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Lausanne (Switzerland), 1–3 juin 2022 / 1.–3. Juni 2022

Abstracts

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Communications libres SSMIG / Freie Mitteilungen SGAIM

FM1–FM10 Meilleures communications libres / Beste Freie Mitteilungen

Société conviée SPSG / Gastgesellschaft SFGG

FM11–FM17 Communications libres / Freie Mitteilungen

Posters SSMIG / Poster SGAIM

P1–P10 Meilleurs posters / Beste Poster

P11–P20 Meilleurs posters des jeunes chercheurs/euses / Beste Poster junger Forschenden

Posters / Poster

P21–P31 – Prevention

P32–P56 – Hospital medicine

P57–P67 – Clinical epidemiology

P68–P78 – Quality of care

P79–P91 – Outcomes and prognosis

P92–P93 – Economic and ethical aspects

P94–P108 – General practice / Family medicine

P109–P151 – Case reports

P152–P157 – Medical education

P158–P162 – Digital medicine

Société conviée SSPTC / Gastgesellschaft SGKPT

P163–P175 Présentations de posters / Posterpräsentationen

P176–P177 Posters / Poster

Société conviée SPSG / Gastgesellschaft SFGG

P178–P179 Posters / Poster

Liste des auteurs / Autorenverzeichnis

Liste des auteurs / Liste der Autoren

Meilleures communications libres SSMIG / Beste Freie Mitteilungen SGAIM

FM1

The gender biased hidden curriculum of clinical vignettes in undergraduate medical training

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Introduction: Clinical vignettes are widespread in medical education and are known to participate to the hidden curriculum.[1] Earlier studies have shown that elements of the hidden curriculum convey gender stereotypes.[2] Our research aimed to identify whether the way men and women are portrayed in clinical vignettes used in the Master years transmit a gender biased hidden curriculum.

Methods: We used a mixed quantitative and qualitative method to analyse the clinical vignettes found in the teaching and evaluation material in the field of internal general medicine, paediatric and psychiatry of the Master years of the Faculty of Medicine of the University of Geneva. Descriptive quantitative analyses were done and chi-squared tests were used to investigate the association between categorical variables. The whole dataset was analysed qualitatively with a thematic analysis framework, and a code list based on a mixed inductive and deductive method.

Results: 2359 vignettes were found in the teaching and evaluation material, of which 955 met inclusion criteria for analysis (at least 2 patient's characteristics and no duplicates). Male patients were slightly more present and only few vignettes portrayed gender neutral patients. (table 1) Profession, relational status or children were mentioned slightly less often in male than female patients. The type of profession differed also greatly between male and female patients. Three main themes emerged from the qualitative analysis: stereotyped gender roles; stereotyped gender expression; and stereotype free or gender transformative formulations, this last category being rare. Both quantitative and qualitative analyses indicate that men and women represented in clinical vignettes differed on the basis of their gender and that their representation is stereotyped. These stereotypes touched all protagonist represented in the clinical vignettes: patient, their significant other and health care providers. (table 2)

Conclusions: Our study reveal that the clinical vignettes used in education and evaluation materials in undergraduate medical education convey a gender-biased hidden curriculum. This might impact negatively on patient care and undermine efforts to promote equal opportunity between men and women in medicine.[3] These results advocate for an active revision using a gender lens of the content and the form of clinical vignettes used in undergraduate medical teaching and evaluation.

	Female n (%)	Male n (%)	Neutral n (%)	Total n
OSCE	56 (47.9%)	30 (25.6%)	31 (26.5%)	117
Teaching material	116 (44.1%)	145 (55.1%)	2 (0.8%)	263
Written exam	267 (46.4%)	307 (53.4%)	1 (0.2%)	575
Total	**439 (46.0%)**	**482 (50.5%)**	**34 (3.5%)**	**955**

Table 1 : Patients by gender depending on type of clinical vignettes.

	Female n (%)	Male n (%)	Unspecified n (%)	Total n
Health care providers	82 (96.5%)	2 (2.3%)	1 (1.2%)	85
Of which :				
• Nurses	45 (97.8%)	1 (2.2%)	0	46
• Doctor assistants	27 (93.1%)	1 (3.4%)	1 (3.4%)	29
• Midwifes	9 (100%)	0	0	9
• Dietician	1 (100%)	0	0	1
Medical doctors	25 (11.9%)	182 (86.7%)	3 (1.4%)	210
Total	107	184	4	295

Table 2 : Health care providers by type and gender

FM2

Comparison of the 2016 and 2021 European Society of Cardiology and 2019 American Heart Association/American College of Cardiology guidelines for primary cardiovascular prevention

B. Delabays[1], R. De La Harpe[1], P. Vollenweider[1], S. Fournier[2], O. Müller[2], D. Strombo[3], D. Nanchen[4], P. Marques-Vidal[1], J. Vaucher[1]

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Introduction: The European Society of Cardiology (ESC) released in 2021 a new cardiovascular risk prediction model, SCORE2. We aimed to 1) compare the proportion of individuals in primary prevention included in each category of risk according to 2016 and 2021 ESC and American Heart Association/American College of Cardiology (AHA/ACC) guidelines and 2) assess the discriminative and calibration performances of ESC SCORE 1 and 2, and AHA/ACC Pooled Cohort Equations (PCE) risk prediction models to predict atherosclerotic cardiovascular disease (ASCVD).

Methods: We used 10-year prospective data from the first follow-up of the CoLaus|PsyCoLaus study, a Swiss population-based cohort including 5,064 individuals aged 40-80 years between 2009-2012. We computed SCORE1, SCORE2 (SCORE2-OP in people >70 years) and PCE in participants without lipid-lowering treatment and free from ASCVD or comparable conditions at baseline (according to guidelines). We assessed the performance of the scores based on discrimination and calibration metrics using first incident ASCVD as outcome.

Results: 323 (7.1%) participants experienced an incident ASCVD during a mean follow-up time of 8.1 (±1.9) years. 3'456 (58.2% women), 3'318 (57.1%) and 3'384 (56.7%) participants in primary prevention were included in the analysis according to ESC 2016, ESC 2021 and AHA/ACC 2019 guidelines, respectively. Statins would be recommended or considered in 38.2% (95% of confident interval [CI], 36.0-40.3), 19.4% (17.7-21.3) and 29.6% (27.5-31.7) of women, and in 57.1% (54.5-59.7), 52.6% (50.0-55.2) and 61.7% (59.1-64.2) of men according to ESC 2016, ESC 2021 and AHA/ACC 2019 guidelines, respectively. SCORE2 and PCE presented comparable discriminative capacities with area under the receiver operating characteristic (AUROC) of 0.776 (95% CI, 0.730-0.822) and 0.775 (0.729-0.821), respectively. SCORE1 presented a lower AUROC (0.717 [95% CI, 0.665-0.769], p-value=0.0001). Calibration of scores was similar and characterized by an underestimation of risk in subjects in intermediate deciles of risk and an overestimation of risk in people in high deciles of risk.

Conclusions: Application of 2021 ESC guidelines would translate into a lower proportion of women in primary prevention eligible for a lipid-lowering treatment compared to ESC 2016 and AHA/ACC 2019 recommendations. In this cohort, both SCORE2 and PCE presented good predictive capacities and could be interchangeably used in comparable populations.

FM3

Diagnostic performance of pneumonia on CXR by artificial intelligence varies according to the gold standard used

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Background: Pneumonia diagnosis is based on clinical, biological and radiological criteria. However, the evaluation of chest radiograph (CXR) can be challenging for clinicians and even for con-

firmed radiologists, especially in an elderly population because of the quality of images and concomitant comorbidities.

Many artificial intelligence (AI) tools for diagnosis of pneumonia based on CXR have been developed. The reference diagnosis used to assess their performance is usually based on radiologists' interpretation of CXR, despite of weak sensibility of CXR and inter-agreement rate.
Our study aims to compare the performance of an AI system for the diagnosis of pneumonia with the diagnosis of clinicians based on CXR, of radiologists based on CXR and CT scan, using as reference diagnosis the diagnosis made by an expert panel having access to clinical, biological and radiological criteria including CT scan.

Material and methods: We trained a convolutional neural network (CNN) to automatically identify pneumonia on >500'000 CXRs from public datasets, whose gold-standard was the diagnosis made by radiologists.

CNN performance was assessed on two independent cohorts of patients from a Geneva cohort including elderly patients >65 years (PneumOldCT, N=200) and a French cohort including patients >18 years (PACSCAN, N=165). All patients included had CXR, CT scan and a diagnosis made by a panel of experts. The reference diagnosis was assessed *a posteriori* by a panel of experts using a Delphi method and based on imaging, biological and clinical data. CNN diagnostic performance was compared with that of clinicians and radiologists based on CXR, as well as that of radiologists based on CT scan.
Results: In both cohorts, CNN performance for the diagnosis of pneumonia based on CXR was superior to that of clinicians ($p<0.05$) but not radiologists (p=ns). However, CNN, clinicians and radiologists' performances were inferior to a diagnosis based on CT (all $p<0.05$).
When we compared CNN performance with radiologists' diagnosis on CXR, which is the common practice, its accuracy was significantly better than when compared with the reference diagnosis ($p<0.05$), which raises concerns about its overestimation in current literature.

Conclusion: AI performance in pneumonia diagnosis based on CXR depends highly on the reference diagnosis to which it is compared. However, its performance is superior to clinicians and similar to radiologists, but all are inferior to a diagnosis based on CT.

FM4

Does thyroid hormone therapy improve muscle function and muscle mass in older adults with subclinical hypothyroidism? An ancillary study within two randomized placebo controlled trials

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Introduction: The loss of skeletal muscle strength and muscle mass is common in the older population, with important socioeconomic and prognostic impacts. Subclinical hypothyroidism is more common with increasing age and has been associated with reduced muscle strength. Yet, no randomized controlled trial (RCT) has investigated whether treatment of subclinical hypothyroidism affects muscle function and mass.

Methods: This is an ancillary study within two coordinated randomized placebo-controlled trials (RCTs) conducted among adults aged ≥65 years with persistent subclinical hypothyroidism (thyrotropin (TSH) 4.60-19.99 mIU/L, free thyroxine within the reference range). Participants were randomized to receive daily levothyroxine with TSH-guided levothyroxine dose adjustment or mock titration in the placebo group. In this ancillary study, the primary outcome was gait speed at the final visit (median time to final visit 18 months). Secondary outcomes were handgrip strength at 1-year follow-up and the yearly change in muscle mass measured by Dual Energy X-ray Absorptiometry (DXA).

Results: We included 267 participants from Switzerland and the Netherlands. Mean age was 77.5 years (range 65.1 to 97.1), 129 (47%) were women, and their mean baseline TSH was 6.36 mIU/L (standard deviation [SD] 1.9). At final visit, TSH in the levothyroxine group was 3.8 mIU/L (SD 2.3), TSH in the placebo group was 5.1 mIU/L (SD 1.8, $p<0.05$). Compared to placebo, participants in the levothyroxine group had similar gait speed at final visit (adjusted between-group mean difference [MD] 0.01m/s, 95% confidence interval [CI] -0.06 to 0.09). The results remained similar when examined by gender, age (<75 years, ≥75 years) and TSH categories (TSH <7 mIU/L, ≥7 and <10 mIU/L, ≥10 mIU/L). Compared to placebo, participants in the levothyroxine group had similar handgrip strength at one year (MD -1.14 kg, 95% CI -2.51 to 0.24) and similar yearly change in muscle mass (MD -0.15 m^2, 95% CI -0.49 to 0.18).

Conclusions: In this ancillary analysis of two RCTs, treatment of subclinical hypothyroidism did not affect muscle function and mass in individuals 65 years and older.

FM5

Does in-hospital antihypertensive treatment modification reduce all-cause hospitalisation in multimorbid older adults? A prospective cohort study

J. Oberle[1,2], V. Gastens[2], C. Aubert[1,2], C. Huibers[3], W. Knol[3], D. O'Mahony[4], S. Henrard[5,6], B. Boland[5,7], N. Rodondi[1,2], M. Blum[1,2]

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Introduction: Cardiovascular diseases (CVD) account for the majority of hospitalisations among older patients. Hypertension (HT) is a major modifiable risk factor for CVD. However, some observational evidence associated HT treatment intensification during hospitalisation with a higher risk of rehospitalisation in older patients, but evidence in multimorbid patients is insufficient. We therefore aimed to investigate the impact of intensification and deintensification of HT treatment in hospitalised, multimorbid, older patients on clinical outcomes.

Methods: We used prospectively collected data from all participants with HT of the OPERAM trial, which included hospitalised, multimorbid, older patients with polypharmacy and assessed the effects of pharmacotherapy optimisation on drug-related admissions. HT treatment intensity was defined by the cumulative Defined Daily Dose. Primary outcome was first all-cause hospitalisation within 1 year. Secondary outcomes included all-cause death and first fall within 1 year. We used Cox proportional hazard models with inverse probability of treatment weighting (IPW) to compare deintensification or intensification with stable HT treatment. Sensitivity analyses used Cox models with covariate adjustment and death as competing risk.

Results: Of 1,355 participants with HT, 238 (18%) received intensification, 337 (25%) deintensification, and 1084 (57%) stable treatment. All-cause hospitalisation within 1 year occurred in 399 (51%) participants with stable treatment, 124 (52%) with intensification and 153 (45%) with deintensification. Compared to stable treatment, deintensification was associated with a reduced risk of all-cause hospitalisation (hazard ratio [HR] 0.77, 95% CI 0.62-0.95), while intensification compared to stable treatment did not differ (HR 1.05 [0.84-1.31]; Fig. 1). Deintensification was also associated with a significantly lower risk of first falls (HR 0.73 [0.55-0.96]). Patients subjected to treatment intensification showed a trend towards a higher risk of death compared to those on stable therapy (HR 1.34 [0.94-1.92]; Fig. 2).

Conclusion: In-hospital deintensification of HT treatment was associated with a lower risk of all-cause hospitalisation and falls within 1 year. Trials are needed to investigate the safety and potential benefit of deintensifying HT treatment in hospitalised, multimorbid older patients.

Fig. 1 All-cause hospitalisation

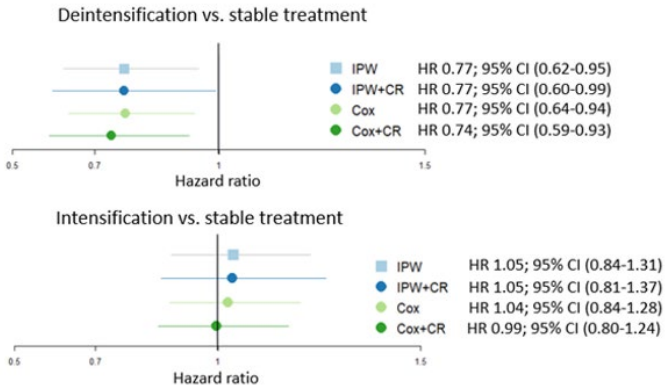


Fig. 2a All-cause death

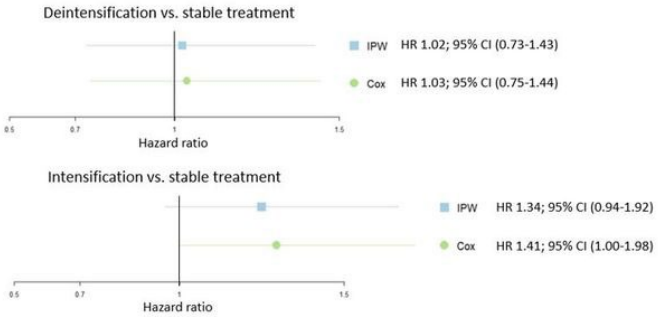
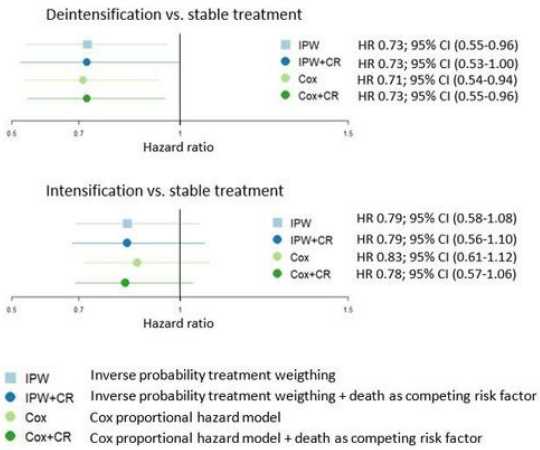


Fig. 2b First fall



IPW Inverse probability treatment weigthing
IPW+CR Inverse probability treatment weigthing + death as competing risk factor
Cox Cox proportional hazard model
Cox+CR Cox proportional hazard model + death as competing risk factor

Abbreviation: CI, confidence interval; CR, competing risk; HR, hazard ratio

FM6

The CoronaGraben: differences in adherence to preventive measures against SARS-CoV-2 infection between German, French, and Italian speaking cantons during the second pandemic wave in Switzerland

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Introduction: During the second pandemic wave (autumn 2020), regional differences emerged in the incidence of SARS-CoV-2 infections and confirmed Covid-19 cases, with a disproportionate burden in the French-speaking region of Switzerland (so called "CoronaGraben"). To understand some of the underlying factors leading to these regional differences, we compared adherence to preventive non-pharmaceutical interventions (NPIs), including wearing masks, social distancing (keeping distance from other people, limiting social gatherings), hygiene measures (coughing or sneezing in the elbow, cleaning and disinfecting frequently) and staying at home across the three major language regions of the country.

Methods: We used data from Corona Immunitas, a national research programme of representative seroprevalence studies, which also included a weekly digital follow-up with standardized questionnaires. We compared the adherence to the NPIs between French (Geneva, Fribourg, Neuchatel), German (Zurich, Basel), and Italian (Ticino) speaking cantons between September 1st 2020 and February 14th 2021 adjusting for age, gender and the KOF Stringency index. Additionally, we used GPS-based daily activity data from the Google community mobility reports, which includes the average mobility per canton regarding the following areas: 'Retail and recreation', 'Grocery and Pharmacy', 'Parks', 'Transit Stations', 'Workplaces' and 'Residential' adjusted for weather reports and the KOF Stringency Index. Finally, we qualitatively compared the difference in restrictions implemented in different cantons based on press releases and legal ordinances.

Results: We included 10952 participants from Corona Immunitas aged 20 years and older. In all regions, people were likely to follow the NPI recommendations, but with slightly different trends. The greatest difference was for the "stay at home" measure, with Ticino reporting a lower adherence during the second wave. Consistently, the mobility data showed a significant difference with higher mobility in Ticino than in German speaking cantons in terms of grocery activity and park activity. In terms of ordinancies, the French speaking cantons were more preventive than the other regions (more restaurant closures and other measures applied earlier than in the other regions).

Conclusion:While the second wave of the pandemic was stronger in French-speaking Switzerland, our results suggest that adherence to NPIs cannot explain this difference.

Figure 1. Adjusted mean adherence to non-pharmaceutical preventive measures in three language regions of Switzerland. Corona Immunitas September 2020-February 2021.

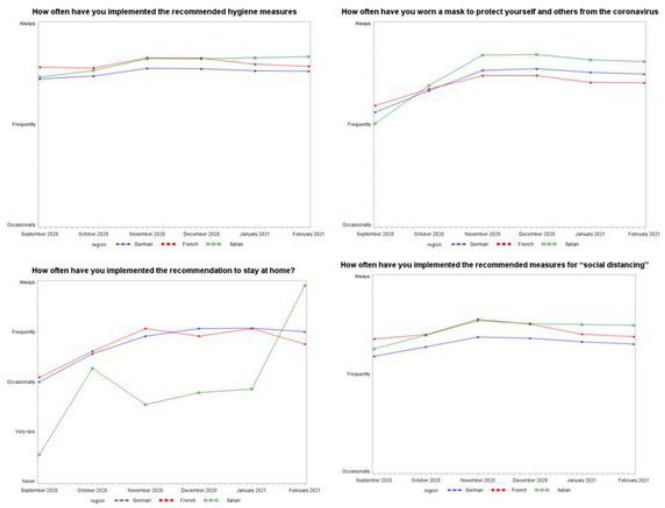
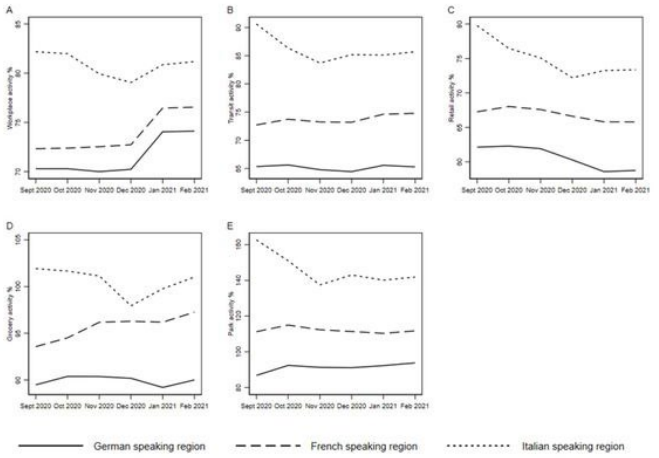


Figure 2. Adjusted predictive margins from GPS-based mobility data for three language-regions in Switzerland. Google Mobility Reports September 2020-February 2021



FM7

Association of thromboprophylaxis with clinically relevant bleeding and hospital-acquired anemia in medical inpatients: the RISE study

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Introduction: Pharmacological thromboprophylaxis (TPX) is widely used to prevent venous thromboembolism (VTE) in medical inpatients, but it may increase the risk of bleeding, particularly in older and multimorbid patients who have additional bleeding risk factors. Furthermore, these patients are at increased risk of hospital-acquired anemia (HAA), which may be exacerbated by TPX use. Therefore, we aimed to evaluate the association of TPX use with clinically relevant bleeding and HAA.

Methods: We used data from a prospective cohort study on hospital-acquired VTE prevention in 3 Swiss hospitals. Adult patients admitted to internal medicine wards for at least 24 hours who did not have an indication for therapeutic anticoagulation were included. Use of TPX was collected during hospitalization. The primary outcome was clinically relevant bleeding (major bleeding + clinically relevant non-major bleeding). The secondary outcome was HAA, defined as new onset anemia or a drop of 20 g/l of hemoglobin during hospitalization. Overall incidence rates were calculated by status of TPX. We assessed the association of TPX with clinically relevant bleeding and HAA using logistic regression adjusted for age, gender, length of stay and IMPROVE Bleeding risk score, and we stratified regarding whether TPX was prescribed alone, with aspirin (ASA) or with double anti-platelet therapy (DAPT).

Results: Among 907 patients (mean age 63.6 years; 45% women, 90% at low risk of bleeding (BRS < 7), 30% receiving anti-platelet therapy) included, 540 received TPX (Table 1).
The incidence rate of clinically relevant bleeding at discharge was 2.62 per 1000 patient-days (95% confidence interval (CI): 1.71 - 4.02) and was not higher in patients receiving TPX vs. those not receiving TPX (Table 2). No association between TPX use and clinically relevant bleeding was found (HR 0.72 [95% CI: 0.18 – 2.85; p-value 0.64]).
Overall, HAA was frequent (20.2%) and higher in patients receiving TPX (23.7% vs 15.3%). The incidence rate of HAA was 22 per 1000 patient-days without a significant difference between patients with and without TPX (Table 2). In multivariate analysis, we found no association between TPX use and HAA (OR 1.41 [95% CI: 0.94 – 2.11]; p-value 0.10).
The results remained similar in patients receiving TPX plus ASA or DAPT.

Conclusion: Our study confirms the safety of TPX in medical inpatients mostly at low risk of bleeding, and showed that TPX use do not either increase the risk of HAA.

Table 1. Characteristics of medical inpatients

	All (n=907) *n (%) or mean* (SD)
Age, years	63.6 (17.8)
Women	406 (44.8%)
Body mass index (kg/m^2)	25.7 (6.1)
Charlson Comorbidity Index (CCI) [a]	4.0 (2.9)
Length of stay, days	9.2 (8.2)
Active bleeding [b]	63 (6.9%)
Prior bleeding within last 3 months	75 (8.3%)
Blood dyscrasia	29 (3.2%)
Anemia present at admission [b]	409 (45.1%)
Thrombocytopenia [b]	
Platelets count < 150 G/l	147 (16.2%)
Platelets count < 50 G/l	24 (2.7%)
INR > 2 [b]	2 (0.2%)
Anti-platelet therapy [b]	
Aspirin therapy	244 (26.9%)
Double anti-platelet therapy	26 (2.9%)
IMPPROVE-bleeding risk score	
High risk (≥7 points)	88 (9.7%)
Low risk (<7 points)	818 (90.3%)
TPX use [c]	540 (59.5%)

[a]calculated based on the report of the electronic health record (EHR);[b]at admission;[c]the patient received TPX at least once during the hospital stay; INR, International Normalized Ratio. SD, standard deviation. TPX, thromboprophylaxis, IMPROVE-BRS, IMPROVE-bleeding risk score.
Results are expressed as number of participants (percentage) for categorical data, as mean ± standard deviation

Table 2. Incidence rates of clinically relevant bleeding and hospital-acquired anemia

	All(n=907)	**No TPX**(n=367)	**TPX**(n=540)	**p-value**
Clinically relevant bleeding				
Incidence rate [a]	2.62 (1.71 – 4.02)	3.83 (2.06 – 7.13)	2.03 (1.13 – 3.67)	0.156
Number of events	21 (2.3%)	10 (2.7%)	11 (2.0%)	0.499
Patient-days	8018	2608	5410	
Hospital-acquired anemia				
Incidence rate [a]	21.98 (19.02 – 25.39)	20.64 (15.89 – 26.82)	22.61 (19.02 – 26.89)	0.574
Number of events	184 (20.3%)	56 (15.3%)	128 (23.7%)	0.002
Patient-days	8373	2713	5660	

[a] expressed asevents per 1000 patient-days (95% confidence interval); TPX, thromboprophylaxis.

FM8

What factors are associated with poor medication adherence in multimorbid older patients with hyperpolypharmacy?

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Introduction: Knowledge of medication adherence is important to assess treatment effectiveness, prevent unnecessary drug escalation or support deprescribing. Adherence data comes mainly from polypharmacy studies (≥5 concurrent drugs), yet studies on adults with hyperpolypharmacy (HPP) (≥10 drugs) are lacking - but are

needed to reflect our aging multimorbid /multi-drug patients. Thus, we aim to determine prevalence, and uncover potential factors associated with poor medication adherence in hospitalized patients with HPP.

Methods: We used baseline data from the OPERAM ("**O**ptimising **P**harmacoth**ERA**py in **M**ultimorbid elderly") trial conducted in 4 European centers. Inpatients aged ≥70yrs with ≥3comorbidities were included in this analysis if they had HPP on admission. Data were collected on demographics, clinical characteristics, health care contacts and quality of life (QoL) using the EQ5D-VAS (0-100 points, with higher scores relating to higher QoL). Adherence was assessed with the Morisky Medication Adherence Scale-8 (MMAS-8)©[1], and patients were categorized into 2 groups: high (MMAS 8points) vs low/medium adherence (MMAS <8points). Potential risk factors for low/medium adherence were first identified using univariable logistic regression. All variables with p-value<0.20 were included in a multivariable model.

Results: Of 978 patients with HPP (median number of drugs 13, interquartile range[IQR] 11-16) and MMAS-8 data, 517 (52.9%) had low/medium adherence, with a median MMAS-8 of 6.75 (IQR 5.75-7). Compared to the high adherence group, patients with low/medium adherence were younger (median 78 vs 80yrs) and had more comorbidities (median 14 vs 12). In multivariable analyses, an increasing number of comorbidities was associated with higher odds of low/medium adherence (p for trend 0.004, Table 1); while the odds were lower with older age (odds ratio [OR] 0.71, 95% confidence interval[CI] 0.53–0.94 for ≥80 vs <80yrs), community nurse visits (OR 0.58, 95%CI 0.43–0.78), and QoL (OR 0.99, 95%CI 0.98–0.99 per 1-point increase in EQ5D-VAS).

Conclusions: Suboptimal medication adherence was highly prevalent in this older population with HPP, and was associated with age, number of comorbidities and absence of community nurse visits. These findings highlight the important role of community nurse visits to improve medication adherence; and suggest that GPs should address poor medication adherence in highly multimorbid patients with HPP, to look for deprescribing opportunities.

Table 1: Factors associated with low/medium medication adherence in multivariable analyses[1]

Variable	OR	95% CI	P-value
Age ≥80 years (vs. <80 years)	0.71	0.53 – 0.94	**0.016**
Female sex (vs. male sex)	1.19	0.90 – 1.58	0.23
Number of chronic medications at baseline			
- 10 - 11	Reference		
- 12 - 13	0.88	0.61 – 1.27	0.32
- 14 - 15	0.80	0.52 – 1.22	
- 16 - 17	0.66	0.41 – 1.05	
- 18 - 19	1.39	0.74 – 2.62	
- ≥ 20	1.01	0.60 – 1.70	
Current smoking (vs. non-smoking)	1.20	0.72 – 2.01	0.48
Education level			
- less than high school	Reference		0.06
- High school	0.90	0.66 – 1.23	
- University	1.42	0.95 – 2.11	
Number of chronic comorbidities			
- ≤ 5	Reference		**0.004** [4]
- 6 - 10	1.07	0.53 – 2.14	
- 11 - 15	1.33	0.66 – 2.69	
- 16 - 20	1.91	0.92 – 3.97	
- ≥ 21	2.32	1.10 – 4.89	
GP contact[2] (yes vs. no)	1.35	0.73 – 2.48	0.34
Community nurse contact (e.g. *Spitex / soins à domicile* visits)[2] (yes vs. no)	0.58	0.43 – 0.78	**<0.001**
EQ5D-VAS for QoL[3] (per 1-point increase in score)	0.99	0.98 – 0.99	**0.001**

Legend: CI, confidence interval; EQ5D-VAS for QoL, EQ5D-Visual Analogue Scale for quality of life; GP, general practitioner/ primary care physician; OR, odds ratio; vs., versus.

[1] results from a multivariable logistic regression model adjusted for all variables shown in the table (i.e. age, sex, and all variables with a p-value <0.2 in the univariable analyses). Low/medium adherence was defined as <8 points on the Morisky Medication Adherence | Scale-8 (MMAS-8)©. (*Use of Morisky medication adherence measure questionnaire is protected by US copyright laws. Permission for use is required. A license agreement was obtained from Donald E Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA Fielding School of Public Health, 650 Charles E Young Drive South, Los Angeles, CA 90095-1772, USA (dmorisky@ucla.edu)*).
[2] at least one contact in the last 6 months.
[3] EQ5D-VAS for QoL: patient self-reported health-related quality of life, ranging from 0 to 100 points, with higher scores relating to higher quality of life. In the statistical model, the odds ratio relates to a 1-point increase in the EQ5D-VAS QoL score.
[4] p-value for linear trend is 0.004. p-value for overall significance is 0.002.

FM9

What is the impact of part-time clinical work on well-being and satisfaction of attending physicians in General Internal Medicine?

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Introduction: Physician burnout and a low job satisfaction are increasing among the General Internal Medicine (GIM) workforce. Whether part-time compared to full-time clinical work is associated with improved well-being, job satisfaction and health among GIM attending physicians in Switzerland remains unclear.

Methods: We conducted an anonymized survey among attending physicians in GIM departments of 14 Swiss hospitals. Part-time clinical work was defined as employment of <100% as a clinician (i.e. not considering protected time for non-clinical tasks). The primary outcome was well-being as measured by the extended Physician Well-Being Index (ePWBI). ePWBI scores range from -2 (highest) to 9 (lowest wellbeing), with a score of ≥3 indicating poor wellbeing. Secondary outcomes included job satisfaction, quality of life, burnout symptoms, work-life balance, depression and fatigue. We compared characteristics and outcomes in part-time and full-time workers using chi-squared and t-tests or Wilcoxon rank sum tests. We assessed the independent association between full-time or part-time work and wellbeing using a propensity-score adjusted multivariate regression model.

Table 1. Characteristics of participating attending physicians in General Internal Medicine

	Full-time clinical employment (n=55)	Part-time clinical employment § (n=61)	p-value*
Clinical employment level in %, median (IQR)	100 (100-100)	80 (50-80)	**<0.001***
Overall employment level in %, median (IQR) †	100 (100-100)	80 (60-90)	**<0.001***
Female gender, n (%)	30 (55%)	47 (77%)	**0.010***
Age, n (%)			
<40 years	52 (95%)	47 (77%)	**0.008***
≥40 years	3 (5%)	14 (23%)	
Parenthood, n (%)			
No children	28 (60%)	18 (34%)	**0.010***
≥1 children	19 (40%)	35 (66%)	
Relationship status, n (%)			
Partnership or married	45 (82%)	53 (90%)	0.22
No partnership	10 (18%)	6 (10%)	
Time since graduation in years, median (IQR)	7 (6-9)	8.5 (7-11)	**0.001***
Experience as an attending in years, median (IQR)	2 (1-5)	4 (2-6.7)	**0.028***
Long-term goal, n (%)			
Clinical hospitalist	29 (53%)	30 (49%)	0.26
Academic position	2 (4%)	2 (3%)	
General practitioner	6 (11%)	15 (25%)	
Specialist in other discipline	10 (18%)	5 (8%)	
Undecided	8 (15%)	9 (15%)	
Overtime per week in hours, median (IQR)	8 (8-13)	7.8 (4.4-12.2)	0.47
Average adjusted number of night shifts per month, median (IQR) ‡	3 (0-4)	2.3 (0-4.7)	0.41
Average number of patients to care for per day, mean (SD)	20.0 (5.8)	18.3 (5.2)	0.09

Abbreviations: CI: confidence interval; IQR, interquartile range.
*p-values were calculated using chi-squared tests for categorical variables and t-tests or Wilcoxon rank sum tests for continuous variables. A p<0.05 was interpreted as statistically significant difference.
§ part-time clinical work was defined as an employment of <100% for clinical work (i.e. not encompassing protected time for non-clinical tasks)
† overall employment level refers to employment for clinical work plus any additional protected time for non-clinical tasks (e.g. for research, administrative or educational tasks)
‡ adjusted to 100% clinical employment

Results: Among 199 invited attending physicians, 116 (58%) were analyzed, of whom 55 (47%) worked full-time and 61 (53%) part-time. Part-time clinicians were more likely to be female, older, to have children and longer experience as an attending compared to full-time clinicians (Table 1). Full-time clinicians were more likely to have an ePWBI ≥3 compared to part-time clinicians (54% vs. 29%, p=0.007; Table 2). Part-time compared to full-time work was significantly associated with a lower risk of poor well-being in adjusted analyses (odds ratio 0.23, 95% confidence interval 0.08-0.69, p=0.008). In part-time compared to full-time clinicians, risk for depression was significantly lower (2% vs. 16%, p=0.005), and there was a trend towards fewer burnout symptoms and higher ratings for job satisfaction, quality of life, work/life balance and fatigue (Table 2).

Conclusions: Full-time clinical attending physicians in GIM have a high risk for poor well-being. Part-time compared to full-time clinical work is associated with better well-being and lower risk for depression, with trends towards improved job satisfaction and quality of life, and fewer burnout symptoms. Enabling part-time clinical work may contribute to improving well-being among GIM attending physicians and their retention in hospital settings.

Table 2. Well-being, job satisfaction, and health among part-time and full-time attending physicians

	Full-time clinical employment (n=55)	Part-time clinical employment (n=61)	p-value*
ePWBI score, mean (SD)	2.1 (2.2)	1.4 (2.5)	0.12
Poor well-being (ePWBI ≥3), n (%)	29 (54%)	16 (29%)	**0.007***
Poor well-being (ePWBI ≥3), OR (95% CI) §	reference	0.23 (0.08-0.69)	**0.008***
Depersonalisation, n (%)	30 (56%)	25 (41%)	0.12
Emotional exhaustion, n (%)	21 (38%)	15 (25%)	0.11
At least 1 symptom of burnout in the last month †, n (%)	34 (62%)	30 (50%)	0.17
Work-life balance (my work schedule leaves me enough time for my personal/ family life), n (%)			0.067
Agree/strongly agree	8 (15%)	19 (32%)	
Neutral	7 (13%)	9 (15%)	
Disagree/strongly disagree	40 (73%)	32 (53%)	
Job satisfaction, n (%)			0.65
Extremely dissatisfied	0 (0%)	1 (2%)	
Dissatisfied	3 (6%)	3 (5%)	
Neutral	12 (23%)	8 (14%)	
Satisfied	30 (58%)	35 (61%)	
Extremely satisfied	7 (13%)	10 (18%)	
Quality of life ‡, mean (SD)	6.2 (1.7)	6.8 (1.9)	0.052
Fatigue ¶, median (IQR)	1 (1-3)	1 (0-2)	0.065
Depression, n (%)	9 (16%)	1 (2%)	**0.005***

Abbreviations: CI, confidence interval; ePWBI, extended Physician Well-Being Index; IQR, interquartile range; OR, odds ratio.
*p-values were calculated using chi-squared tests for categorical variables and t-tests or Wilcoxon rank sum tests for continuous variables. A p<0.05 was interpreted as statistically significant difference.
§ analyzed using a propensity-score adjusted logistic regression model, considering age, sex, parenthood, relationship status, reduced work capacity due to health reasons, academic ambition, time since transition to attending and number of patients as potential confounders
† assessed with a positive answer to the single-item measures of depersonalisation or emotional exhaustion of the ePWBI
‡ assessed by Likert scale going from 0 (as bad as can be) to 10 (as good as can be)
¶ assessed using the Stanford Sleepiness Scale (score 0 to 6 with a higher score indicating more fatigue)

FM10

Does lipid-lowering therapy increase the risk of hemorrhagic stroke? A systematic review and meta-analysis of randomized controlled trials

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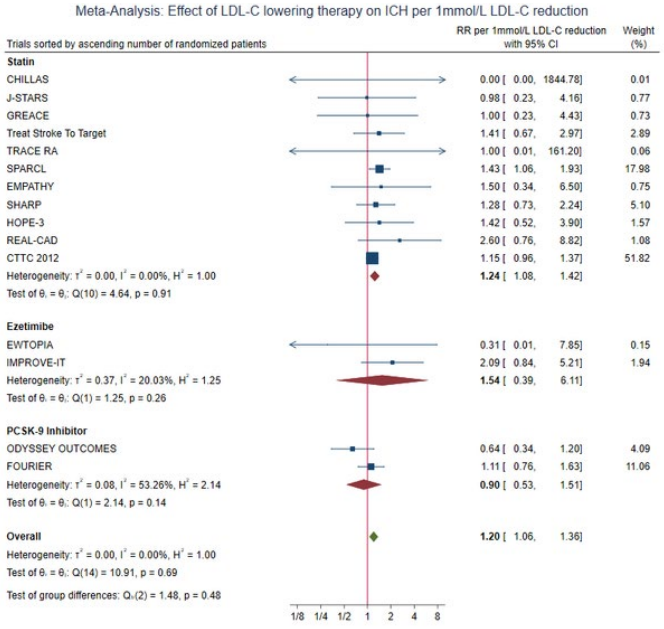
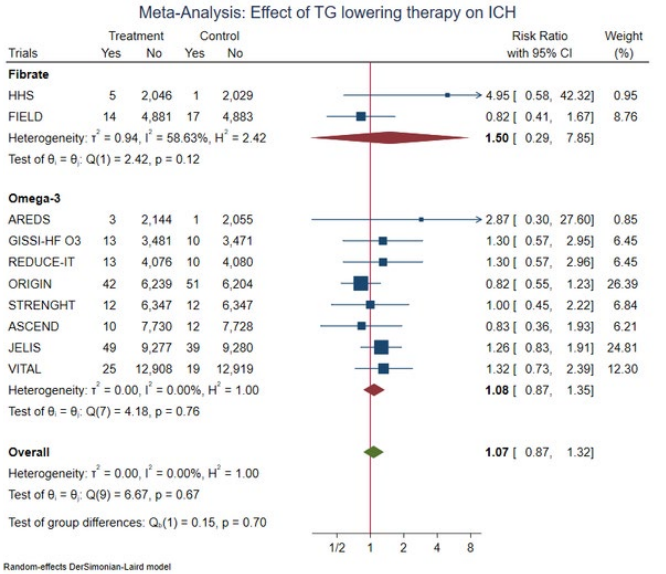
Background: Some randomized controlled trials (RCTs) reported an association between the use of statin and the risk of hemorrhagic stroke (HS), especially after a cerebrovascular event. It remains unclear whether this rare complication also occurred in other statin or lipid-lowering therapy trials.

Methods: We performed a systematic review of large RCTs (≥1000 patients with at least two years of follow-up) of low-density lipoprotein cholesterol (LDL-C) lowering therapy (defined as statin, ezetimibe and PCSK-9 inhibitor) to update a statin meta-analysis of 27 trials published in 2012, as well as RCTs of triglyceride (TG) lowering therapies (defined as omega-3 and fibrates). We used a random-effect model to summarize the relative risk (RR) of HS (or similar reported outcomes such as intracranial hemorrhage (ICH)) per 1mmol/L LDL-C reduction for LDL-C lowering therapy. We did a meta-regression to assess the relationship between achieved LDL-C levels and the risk of HS. We also performed a meta-analysis to assess the RR of HS for TG lowering therapy trials.

Results: After a screening of 5501 recordings (MEDLINE, Embase, Cochrane Central and other sources), we identified 41 trials for LDL-C lowering (297'849 participants) and 10 for TG lowering (118'989 participants). There was a higher risk of HS per 1mmol/L LDL-C lowering (573 vs. 467, RR 1.20, 95%CI 1.06-1.36, p<0.01). This risk was statistically significant for statin (37 trials, 229'448 participants, 468 vs. 372, RR 1.24, 95%CI 1.08-1.42, p<0.01), but not for PCSK-9 inhibitor (2 trials, 46'488 participants, 38 vs. 41, RR 0.90, 95%CI 0.53-1.51, p=0.68) and ezetimibe (2 trials, 21'913 participants, 67 vs. 54, RR 1.54, 95%CI 0.39-6.11, p=0.54). After excluding 3 statin trials that exclusively enrolled patients with stroke/TIA, the risk was attenuated but remained increased with statin (383 vs 314, RR 1.18, 95% CI 1.01-1.39, p=0.041). For each 1 mmol/L difference in achieved LDL-C, the RR for HS was 1.03 (95%CI 0.53-2.01, p=0.92) and there was no increased risk in TG lowering trials (186 vs. 172, RR 1.07, 95%CI 0.87-1.32, p=0.53).

Conclusion: There is a significant increased risk of HS in statin trials, including in those not limited to patients with stroke/TIA. No association was observed for other lipid lowering therapies and the risk appeared to be unrelated to the achieved LDL-C level. Patients should be informed of this rare complication, especially when they are at higher risk of bleeding.





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FM11

Assessment at four years after the opening of an orthogeriatric unit at the Valais Hospital

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Background: In order to limit the adverse impact of hip fractures on morbidity/mortality in the older population, implementing a coordinated interdisciplinary management between the geriatrician and the orthopedist in an orthogeriatric unit seems to improve overall prognosis.

Method: This retrospective study analyses the results of a 4-year follow-up hip fracture management in a dedicated orthogeriatric unit (with implementation of standardized care protocols) since its opening on January 1, 2018 in the Valais Hospital, Switzerland.

Results: From January 1, 2018, to December 31, 2021, 517 patients with hip fractures were hospitalized in the ortho-geriatric unit. The mean age was 84.1years (62-104) and included mostly women (78.3%). Most (82%) lived at home, while 17.4% were residents of a nursing home. 45% of the patients suffered from cognitive disorders (MMS score < 25), 84.4% had a poor nutritional status, with malnutrition described as moderate to severe for more than half of the group. Applying the American Diabetes Association criteria for their health profile, 24.6% were considered healthy, 54.9% complex and 20.1% very complex. Only 8.7% of the patients were receiving anti-osteoporotic treatment before the fall.
From an orthopedic point of view, 50.2% presented a pertrochanteric fracture, 43.3% a femoral neck fracture and 3.7% a peri-prosthetic fracture.
The mean delay until surgery was 32.19 hours (h), the median being 23.53 hours. In the more complex patient, the operating time was longer: with 30.54 hours for the healthy, 32.2 hours for the complex and 34.1 hours for the very complex.
48% of the group had no postoperative complications; 36.6% had one complication, 11.4% had two complications and 3.3% had three complications.The frequency of complications for the whole group was as follows: delirium (18.2%), pulmonary, urinary or wound infections (15.9%), acute renal failure (14.5%), heart failure (12.2%), and intermediate care monitoring (4.2%).
Mortality at 6 weeks was 6.7% (33 deaths of 492 patients).

Conclusions: We observe that the opening of an orthogeriatric unit for patients suffering from hip fractures allows for a satisfactory operating time, an acceptable rate of postoperative complications and an equally acceptable rate of 6-week mortality for an elderly and mostly frail population.

FM12

Fighting social isolation in times of pandemic COVID-19 using video-calls for older hospitalized patients: the SILVER study

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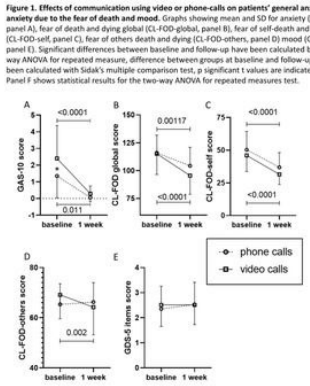
Introduction: The ban on visits to hospitalized patients during the COVID-19 pandemic especially affected the older frail patients and thus highlighting the need to prevent loneliness and social isolation. Indeed, loneliness and social isolation have been associated with negative health impact, including increased anxiety and psychological discomfort (1-3). During COVID-19 pandemic, the use social technologies and, in particular, of video-calls has been proposed to nursing homes residents and to hospitalized patients (4-6). However, the efficacy of these interventions on specific patients' outcomes and the appreciation of this type of communication by older subjects have still to be clarified.
SILVER aims to evaluate the appreciation of video-calls as communication technology by old hospitalized patients and their relatives, and their utility in reducing anxiety, fear of self and of others' death and mood.

Methods: SILVER is an observational multicentre study. Video-calls were performed at least twice a week. Phone-calls were allowed without any restriction in both groups over the study period. Patients hospitalized in two acute and post-acute geriatric units in Switzerland and in one orthogeriatric unit in Italy and their relatives were enrolled during the ban on visits due to the COVID-19. Patients and their relatives were evaluated for anxiety, fear of death and mood at baseline and after one week with standardizes scales. The effects of video or phone-calls on these parameters was evaluated by two-way ANOVA for repeated measures

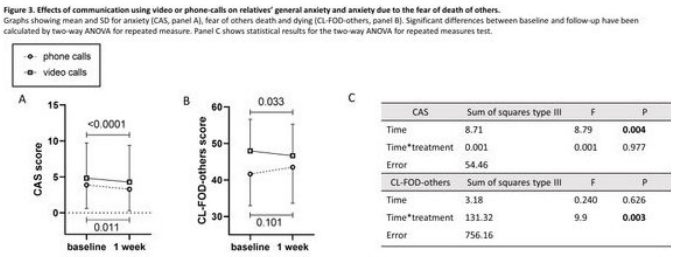
Results: Sixty-four patients and relatives were enrolled, among those 26.5% chose phone-calls and 73.5% chose video-calls as communication technology. Anxiety and fear of death were significantly reduced in patients using video-calls, whereas we observe no effect on mood (Figure 1).



F

GAS-10	Sum of squares type III	F	P
Time	10,273	6.039	0.017
Time*treatment	7,148	4.202	**0.045**
Error	105.47		
CL-FOD total	**Sum of squares type III**	**F**	**P**
Time	5200.6	46.43	<0.0001
Time*treatment	506.6	4.5	**0.038**
Error	105.47		
CL-FOD-self	**Sum of squares type III**	**F**	**P**
Time	4168.8	99.4	<0.0001
Time*treatment	10.8	0.26	0.061
Error	2139.5		
CL-FOD-others	**Sum of squares type III**	**F**	**P**
Time	57.0	1.33	0.255
Time*treatment	369.4	8.6	**0.005**
Error	2190.5		
GDS-5 items	**Sum of squares type III**	**F**	**P**
Time	0.19	0.54	0.464
Time*treatment	0.19	0.54	0.464
Error	22.2		

In relatives using video-calls, we observed a significant reduction of the fear of death of their loved one, but no significant effect on anxiety (Figure 2).



C

CAS	Sum of squares type III	F	P
Time	8.71	8.79	**0.004**
Time*treatment	0.001	0.001	0.977
Error	54.46		
CL-FOD-others	**Sum of squares type III**	**F**	**P**
Time	3.18	0.240	0.626
Time*treatment	131.32	9.9	**0.003**
Error	756.16		

Conclusions: Old patients and their relatives appreciate the use of video-calls as communication tool during hospitalization. The effects of video-calls in relieving anxiety and fear of death in hospitalized patients and their in relatives suggest that video-calls may be useful for old patients in order to keep social relationship with relatives unable to come to the hospital to visit the patient even in the absence of quarantine measures.

FM13

How do geriatric scores predict 1-year mortality in elderly patients with suspected pneumonia?

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Introduction: Pneumonia has an impact on long-term mortality in elderly patients. The risk factors associated with poor long-term outcomes are understated. We aimed to assess the ability of scores that evaluate patients' comorbidities (cumulative illness rating scale—geriatric, CIRS-G), malnutrition (mini nutritional assessment, MNA) and functionality (functional independence measure, FIM) to predict 1-year mortality in a cohort of older patients having a suspicion of pneumonia.

Methods: Our prospective study included consecutive patients over 65 years old and hospitalized with a suspicion of pneumonia

enrolled in a monocentric cohort from May 2015 to April 2016. Each score was analysed in univariate and multivariate models and logistic regressions were used to identify contributors to 1-year mortality.

Results: 200 patients were included (51% male, mean age 83.8 ± 7.7). Their 1-year mortality rate was 30%. FIM (p< 0.01), CIRS-G (p< 0.001) and MNA (p< 0.001) were strongly associated with poorer long-term outcomes in univariate analysis. CIRS-G (p< 0.05) and MNA (p< 0.05) were significant predictors of 1-year mortality in multivariate analysis.

Conclusions: Long-term prognosis of patients hospitalized for pneumonia was poor and we identified that scores assessing co-morbidities and malnutrition seem to be important predictors of 1-year mortality. This should be taken into account for evaluating elderly patients' prognosis, levels and goals of care.

Table 2. Association between scores evaluating comorbidities, malnutrition and functionality and 1-year mortality (univariate and multivariate analysis).

A. Univariate

Variable	OR	95% CI	p
CIRS-G	1.09	1.06-1.12	0.001
MNA	0.76	0.71-0.81	< 0.001
FIM	0.98	0.97-0.99	0.02

B. Multivariate

Variable	OR	95% CI	p
CIRS-G	1.08	1.01-1.15	0.014
MNA	0.83	0.71-0.96	0.012
FIM	0.99	0.97-1.0	0.269

Table 3. Sensitivity, specificity, positive and negative likelihood ratio and diagnostic odds ratio (DOR) values for 1-year mortality according to CIRS-G, MNA and FIM at the best cut-off values (computed with Youden index).

Variable	Sensitivity	Specificity	LR+	LR-	DOR(LR+/LR-)
CIRS-G ≥ 26	0.59	0.70	1.94	0.59	3.27
MNA ≤ 8	0.71	0.65	2.0	0.45	4.46
FIM ≤ 63	0.58	0.52	1.21	0.81	1.50

FM14

One year-mortality, institutionalization, and re-hospitalization in older patients after hospitalization for COVID-19

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Introduction: SARS-CoV2 infection has led to more than 5 million deaths worldwide. The elderly were the most severely affected with a mortality rate ranging from 15 to 30% according to the countries. Among predictors of elderly in-hospital mortality, comorbidities, frailty, male sex and delirium at admission have been mentioned. We have previously reported that male sex, crackles and a higher fraction of inspired oxygen at admission as well as functionality were independent risk factors of mortality in oldest old[1]. However, little data are available on the assessment of the middle or long-term mortality and consequences of COVID-19 in elderly patients. Loss of function after Covid-19 hospitalization represents a risk for long term sequelae, such as long-term functional decline, depression, worse quality of life. In this one-year follow-up, we aimed to study the medium-term consequences of COVID-19 on mortality rate, institutionalization, and re-hospitalization in the oldest-old population after SARS CoV-2 infection and what were the predictors of these consequences.

Methods: This is a bicentric (University Hospitals of Geneva and the Hospital of Valais) national prospective study of patients aged 65 years and older discharged after hospitalization for COVID-19. Data were collected from the electronic medical records and completed by a phone call with the patient and/or his legal representative. Logistic regression and Cox models were used to predict the post-hospitalization mortality and institutionalization.

Results: A total of 198 patients (125 women and 73 men) were included in this study. The one-year mortality after hospitalization for COVID-19 in the elderly was 15.6%. A new institutionalization occurred in 28.8% and complications or rehospitalization in 40.9%. The main predictor of post-hospitalization mortality was institutionalization, which was more frequent in older patients with dementia, female sex, and chronic obstructive pulmonary disease which increased the risk respectively by 6.6 (95% CI: 3.02-14.45; p<0.001), 4 (95% CI: 0.10-0.58; p=0.001) and 3.7 (95% CI: 1.38-10.32; p=0.01).
Conclusion: COVID-19 has middle and long-term repercussions in the elderly, particularly concerning the risk of institutionalization. Factors such as gender, age, dementia or co-morbidities are independent predictors of this risk.

FM15

Projet VIeSA «Vieillissement enSanté» Promotion du vieillissement en santé après 65 ans, quelle place pour un itinéraire de santé intégré visant la prévention primaire et secondaire dans cette population ? Projet VIeSA, une étude de faisabilité

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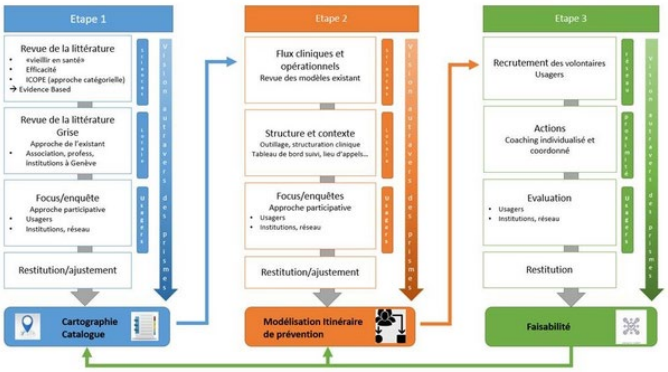
Introduction: Le vieillissement démographique, la forte prévalence des maladies chroniques, le risque accru de dépendance fonctionnelle et l'hétérogénéité de la population âgée de plus de 65 ans constituent un enjeu pour les systèmes socio-sanitaires encore très orientés sur les soins curatifs.Les disparités dans le vieillissement sont notamment en lien avec l'exposition à des facteurs de risque, et justifient la mise en place de programmes intégrés au sein de la communauté basés sur la promotion des comportements sains et la prise en charge précoce des facteurs de risque (1)(2). Le défi est d'adapter les politiques de soins vers une logique préventive au niveau local avec comme objectifs dans cette population, la prévention de la fragilité et des maladies chroniques, et le dépistage des syndromes gériatriques selon les 6 domaines de l'OMS (3).
Basé sur les recommandations de l'OMS/ICOPE (4), le projet VIeSA (**VI**eillissement **e**n **SA**nté) a pour objectif de développer un itinéraire de santé coordonné et de proximité, pour aider les personnes âgées de 65 ans ou plus vivant à domicile dans le Canton de Genève, à renforcer leur capacités fonctionnelles (capacités intrinsèques et extrinsèques). Tous les acteurs locaux de la santé, bénéficiaires, proches, professionnels de la santé, associations et institutions seront impliqués dans ce parcours de soins à travers les prestations déjà existantes.

Méthode: 1) Un catalogue de prestations sera fondé sur la base d'une revue de la littérature identifiant à la fois les capacités et les interventions favorisant un vieillissement en santé et réalisation d'une cartographie les localisant dans le canton de Genève. 2) Un itinéraire clinique interprofessionnel sera élaboré par «consensus d'experts» mobilisant tous les acteurs concernés de la communauté 3) Une étude de faisabilité sera effectuée auprès de 30 participants issu de la communauté. VIeSA se basera sur l'approche relevant des sciences de l'implémentation (5).

Résultats: Présentation du protocole du projet VIeSA et des 3 étapes (cf. figure).



Discussion: VIeSA sera le pilote pour une étude ultérieure d'efficacité à plus large échelle. A terme, la mise en place d'actions précoces et de prestations ciblées aux besoins individuels des bénéficiaires devrait promouvoir un «vieillissement en santé» à domicile et ainsi retarder l'entrée dans les soins (ambulatoires ou stationnaires).

FM16

Qualitative evaluation of a pilot program in French-speaking Switzerland for postgraduate training of physicians in long-term care facilities

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Background: In Switzerland, residents specializing in family or internal medicine are not required to train in long-term care (LTC) medicine. Ensuring that future physicians are adequately prepared to care for institutionalized older patients is increasingly challenging. Thus, we developed a specific post-graduate training program where residents spend 20% of their time for 6-12 months in an LTC facility under the supervision of LTC physicians, along with monthly training sessions focusing on LTC-specific topics related to geriatric and palliative care medicine.

Objectives: To assess the feasibility and acceptability of the LTC pilot training program from multiple stakeholders' perspectives.

Methods: This qualitative study used semi-structured interviews conducted with in-training residents (n=4) before and after completing the training program. In addition, supervising physicians (n=5) and public health stakeholders (n=3) participated in semi-structured focus groups. Issues discussed related to the conditions of development and long-term sustainability of the training program. Finally, directors of LTC facilities (n= 2) were interviewed about conducive and inhibiting organizational factors for successful long-term implementation of the training program. Content analysis was performed on the transcripts.

Results: All in-training residents indicated a positive influence on their motivation to work in LTC after completing the program and one decided to accept a position as LTC physician. All also highlighted several areas for improvement, such as the need for a smoother integration into the LTC facility and improved information about the conditions to fulfil when contemplating to become an LTC physician.
LTC physicians noted organizational challenges related to billing and patient allocation, but all supported the program as essential to ensuring adequate physician training and resources for future LTC demand. Public health stakeholders and LTC directors also supported the need to enhance physicians' training in LTC setting, with emphasis on the development of geriatric and palliative care competencies.

Conclusions: This preliminary analysis provides insights into challenges to address in order to further develop this pilot program. Attracting residents and exposing them to LTC medicine is essential for promoting a sustainable workforce specifically trained in LTC medicine in the future.

FM17

Transfer to acute care during inpatient geriatric rehabilitation: incidence, causes, risk factors, and associated outcomes

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Introduction: Unplanned transfers from a geriatric rehabilitation unit back to an acute ward disrupt patients' recovery. Data about patients' characteristics or predictive factors associated to a higher risk of transfer are scarce. This study aimed to determine the incidence and causes of unplanned transfers, to identify patients' characteristics associated with such transfers, and to describe associated outcomes.

Methods: Consecutive stays (n=2375) occurring in an academic geriatric rehabilitation unit were examined. All discharge summaries of patients with unplanned transfers were reviewed to gather information on the cause. Data on demographics, medical, physical, social and mental status, as well as information on length of rehabilitation stay, discharge destination, and death, were extracted from the hospital database. Multivariable logistic analyses were performed to examine the association between patients' characteristics and unplanned transfers.

Results: One in six (16.7%) rehabilitation stays was interrupted by at least one unplanned transfer, most often because of infectious (19.3%), cardiac (16.8%), digestive (12.7%), trauma (12.2%) and neurological (9.4%) problems. Being older ($_{adj}OR_{per\ year}$: 0.98; 95%CI: 0.96-0.99, P=.013); and being admitted for gait disorder ($_{adj}$OR: 0.72; 95%CI: 0.53-0.99, P=.041) were independently associated with lower odds of unplanned transfer, whereas being a man (adjOR: 1.69; 95%CI: 1.28-2.22, P<.001); medical severity measured by the CIRS ($_{adj}OR_{CIRS}$: 1.04; 95%CI: 1.02-1.07, P<.001), and functional impairment in instrumental ($_{adj}$OR: 1.73; 95%CI: 1.08-2.78, P=.023) and basic ($_{adj}$OR: 2.11; 95%CI: 1.58- 2.82, P<.001) activities of daily living were associated to higher odds of transfer. Patients with any unplanned transfer were less likely to return home, and more likely to be admitted to a nursing home or to die than those without transfer (P< .001).

Conclusion: A significant proportion of patients experienced an unplanned transfer that potentially interfered with their rehabilitation program and translated into poorer outcomes as compared with patients without transfer. Male patients, those with more severe illness and functional impairment are at greater risk of unplanned transfer. Further studies should investigate whether and how some transfers might be prevented.

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P1

Association of statin use and lipid levels with cerebral microbleeds and hemorrhagic stroke in patients with atrial fibrillation: a prospective cohort

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Background: Some studies reported an increased risk of hemorrhagic stroke (HS) associated with statins, but the relationship between statin use and cerebral microbleeds (CMBs) as well as HS in patients with atrial fibrillation (AF) has not been previously examined.

Methods: We used the data of the Swiss-AF study, a prospective cohort of patients with established AF. The associations of statin use and low-density lipoprotein (LDL) levels with CMBs at baseline and new CMBs were assessed using logistic and linear regression models. Association with adjudicated HS during follow-up was assessed with Cox-proportional hazard models. Models were first adjusted for age and sex, and further for hypertension, smoking, alcohol, body mass index (BMI), anticoagulation, education, diabetes, stroke/transient ischemic attack (TIA), coronary heart disease, white matter volume and physical activity at baseline.

Results: Of the 1,693 patients with baseline MRI (mean±SD age 72.5 ±8.4 years, 27.6% women, 90.1% on oral anticoagulants), 802 patients (47.4%) were statin users. The number of CMBs at baseline was 213 (26.5%) and 163 (18.3%) in statin, respectively non-statin users. The age and sex adjusted odds ratio (OR) for CMBs at baseline for statin users vs non-users was 1.46 (95% confidence interval [CI] 1.15-1.85); following multivariable adjustment the adjusted OR (adjOR) was 1.16 (95% CI 0.88-1.58). AdjOR for LDL was 0.93 (95% CI 0.80-1.07).
At 2 years follow-up, 44 (8.0%) statin users and 47 (7.4%) non-statin users had CMBs progression. The multivariable adjOR for statin users was 1.08 (95% CI 0.66-1.77). At follow-up, 14 (1.2%) statin users had HS vs 16 (1.3%) non-users. The multivariable adjusted Hazard Ratio (adjHR) was 0.72 (95% CI 0.27-1.91). There was no significant association between LDL and CMBs progression (adjOR 1.02, 95% CI 0.79-1.33) or development of HS (adjHR 0.96, 95% CI 0.56-1.65). Results remained robust in sensitivity analyses adjusting for new statin introduction or increase in intensity or by classifying statins in low, medium or high intensity. Furthermore, results were similar across all analyzed subgroups, including people of age ≥75 years or patients with prior history of ischemic stroke or with baseline CMBs.

Conclusions: According to this prospective analysis, the use of statins in patients with AF, a population at increased hemorrhagic risk due to anticoagulation is not associated with an increased risk of new CMBs or HS.

Table 1. Baseline characteristics of included participants (with **MRI at baseline**) stratified by statin use

Variable	Statin users (n=802, 47.4%)	Non-Statin users (n=891, 52.6%)
Age, y (mean, SD)	73.7 (7.6)	71.5 (8.9)
Female (n, %)	166 (20.7%)	302 (33.9%)
BMI kg/m² (mean, SD)	28.1 (4.7)	27.2 (4.7)
Smoking (n, %) [a]		
Never	316 (39.4%)	431 (48.4%)
Past	422 (52.7%)	395 (44.4%)
Current	63 (7.9%)	64 (7.2%)
Average alcohol intake (n, %)[b]		
Low	686 (85.6%)	759 (85.3%)
High	115 (14.4%)	131 (14.7%)
TCHOL mmol/L (mean, SD)	4.0 (0.9)	5.1 (1.0)
LDL mmol/L (mean, SD)	2.0 (0.7)	3.1 (0.9)
HDL mmol/L (mean, SD)	1.3 (0.4)	1.4 (0.4)
TRG mmol/L (median, IQR)	1.5 (1.1-2.0)	1.5 (1.1-2.1)
History of Hypertension (n, %)	639 (79.7%)	534 (59.9%)
History of Diabetes (n, %)	189 (23.6%)	77 (8.6%)
Known cardiovascular disease[c] (n, %)	356 (44.4%)	82 (9.2%)
History of stroke or TIA (n, %) [d]	233 (29.1%)	104 (11.7%)
Aspirin (n, %)	182 (22.7%)	61 (6.9%)
Vitamin K Antagonist (n, %)	330 (41.2 %)	275 (30.9%)
Direct oral anticoagulation (n, %)	409 (51.0%)	512 (57.5%)
Other Antiplatelets (n, %)[e]	222 (27.8%)	66 (7.4%)

[a]Missing 2 [b]defined according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA); Missing 2 [c]defined as previous myocardial infarction, bypass, peripheral arterial disease; Missing 1 [d]Missing 2 [e]Missing 3. Abbreviations: BMI, Body mass index; TCHOL, total cholesterol; TRG, Triglycerides.

Table 2. CMBs at baseline, progression of CMBs and occurrence of HS at follow up by statin use in all participants

	Statin users (n=802)	Non-Statin users (n=891)
CMBs at baseline (n, %)	213 (26.5%)	163 (18.3%)
OR[a] (95% CI)	1.46 (1.15-1.85)	
adjOR[b] (95% CI)	1.16 (0.88-1.58)	
CMBs Progression (n, %)	44 (8.0%)	47 (7.4%)
OR[c]	1.10 (0.71 – 1.68)	
Age- and sex-adjusted OR (95% CI) (for yes/no)	1.05 (0.68-1.62)	
Multivariable adjusted OR (95% CI)[b] (for yes/no)	1.08 (0.66-1.77)	
HS (n, %)	14 (1.2%)	
Incidence rate[c]	2.76 (1.63-4.65)	
Age- and sex-adjusted HR (95% CI)	0.75 (0.36-1.55)	
Multivariable adjusted HR (95% CI)[b]	0.72 (0.27-1.91)	

[a]age and sex adjusted; [b]adjusted for sex, age, history of hypertension, smoking status, alcohol, BMI, Vit-K-Antagonist, non Vit-K-Antagonist, education, history of diabetes, history of stroke or TIA, coronary heart disease, white matter volume, regular physical exercise; [c]per 1000 person-years; Abbreviations: CMBs, cerebral microbleeds; HS, hemorrhagic stroke

P2

Is there a shift from cardiovascular death to cancer death in lipid-lowering trials? A systematic review and meta-analysis

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Background: Lipid-lowering therapy (LLT) has been shown to reduce major vascular events in a wide range of patient groups, but results have been contradictory for all-cause mortality, especially among older people. Some randomized clinical trials (RCTs) have found a pattern of increased cancer death in the group treated with LLT. Though meta-analyses have shown that statins do not induce cancer, the question remains on the potential reasons for this pattern. The purpose of our work was to assess a possible shift from cardiovascular (CV) to cancer death in LLT trials among the elderly and to investigate potential subgroups at risk.

Methods: We retrieved all trials from the Cholesterol Treatment Trialists' Collaboration (CTTC) and completed it with a systematic review of large RCTs (≥1000 patients) of LLT (defined as statin, ezetimibe and PCSK-9 inhibitor) reporting CV outcomes for a minimum follow-up of 2 years. We included trials using as a control group placebo or no treatment. To assess a potential shift, we calculated the relative risk (RR) using the number of CV and cancer deaths under treatment vs. in the control group. We used a random-effect meta-analysis to summarize the RR for CV and cancer death. Subgroup analyses were performed on primary vs secondary prevention, on trials with different prevalence of participants aged over 75 years and on trials with a mean age over or under 70 years.

Results: We included 30 trials (21 trials from the CTTC and 9 additional trials) with a total of 232'325 patients; 24 statin trials, 4 ezetimibe trials, 2 PCSK-9 inhibitor trials. Overall, there was no increase of cancer mortality (RR 1.03, 95%CI 0.97-1.10). The RR for cancer mortality was 0.99 (95%CI 0.79-1.23) in primary prevention and 0.99 (95%CI 0.88-1.10) in secondary. The RR for CV death was significantly reduced in both groups (RR 0.79, 95%CI 0.69-0.90; resp. RR 0.86, 95%CI 0.78-0.96). In the subgroup analyses with more than 15% of participants aged over 75 years, the risk of cancer death was increased (RR 1.11, 95%CI 1.00-1.23), while the RR for CV death was 0.96 (95%CI 0.91-1.01). For trials with mean age over 70 years, the RR for cancer death was 1.21, 95%CI 0.99-1.47.

Conclusion: We found no clear shift from CV to cancer death in LLT takers. However, we observed a possible shift with increased cancer deaths in trials with >15% of participants aged over 75 years. This should be taken into consideration in the prescription of LLT in the elderly.

Figure 1: Relative risk for cancer mortality according to prevalence of patients ≥75years old

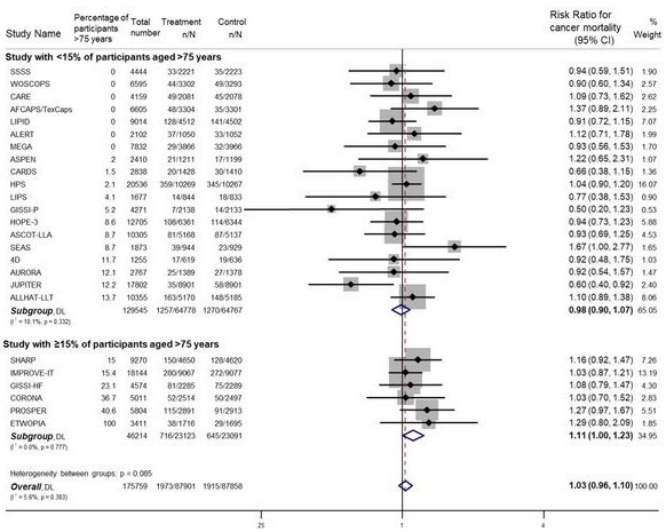
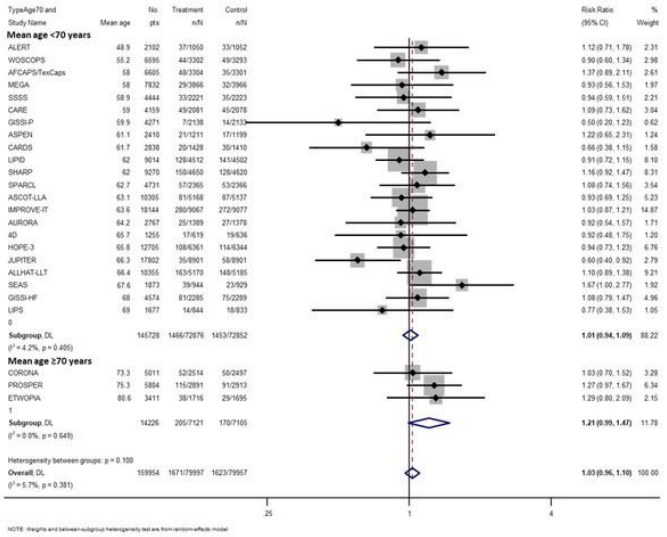


Figure 2: Relative risk for cancer mortality according to mean age under or over 70 years



P3

Interns and senior residents' perspectives on barriers to depression care: what should we look out for?

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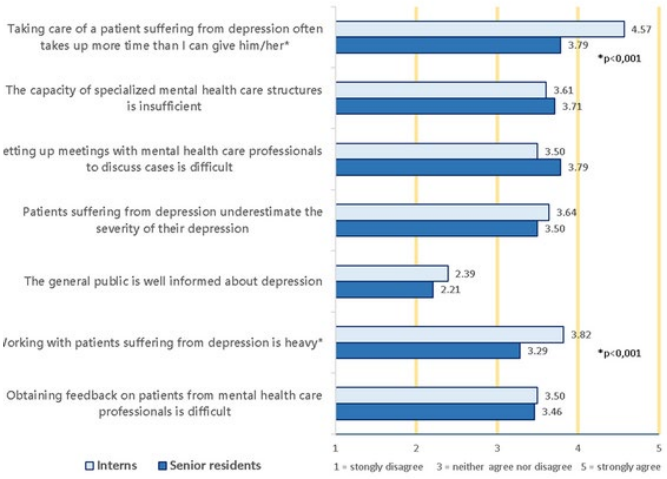
Introduction: A better knowledge of physicians' perspectives on barriers to depression care during their training years is key to support best practice in the long run. The main objective of this study was to identify and compare barriers to depression care encountered by interns and senior residents (SR).

Methods: We conducted a cross-sectional study surveying interns and SR in the Primary Care Division of the Geneva University Hospitals between September and October 2021. The survey was administered online using Qualtrics®. We used both the validated Barriers to Depression Care questionnaire (BDCQ) and the Revised Depression Attitudes Questionnaires (RDAQ) to assess barriers (25 items covering 5 dimensions) and professional confidence (7 items). All items were rated on a 5 points Likert scale. We analysed the data using descriptive statistics to compare each item and dimension by professional rank (interns vs SR). Pearson r test was used to determine correlation between each of the 5 dimensions of the BDCQ and professional confidence (RDAQ).

Results: The survey was distributed to 109 physicians and completed by 56 (57% response rate and 90% completion rate). Interns and SR were evenly distributed (50% each). Participants were 66% female with a mean age of 34 y/o. The strongest barriers were reported in three dimensions: provision of care by the general practitioner, patients' attitudes towards depression, and collaboration with mental health specialists. This pattern suggested an overall feeling of isolation among physicians in their practice. The weakest barriers were reported in two dimensions: guidance for care and access to mental health care. This pattern suggested trust and openness to work with mental health services. Compared to SR, interns were most likely to report that working with depressed patients is heavy and takes up more time that they can give (see Fig1). The barriers reported on the dimensions: provision of care, patients' attitudes towards depression and guidance for care were correlated with lower professional confidence (r=0.57, r=0.59, r=0.5 respectively; p<0.001).

Conclusions: Interns and SR reported similar perspectives on barriers to depression care. These were mostly correlated with their professional confidence. Improvement interventions should preferably target time constraint management, patients' empowerment strategies and transfer of skills from mental health specialists to primary care physicians to secure their autonomy.

Fig 1. The strongest barriers to depression care reported by interns (N=28) and senior residents (N=28) at the Division of Primary Care Medicine, Geneva University Hospital.



P4

Efficacy and safety of digoxin in acute heart failure triggered by tachyarrhythmia

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Introduction: Acute heart failure (AHF) is the most common diagnosis in the emergency department (ED).[1,2] The morbidity and mortality remain very high in patients with AHF.[2] Dismal outcome in patients with AHF is at least in part due to major uncertainty regarding treatment.[1-2] Although tachyarrhythmia is the most common trigger of AHF, the optimal treatment for reducing the heart rate in AHF triggered by tachyarrhythmia is largely unknown.Particular controversy exists regarding the efficacy and safety of digoxin in AHF triggered by tachyarrhythmia and few have questioned the possible effectiveness of digoxin in AHF.[3] Among all currently available negative chronotropic agents, digoxin is the only one with positive inotropic effects and it is inexpensive and widely available, rendering digoxin a very attractive option.Therefore, the aim of this study was to evaluate the short-term efficacy and safety of digoxin loading in consecutive patients presenting with AHF triggered by tachyarrhythmia to the ED.

Methods: This was a single-center, retrospective cohort study including patients from January 2012 until December 2018 admitted to the University Hospital Basel, with AHF triggered by tachyarrhythmia. The patients were eligible if they were naïve to digoxin and received at least 0.75mg i.v. or per os (the minimal expected effective dose) digoxin for heart rate control .[4] The primary efficacy outcome was heart rate reduction at 24h and 48h after 0.75mg or more of digoxin were given. The primary safety outcomes were adverse events (AE) possibly related to digoxin and observed compared to predicted 30-days mortality. Secondary endpoints included change in systolic and diastolic blood pressure at 24h and 48h.

Results: Among 210 consecutive AHF patients treated with at least 0.75mg digoxin for rate-control of tachyarrhythmia, heart rate was significantly reduced from 141±22 beats per minute (bpm) to 101±23 bpm at 24h and 98±22 bpm at 48h (both p<0.0001). AE possibly related to digoxin were infrequent (0.5%) and observed 30-days mortality was comparable to predicted 30-days mortality. Systolic blood pressure increased from 115.86±19.82 mmHg to 122.10±19.04 mmHg at 24h and 122.86±19 mmHg at 48h (both p<0.0001).

Conclusion and relevance: Digoxin was very effective in reducing heart rate among patients with AHF triggered by tachyarrhythmia and had a favorable safety profile. It offers physicians a widely available and inexpensive treatment option in these vulnerable patients.

Table: Baseline characteristics

	All patients	Alive	Dead	«p value»
	n=210	n=191	n=19	
Sociodemographic findings				
Age (mean [SD])	78.9 (9.8)	78.7 (9.7)	80.8(11.2)	0.36
Sex Female (%)	128 (61)	118 (61.8%)	10 (52.6%)	0.44
Medical history				
Heart Failure (%)	112 (53)	104 (54.5)	8 (42.1)	0.34
CAD (%)	59 (28)	55 (28.8%)	4 (21.1%)	0.60
History of MI (%)	26 (12)	25 (13.1%)	1 (5.3%)	0.48
LVEF (median [IQR])	45.0 [33.0, 55.0]	45.0 (32.0, 55.0)	47.5 (39.0, 65.0)	0.21
Valvular Heart Disease (%)	117 (59)	110 (60.4%)	7 (41.2%)	0.13
Active cancer	27 (13)	21 (11.0%)	6 (31.6%)	0.011
COPD	31 (14.8%)	28 (14.7%)	3 (15.8%)	1.00
Devices				0.548
No devices	194 (92)	177 (93)	17 (89)	
ICD/CRT	5 (2)	5 (3)	0 (0)	
Pacemaker	11 (5)	9 (5)	2 (11)	
Chronic Medication				
Beta-blocker (%)	129 (61.4)	120 (62.8%)	9 (47.4%)	0.19
Amiodarone (%)	8 (3.8)	7 (3.7%)	1 (5.3%)	0.54
OAC/NOAC (%)	110 (52.4)	103 (53.9%)	7 (36.8%)	0.16
ACE-inhibitor/ARB (%)	100 (47.6%)	94 (49.2%)	6(31.6%)	0.14
Aldosterone Antagonist (%)	32 (15.2%)	29 (15.2%)	3 15.38%)	1.00
Laboratory values (median [IQR])				
Potassium, mmol/L	4.2(3.8, 4.6)	4.2 (3.8, 4.6)	4.5 (4.0, 5.3)	0.028
Creatinine, µmol/L	98.0 (81.0, 128.0)	98.0 (81.0, 127.0)	96.0 (67.0, 148.0)	0.87
GFR (CKD-EPI) ml/min/1.73m2	57.7 (41.2, 74.4))	53.5 (39.0, 70.0)	55.9 (32.4, 80.4)	0.72
CRP, mg/l	18.7 (5.9, 58.4)	17.4 (5.7, 51.9)	109.0 (9.8, 250.5)	0.003
Hemoglobin, g/L	128.0 (111.0, 139.0)	128.0 (112.0, 139.0)	116.0 (96.0, 127.0)	0.003
Natrium, mmol/L	139.0 (135.0, 141.0)	139.0 (135.0, 141.0)	138.0 (135.0, 144.0)	0.71
Cardiac troponin T, ng/L	34.0 (23.0, 53.0)	33.0 (22.0, 51.0)	60.0 (33.0, 108.0)	0.072

ACE-inhibitor= Angiotensin converting enzyme inhibitor;ARB= Angiotensin receptor blocker; CAD= coronary artery disease; COPD= chronic obstructive pulmonary disease; CRP= C - reactive protein; CRT= cardiac resynchronization therapy; GFR (CKD-EPI) = Glomerular filtration rate (according to chronic kidney disease epidemiology collaboration) ; ICD: Implantable cardioverter defibrillator; IQR=Interquartile range; IV= intravenous; LVEF= left ventricular ejection fraction; MI= myocardial infarction; NOAC= Novel anticoagulants; OAC= Oral anticoagulants; Valvular Heart Disease= Moderately Severe-Severe aortic/tricuspid, mitral valve stenosis or insufficiency

P5

Inadequate reporting of co-interventions is associated with exaggerated treatment estimates in recent cardiovascular trials: a meta-epidemiological study

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Introduction: Recent large randomized controlled trials (RCTs) have found benefits of new drugs for cardiovascular prevention, but study quality varied. Our aim was to assess which methodological study quality factors might be associated with increased treatment estimates in recent cardiovascular trials.

Methods: We did a systematic search of RCTs evaluating pharmacological interventions on cardiovascular outcomes, published in five high impact general medical journals from 2011-2021. Two reviewers independently extracted information on co-interventions (adequately reported vs inadequately reported), blinding of participants and personnel (adequate vs inadequate), risk of bias due to deviations of intended interventions (low vs high/some concerns), funding (non-industry vs industry), design (superiority vs non-inferiority) and primary endpoint results as well as conclusions. We assessed the association of these factors with effect sizes using meta-regression random effect analysis, expressed as the Ratio of Odds Ratio (ROR). RORs >1.0 indicates larger treatment effects in trials characterized with methodological factor pointing towards lower quality. We also examined if the conclusions drawn by the trial authors were congruent with the results, by identifying manipulation of conclusions.

Results: 164 RCTs were included in this analysis. 63 (38%) trials were conducted in the field of antiplatelets/anticoagulants, 25 (15%) in antidiabetics and 19 (12%) were lipid-modifying trials. 124 (74%) trials did not adequately report co-interventions and 71 (43%) were at risk of blinding. In the meta-analytic approach, inadequate reporting of co-interventions was associated with an 8% larger treatment effect for the primary endpoint (ROR 1.08, 95% CI 1.01-1.15, figure 1). We found no statistically significant association with inadequate blinding (0.97, 95% CI 0.91-1.03), risk of bias due to deviations of intended interventions (ROR 0.97, 95% CI 0.91-1.03) and funding type (ROR 1.01, 95% CI 0.93-1.09). Among the RCTs with null results, we identified 8 trials (5%) with manipulation of the conclusions.

Conclusions: Inadequate reporting of co-interventions is associated with increased treatment effects, potentially indicating overestimation of therapeutic benefit from recent large cardiovascular RCTs. Physicians should be cautious about the use of novel drugs, not overstating their benefits when discussing them with patients.

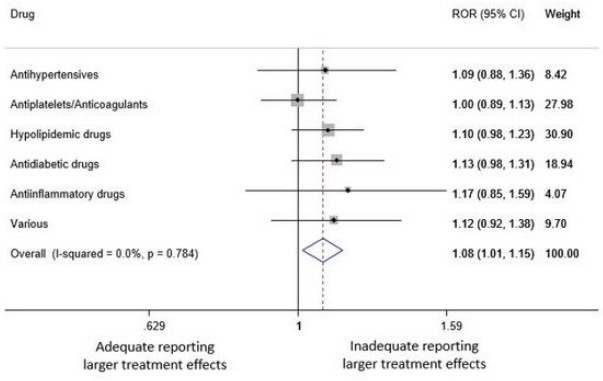

Figure 1. Forrest plot on the association of co-interventions and treatment effects. A Ratio of Odds Ratio >1.0 indicates larger treatment estimates in trials with inadequate reporting of co-interventions.

P6

Combining European Society of Cardiology and American College of Cardiology/American Heart Association risk prediction model with polygenic risk scores to refine cardiovascular prevention: the CoLaus|PsyCoLaus cohort study

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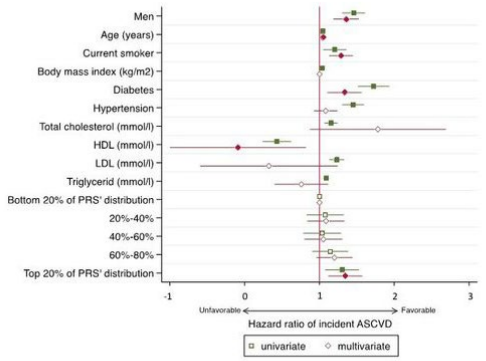
Introduction: Polygenic risk scores (PRS) can predict the risk of developing atherosclerotic cardiovascular disease (ASCVD). However, their utility in combination with existing clinical risk scores remains uncertain. We first validated four different PRS in a Swiss population-based cohort. Second, using the PRS with the best predictive capacity, we assessed its benefit when combined with two clinical risk scores: the Systematic COronary Risk Evaluation 2 (SCORE2) and the Pooled Cohort Equation (PCE).

Methodology: We used data from the prospective CoLaus|PsyCoLaus study, involving 6733 participants at baseline (2003-2006). Non-European ancestry were excluded. The predictive accuracy of the PRS was assessed with discrimination and calibration metrics. For the second aim, subjects with prevalent ASCVD or statin therapy at baseline were also excluded. We tested associations between risk prediction models (PRS alone and combined clinical and PRS) and incident ASCVD, using Cox proportional hazard regressions. Net reclassification index (NRI) detected any improvement of ASCVD risk categorisation following the addition of the PRS to clinical risk scores in overall sample and in subgroups (e.g., sex, age, clinical intermediate-risk).

Results: For the first aim, 4215 subjects (53% women; mean age 53.7±10.7), with 357 prevalent ASCVD, were analysed. The PRS developed by Inouye et al[1], comprising >6 million variants, presented the best predictive capacity (area under the receiver operating characteristic of 0.77) and was used in the following analyses. For the second aim, 3390 subjects (mean follow-up of 12.0±3.3 years), with 188 incident ASCVD, were analysed. Individuals in the top 20% of the PRS distribution had the same magnitude of association with ASCVD as current smokers or diabetic subjects (Figure 1). Combining the PRS with SCORE2 led to a reclassification of 17.1% (95% CI, 4.7-29.5) of subjects in the intermediate-risk category (Figure 2). Likewise, adding the PRS to PCE translated into an NRI of 19.2% (95% CI, 4.8-22.4) in the intermediate-risk category (not shown).

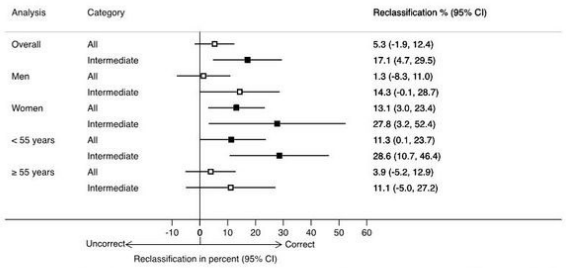
Conclusion: Using a Swiss population-based cohort, PRS presented good predictive capacities for ASCVD. Combining a PRS with clinical risk scores improved reclassification of risk for ASCVD, especially for subjects in the intermediate-risk category. Introducing PRS in clinical practice may refine cardiovascular prevention for subgroups of patients in whom prevention strategies are uncertain.

Figure 1 Associations of traditional risk factors and PRS (in quintiles) with incident atherosclerotic cardiovascular disease



PRS is presented by quintiles, with those in the top 20% of the PRS distribution corresponding to the high- risk category.
Cox proportional hazard regressions were used to test associations with incident atherosclerotic cardiovascular disease. For each factor, a univariate analyse is first presented (green squares and lines). Second, a multivariable analysis, incorporating other factors presented here, has been performed (red diamonds and lines). Hollow squares/diamonds correspond to non-significant associations.
HDL, high-density lipoprotein; LDL, low-density lipoprotein; PRS, polygenic risk score.

Figure 2. Net reclassification improvement when combining the polygenic risk score with the clinical risk SCORE2



The PRS used was developed by Inouye et al. (in Journal of the American College of Cardiology, 2018, doi: 10.1016/j.jacc.2018.07.079). The net improvement in reclassification (NRI) was quantified as the sum of differences in proportions of individuals moving up minus the proportion moving down for those with ASVCD, and the proportion of individuals moving down minus the proposition moving up for those without ASCVD. Results are presented overall, by subgroups and, then, specifically for subjects in the clinical intermediate-risk category. Hollow squares correspond to non-significant associations. CI, confident interval.

P7

Trends and regional variation of transcatheter and surgical aortic valve replacement in Switzerland: a population-based cross-sectional small area variation analysis

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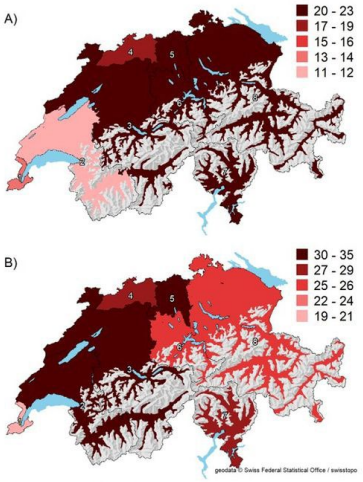
Introduction: Aortic valve stenosis (AS) is the most common valvular heart disease and is treated with transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR). We assessed trends and regional variation of these interventions in Switzerland and examined potential determinants of variation.

Methods: We conducted a population-based analysis using patient discharge data from all Swiss acute care hospitals from 2013–2018. We generated hospital service areas (HSAs) by analyzing patient flows, calculated age-standardized mean procedure rates, and measures of regional variation (extremal quotient [EQ], the highest divided by the lowest rate, systematic component of variation [SCV], the non-random part of variation). We calculated the influence on variation with multilevel regression models, adjusting for demographics, socioeconomic factors (language, insurance status), burden of disease, and density of cardiologists.

Results: Overall, 8074 TAVR and 11825 SAVR procedures were performed in 8 Swiss HSAs between 2013 and 2018. The overall SAVR procedure rate decreased by 27%, whereas the TAVR procedure rate increased by 83%. The fully adjusted TAVR and SAVR rates varied from 12-23 and 20-35/100,000 persons across HSAs (Figure), respectively. The overall regional variation was low to moderate in TAVR (EQ 1.9, SCV 3.9) and SAVR (EQ 1.6, SCV 2.2). After adjustment, women had 35% lower TAVR and 65% lower SAVR rates than men. TAVR were mainly performed in persons aged ≥80years (67%) whereas SAVR were mainly done in persons aged 60-79years(68%). French/Italian speaking regions had a 21% lower TAVR rate than Swiss German regions. A 10% higher regional proportion of private/semiprivate insurance was associated with a 40% increase in TAVR rates and a 21% decrease in SAVR rates. The presence of 1 additional comorbidity per 1000 persons was associated with a 4-fold increase in TAVR, without significant impact on SAVR. The regional density of cardiologists was not significantly associated with procedure rates. After full adjustment, 10% of the variance in TAVR and 17% in SAVR remained unexplained.

Conclusion: TAVR rates increased over the last years, apparently at the expense of SAVR. The regional variation for both procedure rates was low to moderate across Swiss regions and largely explained by differences in patient demographics and socioeconomic characteristics. TAVR was appropriately mainly performed in older persons and those with comorbidities.

Figure: Fully adjusted map of (A) TAVR and (B) SAVR across 8 Swiss HSAs



Abbreviation: HSA = hospital service area. TAVR = transcatheter aortic valve replacement. SAVR = surgical aortic valve re-placement.
Average predicted procedures rates for each HSA per 100,000 persons. Adjusted for year of intervention, age, sex, language region, insurance status, burden of disease, and density of cardiologists/cardiovascular surgeons.

P8

Do we need blood culture stewardship programs? A quality control study to assess the appropriatenss of blood culture collection

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Background: Inapproriatetely collected blood cultures (BC) are associated with potentially harmful consequences for patients including unnecessary diagnostic tests, treatments and costs. As data regarding unnecessarily collected BC are scares, we assessed the appropriateness of BC collection at a tertiary care hospital.

Materials: We conducted a single-center, quality control study to evaluate the appropriateness of BC collection practices at a Swiss tertiary care hospital according to local guidelines in 2020. We performed 3 analysis (A1-A3): a point prevalence survey (A1, including all BC collected on two days in January and September 2020), a patient-individual longitudinal analysis (A2, analyzing all BC from individual patients) and an analysis of BC collection according to predefined diseases (A3) (Table 1).

Pretest probability	Underlying disease	
very low/low pretest probability (<10%)	respiratory tract infection	**mild or moderate CAP***, HAP
	skin or soft tissue infection	**uncomplicated cellulitis***
	genitourinary tract infection	cystitis, prostatitis
	isolated fever, postoperative fever within 48h after surgery	
intermediate pretest probability (10-50%)	respiratory tract infection	severe CAP, VAP
	intra-abdominal infection	**cholangitis***, liver abscess, nonvascular shunt infections (e.g. ventriculoperitoneal shunt)
	skin or soft tissue infection	complicated cellulitis
	genitourinary tract infection	**acute pyelonephritis***
high pretest probability (>50%)	septic shock	
	endovascular infection	infective endocarditis, septic thrombophlebitis, vascular graft infection, catheter-related BSI ventriculoatrial shunt infectio
	bone and joint infection	nontraumatic native septic arthritis, discitis, native vertebral osteomyelitis
	central nervous system infection	meningitis, epidural abscess

Table 1. Overview of pretest probabilities for positive blood cultures (BC) based on the underlying disease. *Diseases in font bold were included into analysis 3 (A3). Abbreviations: CAP: community acquired pneumonia; HAP: hospital acquired pneumonia; VAP: ventilator associated pneumonia; BSI: bloodstream infection.

		BC collection according to local guidelines	Growth of a relevant pathogen**
		Number of BC, n (%)	Number of BC, n (%)
Index BC (n=370)		228 (61.6)	46 (12.4)
	Pretest probability for BSI		
	Intermediate (n=71)	68 (95.8)	10 (14.1)
	High (n=109)	102 (93.6)	34 (31.2)
	Categorization not possible (n=27)	18 (66.7)	2 (7.4)
	No indication documented (n=49)	20 (40.8)	0 (0)
	Low (n=114)	20 (17.5)	0 (0)
FUBC (n=255)		84 (32.9)	23 (9)
	Indication for BC collection		
	FUO (n=6)	5 (83.3)	0 (0)
	Intravascular infection (n=48)	28 (58.3)	12 (25)
	Abdominal tract infection (n=35)	16 (45.7)	0 (0)
	Bone and joint infection (n=17)	7 (41.2)	4 (23.5)
	Skin and soft tissue infection (n=11)	4 (36.4)	1 (9.1)
	Septic shock (n=20)	5 (25)	3 (15)
	Respiratory tract infection (n=43)	9 (20.9)	0 (0)
	Categorization not possible (n=54)	10 (18.5)	1 (1.9)
	Genitourinary tract infection (n=17)	0 (0)	2 (11.8)
	Isolated/postsurgical fever (n=4)	0 (0)	0 (0)
BC according to department (n=625)			
	Surgical departments (n=154)	87 (56.5)	27 (17.5)
	Emergency Department (n=152)	79 (52)	25 (16.4)
	Intensive care unit (n=132)	63 (47.7)	6 (4.5)
	Medical departments (n=187)	83 (44.4)	11 (5.9)

Table 2. Appropriateness and growth of significant pathogens according to the pretest probability for BSI, indication for BC collection and department in analysis 2 (A2). Abbreviations: BC: blood culture; BSI: bloodstream infection; FUBC: follow-up blood culture; FUO: fever of unknown origin. **Definition of relevant pathogen: Growth of a pathogen, excluding contaminations.

Results: We included 69 patients and 127 BC in A1, 130 patients and 625 BC in A2 and 362 BC of 145 patients in A3. BC were not collected according to local recommendation in 40-48% of cases. The positivity rate was 10% and the contamination rate 25%. Growth of a relevant pathogen was more frequently observed when the pretest probability of bloodstream infection (BSI) was high (Table 1 and 2) and was associated with appropriateness of BC collection (18.6% vs. 3.0%, p<0.001). The positivity rate was <3% in infections with low pretest probability (A1: n=0/174; A2: n=0/120; A3: n=4/183; 2.2%), especially in non-severe respiratory tract infections (n=16; 48.5%). The majority of BC with low pretest probability of bacteremia was collected in the emergency department (n=48/114; 42.1%, A2). Appropriateness was not influenced by the COVID-19 pandemic (p=0.85). 40% of follow-up BC in BSI with *Staphylcoccus aureus* and *Candida spp.* were considered as not necessary (Table 2). The costs for inappropriately collected BC amounted to approximately 626'000 EUR a year with a blood volume of 357 mL unnecessarily drawn per day.

Conclusions: Almost half of the BC are not collected according to the guidelines in a Swiss tertiary care hospital, especially in non-severe respiratory tract infections. The implementation of diagnostic stewardship programs including the use of electronic decision support systems should be reinforced to improve BC collection practices and to increase the adherence to local guidelines.

P9

Management of acute non-specific low back pain – do emergency physicians follow the guidelines?

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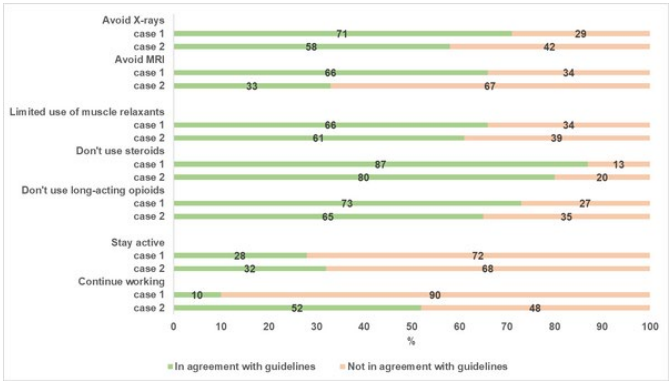
Introduction: Clinical guidelines for acute non-specific low back pain (LBP) recommend to avoid imaging studies or invasive treatments and to advise patients to stay active. It is unknown how emergency physicians adhere to clinical guidelines when managing patients with acute non-specific LBP in emergency departments (ED).
We evaluated the management of acute LBP among ED physicians in Switzerland, and assessed adherence with clinical guidelines.

Methods: We invited all department chiefs of Swiss EDs and their staff to participate a web based survey using two clinical case vignettes of patients with acute non-specific LBP presenting to an ED. The main differences between the two cases were sex, age, profession, pain duration, previous history of back pain and presence vs. absence of yellow flags.

Results: In total, 262 ED physicians completed the survey (43% residents, 32% senior/attending physicians, 24% chief physicians). ED physicians considered the vignettes to be representative for the current work situation. Overall, 49% reported to know current clinical guidelines, and 65% were aware of the «Swiss choosing Wisely-Smarter Medicine» recommendations. Whereas the minority (46%) considered lumbar disc herniation as the underlying specific cause for the pain in vignette 1, this was the case in the majority (66%) in vignette 2. ED physicians chose not to perform further diagnostics in 60% in vignette 1 and in 23% in vignette 2.
Though in both vignettes no neurological deficits or red flags were present, ED physicians would perform x-rays (29% and 42%,Figure) and MRI (34% and 67%). Laboratory tests were considered by every second ED physician (44% and 52%). For pain management, NSAIDs, paracetamol, and metamizole were mostly used. One third reported to prescribe muscle relaxants and long-acting opioids. A short course of prednisone was considered by 13% and 20%. Activity restrictions were recommended in 72% (vignette 1) and 68% (vignette 2), in contrast to guidelines recommendations to stay active. ED physicians issued a certificate for absence from work in 90% and 48%.

Conclusion: A substantial proportion of the diagnostic and therapeutic management of two non-specific low back pain case vignettes in the ED was not in agreement with current guideline recommendations although Swiss ED physicians appear to be aware of them. Ineffective management of low back pain may result in unintended and costly consequences.



P10

First-year medical students at the patient bed – early clinical exposure through a project-based learning tool in internal medicine

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Introduction: Project-based learning is part of the medical curriculum of the Faculty of Medicine, University of Basel, aiming at early patient contact. In brief, medical students participate in one of 20 projects in various clinical settings during the first year of studies. We introduced an internal medicine program "Where Dr. House seeks advice" (Dr. House program) in 2016, consisting of (Figure 1):

- Practically orientated teaching units (theoretical seminars and patient encounters with demonstration of clinical skills)
- Shadowing clinicians of different subspecialties and during interventions (e.g. wards, outpatient clinic, emergency department, cardiac catheterization laboratory)
- Thematic workshops and clinical reasoning seminars
- Social events including commented watching of Dr. House TV series.

The aim of this study is to get an understanding on students' experience with regard to their professional development.

Methods: Eight to ten medical students with two peer tutors take part in this program every year. Eighteen students who participated in 2018 and 2021 wrote a reflective report on their experiences of the program. Content analysis with an inductive coding frame was used to analyze students` reflections, emphasizing in overacting themes.

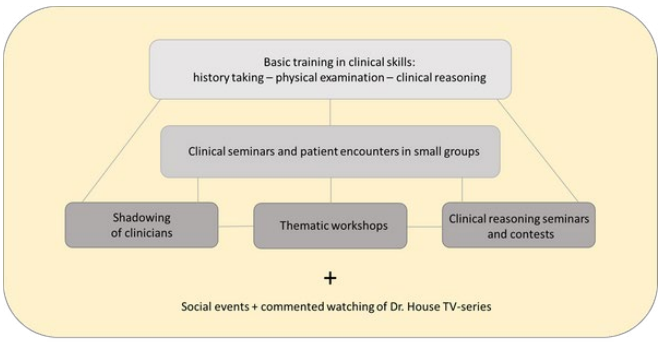

Figure 1: Setup of Dr. House program

Results: Five main themes emerged: professional identity formation, motivation for the professional development, dealing with own emotions facing patients, and experiencing senior physicians as role models. The patient contact was particularly emphasized. The students described going through an emotional process, e.g. while experiencing the role of a future physician as a moving moment, or learning to overcome the initial "fear" of patients, as well as dealing with their own emotions in regard to the different patient fates. Observing clinicians at work and learning how they achieve a satisfactory work-life balance was a crucial experience for them. Overall, the students felt being at the right place professionally.

Conclusion: Dr. House program enables the first-year medical students to experience the first contact with medical staff and patients. The lack of theoretical knowledge does not hinder them to attain relevant insights into the clinical practice and to increase their motivation for further professional development. Thus, early exposition to the clinical setting in internal medicine seems to be a valuable first step in the career of a medical student.

Meilleurs posters SSMIG des jeunes chercheurs/euses / Beste Poster SGAIM junger Forschenden

P11

Development of tools to implement shared decision-making for guideline- recommended antibiotic prescriptions in primary healthcare physician practices in Switzerland

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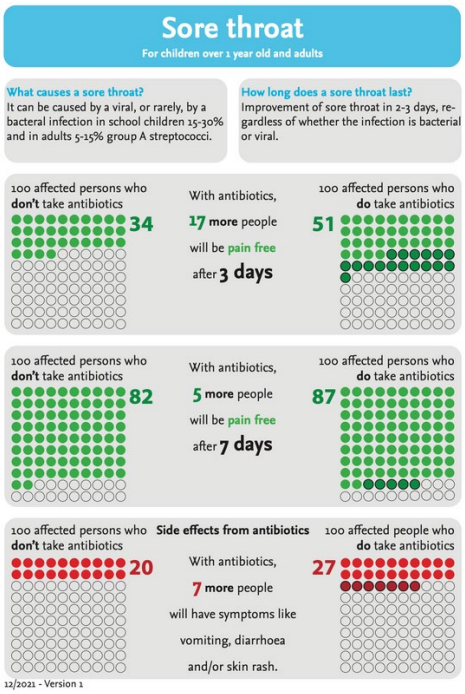
Introduction: If primary care physicians (PCP) prescribe fewer antibiotics, this should reduce the rate of antibiotic resistance. PCP prescribe fewer antibiotics when they engage in shared decision making (SDM) with their patients, which encourages patients to express their preferences and receive treatment that aligns with their values. Effective SDM tools for antibiotic prescription in primary care should thus be developed, tested, and integrated into daily routine practice.

Methods: We developed and tested evidence-based summary information (EBSI) for PCP and SDM instruments over four Plan-Do-Study-Act (PDSA) cycles conducted with quality circles (QC) of PCP. The EBSI and SDM instruments addressed symptomatic patients who presented with otitis media acuta, tonsillopharyngitis, and (in women) lower urinary tract infection. We began by retrieving evidence-based information, analysing existing guidelines in Europe, and finding existing patient decision aids (PDAs) in the literature for these infections. PCPs then gave us feedback in QC. To capture PCPs' knowledge and attitude towards treatment options before and after presenting the document to gain insight in knowledge increase over time, we developed a questionnaire for QC to complete before the first QC and after the second QC. We also received feedback from expert physicians and interviewed patients to improve the documents.



Results: Three QC (39 PCP) participated in two out of four PDCA cycles. Six expert physicians commented on the EBSI and SDM instruments. We interviewed 11 patients in separate one-hour interviews. Most PCPs said they would use our materials in clinical practice, though role plays revealed they might find it hard to implement SDM. Discussing the EBSI in QC increased PCP knowledge about antibiotic prescription. The patients we interviewed appreciated the SDMI and participating in decision making.

Conclusion: While both PCP and patients appreciated the developed tools, future efforts should enable PCP to be more confident about the current evidence and PCP need to practice communication skills in the safe environment of a QC to become familiar with the process of SDM. We successfully worked with QC to develop, adapt and test materials that encouraged PCP to engage in SDM about antibiotic prescription in primary care.

P12

Prevalence and determinants of common mental health problems in primary care: a cross-sectional study in Switzerland

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Introduction: General practitioners (GPs) are confronted daily with patients who have mental health problems but most studies about psychic symptoms are conducted in general population. In this context,the aim of this study was to figure out the prevalence of the most common mental health symptoms in a large primary care population, to characterize them and describe their determinants.

Methods: Data were based upon a cross-sectional study in a primary care population in Switzerland called SPAM Prev (Swiss Primary Health Care Active Monitoring, Prevention) conducted in 2015-2016. 1200 randomly drawn patients participated from a research network of 170 GPs. Questionnaires were handed to the patients by fieldworkers present at GPs' practices. Stress in daily life, PHQ-4 and sleep disorders were measured.

Results: 7.7% of patients had moderate to severe anxious and depressive symptoms, 30.9% felted stressed at least once a week and 17.2% had severe sleep disorders. Women, young people and people living alone with kid-s were globally more at risk to report mental health problems. A high number of visits to the GP during the 12 last months was associated with a high PHQ-4 score and severity of sleep disorders. Participants taking psychotropic medication still had high PHQ-4 scores, high level of stress and high severity of sleep disorders.

Conclusion: Even though most of the patients included in our study were followed regularly by a GP, a significant number of mental health problems were found. Concrete tools should be given to GP in order to better take care of patients suffering from mental health problems. Interprofessional collaboration between GP and mental health specialists should especially be encouraged.

P13

Is prealbumin a useful clinical biomarker for medical inpatients at nutritional risk? Results of a secondary analysis of a randomised clinical trial

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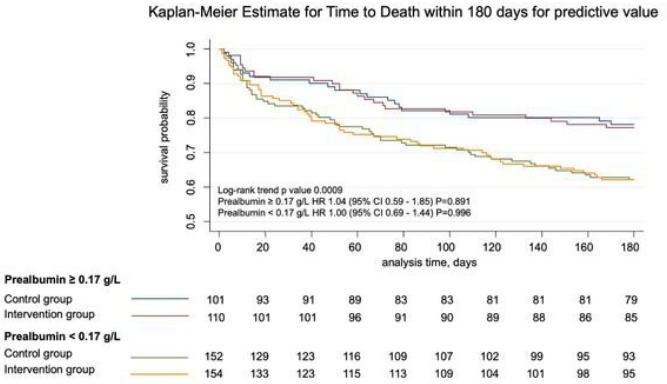
Introduction: Serum prealbumin levels have been proposed to be useful biomarkers for the nutritional assessment of patients due to its shorter half-life time compared to albumin. However, it is unclear whether prealbumin levels have prognostic implications and can be used as an indicator for the response to nutritional therapy and help identify patients benefitting from nutritional support.

Methods: This study is a secondary analysis of the EFFORT trial, a Swiss multicentre randomised controlled trial comparing the effects of individualised nutritional support with usual care in medical inpatients. We included a total of 517 of 2028 patients from one participating centre with available admission prealbumin concentrations. Patients were stratified into groups of low vs. normal prealbumin levels based on the cut-off of 0.17 g/L.

Results: 306/517 (59.2%) patients (mean age 71.9 years, 53.6% men) had low admission prealbumin levels (<0.17 g/L). There was a significant association between low prealbumin levels and 180-day mortality [115/306 (37.6%) vs. 47/211 (22.3%), fully adjusted HR 1.59, 95%CI 1.11 to 2.28, p=0.011]. The response to nutritional support was similar for patients with low prealbumin levels compared to patients with normal prealbumin levels (HR 0.9, 95%CI 0.51 to 1.59 vs. HR 0.88, 95%CI 0.35 to 2.23), showing no evidence for a subgroup effect (p for interaction=0.823).

Conclusion: In medical inpatients at nutritional risk, low admission prealbumin levels correlated with higher mortality risk and other adverse clinical outcomes. However, serum prealbumin levels were not helpful in identifying patients benefitting from nutritional interventions.



P14

Overuse and underuse of thromboprophylaxis in medical inpatients

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**co-last authorship*

Introduction: To simplify venous thromboembolism (VTE) risk stratification and to improve the use of thromboprophylaxis (TPX) in medical inpatients, risk assessment models (RAMs) have been developed. Although provision of TPX is recommended only in patients categorized as high risk for VTE by a validated RAM, previous studies have reported underuse of TPX in high risk and overuse in low risk patients. How the various RAMs differ in categorizing patients in risk groups, and whether the choice of a particular RAM may influence estimates of overuse and underuse of TPX is currently unknown. We aimed to determine the proportion of medical inpatients categorized at high or low VTE risk according to validated RAMs, and to investigate the appropriateness of TPX in high and low risk patients based on each RAM.

Methods: We used data from a prospective cohort study conducted in 3 Swiss university hospitals in 2020 and 2021. Adult inpatients were enrolled if they were admitted to general internal medicine due to acute illness. Data on demographics, clinical characteristics and all items of 4 validated RAMs (Padua Score, IMPROVE Score, simplified Geneva Score, Geneva Score) were collected at baseline (within 72 hours of admission). Participants were categorized as high or low risk for VTE according to each RAM. The proportion of patients consistently categorized as high or as low risk by all 4 RAMs was calculated. We assessed prescription of pharmacological or mechanical TPX at baseline and anytime during hospitalization in high and low risk groups according to each RAM.

Results: Among 1350 medical inpatients, the proportion of patients categorized as high risk for VTE ranged from 29.9% with the IMPROVE Score to 65.8% with the Geneva Score. Overall, 24.5% of patients were consistently categorized as high risk, and 26.6% as low risk by all 4 RAMs. Depending on the RAM used, 59.6% to 64.3% of high risk patients had a prescription of TPX at baseline (Table), while the proportion increased to 70.7% to 74.8% during the entire hospitalization. TPX was prescribed to 37.6%-48.5% of patients categorized as low risk.

Conclusions: The proportion of patients considered at high risk of VTE varies widely according to different RAMs. Both Geneva Scores classify more patients at high risk of VTE than others, which potentially generates a greater use of TPX. While TPX remains underused in high risk patients, overuse in low risk patients is even more pronounced.

Table. Proportion of patients at high and low VTE risk according to validated RAMs* and receipt of pharmacological or mechanical TPX

VTE RAM	High VTE risk			Low VTE risk		
	Overall	TPX at baseline§	TPX during hospitalization‖	Overall	TPX at baseline§	TPX during hospitalization‖
	n (%)	n (%)†		n (%)	n (%)†	
Padua Score	642 (47.6)	413 (64.3)	480 (74.8)	708 (52.4)	296 (41.8)	373 (52.7)
Improve Score	404 (29.9)	250 (61.9)	293 (72.5)	946 (70.1)	459 (48.5)	560 (59.2)
Simplified Geneva Score	847 (62.7)	520 (61.4)	612 (72.3)	503 (37.3)	189 (37.6)	241 (47.9)
Geneva Score	888 (65.8)	529 (59.6)	628 (70.7)	462 (34.2)	180 (39.0)	225 (48.7)
Concordant categorization in all 4 RAMs	331 (24.5)	209 (63.1)	248 (74.9)	359 (26.6)	118 (32.9)	158 (44.0)

Abbreviations: RAM, risk assessment model; TPX, thromboprophylaxis; VTE, venous thromboembolism
* variables to calculate VTE risk according to each RAM were collected at baseline visit (i.e. within 3 days [median 1 day] of admission)
§ receipt of TPX refers to any TPX at baseline
‖ receipt of TPX refers to any TPX during the entire hospitalization
† among the subgroup of patients categorized at high or low VTE risk, respectively

P15

Effects of discussing sensitive health topics during internal medicine ward rounds: ancillary analysis of the BEDSIDE-OUTSIDE Trial

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Introduction: Discussing sensitive health topics, (e.g., medical ambiguity and uncertainty, social issues, non-adherence) during the ward round is challenging and may negatively impact patient satisfaction with health care. We compared patients with and without sensitive topics and investigated risk factors for low satisfaction with care.

Methods: Within this ancillary project of a large multicenter randomized trial, we analyzed sensitive topics discussed during the ward rounds as well other specific communication elements. The

primary endpoint was patients' overall satisfaction measured on a visual analogue scale from 0 to 100.

Results: Overall, 906 patients were included in the analysis and in 643 patients, sensitive topics were discussed. Patients with sensitive topics had more psychiatric comorbidities (14[5.3%] vs. 86[13.4%], p<0.001) and a lower mean satisfaction with care (90.62±12.24 vs. 88.25±13.93, adjusted difference -2.13 [95%CI -4.10 to -0.17], p=0.033) compared to patients without sensitive topics. Most important risk factors for low satisfaction with care among patients with sensitive topics were not addressing emotion but instead providing medical information (20[6.6%] vs. 39[11.4%], OR 1.82 (95%CI 1.04 to 3.10, p=0.04) and dismiss of concerns raised by patients (12[3.5%] vs. 1[0.3%], OR 11.10 (95%CI 1.42 to 85.10, p=0.03).

Conclusions: Patients with sensitive topics have lower satisfaction with care, particularly, if emotions were not properly addressed. Education of physicians on how to communicate emotions may help to improve the care of these patients.

P16

Risk factors of nosocomial SARS-CoV-2 infection in the Service of internal medicine at CHUV

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Introduction: Nosocomial SARS-CoV-2 infections are one of the multiple challenges faced by hospitals in the management of this virus-induced pandemia. Between February and March 2021, despite stringent preventive measures, several nosocomial cases occurred in our Service of internal medicine at CHUV.

Method: In order to assess potential risk factors for these nosocomial infections, we retrospectively compared demographic, clinical and environmental factors in 65 patients with hospital-acquired COVID-19 and 51 patients hospitalized during the same period that did not display a SARS-CoV-2 infection despite presenting a high risk for this viral infection.

Results (Table 1): Sex, age and comorbidities (BMI, diabetes, hypertension, active cancer nor immunosuppression) were similar in both groups.
Patients with nosocomial infection had an inferior number of contact with both caregivers (doctors and physiotherapists) and family members.
However, a significantly higher percentage of patients with nosocomial infection stayed in a 5-bed capacity rooms instead of 1-2 beds (56.9 % vs 33.3 %, p = 0.01) and shared toilets in these rooms (61.5 % vs 43.1 %, p < 0.05).
Nosocomial infection was associated with a significantly longer hospitalization and a 5-fold increased mortality (38.4 % vs 7.8 %, p < 0.001).
The reduction from 5 to 3 patients per room, combined with an increased frequency of toilet cleaning led to a subsequent almost complete drop of nosocomial SARS-CoV-2 infections.
Conclusion: Patient promiscuity appears to be a major determinant of nosocomial SARS-CoV-2 infections. Simple distancing measures may help to prevent this condition that is associated with an important morbidity and mortality.

TABLE 1

	Control group [n = 51]	Nosocomial COVID-19 cases [n = 65]	p
Demographic factors			
Sex			
• Male [%]	34 [66.7]	40 [61.5]	0.6
• Female [%]	17 [33.3]	25 [38.5]	0.6
Age (years)	74.4 ± 15.1	72.5 ± 12.1	0.5
Comorbidities			
BMI (kg/m²)	23.1 ± 5.8	24.5 ± 6.0	0.2
Patients with diabetes [%]	11 [21.6]	22 [33.9]	0.1
Patients with hypertension [%]	23 [45.1]	29 [44.6]	1.0
Patients with active cancer [%]	20 [39.2]	26 [40.0]	0.9
Immunosuppression			
• Patients immunodepressed [%]	27 [52.9]	22 [33.9]	0.04
• Treated by corticosteroids	20 [74.1]	14 [63.6]	0.4
Contacts with caregivers or family			
Patients with physiotherapy session outside their bedroom [%]	35 [68.6]	31 [47.7]	0.02
Number of visits by external physician	5.5 ± 4.3	4.0 ± 3.0	0.03
Patients visited by family members [%]	15 [29.4]	12 [18.5]	0.2
Environmental factors			
Patients stayed in a 5-bed capacity room [%]	17 [33.3]	37 [56.9]	0.01
Use of common bathroom [%]	22 [43.1]	40 [61.5]	< 0.05
Clinical course			
Deceased [%]	4 [7.8]	25 [38.4]	< 0.001
Mean length of stay in days (min.-max.)	23.9 ± 11.6 (14-64)	30.8 ± 25.3 (9-155)	0.05

P17

Ten-year evolution of statin eligibility and use in a population-based cohort: the CoLaus|PsyCoLaus study

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Introduction: Recent studies on management of dyslipidemia show that eligible individuals are undertreated and that a large proportion of them do not reach LDL-cholesterol target levels.
Using contemporaneous data (2003-2017), we assessed the use of statins, including their intensity, in primary and secondary prevention.

Methods: Data from the CoLaus|PsyColaus study, involving 4,655 participants at baseline (2003-2006) and 3,587 at 10-year follow-up (2014-2017). We estimated 10-year cardiovascular risk using clinical risk scores, namely the European Systematic Coronary Evaluation Score (SCORE; recommended by the European society of cardiology [ESC]) and Pooled Cohort Equation (PCE; recommended by the American Heart Association/American College of Cardiology [AHA/ACC]). We first determined eligibility for statins and adherence to recommendations in primary prevention. Additionally, we assessed the prevalence of statin users in 2014-2017 in people free from ASCVD at baseline and who developed an ASCVD during the follow-up (secondary prevention).

Results: During follow-up, 219 people developed a first ASCVD. In eligible individuals in primary prevention based on ESC guidelines, 25.9% in 2003-2006 and 35.9% in 2014-2017 used statins. According to AHA/ACC guidelines, 24.0% of eligible individuals in 2003-2006 and 26.3% in 2014-2017 reported statin use. Only 28.2% of treated people achieved LDL-C target levels recommended by ESC in 2014-2017 (15.8% in 2003-2006), women less frequently attaining goals. Only 18% of individuals used high-intensity statins in 2014-2017, women less often receiving them (14% vs. 22%). In secondary prevention, only 74% of individuals were using statins when recommended.

Conclusions: In our population-based cohort, management of dyslipidemia is suboptimal in both primary and secondary preventions, especially with an underuse of high-intensity statins with adapted posology. Women were less frequently treated and, if treated, received high-intensity treatment less frequently.

P18

Counselling for chronic insomnia in Swiss pharmacies: a survey study based on case vignettes

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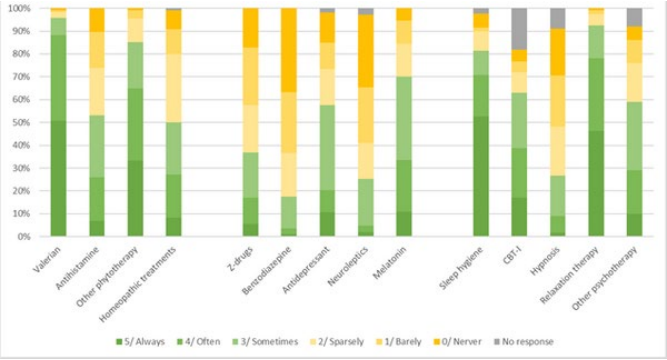
Background: Pharmacies are a first low-threshold access point for treating health conditions like chronic insomnia (CI), but CI guidelines recommend cognitive behavioural therapy (CBT-I) as a first-line treatment, rather than pharmacotherapy. We aimed to determine if Swiss pharmacists suggested treatments in line with CI treatment guidelines.

Methods: Our interprofessional team of pharmacists, primary care providers, and specialist physicians created a survey to determine whether pharmacists recommend CBT-I to their clients and determine how well-informed they are about this therapy. The survey included three case vignettes describing clients with chronic insomnia, one without a medical diagnosis (women, 50 y.o.) and two with a diagnosis but a significant age difference (women, 45 y.o. and men, 79 y.o.). A short explanation about CBT-I was given to the pharmacists before they answered questions about CI prevalence, treatment options for CI, and their interest in learning more about these topics. The link to the online survey, accessible from April until June 2021, was sent out by the main pharmacist association in Switzerland (pharmaSuisse), followed by one email reminder. We also mailed paperbased surveys to pharmacies in Cantons Bern and Lucerne.

Results: Of the 1523 Swiss pharmacists who received the link, 149 (10%) fully filled out a questionnaire (61% German-speaking pharmacists; 79% female). For the first clinical vignette, 96% of the pharmacists would recommend valerian, 94% relaxation therapy, and 63% CBT-I. Almost all pharmacists thought Z-drugs (97%) and benzodiazepines (94%) were the most effective treatments, but they only recommended Z-drugs in 37% of cases and benzodiazepines in 18%.
Pharmacists varied widely in their estimates of the number of their clients who had sleep disorders, acute insomnia, or CI with acute insomnia. Their estimates of the percentage of patients with CI ranged from less than 5% to more than 75%. Most pharmacists (72%) had not heard of CBT-I before the survey, but 64% expressed interest in learning more about it.

Conclusion: Even though guidelines recommend CBT-I as a first-line treatment for CI, participating pharmacies usually recommended phytotherapy and relaxation therapy and few recommended CBTI.
Though most were unfamiliar with CBT-I, they wanted to learn more about it. To increase the likelihood CI patients will be offered CBT, researchers should test interventions that promote CBT-I to pharmacists.



P19

Choosing an eco-responsible single-use hospital medical device: the example of a life cycle analysis of medicine cups

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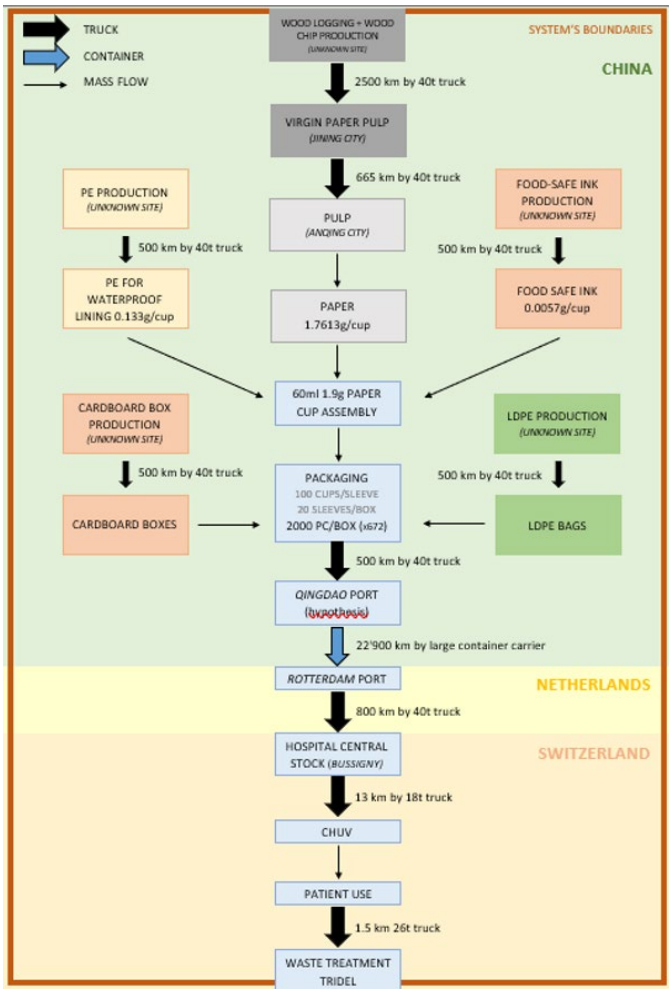
Introduction: Human health depends on environmental health: climate change causes famine, migration, infectious diseases, psychological disorders, threatening the health progress made over the past century. However, the healthcare system (HS) has a significant environmental impact. In Europe, it is the fourth largest emitting sector after the energy, transport and construction sectors. The Swiss HS is the third largest in terms of CO_2equivalent (CO_2e) emissions per year and per inhabitant (>1t vs world average of 0.28t). Hospitals are responsible for 50% of it, among others due to single-use hospital waste. Life cycle assessment (LCA) is the gold standard to assess the impacts of the production, transport, use and disposal of objects or processes from cradle to grave. At the Centre hospitalier universitaire vaudois (CHUV), the polypropylene (PP) medicine cup is the most ordered single-use item. Our aim is to find alternatives and compare them through LCA.

Methods: An internet search with "medical measure", "medical cup", "gobelet à médicaments" and "Medizinbecher" and mail contacts with current CHUV suppliers found two mains alternatives to the PP cup: PP Eco+ fossil free (PP+ from Sweden) and PAPER cup (from China). Boundaries of LCA's PAPER cup production system are shown in Figure 1. The impact on climate change, human health, ecosystem quality and resource depletion were carried out using the Ecoinvent 3.7.1 database.

Results: The LCA of the PP+ cup could not be completed as its raw material, black liquor soap, is not included in the Ecoinvent inventory. However, for PP, respectively PAPER, LCAs show that the biggest impact is attributable to the production phase (55% vs 46% of total CO_2e). The impact of the disposal phase is reduced thanks to the waste-to-energy system of the incineration plant savings on global warming through thermal energy production (28% vs 47%).

The PP cup is responsible for five times more CO2e (13,1 vs. 2,5 Kg CO_2e/year) and has eight times more effect on resources (207,2 vs. 25,6 MJ/year) but has a 1.2 time lower impact on ecosystems (2,6 vs. 3,2 PDF*M2*year/year) (see Table1).

Conclusions: The PAPER alternative is to recommend as having much lower impact on climate change and resource use, even if having a higher one on ecosystems and although transport is 14 times longer (China vs Sweden). Health actors need to know the environmental impacts of the material ordered through LCA and add this criterion to those of safety of use and cost effectiveness.



P20

Teaching "therapeutic communication" ("hypnosis without hypnosis") in the bachelor of medicine. The experience of Geneva University

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Introduction: Therapeutic communication (or *"hypnosis without hypnosis"*[1]) is a set of technics inspired by clinical hypnosis capable of influencing the person in distress to make her feel/behave differently, in a more beneficial/adaptive way.[2]This type of communication is particularly effective in situations with a strong emotional/affective impact, where the patient quickly and spontaneously enters a state of altered consciousness (trance state) characterized by an increased susceptibility to suggestions.[3] The clinical value of thy type of communication, particularly in managing perioperative pain and anxiety, has been demonstrated in several works.[4]TC is currently taught to health care workers of the University Hospitals of Geneva; nevertheless, participants often report that this teaching is delivered too late in their *curriculum*, after they have already developed potentially noxious habits (e.g. voicing negatively loaded suggestions, or warning before potentially noxious stimuli). In order to prevent bad communication habits from forming, we developed an introductory course to therapeutic communication, which was this course was finally approved for implementation in 2021 in the*curriculum* of the Medical Faculty of the University of Geneva (Bachelor's program, third year).

Methods: In order to analyze and evaluate the efficacy of this course, a survey was submitted to third-year students before the course and 1 month after. The survey was built upon the Kirkpatrick's levels of training evaluation,[5] and contained 5 questions to ascertain what the participants thought about the course (level 1, reaction), what knowledge and skills did they acquire (level 2, knowledge), and whether they were able to apply what they learnt (level 3, behavior). Students' answers before and after the course were compared.

Results: The major results of the preliminary analysis of the surveys showed that students are initially unaware of how hypnotic techniques can be integrated in clinical communication, but are curious and eager to learn. Moreover, they rapidly understand the potential implication of therapeutic communication, and its bases, and are keen to use it in their future clinical practice.

Conclusions: Students are interested in improving their communication skills, and that therapeutic communication seems to be a tool that can be easily and quickly grasped and integrated into everyday clinical practice.

Posters SSMIG / Poster SGAIM

P21

Adherence to European Society of Cardiology guidelines' recommendations for physical activity in a population with different cardiovascular risk levels: theCoLaus|PsyCoLaus Study

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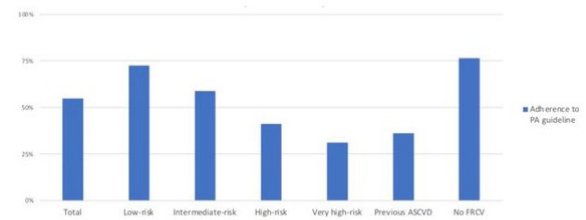
Introduction: Physical activity (PA) is an important modifiable lifestyle factor with a favourable effect on atherosclerotiCcardiovascular diseases (ASCVD). However, the level of adherence to PA guidelines remains unclear.Using a population-based cohort (CoLaus|PsyCoLaus study), we first aimed to assess level of adherence to ESC PA guidelines using accelerometer measurement in subjects with different cardiovascular risk levels. Second, we assessed characteristics associated with adherence to PA.

Methodology: We identified, between 2013-2016, 4'882 eligible subjects, of them 2'187and 143 subjects had no accelerometry data or ESC SCORE, respectively, available, leaving a sample of 2558 subjects for analysis.PA was assessed using an accelerometer worn on the wrist continuously during 14 days in free-living conditions. European Society of Cardiology (ESC) recommends 150 minutes per week of moderate intensity or 75 minutes per week of vigorous-intensity PA. Adherence to PA recommendations was reached if >80% of the recommended PA levels were performed. Participants' cardiovascular risk levels were calculated according to a clinical score supported by the ESC, the Systematic Coronary Risk Evaluation SCORE-1. Levels of adherence across risk groups were assessed. Univariate analysis was used to test associations between subjects' characteristics and adherence. Finally, we used multivariate logistic regression to assess factors independently associated with PA adherence.

Results: Of 2558 subjects (mean age 61.9±9.9, 53.5% women),overall 55% were adherent to PA guidelines. Subjects free from ASCVD were more likely to be adherent compared to those with prevalent ASCVD (56% vs 36%; p-value <0.001). The level of adherence varied significantly according to cardiovascular risk categories (Figure 1). Bringing factors significantly associated with adherence to PA recommendations in univariate analysis to multivariate analysis, only age, body-mass index, benzodiazepine treatment, current smoking for men and being diabetic for women remained associated with adherence to guidelines.

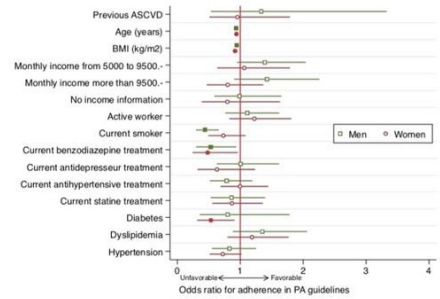
Conclusion: Adherence to ESC guidelines on PA was poor, in particular a third of subjects with previous ASCVD adhered to PA recommendations. Age, BMI, benzodiazepine treatment, current smoking (men), being diabetic (women), play an important role in adherence to PA recommendations.

Figure 1. Distribution of adherence to ESC PA guidelines according to cardiovascular risk levels, using ESC-SCORE1 categories of risk



ASCVD is defined as any acute myocardial infarction, symptomatic coronary artery disease with greater than 50% stenosis treated by percutaneous coronary intervention or coronary artery bypass graft, fatal or non-fatal stroke or death of cardiovascular origin.
Abbreviations : ASCVD, atherosclerotic cardiovascular disease ; FRCV: cardiovascular risk factors; PA, physical activity,

Figure 2. Multivariate logistic regression between individuals' characteristics and adherence to ESC PA guidelines, by sex



Multivariate logistic regression analysis was used to test associations with adherence to ESC PA recommendations. It included all significantly associated individual's characteristics from univariate analysis. Hollow squares/circles correspond to non-significant associations. Abbreviations : ASCVD, atherosclerotic cardiovascular diseases; PA, physical activity,

P22

Association of trimethylamine N-oxide with impaired cognitive function in patients with atrial fibrillation: a Swiss-AF cohort study

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Introduction: As patients with atrial fibrillation (AF) are predisposed to suffer from major adverse cerebrovascular events (MACE), they are also more likely to suffer MACE linked sequelae such as cognitive impairment. We hypothesized that the gut microbiome derivate trimethylamine N-oxide (TMAO) may amplify this pathomechanism through its hypercoagulative, proinflammatory and proatherogenic effects.

Methods: Patients of the Swiss-AF cohort with determined TMAO plasma levels, cognitive testing (n = 2'379) and cerebral magnetic resonance imaging (cMRI) (n = 1'722) at baseline were included. Overall cognitive performance was indicated by the Cognitive Construct (CoCo) score, which is a factor score reflecting different cognitive functions measured by four validated neuropsychological assessments within the Swiss-AF cohort: the Montreal Cognitive Assessment (MoCA), Trail Making Test (parts TMT-A and TMT-B), Semantic Fluency Test (SFT) and Digital Symbol Substitution Test (DSST). All cognitive test scores obtained were correlated with quartiles of patients' TMAO plasma levels (Q1: 0.6-4, Q2: 4-5.8, Q3: 5.8-9.1, Q4: 9.1-164µmol/l). The relevance of co- existence of stroke in cMRI (i.e., clinically overt, silent, or no stroke) and high TMAO plasma levels was evaluated. Linear effect models with multiple TMAO- and cognition-relevant covariate adjustment were employed.

Results: After multivariable adjustment, patients in the highest quartile of TMAO levels was associated with significant poorer cognitive performance according to the global cognitive score (CoCo: estimate -0.11, 95% CI [-0.17, -0.49], p<0.001) and the well-established MoCA test (-0.53, 95% [-0.93, -0.12], p = 0.011) compared to patients in the lowest quartile. This was observed accordingly in the SFT, DSST, TMT-A and TMT-B. In the subgroup analysis, lower CoCo score and MoCA scores were significantly associated with overt (-0.18, 95% [-0.33,-0.04], p=0.012) or silent (-0.126, 95% [-0.25,0.002], p=0.053) strokes. Furthermore, high TMAO levels and silent strokes were associated with lower MoCA scores (-1.03, 95% CI [-1.91,-0.15], p=0.023).

Conclusion: This analysis shows an association between elevated TMAO plasma levels and cognitive impairment in AF patients. This association seemed especially in patients with previous cryptogenic strokes. More longitudinal data is necessary to clarify the causality and dynamics between TMAO and cognitive impairment in patients with AF.

P23

Attitudes and intentions of pharmacists towards the controlled distribution of cannabis for non-medical use in Swiss pharmacies

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Introduction: Several countries have regulated or are considering regulating sale of cannabis for non-medical use (CNMU). The Swiss government amended the law on narcotics in 2021 to allow researchers to test alternate models for selling CNMU. Point-of-sale pilot trials in pharmacies are planned or underway in several Swiss cities. We set out to assess pharmacists' attitudes towards regulating sale of cannabis for medical use (CMU) and CNMU and to ask where they thought it should be sold.

Methods: Our interprofessional team of pharmacists, primary care providers, psychiatrists and public health professionals designed a survey to determine pharmacists' willingness to sell CNMU and CMU in their own pharmacies, and the locations where they thought it should be sold. Between April 2021 and June 2021, the main pharmacist's organization in Switzerland sent an electronic link to all their members to fill out our electronic survey, followed by one email reminder. We summarized the results with descriptive statistics.

Results: Of the 1523 pharmacists who received the link, 198 (13%) completely filled out the survey. Most respondents were women (62%) and under 50 (57%). Most (62%) were willing to sell CNMU during a pilot research project; 53% would sell regulated CNMU in their pharmacy over the long-term; 93% would sell CMU. Slightly under half (48%) preferred selling CNMU in pharmacies, followed by state owned cannabis-shops (20%), profit-oriented specialized cannabis shops (18%), and cannabis-clubs (5%); 0.5% would relegate sale to the illicit cannabis market.

Conclusion: Most participating pharmacists were willing to participate in pilot projects for regulated CNMU sales, would involve their pharmacy in a pilot experiment, and recommended CNMU be sold in pharmacies. Almost none would relegate sales to the illicit market. Nearly all supported the sale of CMU. Though the low response rate to our survey limits its generalizability to the whole population of pharmacists in Switzerland, researchers planning pilot trials on cannabis sale for non-medical use in pharmacies can be confident that some pharmacists will volunteer their pharmacies as sites of sale.

Figure 1: Self-reported willingness to sell cannabis for medical use, cannabis for non-medical use within the context in a pilot trial and on long term of participating pharmacists.

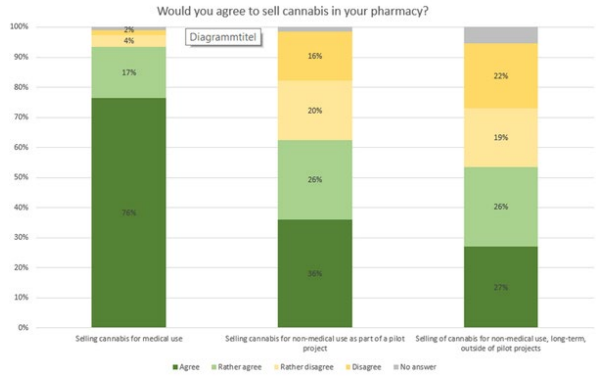
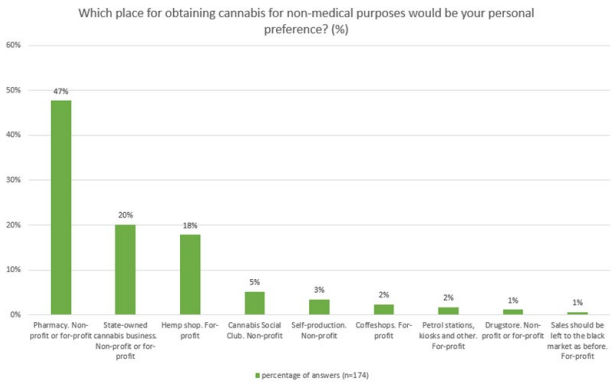


Figure 2: Recommended place for selling cannabis for non-medical use according to participating pharmacists.



P24

Attitudes of primary care physicians towards policy and regulation of cannabis for medical and non-medical use in Switzerland: a cross-sectional survey

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Introduction: Changes in regulation for cannabis sale for non-medical use (CNMU) and prescription of cannabis for medical use (CMU) are heavily debated internationally. Swiss government recently amended the law on narcotics to enable researchers to conduct trials testing alternate models of selling CNMU and simplified the regulation for physicians to prescribe CMU. Since the general population trusts primary care physicians (PCPs), we aimed to assess PCPs attitude and propositions for those changes in regulations. We further queried PCPs if they agree with regulated sale of further illicit drugs such as heroin, cocaine, psilocybin/LSD and MDMA.

Methods: An interprofessional team of PCPs, pharmacists, public health professionals and psychiatrists designed a survey to solicit PCPs attitudes towards and recommendations about cannabis regulation. From September to November 2021, we invited PCPs working as medical educators for the Institute of Primary Health Care at the University of Bern (BIHAM), to take the survey either online or in hard copy.

Results: 984 PCPs were invited to participate and 210 responded and were included in final analyses (21%). Participants were mostly men (62%), over 50 (62%), working in adult primary care (89%); 11% were pediatricians. Most (56%) would support a hypothetical popular initiative that regulates the sale of CNMU; 83% approved research trials that test alternate models for selling CNMU. When asked where CNMU best should be sold, most PCP recommended cannabis shops (44%) and pharmacies (32%); only 4 % recommended relegating it to the illicit market. Most PCPs approved the new law simplifying CMU prescription. Regulated sale of heroin was approved of by 17%, cocaine by 13%, psilocybin/LSD by 14%, and MDMA by 7%.

Conclusions: A small majority of Swiss PCPs who participated in the survey would approve a hypothetical popular initiative regulating the sale of CNMU. Most approved of the new regulation allowing trials to test alternate models for regulating CNMU. They preferred cannabis to be sold in shops and pharmacies and almost all disapproved relegating the sale to the illicit market. Most favored the simplification of CMU prescription. Few PCPs would extend regulated sale to other illicit drugs. We expect PCPs to support planned trials on cannabis regulation in Switzerland.

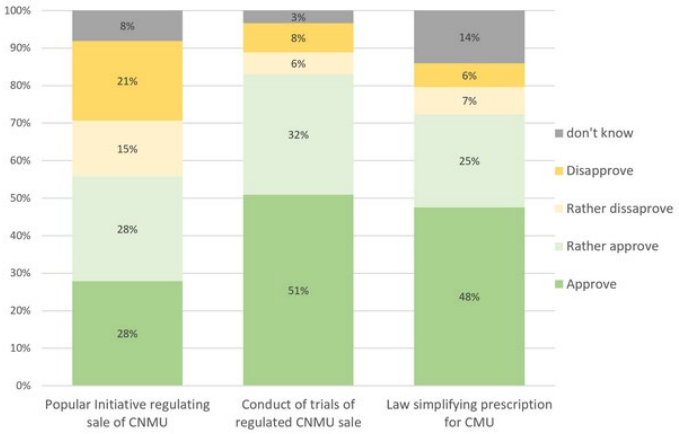

Figure 1.

Attitude of PCPs towards policy and regulations of cannabis for non-medical use (CNMU) and cannabis for medical use (CMU)

P25

Concomitant administration of the adjuvanted Recombinant Zoster Vaccine (RZV) with 13-valent Pneumococcal Conjugate Vaccine (PCV13) is safe and does not interfere with immunogenicity of either vaccine in adults aged ≥ 50 years

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Introduction: This study assessed non-inferiority of humoral immunogenicity, reactogenicity, and safety of RZV when the 1st dose was co-administered with PCV13 in adults ≥ 50 years of age (YOA) compared to sequential administration.

Methods: In this phase 3b, open-label, multi-center study (NCT03439657), adults were randomized 1:1 to receive either the 1st RZV dose co-administered with PCV13 at day (D)1 and the 2nd RZV dose at month (M)2 (Co-Ad group), or PCV13 at D1, the 1st RZV dose at M2 and the 2nd RZV dose at M4 (Control group). Co-primary confirmatory objectives were: (i) vaccine response rate (VRR) to RZV at 1 month post-dose 2 in Co-Ad group; (ii) non-inferiority of humoral responses to RZV (1 month post-RZV dose 2) and PCV13 (1 month post-PCV13) in Co-Ad group compared to Control group. Solicited adverse events (AEs) until D7 post-vaccination and unsolicited AEs until D30 post-vaccination were recorded. Serious AEs (SAEs) and potential immune-mediated diseases (pIMDs) were collected through 12 months post-RZV dose 2. Immunogenicity was performed in the per-protocol set (PPS) and safety analyses in the exposed set.

Results: Of 912 vaccinated adults, 863 were included in PPS (Co-Ad: 427; Control: 436). VRR for anti-glycoprotein E antibody concentrations was 99.1% in Co-ad group. The predefined non-inferiority criteria for the humoral immune responses to RZV and PCV13 were met. The overall frequency of solicited local AEs after RZV and PCV13 was comparable between Co-Ad and Control groups. The frequency of solicited general AEs was similar for the 1st RZV dose when co-administered with PCV13 or alone (57.4%vs 54.6%). The frequency (Co-Ad: 21.2%; Control: 23.1%) and nature of unsolicited AEs were balanced between groups. None of the reported SAEs, fatal SAEs, or pIMDs were vaccine-related.

Conclusion: Co-administration of the 1st RZV dose with PCV13 showed non-inferior immune responses to sequential administration. The reactogenicity and safety of RZV in the Co-Ad group were within the range of the established safety profile of RZV.Co-administration of RZV with PCV13 may improve vaccination rates in ≥ 50 YOA population.

P26

Deaf patients are vulnerable patients and health professionals are helpless when dealing with them

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Learning objectives: Be aware of the health vulnerability and lack of health literacy of deaf people.

Case: A 56-year-old deaf male patient presents to the emergency department with chest pain, which started 5 hours earlier. The patient has been deaf since age two, speaks a few words of German, reads on the lips but uses mostly German sign language. The medical history is not clear, as the patient is not able to understand our questions. He mimes things we don't understand. His vital parameters are normal. The ECG shows no change. Troponin and CK are increased. We diagnose an NSTEMI. The patient receives appropriate medication and is admitted to the intensive care unit. A coronography is scheduled for the next day.

Discussion: From a medical point of view, the case did not present a major challenge, as NSTEMIs are common and their treatments well known. The communication with the patient (anamnesis, diagnostic & therapeutic procedures) was difficult. Lip-reading allows a maximum of one word out of three to be understood, the rest being guessed with the help of acoustic clues and context. Communicating through written word is also complicated. The level of knowledge of oral and written languages varies greatly from one Deaf person to another. Studies have shown that at age 18, only

10% of Deaf people have a high school-leaving reading level. To improve the communication with this patient, we used visual supports (images). We were note able to contact an interpreter, but by chance a young medical doctor knew some French sign language (sign language is not universal but varies from region to region). The communication remained difficult but the patient felt better taken care of.
It is unclear why this patient was seeking care 5 hours after the onset of chest pain. This may be due to low health literacy: only 49% of Deaf people are able to name a symptom of a heart attack compared to 90% of the general population. Deaf people benefit little from "general public" health information: they have limited access to information conveyed by usual media and often have difficulty understanding the conversations of their relatives and prevention campaigns.

Conclusion: Deaf population is a vulnerable population with higher cardiovascular, sexual and mental health risks than the general population. They represent a challenge for health professionals since communication is difficult and symptoms can be expressed in a different way than those from the general population.

P27

Glucagon-like peptide-1 analogues: a new way to quit smoking? SKIP – a randomised controlled study

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Background: Cigarette smoking is the leading preventable cause of premature death. Despite dedicated programs, quit rates remain low due to barriers (i.e. nicotine withdrawal syndrome, weight gain).Glucagon-like peptide-1 (GLP-1) analogues reduce energy intake and body weight and seem to modulate addictive behavior. These GLP-1 properties are of major interest in the context of smoking cessation. The aim of this study was to evaluate the GLP-1 analogue dulaglutide as a new add-on therapy for smoking cessation.

Methods: This was a placebo-controlled, double-blind, parallel group, superiority, single-center randomized study including 255 patients. The intervention consisted of a 12-week treatment phase with dulaglutide or placebo injected subcutaneously at a weekly study visit, in addition to standard of care (behavioral counselling and pharmacotherapy with varenicline).The primary outcome was the point-prevalence abstinence rate (self-reported smoking status with biochemical confirmation) at week 12. We further investigated changes in weight and glucose homeostasis. In a substudy (n=71), we compared behavioral (i.e. nicotine craving) and brain activity changes in response to smoking cue videos using functional magnetic resonance imaging at baseline and week 12.

Results: The point-prevalence abstinence rate after 12 weeks of treatment was 80/127 (63%) in the dulaglutide group and 82/128 (65%) in the placebo group (difference in proportions [95% CI] -1.9% [-10.7, 14.4], p=0.859). We observed an increase in weight in the placebo (+1.8kg [SD 2.4]) and a decrease in the dulaglutide group (-0.7kg [SD 3.3]) between baseline and week 12; baseline-adjusted difference in weight change [95% CI] -2.5kg [-3.3, -1.7], p<0.001. Craving in response to smoking cue videos decreased from baseline to week 12 (estimated mean difference [95% CI] -3.0 [-3.7, -2.3], p<0.001), with no difference between the groups. Similarly, no difference in whole brain functional activity was seen between the groups, at both time points and between baseline and follow-up.

Conclusion: In this study, an exceptional high point prevalence abstinence rate in both groups was observed, most probably due to the very close (weekly) supervision of the patients. Our data provides no evidence that dulaglutide modulates nicotine craving or smoking cessation rates.Nevertheless, GLP-1 analogues such as dulaglutide may be a promising treatment during smoking cessation as it may avoid post-cessation weight gain.

P28

Human papillomavirus vaccination in general practice – a missed opportunity for cancer prevention? Results from a survey among Swiss students

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Introduction: Human papillomavirus vaccination (HPVv) coverage rates among young adults in Switzerland are dissatisfactory, and general practice may pose an additional opportunity to provide catch-up HPVv in this group. Previous research has revealed that Swiss general practitioners (GPs) are well aware of HPVv and that they consider their setting appropriate for providing it. On the other hand, whether this readiness finds a correspondence among young adults remains unknown. With our study, we therefore explored knowledge, experience and attitudes concerning HPVv in general practice among Swiss students.

Methods: We conducted a self-administered, web-based survey using a commercial web tool. Invitations to the questionnaire were sent to the e-mail lists of university students enrolled in different departments of three universities and one training institution for healthcare professions in the Zurich area. The questionnaire comprised different sections addressing knowledge, experience and attitudes concerning HPVv in general practice. We used logistic regression to explore determinants of binary outcomes.

Results: We analyzed the responses of 5,524 participants (age median 23 years, 70.2% female, 28.9% enrolled in a healthcare-related program). 46.2% of female and 14.6% of male respondents reported having received HPVv. Among those who had obtained HPVv by their GP (32.6% of female and 64.6% of male students who had received HPVv), 41.6% of female and 74.2% of male respondents reported that its administration occurred upon their request rather than on their GP's initiative. 86.5% of respondents wished to obtain more information about HPVv at their GP's office, and 44.8% rated acute consultations in general practice as non-inappropriate for addressing HPVv. Upon adjustment for age and enrolment in a healthcare-related program, female participants were more likely to know about HPVv (OR 2.4, 95% CI 2.1–2.7) and to have received HPVv (OR 4.7, 95% CI 4.1–5.5).

Conclusions: The acceptance of general practice as a setting for informing about and administering HPVv is high among Swiss students. Most respondents who received HPVv by their GP had asked for it explicitly. While general practice shows a high potential for increasing HPVv coverage rates, there is room for improvement in GPs' proactivity towards HPVv, especially with young male patients.

P29

Narrowing the gap: colorectal cancer screening completion by race and ethnicity subgroups after outreach strategies of an organized screening program in Northern California, USA

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Introduction: Black and Latino people have lower screening rates for colorectal cancer (CRC). Kaiser Permanente Northern California (KPNC), an American integrated healthcare delivery system, closed gaps in CRC outcomes across racial and ethnic minority groups among its members, likely due to improvements in CRC screening from implementation of an organized screening program. The relative importance of individual outreach strategies (automated and personalized) for each race and ethnic subgroup in the screening program is not well known.

Methods: Retrospective cohort study of screen-eligible people in 2019 in KPNC. The automated outreach program mailed pre-letters (7 days prior) and fecal immunochemical tests (FIT) to those not up-to-date with screening, followed by a robocall and postcard reminder (28 and 42 days after). Personalized outreach was done by telephone by local primary care office staff (between 56 and 90 days after) and by staff reminding patients about CRC screening and distributing FITs during office visits (throughout the year, counted as outside of 90-day window after FIT mailing). Colonoscopy and sigmoidoscopy were available upon request. We compared CRC screening completion after each step of the process by race and ethnic groups among individuals who self-identified as Asian-Pacific Islander (API), Latino, non-Latino Black (NLB) and non-Latino White (NLW) people.

Results: We identified 1,039,561 individuals aged 51–74 years as of January 1st 2019; 21% self-reported as API, 16% as Latino, 7% as NLB and 57% as NLW. Completion of CRC screening after each step of outreach, stratified by race and ethnicity is shown in the Table. When added to those already up-to-date with screening due to prior colonoscopy or sigmoidoscopy, automated mailing of FIT and subsequent reminders achieved screening coverage of 71% among API, 62% among Latino, 64% among NLB, and 71% among NLW individuals, respectively. Personalized FIT outreach and colonoscopy yielded an additional uptake of 13% among API, 15% among Latino, 14% among NLB, and 12% among NLW individuals. Overall screening coverage was 83% among API, 77% among Latino, 78% among NLB, and 82% among NLW individuals.

Conclusions: Personalized outreach approaches were most important in increasing coverage in Latino and NLB individuals, allowing this organized program to narrow gaps in screening uptake. Screening programs wishing to achieve equity should consider investing in personalized outreach strategies.

		Asian-Pacific Islander (API)		Latino		Non-Latino Black (NLB)		Non-Latino White (NLW)	
		Number	%	Number	%	Number	%	Number	%
	Already up to date on Jan 1st	66,347	33%	50,915	30%	26,144	35%	215,600	36%
Automated	Completed FIT within 28 days*	58,360	29%	38,795	23%	15,976	21%	148,448	25%
Automated	Completed FIT in 28-56 days*	18,068	9%	15,131	9%	6,210	8%	55,924	9%
Personalized	Completed FIT in 56-90 days*	5,320	3%	5,060	3%	1,974	3%	15,121	3%
Personalized	Completed FIT outside 90-day window*	15,327	8%	15,822	9%	6,395	8%	38,517	7%
Personalized	Colonoscopy / Sigmoidoscopy	4,655	2%	4,404	3%	1,965	3%	13,059	2%
	Not screened by Dec 31st	33,945	17%	39,903	23%	16,771	22%	105,405	18%
	Total	202,022	100%	170,030	100%	75,435	100%	592,074	100%

P30

Prognostic impact of carotid plaque imaging using total plaque area added to SCORE2 in middle-aged subjects: the Arteris Cardiovascular Outcome (ARCO) cohort study

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Introduction: A large number of cardiovascular events occur in seemingly healthy individuals. Atherosclerosis imaging can improve the outcome and treatment regime of such subjects.
We aim to assess the predictive value of atherosclerosis imaging beyond cardiovascular risk calculators in subjects aged 40-65 years.
Methods: We compared PROCAM, SCORE and SCORE2 with carotid ultrasound (total plaque area, TPA) in subjects without known cardiovascular diseases. Follow-up was obtained by phone or mail.

Results: In 2842 subjects (age 50±8, 38% women) 154 (5.4%) cardiovascular events occurred (ASCVD: 41 myocardial infarctions, 16 strokes or TIA, 21 CABG, 41 PTCA, 35 coronary artery disease defined by invasive angiography) during a mean follow-up time of 5.9 (1-12) years. PROCAM risk was 5±6%, SCORE risk 1.3±1.6% and SCORE2 5±3%. Both for the primary outcome (AMI, STROKE=MACE) and the secondary outcome (adding CABG, CAD and PTCA=ASCVD) hazards increased significantly for TPA 3rdtertile (MACE 6.7, ASCVD 22.5) and for SCORE2ptp Code 3 (MACE 7.7, ASCVD 10.1) after adjustment for risk factors (age, smoke, sex, systolic BP, lipids, medication). Model performance was statistically improved regarding model fit in all models using TPA. Net reclassification improvement (NRI) for SCORE2ptp increased significantly by 32% for MACE (p=0.0001) and 44% for ASCVD (p<0.00001).

Conclusion: TPA posttest risk integrated into SCORE2 added prognostic information to SCORE2 alone, supporting the assessment of ASCVD risk with carotid ultrasound in subjects aged 40-65 years.

Figure 4: Display of the Cox proportional Hazards with SCORE2ptp as the categorical variable, stratified for clinical variables and risk tools according to tables 5 and 6.

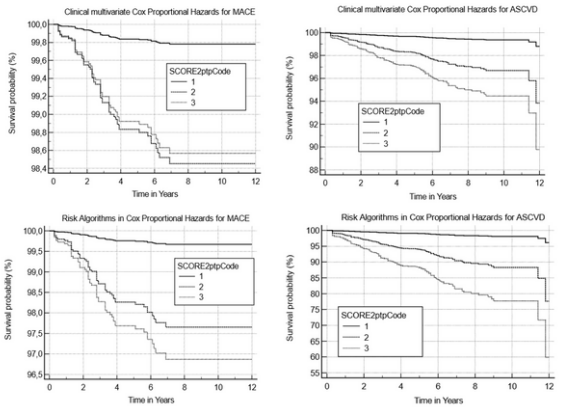

Table 5: Cox proportional Hazards model using clinical variables and posttest risk categories of SCORE2 for MACE and ASCVD

	Coefficients and Standard Errors for MACE					
Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
cAge	0,05236	0,02137	6,0039	0,0143	1,0538	1,0105 to 1,0988
Sex_Code	-1,6124	0,577	7,8099	0,0052	0,1994	0,0644 to 0,6178
SMOKE_Code	1,4975	0,2837	27,859	<0,0001	4,4704	2,5636 to 7,7954
Fam_Code	0,6265	0,2803	4,9951	0,0254	1,871	1,0801 to 3,2408
BPs	0,03067	0,00754	16,555	<0,0001	1,0311	1,0160 to 1,0465
SCORE2ptpCode=2	1,9659	0,7207	7,4406	0,0064	7,1412	1,7390 to 29,3252
SCORE2ptpCode=3	2,0354	0,6282	10,497	0,0012	7,6554	2,2347 to 26,2253

Excluded: CHOL, HDL, LDL, TG

	Coefficients and Standard Errors for ASCVD					
Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
cAge	0,06947	0,01394	24,844	<0,0001	1,0719	1,0431 to 1,1016
Sex_Code	-1,332	0,3237	16,938	<0,0001	0,2639	0,1400 to 0,4977
SMOKE_Code	1,071	0,1712	39,126	<0,0001	2,9182	2,0863 to 4,0819
Fam_Code	0,6247	0,1718	13,219	0,0003	1,8678	1,3337 to 2,6157
LDL	0,165	0,07513	4,8235	0,0281	1,1794	1,0179 to 1,3665
SCORE2ptpCode=2	1,6346	0,4412	13,728	0,0002	5,1276	2,1596 to 12,1746
SCORE2ptpCode=3	2,3154	0,3892	35,399	<0,0001	10,129	4,7239 to 21,7187

Excluded: BP, CHOL, HDL, TG

P31

Where to intervene? A fine-scale spatial analysis of variation in breast cancer screening participation in the canton of Geneva, Switzerland

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Introduction: Breast cancer remains among the most common and deadliest cancer in developed countries. In the last decades, breast cancer mortality has decreased due to, at least partially, the advent of mammography screening. Organized programs aim to increase

participation and decrease social inequalities in screening access. Our study aims to evaluate disparities in participation in a mammography screening program at fine geographical scale.

Methods: Data on 118,963 screened and non-screened women, aged 50-74 years, were extracted from the mammography screening program 1999–2018 datasetin the canton of Geneva, Switzerland. We aggregated the data at the hectare level and by two-year intervals to account for the biannual invitation pattern. We used the local Moran'slstatistics to identify clusters of significantly higher and lower prevalence of participation in mammography screening. We evaluated the persistence of clusters with a score cumulating high and low clusters identified across each two-year interval for spatially smoothedparticipationrates.

Results: Almost half of women (48.7%) were screened at least once. Spatial analyses and the cumulated cluster score revealed areas of consistently high and low participation and a clear East-West divide. Women living in deprived areas tended to participate more than women in affluent areas suggesting that the program may be successful in decreasing social inequalities in screening access. Interestingly, in areas with consistently high participation rates the participation rate was lower in deprived areas compared to their more affluent counterparts.However, we also identified several areas cumulating consistently low participation rates and high socioeconomic deprivation.

Conclusion: Our fine-scale spatial analyses identified areas of consistently high and low participation rates. By shedding light on areas of low participation and particularly on the ones cumulating socioeconomic deprivation and low participation, we provide important information for future prevention efforts. Future research should focus on adjusting for socioeconomic deprivation, opportunistic screening, and physical accessibility to screening centers to identify areas where clusters may be explained by the unequal distribution of these indicators across the study area.

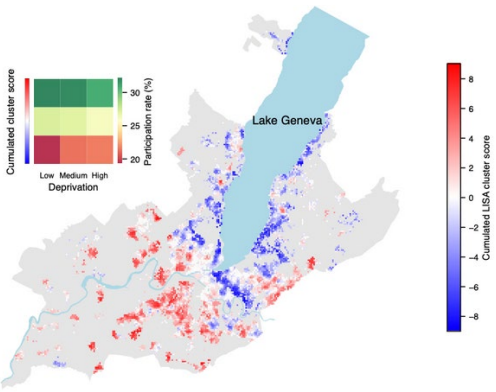

Figure 1 – Spatial distribution of the cumulated LISA cluster score.

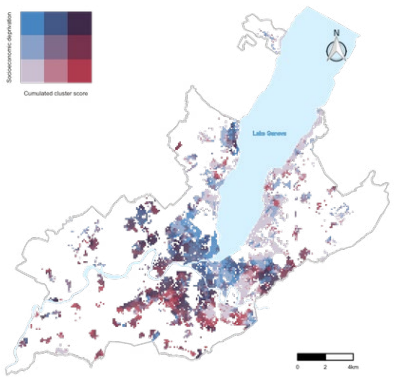

Figure 2 – Bivariate map of the socioeconomic deprivation index and the cumulated LISA cluster score.

P32

Prevention of hepatitis B reactivation in patients with resolved hepatitis B infection receiving immunosuppressive therapy: case series and review of society guidelines

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Introduction: Hepatitis B (HBV) reactivation (HBVr) is a potentially fatal complication in patients with past HBV exposure receiving immunosuppressive therapy (IST). HBVr can occur in patients with chronic HBV infection (hepatitis B surface antigen (HBsAg) positive, hepatitis core antibody (anti-HBc) positive) as well as in patients with resolved HBV infection (HBsAg negative, anti-HBc positive). Screening of at-risk patients and allocation to an appropriate treatment strategy are paramount to prevent HBVr. As four patients with resolved hepatitis B suffered from HBVr at our institution during 2021 (Table 1), of whom two died as a consequence of HBVr, we decided to review current society guidelines.

	Indication for IST and IST regimen	HBV PPX	HBV reactivation			Treatment	Outcome	HBVr caused by IST
			Timing (since IST start)	Laboratory parameters	Clinical, sonographical and histopathological characteristics			
Patient 1 (m, 85)	DLBCL RTX-based chemotherapy (EPOCH-R)	no	11 months	Serology: HBsAg+ HBV DNA: >170 Mio IU/l ASAT 314 U/l ALAT 275 U/l Bili 82 umol/l	Jaundice Ascites Ultrasound: normal liver morphology	TDF	Liver failure, death	Probably yes
Patient 2 (m, 71)	Kidney transplant MMF, MTX and prednisone 7.5 mg/d	no	8 years	Serology: HBsAg+ HBV DNA: >170 Mio IU/l ASAT 42 U/l ALAT 31 U/l Bili 23.4 umol/l	Ascites Fibroscan: progression of previously known liver fibrosis Liver biopsy: chronic hepatitis, cirrhosis	TAF	Cirrhosis	Possibly
Patient 3 (m, 76)	Rheumatoid arthritis MTX and RTX	no	16 months	Serology: HBsAg- HBV DNA: >170 Mio IU/l ASAT 319 U/l ALAT 311 U/l Bili 49.7 umol/l	Ascites Ultrasound: normal liver morphology Liver biopsy: acute hepatitis, cirrhosis	TDF	Liver failure, death	Probably yes
Patient 4 (f, 63)	DLBCL RTX-based chemotherapy (R-CHOP)	yes: lamivudine until 12 months after IST cessation	7 years	Serology: HBsAg+ HBV DNA: 4 Mio IU/l ASAT 1491 U/l ALAT 1233 U/l Bili 386 umol/l	Jaundice Ultrasound: normal liver morphology Liver biopsy: acute hepatitis, no fibrosis	TAF	Resolution of HBV infection and of hepatitis	Probably no

Table 1: Demographic and clinical characteristics of the four patients who suffered from HBVr during 2021 at our institution. All patients had serologies compatible with resolved HBV infection (HBsAg-/anti-HBc+) and normal liver function tests before IST start. **Legend:** m: male; f: female; HBV: hepatitis B virus; IST: immunosuppressive therapy; PPX: prophylaxis; DLBCL: diffuse large B-cell lymphoma; EPOCH-R: etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; RTX: rituximab; MMF: mycophenolate mofetil; MTX: methotrexate; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; HbsAg: hepatitis B surface antigen; ALAT: alanine aminotransferase; ASAT: aspartate aminotransferase; Bili: bilirubin; TDF: tenofovir disoproxil fumarate; TAF: tenofovir alafenamide; HBVr: hepatitis B virus infection reactivation.

Methods: We summarized recommendations of four major societies for the screening and management of previously HBV exposed patients planned to receive IST: the American Gastroenterological Association (AGA) [1], the European Association for the Study of the Liver (EASL) [2], the American Association for the Study of Liver Diseases (AASLD) [3], and the Asian Pacific Association for the Study of the Liver (APASL) [4].

Results: Current guidelines recommend screening for HBV in all patients planned to receive IST. HBsAg+ patients and among HBsAg-/anti-HBc+ patients, those receiving B-cell depleting therapy or undergoing hematopoietic stem cell transplantation (HSCT), are at high risk for HBVr and should receive antiviral prophylaxis (PPX) (Figure 1). PPX should be initiated before start of IST start and continued for 6-12 months after cessation of IST. Monitoring of HBsAg, HBV DNA and liver function tests every 1-3 months during IST is recommended for HBsAg-/anti-HBc+ patients receiving various other IST regimens. HBV vaccination is recommended for those without evidence of prior exposure to the virus.

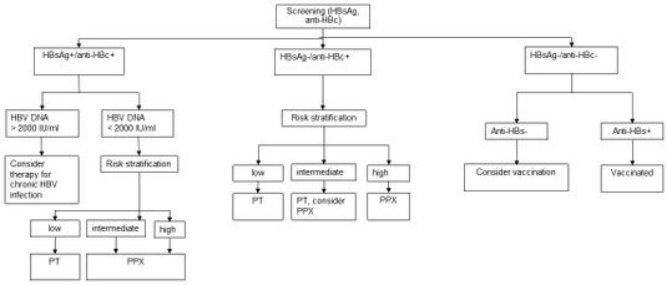

Figure 1: proposed algorithm for the management of patients with past hepatitis B exposure planned to receive immunosuppressive therapy based on current society guidelines, adapted from [4, 5]. **Legend:** + positive; - negative; HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; risk stratification: AGA [1] and APASL [4] have issued classifications based on serological status and the type and duration of immunosuppressive therapy, risk is defined as low if the incidence of HBVr is <1%, intermediate if HBVr incidence is between 1 and 10%, and high if the risk is >10%; PT: preemptive therapy, consisting of monitoring of liver function tests, HBV DNA and HBsAg every 1-3 months and start of antiviral therapy if elevated HBV DNA or a positive HBsAg is detected; PPX: antiviral prophylaxis with nucleos(t)ide analogues. For details consult society guidelines.

Conclusion: In a low endemicity setting, greater awareness is needed among clinicians regarding the risk of HBVr in patients receiving IST. There is broad consensus among current society recommendations about the management of these patients. Implementation of screening and management programs based on

these guidelines in IST prescribing institutions may improve the management of these patients. Future studies should clarify the risk of HBVr and prophylactic strategies for certain old and new IST regimens, such as immunosuppressive drugs combinations (e. g. after solid organ transplantation), or new biologicals (e.g. daratumumab).

P33

Acute kidney injury and cefepime-induced neurotoxicity: discussion of preventive measures based on two case reports

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Learning objective(s): Neurotoxicity is a well described adverse effect of cefepime. Nonetheless, it might be a challenge to identify cefepime as the causative agent of a neurological deterioration in critically ill or multimorbid patients with an altered mental status. Clinical presentation includes mild neurological deficits, but also non-convulsive status epilepticus (NSCE) which may result in a higher mortality. Impaired kidney function is considered the most important risk factor for cefepime-induced neurotoxicity (CIN) [1]. Acute kidney injury (AKI) frequently occurs in the course of critical diseases, which increases the potential of overdosing. Physicians should be aware of situations with an increased risk for AKI and actions to prevent CIN.

Case: We present two patients with CIN who were admitted to the University Hospital Basel. Both patients were treated with cefepime for healthcare-associated infections and had AKI, which was related to septic shock and vancomycin nephrotoxicity, respectively. One patient presented with intermittent confusion and vision impairment and the other with NSCE. At this time, cefepime levels were markedly elevated (trough concentration of 94.4 mg/L and 69.7 mg/L, respectively). Both patients fully recovered after admission to the intensive care unit and treatment with intermittent hemodialysis (HD).

Discussion: Diagnose of CIN might be challenging because of variable clinical presentation (intensity and latency of symptoms), in particular in a setting of severely ill patients. It is therefore all the more important to consider therapy-induced neurotoxicity in a patient treated with cefepime, especially in those with impaired renal function or being susceptible to AKI. A trough cefepime concentration between 15 and 20 mg/L has been identified as the threshold for increased neurotoxicity. Based on recent data a cefepime trough concentration of <7.5 mg/L is recommended to prevent CIN [2]. Preventive measures of CIN include therapeutic drug monitoring, reconsideration of a therapeutic alternative, being aware of potential glomerular filtration rate overestimation and using alternative formulas to determine kidney function in special populations and electronic alert systems warning health-care professionals about risk constellations for potential overdosing.

Table 1: Characteristics of the two patients

Case	Age, y	Sex	Weight, kg	Diagnosis	Cefepime trough level in plasma (max.), mg/L	eGFR,mL/min/1.73m²	Cause of AKI	Concomitant nephrotoxic Therapy
Case 1	44	F	59.0	Hospital-acquired pneumonia	94.4	13 (intermittent HD)	Sepsis/multi organ failure	-
Case 2	75	F	95.0	Postoperative implant-associated infection	69.7	17	Vancomycin-induced renal toxicity	Vancomycin, NSAID

P34

Burden of night shifts on physician's burnout in a Swiss hospital

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Introduction: Recent studies on Swiss hospital-based internists show a high level of burnout that calls for measures to improve physician's well-being[1]. Night shifts are an important part of postgraduate medical training. The impact of repeated night shifts periods on physicians' level of stress, burnout and quality of sleep is unknown.

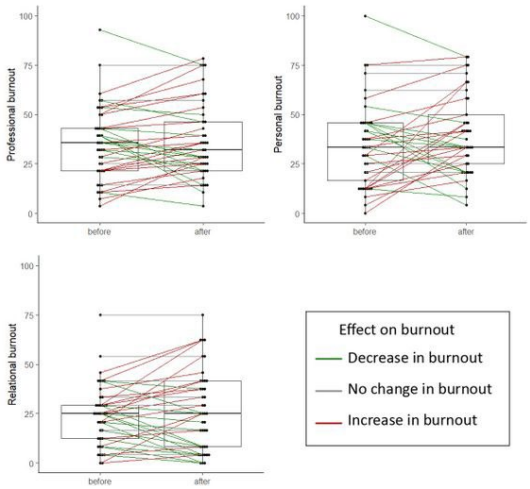
Methods: We conducted an ecological study of night shifts in the division of general internal medicine at the University Hospitals of Geneva, between 2019 and 2020 (before the pandemic). Trained medical students directly observed residents work during their night shifts, and residents fulfilled an e-survey once at the beginning of their 4 weeks rotation of night shifts and once 2 to 4 weeks after their rotation. We assessed burnout using the Copenhagen Burnout Inventory (CBI), a self-reported questionnaire covering 3 dimensions: personal burnout, professional burnout, and relational burnout. The scores (ranging from 0 to 100) were categorized as: low burnout (0-49), moderate burnout (50-74) and high burnout (75-100). Our secondary outcome was sleep medications intake, using a validated item from the Pittsburgh Sleep Quality Index. We compared continuous outcomes before and after their night shifts using Wilcoxon rank sum tests and categorical outcomes using the McNemar exact test.

Results: Amongst the 41 included physicians, a higher proportion presented an increase in their burnout score after their night shift rotation, (all p-values>0.05) (Figure). The proportions of those with moderate or high burnout increased or remained stable on all tested dimensions: moving from 7 (17.1%) to 11 (26.9%) for personal burnout, from 10 (24.4%) to 10 (24.4%) for professional burnout, and from 2 (4.8%) to 6 (14.6%) for relational burnout (Table). The proportion of high professional burnout increased from 2 (4.9%) to 4 (9.8%). Regarding the secondary outcome, 3 physicians (7.3%) were taking sleep medications before the rotation and 10 (24.4%) after (p=0.02).

Table: Burnout and Sleep medication use amongst night shift residents

		Before	After
Personal Burnout (%)			
	Low	34 (82.9)	30 (73.2)
	Moderate	4 (9.8)	7 (17.1)
	High	3 (7.3)	4 (9.8)
Professional Burnout (%)			
	Low	31 (75.6)	31 (75.6)
	Moderate	8 (19.5)	6 (14.6)
	High	2 (4.9)	4 (9.8)
Relational Burnout (%)			
	Low	39 (95.1)	35 (85.4)
	Moderate	1 (2.4)	5 (12.2)
	High	1 (2.4)	1 (2.4)
Sleep medication use (%)			
	No	38 (92.7)	31 (75.6)
	<1x/week	3 (7.3)	5 (12.2)
	1-3x/week	0 (0.0)	5 (12.2)
	>3x/week	0 (0.0)	0 (0.0)

Figure: Effect of night shifts on the different categories of burnout scores



Conclusion: After a 4-weeks period of night shifts, physicians tend to score higher in all categories of burnout and the sleep medication intake was significantly higher, suggesting poor sleep related health issues. These data can increase the awareness of healthcare institutions and managers toward the burden of night shifts, and may ultimately lead to a call for better organization and supervision of night shifts to improve resident's well-being and prevent internists' burnout.

P35

Community-acquired pneumonia in the emergency department: age- and sex-related differences in clinical presentation

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Introduction: As one of the leading global causes for morbidity and mortality, early identification and treatment of community-acquired pneumonia (CAP) is essential[1]. It was the aim of this study to investigate age- and sex-related differences in clinical symptoms, radiologic findings and outcome in patients presenting to the emergency department (ED) with CAP to identify associations with atypical presentation and patients at risk.

Methods: In this retrospective cross-sectional study, all adult patients admitted to the ED of the Bürgerspital Solothurn between 01.01.2017 and 31.12.2018 with clinically and/or radiologically confirmed CAP were included. Clinical symptoms, Pneumonia Severity Index (PSI) and radiologic findings were gathered by chart reviews. Symptoms were classified as chest pain, fever, chills, cough, sputum, dyspnea, headache and myalgias[3]. Outcome was measured by need for ICU admission, mechanical ventilation, length of hospital stay, 30-day re-admission, 180-day pneumonia recurrence and in-hospital mortality.

Results: During the study period, 467 patients presented to the ED with confirmed diagnosis of CAP of which 211 were women (45%). In terms of age groups, 317 patients were classified as elderly by an age of ≥65 years (68%). PSI and PSI risk class were significantly higher in the elderly (p<0.001). Regarding clinical presentation of CAP, younger patients significantly more often reported chest pain (27% vs. 13%, p<0.001), fever (53% vs. 39%, p=0.004), chills (20% vs. 6%, p<0.001), cough (57% vs. 44%, p=0.013), headache (15% vs. 5%, p<0.001) and myalgias (19% vs. 5%, p<0.001). Altered mental status and need for supplemental oxygen therapy on the other hand, were more common in elderly patients. Considering sex-related differences, PSI was significantly lower in women (p=0.01) and women significantly less often reported sputum (22% vs 32%, p=0.016). In the multivariable Cox-regression, neither age nor sex was a predictor for mortality in CAP. There were no relevant differences in IMC/ICU referral, need for invasive or non-invasive ventilation, 30-day readmission rate and 180-day pneumonia recurrence when comparing men and women as well as elderly and younger patients.

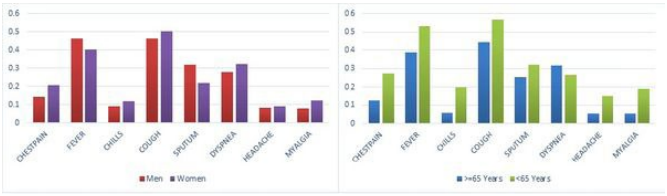

Figure 1: Symptoms of CAP in men, women and age groups.

Table 1: PSI score, PSI risk classes and its components stratified for sex and age groups

	Women (N=211)	Men (N=256)	p-value	<65 Years (N=150)	>= 65Years (N=317)	p-value
PSI	95±31	104±31	0.01	72±30	109±31	<0.001
PSI Risk Class 1	25 (12%)	28 (11%)	0.092	53 (35%)	0 (0%)	<0.001
PSI Risk Class 2	42 (20%)	29 (11%)		52 (35%)	19 (6%)	
PSI Risk Class 3	40 (19%)	47 (18%)		22 (15%)	65 (21%)	
PSI Risk Class 4	71 (34%)	107 (42%)		21 (14%)	157 (50%)	
PSI Risk Class 5	33 (16%)	45 (18%)		2 (1%)	76 (24%)	
Hematocrit < 30%	22 (10%)	23 (9%)	0.638	7 (5%)	38 (12%)	0.012
Glucose > 14 mmol/L	5 (2%)	8 (3%)	0.78	2 (1%)	11 (0.5%)	0.24
Urea > 11mmol/L	48 (23%)	56 (22%)	0.824	9 (6%)	95 (30%)	<0.001
Sodium < 130 mmol/L	13 (6%)	12 (5%)	0.539	10 (7%)	15 (5%)	0.386
Nursing home resident	55 (26%)	49 (19%)	0.075	8 (5%)	96 (30%)	<0.001
Neoplastic disease	41 (19%)	60 (23%)	0.311	25 (17%)	76 (24%)	0.092
Cerebrovascular disease	19 (9%)	34 (13%)	0.187	4 (3%)	49 (15%)	<0.001
Temperature <35 or >39.9°C	2 (1%)	2 (1%)	1.0	3 (2%)	1 (0.5%)	0.1
Altered mental status	18 (9%)	29 (11%)	0.356	5 (3%)	42 (13%)	<0.001
RR systolic < 90 mmHg	4 (2%)	6 (2%)	1.0	3 (2%)	7 (2%)	1.0
Respiratory rate > 29/min	13 (6%)	19 (7%)	0.714	6 (4%)	26 (8%)	0.117
Heart rate > 124/min	16 (8%)	13 (5%)	0.336	8 (5%)	21 (7%)	0.684
pH < 7.35	8 (4%)	9 (4%)	0.798	4 (3%)	13 (4%)	0.578
pO2 < 8 kPa	20 (10%)	22 (9%)	0.699	14 (9%)	28 (9%)	0.674

Conclusion: In this study, no relevant differences were found in laboratory and radiologic findings between men and women with CAP and neither age nor sex was a predictor for mortality or adverse outcome. However, clinical presentation varied significantly between elderly and younger patients. In the elderly, CAP should therefore be considered a differential even in the absence of typical symptoms such as fever and cough[3]. Further studies should evaluate different diagnostic and treatment approaches in elderly patients, especially in the emergency setting.

P36

Do women not want to become senior-level physicians in General Internal Medicine?

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Background: Despite women making up 44% of all physicians in Switzerland, only 13% of general internal medicine senior physicians (Leitende Ärzte/innen und Chefärzte/innen) are female. Among the general internal medicine workforce and medical students, we aimed to compare career ambitions in women and men.

Methods: Ambulatory and hospital general internal medicine physicians in Switzerland and 4th-6th year medical students from the University in Bern were invited by newsletters, advertisements, and e-mail to participate in a cross-sectional survey. Questions were included on demographics and career ambitions. Outcome for the present interim analysis of this ongoing study were the scores of a modified career ambition scale (scores ranging from 0 [minimum] to 24 [maximum]) and the frequency of those who desire to attain a position of senior physician. Sex differences in responses to questions in the dimensions above were tested in physicians and students using non-parametric t-test and Chi-square test.

Results: Of 539 respondents with a median age of 27 years (IQR: 24-33 years), 62% were women and 55% medical students. Among physicians, career ambition scores were 13 (median, IQR: 7-17) in women and 14.5 (IQR: 11-18) in men (p=0.03). Among medical students, career ambition scores were 13 (median, IQR: 10-16) in women and 15 (IQR: 11.5-18) in men (p=0.01). In an analysis restricted to medical students, hospital resident and attending physicians, the desire to attain a position as senior physician was present in 23% of women vs. 29% of men (p=0.42). In medical students, this career goal was present in 31% of women vs. 37% men (p=0.30).

Conclusions: A small sex difference in career ambition responses were observed, but women and men expressed similar frequencies of the career goal to attain a position of senior physician. This indicates that women's original career goals are unlikely the main reason for their underrepresentation among senior physicians.

	Physicians			Medical students		
	Women	Men	p value	Women	Men	p value
	n=75	n=63		n=190	n=83	
Goal to attain a position as senior physician *	23%	29%	0.42	31%	37%	30%
	n=105	n=102		n=192	n=83	
Career ambition score	13 (7-17)	14.5 (11-18)	0.03	13 (10-16)	15 (11.5-18)	0.01

Data reported as median (interquartile range) or percentage. Statistical analysis using Welch or Chi2 test.
*, excluding current senior physicians and general practitioners.

P37

Evidence of gycocalyx damage in COVID-19 patients with moderate disease progression: a prospective multicenter study

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Introduction: The SARS-CoV-2 virus is the pathogen of the COVID-19 pandemic. While the disease causes a mild course in most patients, severe lung damage and hyperinflammatory syndrome occur in some patients. Inflammation-induced degradation of the glycocalyx layer in endothelial cells has been demonstrated in association with COVID-19 infection. Syndecan-1 (SDC-1) is an established parameter for measuring glycocalyx damage1. The aim of this study was to evaluate hospitalized COVID-19 patients with a moderate disease course without oxygenation disturbance for endothelial injury.

Methods: In this prospective, multicenter study (University hospital Muenster, Muenster, Germany; Marien Hospital Steinfurt, Steinfurt, Germany), SDC-1 levels in hospitalized COVID-19 patients with moderate disease progression (n = 17) were compared with healthy control subjects (n = 17). Disease severity was classified according to World Health Organization (WHO) severity categories as critical (life-sustaining treatment required, presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock), severe (oxygen saturation <90% on room air, signs of pneumonia, signs of severe respiratory distress), or moderate (no signs of severe or critical illness)2. Blood sampling was performed within the first 48 hours after hospitalization.

Results: Hospitalized patients with moderate disease course without evidence of oxygenation disturbance showed significantly increased SDC-1 levels (Figure 1, Table 1). Hospitalized COVID-19 patients were older than healthy controls.

Conclusions: In this study, we detected signs of endothelial damage in hospitalized COVID-19 patients with moderate disease course without oxygenation disturbance. These data confirm previous data on endothelial damage in hospitalized patients with critical/severe disease course3 and indicate that even mild disease course may cause endothelial damage.

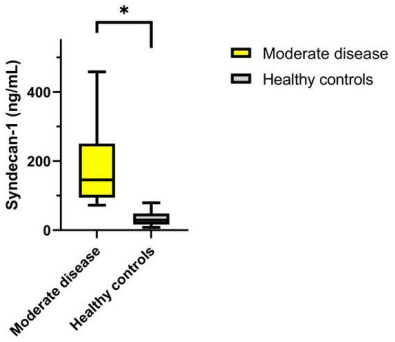

*Figure 1. SDC-1 values of hospitalized COVID-19 patients with moderate disease progression compared with healthy controls. SDC-1, Syndecan-1; * p < 0.05.*

Table 1. Cohort characteristics of hospitalized COVID-19 patients and healthy controls. IQR, interquartile range.

	COVID-19 Patients (n=17)	Healthy Controls (n=17)
Age, years median (IQR)	60 (50-76)	32 (28-43)
Sex, male (%)	53	63
Syndecan-1 (ng/mL)	145 (94-251)	29 (16-48)

P38

From mouth, to pleura and to skin – the power of anaerobes

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Learning objective: Diagnostic approach to pleural empyema and therapeutic interventions when medical treatment fail.

Case: An 83-year-old male patient known for diabetes, Parkinson's disease and cognitive deficit with known risk of aspiration, was admitted for dyspnea and fever. Clinical examination found signs of a right pleural effusion, confirmed by the chest radiography. The lab values revealed a C-reactive protein at 460 mg/l. A pneumonia with parapneumonic effusion was diagnosed. Levofloxacin was started given an allergy to penicillin. After 5 days, fever persisted. A chest tube was inserted and drained purulent liquid. Imipenem and intrapleural fibrinolysis were then started. The empyema culture revealed Fusobacterium nucleatum (n). Despite 9 days of well conducted antibiotic therapy, the fever still persisted, and he developed a broad dermohypodermitis around the tube orifice. The chest CT showed an increase of the effusion, a hydropneumothorax and a parietal abscess along the tube. A pleural debridement and drainage of the abscess by thoracoscopy were performed. Fusobacterium n. was also found in the soft tissue. Imipenem was switched for aztreonam and metronidazole, due to toxidermia suspicion. 10 days after thoracoscopy, antibiotics could be discontinued. 6 weeks after the thoracoscopy, the patient had recovered.

Discussion: Pleural empyema is most often a complication of pneumonia. Pyogenic bacteria such as Streptococcus pneumoniae, oral streptococci and Staphylococcus aureus are the most common causes of parapneumonic effusions. Anaerobes are sometimes found, specially related to aspiration. The Fusobacterium is an anaerobic gram-negative rod found especially in the oral flora. The clinical spectrum is wide, ranging from upper respiratory tract infection, to abscess formation and septic shock. However, Fusobacterium infections are rare with only few case reports describing Fusobacterium n. empyema given its rarity and anaerobic nature being difficult to culture. Anaerobic infections are favoured by advanced age, diabetes, poor dentition and aspiration, all found in our patient. Early recognition of pleural empyema allows the realization of rapid diagnostic and therapeutic gestures, decreasing the morbidity and mortality. Physicians should keep in mind that despite bacteria sensibility to a given antibiotheray in empyema, debridement or even surgery must be considered if systemic inflammatory signs persist.

P39

Goal-directed mobilisation of general medical inpatients: a scoping review of the literature

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Introduction: Patients spend most of their hospitalisation in bed, which can lead to negative physical, social, and psychological outcomes. Goal-directed mobilisation involves setting mobility goals with patients and care teams working together towards achieving these goals. Setting mobilisation goals could potentially improve mobility outcomes by motivating patients to stay active and facilitate communication between staff, patients, and caregivers.

Methods: Three different platforms (SCOPUS, Ovid Medline, PubMed) were searched on 12.07.2021. Search terms included «goal-directed», «goal-attainment» or «goal-setting», and «inpatient» or «hospitalisation» and «mobility» or «mobilisation». Articles were included if mobility goals were set in acutely hospitalised adults. Studies were excluded if mobility or mobilisation were not specifically outlined or focused on surgery or specific illness.

Results: In total, 173 articles were screened for inclusion by two independent reviewers. In the final analysis, thirteen articles (5 randomised controlled trials, 2 post-hoc analyses, 3 quality-improvement projects, 1 pre-post two group analysis, 1 comment and 1 study protocol) were assessed. Goal-directed mobilisation improved mobility-related outcomes, such as higher levels of mobilisation, activity and mobility-related functional independence, daily

walking time and community mobility. However, readmissions, quality of life, discharge disposition and muscle weakness were not significantly altered and there was conflicting evidence regarding length of stay and Activities of Daily Living.

Conclusion: There is a lack of evidence of goal-directed mobilisation in general medical inpatients on relevant outcomes. The quality of evidence was generally low due to the study design used. Further research on goal-directed mobility should use standardised mobility protocols and measurements to assess mobility and the effects of goal-directed mobility more accurately and include broader patient populations.

P40

Humoral immune response in patients with inflammatory bowel disease six months after vaccination with the SARS-CoV-2 mRNA vaccine BNT162b2

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Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the pathogen of the 2019 coronavirus pandemic (COVID-19). Immunization of the population through vaccination is considered the most important approach to prevent severe disease progression. Preliminary studies suggest a shorter duration of humoral immunity in immunocompromised patients with inflammatory bowel disease (IBD)1,2. The aim of this study was to investigate the humoral response in IBD patients on immunosuppressive therapy with anti-TNF agents six months after COVID-19 mRNA vaccination (BNT162b2).

Methods: In this prospective study, a SARS-CoV-2 surrogate neutralization test (sVNT) was performed to assess the potential neutralization capacity in IBD patients (n=14) on immunosuppressive therapy (anti-TNF) and healthy controls (n=9). Sera were analyzed 6 months after the second mRNA COVID-19 vaccination (BNT162b2).

Results: In IBD patients on anti-TNF therapy, we detected significantly lower sVNT levels 6 months after the second vaccination compared to healthy controls (p=0.001, Figure 1). In IBD patients, the median level of antibodies in sVNT was 2.4% (cut off 30%). There were no significant differences between the groups with respect to the characteristics age and sex (Table 1).

Conclusions: IBD patients on therapy with anti-TNF agents showed significantly reduced levels of inhibitory antibodies in sVNT compared to healthy controls. In 64% of IBD patients, neutralizing antibodies could no longer be detected in sVNT 6 months after the second vaccination. In conclusion, early booster vaccination for IBD patients on anti-TNF therapy should be discussed.

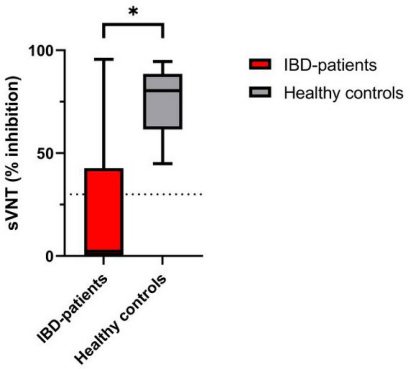

*Figure 1: SARS-CoV-2 sVNT inhibition levels (% inhibition) in IBD patients on immunosuppressive therapy (anti-TNF) and healthy controls 6 months after the second vaccination. Tukey boxplots, *p< 0.01.*

Table 1. Cohort characteristics of IBD patients and healthy controls.

	IBD-Patients (n=14)	**Healthy controls** (n=9)
Age, years median (IQR)	36 (24-49)	42 (37-57)
Sex, male (%)	43	44
sVNT (%), median (IQR)	2.4 (0-43)	80 (62-89)

P41

Hypernatremia in the emergency department - the neglected electrolyte disorder

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Introduction: Dysnatremias are among the most common electrolyte disorders in patients presenting to the emergency department (ED)[1,2]. While research on hyponatremia is growing, evidence on hypernatremia remains scarce. The aim of this study was to investigate the prevalence, symptoms, etiology, treatment and course of community-acquired hypernatremia.

Methods: All adult patients with measurements of serum sodium presenting to the ED of the Bürgerspital Solothurn between 01 January 2017 and 31 December 2020 were eligible for this retrospective cohort study. Exclusion criteria were age younger than 18 years or withdrawal of consent. Chart reviews were performed for all patients with community-acquired hypernatremia defined as a serum sodium >147mmol/L[3].

Results: In total, 376 patients (0.7%) were hypernatremic defined as a serum sodium >145mmol/L on admission and of these 109 patients (0.2%) had community-acquired hypernatremia. Mean age of hypernatremic patients was 67 years (±22) and 47% were women. Main symptoms included somnolence in 42%, disorientation in 30% and recent falls in 17% (Figure 1). An impaired sense of thirst was the main cause of hypernatremia as present in 76 patients (70%), followed by a lack of access to water in 50 patients (46%) for example due to immobility. The main reasons for ED presentation in hypernatremic patients were infection (44%), mainly sepsis (18%) or pneumonia (16%), trauma (9%) and intoxication (9%). Regarding treatment of hypernatremia, only one patient received targeted oral hydration. 38 patients (35%) experienced inadequate correction of hypernatremia as defined as either a decline of <2mmol/L or further increase in serum sodium during the first 24 hours after admission (Table 1). 25% of patients with community-acquired hypernatremia died during hospitalization. Patients who died had significantly lower correction rates of serum sodium (0mmol/L (-3-1.5) versus -6mmol/L (-10-0), p<0.001). Of the 82 patients discharged from the hospital, 33 patients (40%) were still hypernatremic at time of discharge.

Conclusion: With a prevalence of 0.7%, hypernatremia is a relevant electrolyte disorder in the ED not only present in the very elderly population. This study found that initial treatment and correction of hypernatremia was frequently inadequate even though mortality was high. Probably due to the mainly unspecific symptoms, the disorder is often underdiagnosed or overlooked.

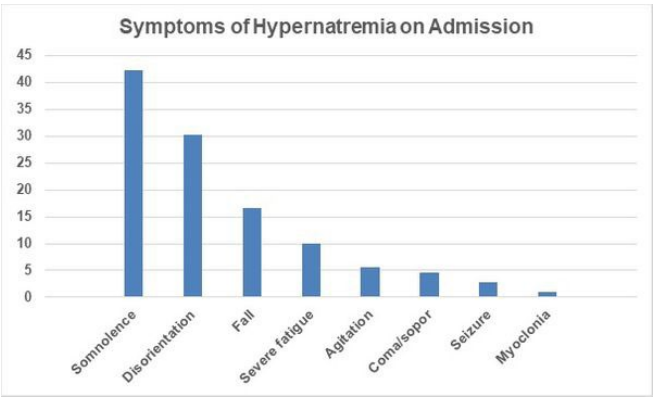

Figure 1: Symptoms of Hypernatremia

Table 1: Comparison of Course and Outcome of Hypernatremia in Patients that survived with Patients that died

	Deceased	Survivors	p-value
N	27 (25%)	82 (75%)	-
Median Serum Sodium	151mmol/L (148-156)	150mmol/L (148-152)	0.32
Median Delta Sodium in 24h	-1mmol/L (-2.25-2.25)	-2mmol/L (-4-1)	0.19
Median Delta Sodium at Discharge	0mmol/l (-3-1.5)	-6mmol/l (-10-0)	<0.001
Median Length of Hospital Stay	5 days (2-7)	6 days (2-10)	0.2

P42

Hypnosis as a useful tool to improve tolerance to non-invasive ventilationin a COVID-19 intermediate care unit

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Introduction: Despite a polymorphic clinical picture, COVID-19 is, in the first instance, a respiratory disease. Lung involvement (from mild pneumonia to acute respiratory distress syndrome) , is common.[1] Several non-invasive respiratory therapies, in particular continuous positive airway pressure and high-flow oxygen therapy,[2] have become essential in the management COVID-19 patient. [3] Even if clinically beneficial, these therapies can be frightening, challenging and traumatic, and have been associated to post-traumatic stress disorder.[4]
In the Division of General Internal Medicine, GEneva University Hospitals, hypnosis is often offered to patients as an integrative tool for pain management and during medical procedures. Since the beginning of COVID-19 pandemics, we have been offering hypnosis to improve patients' tolerance to non-invasive ventilation. We aimed at studying whether hypnosis can indeed improve patients' experience of these type of respiratory therapies.

Methods: Retrospective study including all patients hospitalized in the COVID-19 Intermediate Care Unit (Division of General Internal Medicine, HUG), between March 2020 and February 2021for acute hypoxemic respiratory failure due to COVID-19 and who beneficiated of hypnosis (by certified hypnotherapists) to improve tolerance to non-invasive respiratory therapy. Respiratory rate (RR; cycles/minute), heart rate (HR; beat/minute), and oxygen saturation ($SatO_2$) were monitored before/during/after the hypnotic session. At the end of the session, hypnotherapists evaluated patients' perceived comfort/anxiety, and dyspnea.

Results: Preliminary data from 8 out of 20 patients (males: 87.5%, mean age: 58.2 years; median number of sessions: 2, average length of session: 31.8 minutes) showed a decrease in RR and HR during hypnotic sessions (before: 26.9 and 89.7; after 22.6 and 84.8), as well as a mean increase in SatO2 of 5% for any given FiO2. Moreover, hypnotic sessions seemed to affect the subjective experience of respiratory therapies (more comfort, less anxiety and dyspnea).

Conclusion: This study evaluates for the first time the therapeutic impact of hypnosis in COVID-19 patients hospitalized in an Intermediate Care Unit. Our preliminary results suggest that hypnosis can be a useful non-pharmacological tool to improve patients' tolerance and experience to non-invasive ventilation techniques.

P43

Hypnosis in general internal medicine: "the best treatment yet to prescribe"? Experience in the Division of General Internal Medicine, Geneva University Hospitals

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Introduction: According to the American Psychological Association, hypnosis is "a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion."[1] Although hypnosis has been proven particularly effective in anesthesiology for the management of periprocedural pain and anxiety, its use in internal medicine is still scanty. Indeed, a recent article in the *American Journal of Medicine* defines hypnosis as "the most effective treatment you have yet to prescribe", as a tool to maximize "our effectiveness as healers", an integrative approach that "if […] were a drug, it would be standard of care".[2]

Methods: Retrospective analysis of all adult patients hospitalized in the Division of General Internal Medicine, HUG, between January 2018 and December 2021 and who beneficiated of hypnosis (by certified hypnotherapists). Data analyzed included patient demographic cues, causes of hospitalization, comorbidities, indication for hypnosis, mean length of sessions and number of sessions, results of hypnosis.

Results: Our preliminary data show that hypnosis has become progressively more popular during the 4 years of observations (2018-2021), and that its indicationsrapidly expanded beyondpain and acute procedural distress, to encompass management of both acute and chronic dyspnea, insomnia, and anxiety. Moreover, hypnosis proved to be an interesting tool to improve tolerance to non-invasive respiratory therapies.

Discussion: Although the benefits of hypnosis have been ascertained in different medical disciplines (e.g. in anesthesia, as an integrative tool for the management of both acute and chronic pain), its use in hospital internal medicine is far from being widespread. Our study shows that hypnosis implementation in internal medicine has a twofold purpose: for patients it is a simple and acceptable mean for self-empowerment, for doctors, it is an interesting tool to maximize our effectiveness as healers.

P44

LOw-dose CT cOmPared to Lung UltraSonography vs standard of care based-strategies for the diagnosis of pneumonia in the elderly: a multicentre randomised controlled trial (OCTOPLUS)

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Introduction: Pneumonia is a leading cause of mortality and a common indication for antibiotic in elderly patients. However, its diagnosis is often inaccurate. We aim to compare the diagnostic accuracy, the clinical and cost outcomes and the use of antibiotics associated with three imaging strategies in patients >65 years old with suspected pneumonia in the emergency room (ER): Chest-X ray (CXR, standard of care), low-dose CT scan (LDCT) or lung US (LUS).

Methods and analysis: This is a multicenter randomized superiority clinical trial with three parallel arms. Patients will be allocated in the ER to a diagnostic strategy based on either CXR, LDCT, or LUS. All three imaging modalities will be performed but the results of two of them will be masked during 5 days to the patients, the physicians in charge of the patients and the investigators according to random allocation. The primary objective is to compare the accuracy of LDCT vs.CXR- based strategies. As secondary objectives, antibiotic prescriptions, clinical and cost outcomes will be compared, and the same analyses repeated to compare the LUS and CXR strategies. The reference diagnosis will be establisheda posteriori by a panel of experts. Based on a previous study, we expect an improvement of 16% of the accuracy of pneumonia diagnosis using LDCT instead of CXR. Under this assumption, and accounting for 10% of drop out, the enrolment of 495 patients is needed to prove the superiority of LDCT over CRX (alpha error =0.05, beta error=0.10).

Impact of the study: Superiority of the LDCT or LUS strategy over CXR would affect recommendations for the diagnosis of pneumonia in elderly patients. A higher accuracy of one of the strategies may decrease antibiotics overuse and lead to better outcomes and reduced costs.

P45

Medication reconciliation for internal medicine inpatients: collaboration between clinical pharmacists and internists

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Background: Transition of care is a challenging step at hospital discharge especially regarding medication safety. Medication reconciliation (MedRec) is essential to prevent adverse drug events. MedRec consists of comparing the medication a patient has been taking regularly to the new medication list prescribed, to identify and resolve any discrepancies before hospital discharge.

Objective: To implement a MedRec program in an Internal Medicine department of a regional hospital (114 beds).

Method: This MedRec program was implemented in November 2020 thanks to extra-funding from the RSHL. The program is divided in 3 components:

1. To standardise medication information among all hospital discharge documents (medications order, discharge letter, discharge treatment plan).
2. To develop a continuous education course on this topic for all internal medicine residents
3. To implement a MedRec intervention involving clinical pharmacists focused on polymedicated patients (≥ 5 drugs prescribed).

Results: This program currently allows the following changes in the department:

1. Discharge prescription orders is now systematically edited as a discharge treatment plan, involving a specific list of "medication stopped during hospital stay", useful for patients, general practitioners, community pharmacists and in-home nurses.
2. Every 3 months, a dedicated course on MedRec and medication discharge issues is dispensed to all medical residents. This course has been scheduled 3 times in 2021.
3. A prospective follow-up is performed by a clinical pharmacist every working days. MedRec interventions have been performed in 480 patients between 27 Sept. and 31 Dec. 2021; mean of 6.9 patients/day (min 1-max 17). 1131 interventions were addressed to the medical residents; mean of 3 interventions/patient (min 1-max 9). 22% of patients had no intervention. The time spent by the pharmacist corresponded to a mean of 1.6h/day (min: 0.3h-max: 4.4h).

Conclusion: This interdisciplinary project allows to harmonize medication information transmitted to all caregivers involved in the patient management by providing a structured discharge treatment plan. It enhances the awareness of discharge medication problematic among physicians of the Internal Medicine Department by continuing education courses and regular phone calls from clinical pharmacists. In the future, the challenge will be the sustainability of this program (additional resources needed for MedRec interventions).

P46

Neutralization of SARS-CoV-2 in the serum of COVID-19 aged patients compared to young

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Background: Elderly people are a high-risk group of death from COVID-19. The detection of total immunoglobulins (Igs) against the Spike (S) protein(anti-S Ig) is the basis of most current serological tests but does not predict the biological activity of the fraction of Igs specifically neutralizing the viral entry. The presence of neutralizing antibodies (nAbs) is then more predictive to evaluate viral protection, but not known during infection in the elderly. Through the development of a new technique to identify nAbs, a fusion assay mimicking SARS-CoV-2 entry into the cell, we aimed to quantify the presence of nAbs in elderly people and compare their levels with a population <65 years. Our secondary objective was to correlate the amount of SARS-CoV-2 anti-Spike Ig antibodies with nAbs.

Methods: Elderly patients were recruited among the GEROCOVID cohort (including patients >65 years old admitted for COVID-19 at Geneva University Hospital) and patients <65 years among the STRAT-Cov cohort [2]. Electrochemiluminescence immunoassay for the detection of total SARS-CoV-2 IgG antibodies in blood samples was performed using the Roche anti SARS-CoV-2 IgG quantitative ECLIA kit. In this assay, nAbs were measured for their ability to reduce the luminescent signal (Fig.1). The luminescence is expressed in percent of control i.e. the pool of non-infected patients.

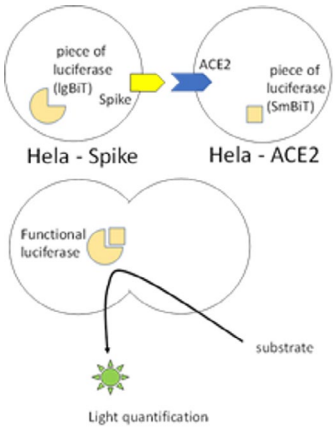

Figure 1. Test developed for the quantification of nAbs

Results: 109 patients were included: 53 (48.6%) in the elderly and 56 in the young group. The luminescence was systematically higher in the older group and the value increased with the serum dilution, meaning that less SARS-CoV-2 nAbs have been detected. The average of the luminescence for youth was 23.0% ± 32.9 and for elderly 33.2% ± 37.1 (p<0.001). In the young group the association between SARS-CoV-2 nAbs and SARS-CoV-2 anti-S IgG antibody level was 9% (p=0.02) for dilution 1/8, 16% (p=0.01) for dilution 1/32, 25% (p=0.01) for dilution 1/128 and 30% for dilution 1/512 (p=0.01) in the young group. So, the higher was the dilution, the better was the association. In the old group, the association was not improved by the dilution. Although this result was statistically significant, it did not reach a clinically relevant level.

	Young n;mean±SD N=56	Old n;mean±SD N=53	N=109
Age (years)	56; 52.3 ± 9.9	53; 85.3 ± 6.9	109; 68.4 ± 18.6
Sexe (male)	46 (82.1%)	20 (37.7%)	66 (60.6%)
Delay PSO-collection (days)	56; 13.2 ± 3.9	53; 15.2 ± 5.5	109; 14.2 ± 4.8
Delay PSO-admission (days)	56; 9.2 ± 4.0	53; 3.7 ± 6.3	109; 6.5 ± 5.9
Chronic cardiac failure	1 (1.8%)	11 (21.2%)	12 (11.1%)
Cognitive disorders	1 (1.8%)	9 (17.0%)	10 (9.2%)
Diabete	9 (16.1%)	8 (15.1%)	17 (15.6%)
Immunosuppression	4 (7.1%)	4 (7.5%)	8 (7.3%)
FRAILTY score			
1	36 (64.3%)	0 (0.0%)	36 (33.0%)
2	11 (19.6%)	0 (0.0%)	11 (10.1%)
3	6 (10.7%)	5 (9.4%)	11 (10.1%)
4	1 (1.8%)	14 (26.4%)	15 (13.8%)
5	1 (1.8%)	8 (15.1%)	9 (8.3%)
6	0 (0.0%)	17 (32.1%)	17 (15.6%)
Symptoms at admission			
Cough	46 (82.1%)	30 (60.0%)	76 (71.7%)
Dyspnea	43 (76.8%)	28 (57.1%)	71 (67.6%)
Asthenia	20 (35.7%)	24 (48.0%)	44 (41.5%)
Diarrhea	15 (26.8%)	12 (24.0%)	27 (25.5%)
WHO severity score			
Mild disease	5 (8.9%)	10 (21.7%)	15 (14.7%)
Moderate	10 (17.9%)	15 (32.6%)	13 (19.7%)
Severe	19 (33.9%)	16 (34.8%)	35 (34.3%)
Critical	22 (39.3%)	4 (8.7%)	26 (25.5%)
CRP(mg/l) at admission	55; 101.9 ± 72.2	52; 50.5 ± 50.9	107; 76.9 ± 67.6
Lenght of stay (days)	56; 18.2 ± 17.8	49; 30.9 ± 25.4	105; 24.1 ± 22.5
Intra-hospital death	7 (12.5%)	6 (11.3%)	13 (11.9%)

Table 1. Clinical and biological characteristics of study participants

Conclusion: Elderly patients have significantly less SARS-CoV-2 nAbs compared to young patients during SARS-CoV-2 infection. SARS-CoV-2 nAbs seems to be correlated with SARS-CoV-2 anti-S Ig antibodies result but did not have a clinical relevance. Our results should be replicated in larger cohorts.

P47

Orthogeriatric rehabilitation: less is more?

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Introduction: Elderly patients are at risk of adverse outcomes (increased morbidity, immobilization, loss of functional independence, institutionalization) following an acute fracture or joint replacement. In this context, a stay in a rehabilitation service is often necessary. This retrospective multicenter study evaluates the predictors of functional progression and destination at discharge, following ortho-geriatric rehabilitation.

Methods: Retrospective multicenter study including patients aged ≥ 75 years, hospitalized in rehabilitation in Geneva between 2018 and 2019 following an acute fracture and/or joint replacement. We performed multivariate logistic regressions to determine which variables were associated with the functional progression (deltaFIM[1] ≥ 10, Montebello score[2] ≥ 0.5) and destination (returning home). The statistical unit is expressed in stays and the results are reported as odds ratios (OR).

Results: On 562 stays, 79% of patients are women, mean age is 84 years old. Fractures, prosthesis and fractures followed by prosthesis represent respectively 43%, 51% and 6% of the diagnoses. Patients are polymorbid (CIRS[3] = 13/56 +/- 6) and malnourished (NRS[4]= 3/7 +/- 1). The admission FIM is 83/126 +/- 22 and the deltaFIM is 9.8 +/- 13.3. On average, patients receive 6 physiotherapie sessions per week, or 8 PPS[5] therapies per week. The average length of stay is 21 +/- 14 days. 78% of the patients return home, while 15% are admitted to a nursing home and 7% remain hospitalized. Being a male (OR 1.64, CI95% 1.02-2.65, p = 0.040), younger (OR 0.93, CI95% 0.89-0.97, p = 0.001), having less comorbidities (OR 0.95, CI95% 0.91-0.99, p = 0.007) and staying hospitalized longer (OR 1.05, CI95% 1.03 - 1.07, p < 0.001) predicts a better functional status at discharge. There is no correlation between the total number of therapies per week and the primary outcomes (deltaFIM, Montebello score and destination at discharge with p = 0.098, 0.213 and 0.985, respectively).

Conclusion: In the elderly, more intensive rehabilitation does not correlate with a better functional status at discharge or returning home. This finding may influence our way to plan ortho-geriatric rehabilitation programs.

[1]deltaFIM: discharge functional independency measure (FIM) - admission FIM

[2]Montebello score: (deltaFIM)/(maximum possible FIM - admission FIM) x 100

[3]Cumulative Illness Rating Scale

[4]Nutrional Risk Screening

[5] PPS: all therapies (physiotherapy, ergotherapy, nutrionnist)

P48

Performance of early lung ultrasound in the diagnosis of SARS-CoV-2 infection in mild- and moderate-severity patients

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Introduction: The SARS-CoV-2 pandemic placed pressure on healthcare systems worldwide. Several institutions, based on the proven accuracy of lung ultrasonography (LUS) in diagnosing community-acquired pneumonia, have implemented LUS to improve precision and rapidity of the diagnostic process of SARS-CoV-2 infections. Results on the diagnostic accuracy of LUS are so far conflicting and no data has been published to date for patients with mild or moderate respiratory failure. The aim of this study is to measure the diagnostic accuracy of LUS for the diagnosis of SARS-CoV-2 infections, in patients with mild to moderate respiratory symptoms.

Methods: Prospective observational study performed among adult patients admitted to the internal medicine ward of a tertiary university hospital, with a suspected SARS-CoV-2 infection. All patients had a nasopharyngeal swab and a bedside LUS performed within 48 hours of admission by a dedicated team, following a standardized protocol. Based on validated criteria, each LUS examination was classified for SARS-CoV-2 as: likely Pneumonia, unlikely Pneumonia and uncertain Pneumonia. Diagnostic accuracy of LUS for a SARS-CoV-2 infection was calculated using RT-PCR from nasopharyngeal swab as gold standard for comparison.

Results: Data from 145 patients was available for analysis. We obtained a moderate overall accuracy of LUS (sensitivity of 74%, specificity of 72% and in the ROC analysis an AUROC of 0.73). Dry cough, fever and dyspnea were significantly associated with an improved diagnostic accuracy of LUS. For patients with dry cough, LUS accuracy was excellent (sensitivity 80%, specificity 89%, AUROC 0.84, PPV 93%). In RT-PCR positive patients without LUS evidence of pneumonia, the duration of symptoms upon admission was significantly shorter (median 3 days, IQR 1-5) than patients with LUS evidence of pneumonia (median 8 days, IQR 7-13). LUS found a pneumonia in 23/83 (27%) RT-PCR negative patients. For 63% of these patients, pneumonia was confirmed radiologically and/or microbiologically.

Conclusions: In patients presenting with mild to moderate respiratory symptoms the overall accuracy of LUS in detecting SARS-CoV-2 infections was moderate. Nevertheless, LUS displays an excellent diagnostic accuracy in patients presenting with dry cough on admission. The absence of LUS signs of pneumonia is more common early in the course of SARS-CoV-2 infections, especially when symptoms last less than 5 days.

Table 1: Overall accuracy of LUS for the diagnosis of SARS-CoV-2 pneumonia and accuracy according to the presence of different clinical variables (95% CI) *.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUROC (%)
LUS Accuracy if "Uncertain" considered as " likely pneumonia"	79 (66.8 – 88.3)	79 (66.8 – 88.3)	79 (66.8 – 88.3)	79 (66.8 – 88.3)	79 (66.8 – 88.3)
LUS Accuracy if "Uncertain" considered as " unlikely pneumonia"	74.2 (61.5 – 84.5)	74.2 (61.5 – 84.5)	74.2 (61.5 – 84.5)	74.2 (61.5 – 84.5)	74.2 (61.5 – 84.5)
Dry cough present (n=53)	80 (63-91)	89 (65.-98)	93 (78-99)	69 (47-87)	0.844 (0.744-0.945)
Fever (≥ 38°C) (n=84)	74 (58.-86)	75 (60-87)	76 (60-88)	74 (58-86.	0.75 (0.656-0844)
Dyspnea present (n=71)	86 (70-95)	66 (48-81)	72 (56-84)	82 (63-94)	0.759 (0.661-0.857)

PPV: Positive predictive value: NPV: Negative predictive value; AUROC: Area under the ROC curve

* In this analysis "uncertain LUS" was considered as "unlikely pneumonia".

P49

Pharmacological thromboprophylaxis in medical inpatients: generalizability of clinical trial eligibility criteria to real world practice

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Background: Randomized pharmacological thromboprophylaxis (TPX) trials in medical inpatients were conducted 10-40 years ago and used complex eligibility criteria. It is unclear whether the results of these trials are applicable to the heterogeneous population of medical inpatients receiving pharmacological TPX in today's real world settings. We therefore examined the proportion of patients who would have been eligible for trial participation and compared the risk of adverse events in eligible and non-eligible patients.

Methods: We included consecutive patients admitted to General Internal Medicine for acute illness, who were enrolled in a prospective multicenter cohort study between 2020 and 2021 at 3 Swiss University hospitals. We restricted the analysis to patients receiving pharmacological TPX with parenteral anticoagulants. We identified 8 randomized trials comparing heparin or fondaparinux with placebo or no intervention through search of guidelines and systematic reviews. Eligibility criteria were abstracted from each trial. First, we calculated the proportion of study patients who would have been eligible for participation in each of the trials. Second, we generated a set of eligibility criteria based on 4 landmark trials (see footnote Table 1). Characteristics of patients who did and did not meet these criteria and the incidence of hospital-acquired anemia, any bleeding event, and venous thromboembolism (VTE) during hospitalization were compared between eligible and non-eligible patients.

Results: Among 823 medical inpatients with TPX, the proportion of patients eligible for trial participation ranged from 19.2 to 57.1%. After application of the generated set of eligibility criteria based on the 4 landmark trials, 367/823 (44.6%) patients were deemed eligible. Eligible vs. non-eligible patients were older (median age 70 vs. 66 years), had a longer hospital stay (median 7 vs. 6 days) and more often a high risk Padua Score of ≥ 4 points (67 vs. 48.6%) (Table 1). There was a statistically significant difference in the occurrence of VTE between eligible and non-eligible patients (2.2% vs. 0.4%, p= 0.028). The risk of hospital-acquired anemia and any bleeding event did not differ (Table 2).

Conclusions: Our results suggest that eligibility criteria of former TPX-trials apply only to a minority of medical inpatients receiving pharmacological TPX in a real world setting and the benefit from TPX remains questionable in patients at lower risk for VTE.

Table 1. Characteristics by eligibility status*

Characteristics	Eligible (n = 367)	Not eligible (n = 456)	p-value
	n (%), unless stated otherwise		
Age in years, median (IQR)	70 (61-78)	66 (53-78)	**<0.001**
Age ≥60 years	290 (79)	279 (61.2)	**<0.001**
Female sex	149 (40.6)	202 (44.3)	0.29
Length of stay in days, median (IQR)	7 (5-10)	6 (3-9)	**<0.001**
Padua Score high risk (≥4 points)	246 (67)	221 (48.6)	**<0.001**
BMI in kg/m^2, mean (SD)	27.0 (6.5)	25.7 (6.2)	**0.004**
BMI ≥30 kg/m^2	98 (26.7)	88 (19.3)	**0.012**
Heart failure	49 (13.4)	33 (7.3)	**0.004**
Respiratory failure	121 (33)	63 (13.9)	**<0.001**
Active cancer	121 (33)	66 (14.5)	**<0.001**
Acute infection	239 (65.1)	165 (36.2)	**<0.001**
Acute rheumatologic disease	18 (4.9)	13 (2.9	0.126
Inflammatory bowel disease	7 (1.9)	7 (1.5)	0.678
Previous venous thromboembolism	21 (5.7)	33 (7.3)	0.379
Ongoing hormonal treatment	9 (2.5)	12 (2.6)	0.867
Chronic venous insufficiency	80 (21.8)	90 (19.7)	0.468
Myeloproliferative syndrome	5 (1.4)	7 (1.5)	0.834
Exclusion criteria			
Active bleeding		22 (4.8)	
Platelet count <100G/L		41 (9)	
Peptic ulcer disease		18 (4)	
eGFR <30mL/min		76 (16.7)	
Liver failure		5 (1.1)	
Known hypersensitivity to heparin or HIT		3 (0.7)	
Surgery within previous 1 month		31 (6.8)	
Pregnancy		1 (0.5)	
Myocardial infarction within previous 1 month		20 (4.4)	
Stroke within previous 30 days		6 (1.3)	

Abbreviations: IQR= interquartile range, BMI= body mass index, SD= standard deviation, eGFR= estimated glomerular filtration rate, HIT= heparin-induced thrombocytopenia, VTE= venous thromboembolism

*eligibility criteria (based on 4 landmark trials):

- **Inclusion**: Age ≥40years, anticipated duration of hospitalization ≥4 days, ≥1 of the following diseases: heart failure, respiratory failure (not requiring ventilatory support), active cancer, or acute infection/acute rheumatic disease/inflammatory bowel disease + ≥1 VTE risk factor (BMI ≥30 kg/m^2, previous VTE, age ≥60 years, hormonal treatment, chronic venous insufficiency, myeloproliferative syndrome)

- **Exclusion**: active bleeding, platelets <100G/L, peptic ulcer, eGFR <30mL/min, liver failure, hypersensitivity to heparin or HIT, surgery within previous 4 weeks, pregnancy, acute myocardial infarction/stroke within last 1 month

Table 2. Outcome by eligibility status

Outcome	Eligible (n=367)	Not eligible (n=456)	p-value
	n (%)		
Hospital-acquired anemia*	99 (27)	115 (25)	0.568
Any bleeding event	6 (1.6)	13 (2.9)	0.351
Venous thromboembolism†	8 (2.2)	2 (0.4)	**0.028**

* defined as new onset anemia or drop of 20 g/L of hemoglobin during hospitalization (hemoglobin value < 120g/L in women [< 110g/L if pregnant], < 130g/L in men)

† symptomatic, objectively confirmed fatal and non-fatal venous thromboembolism

P50

Physicians' views and agreement about patient- and context-related factors influencing ICU admission decisions: a prospective study

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Background: Single patient- and context-related factors have been associated with admission decisions to intensive care (ICU). How physicians weigh various factors and integrate them in the decision-making process is not well known. We aimed to determine
1) which patient- and context-related factors intensivists and internists considered as influencing an admission decision, and their agreement about these determinants,
2) whether factors differed for patients with compared to patients without advanced disease.

Methods: Consecutive ICU consultations for medical inpatients were prospectively included. The involved physicians, i.e. the internist and the intensivist, rated the importance of 13 factors for each decision on a Likert scale (1 = negligible to 5 = predominant). We cross-tabulated these factors by presence or absence of advanced disease, and examined the degree of agreement between internists and intensivists using the kappa statistic.

Results: Of 201 evaluated patients, 105 (52.2%) had an advanced disease, and 140 (69.7%) were admitted to intensive care. The mean number of important factors per decision was 3.5 (SD 2.4) for intensivists, and 4.4 (SD 2.1) for internists. Patient's comorbidities, quality of life, preferences, and code status were most often mentioned (Table 1). Inter-rater agreement was low, for the whole population and after stratifying for patients with and without advanced disease (Table 2). Kappa values ranged from 0.02 to 0.34 for all the patients, from -0.05 to 0.42 for patients with advanced disease, and from -0.08 to 0.32 for patients without advanced disease. Best agreement was found for family preferences.

Table 1. Opinions of the intensivist and the internist about the importance of specific factors in the decision to admit or not a patient to intensive care, in 201 decisions.

Factor	Rated as important* by		P value
	Intensivists	Internists	
	Proportion of decisions (%)		
Patient's age	19.4	40.8	<0.001
Patient's comorbidities	59.2	63.7	0.36
Patient's quality of life	48.3	53.2	0.36
Patient's preferences	40.8	47.8	0.16
Family preferences	12.9	18.4	0.09
Code status	45.3	73.6	<0.001
Knowing the patient	24.9	27.4	0.63
Opinion of a specialist	18.4	24.4	0.14
Opinion of a senior internist	10.4	42.8	<0.001
Workload on medical ward	17.9	12.9	0.17
Discomfort of intensive care for the patient	24.9	10.4	<0.001
Availability of beds in the ICU	16.4	17.4	0.89
Time pressure	7.0	3.5	0.17

* 4 or 5 on 5-point scale from 1 (negligible) to 5 (predominant). Missing and non-applicable ratings were included and treated as less than 4 or 5

Table 2. Agreement beyond chance between intensivist and internist about the influence of specific factors on the admission decision, in 201 patients, and for patients with and without advanced disease

Factor	All patients N=201	Patients	
		No advanced disease N=96	Advanced disease N=105
	Kappa statistic	Kappa statistic	Kappa statistic
Patient's age	0.11	0.11	0.12
Patient's comorbidities	0.21	0.32	0.09
Patient's quality of life	0.03	0.01	0.04
Patient's preferences	0.12	0.07	0.14
Family preferences	0.34	0.19	0.42
Code status	0.11	0.08	0.14
Knowing the patient	0.11	0.11	0.11
Opinion of a specialist	0.18	0.29	0.10
Opinion of a senior internist	0.02	0.01	0.04
Workload on medical ward	0.16	0.14	0.19
Discomfort of intensive care for the patient	0.16	-0.08	0.24
Availability of beds in the ICU	0.12	-0.04	0.27
Time pressure	0.05	0.16	-0.05

Conclusions: Poor agreement between physicians about patient- and context-related determinants of ICU admission suggests a lack of explicitness during the decision making process. Potential consequences are increased variability and inequity regarding which patients are admitted. Timely advance care planning involving families could help physicians make the decision most concordant with patient preferences.

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P51

Renal failure: a non-cardiac source of high sensitivity cardiac troponin T?

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Introduction: Circulating high sensitivity cardiac troponin T (hs-cTnT) levels are frequently elevated in patients with end-stage renal disease (ESRD). The underlying pathophysiology is largely unknown. Currently, accumulation of hs-cTnT due to decreased renal clearance, as well as increased production caused by uremic cardiomyopathy is being discussed. In this study, we used successful renal transplantation as an in-vivo model of rapidly improved renal function to assess the relative contribution of impaired renal clearance to the elevated systemic hs-cTnT concentrations.

Methods: Using the BASEL-PMI study (NCT02573532), we identified 43 patients undergoing successful renal transplantation without evidence of perioperative myocardial injury (infraction). Serial creatinine and hs-cTnT (Elecsys, Roche) measurements were performed pre-transplant (baseline) and post-transplant on day (d) 1, between d2 and d7, and between d14 and d180.

Results: Baseline median serum creatinine concentration was 608 umol/l [interquartile range (IQR): 473-820] and was significantly reduced to 425 umol/l (IQR: 294-629) on d1, 280 umol/l (IQR: 189-514) on d2-7, and 116 umol/l (IQR: 94.75-182.75) on d14-180 (p< 0.001, p< 0.001, and p= 0.043, respectively) (Figure A). Simultaneously, median hs-cTnT concentration was 50 ng/l (IQR: 35-70) at baseline, 28 ng/l (IQR: 15-43) on d1, 28 ng/l (IQR: 18-37) on d2-7, and 24 ng/l (IQR: 15- 29.25) on d 14-180 (Figure B). The only significant reduction of the circulating hs-cTnT levels was observed between baseline and d1 (p=0.001) with a rate of relative change of 36%, while in contrast to the continuously decreasing serum creatinine levels, no further decrease was noticed after the first 24 hours post-transplant (geometric mean of the relative change between d1 and d2-7, 7% for hs-cTnT and 18% for creatinine, p= 0.048). Additionally, the hs-cTnT levels reached after the initial reduction within the first 24 hours a plateau, which significantly remained above the 99th percentile (14ng/l) across the remaining period of observation.

Conclusion: Following renal transplantation, serum hs-cTnT concentrations decreased only during the first 24 hours and then remained elevated above the 99thpercentile. This suggests, that elevated hs-cTnT concentrations in patients with ESRD can only partly be explained by decreased renal function. Further data assessing the long-term effect of renal transplantation on hs-cTnT levels and cardiac function are needed.

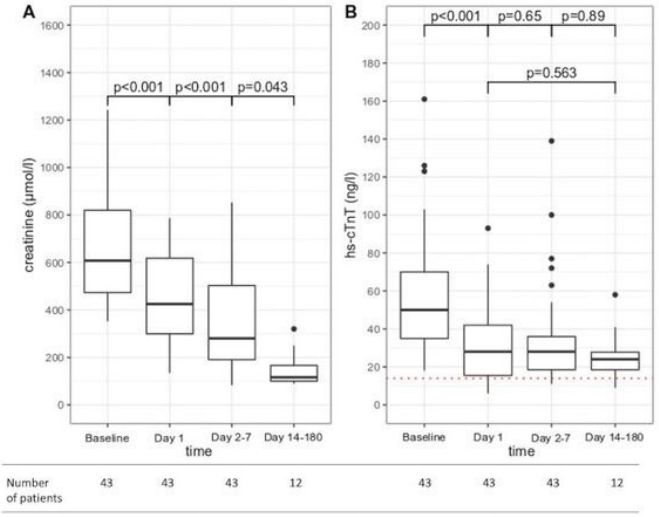

Figure: Serum creatinine (A) and hs-cTnT (B) levels pre- and post-renal transplantation. Dotted line, 99th percentile (14 ng/l)

P52

Sartan-induced enteropathy

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Learning objectives: Sartan-induced enteropathy is a rare side effect of angiotensin-1 receptor antagonists (ARB) and an important differential diagnosis of celiac disease.

Case: A 74-year-old man presented with excessive non-bloody diarrhea, mild nausea and weight loss over 10 days. He denied abdominal pain and food dependence of the diarrhea and had no related travel history. Medical history included hypertension treated with azilsartan (AS). Clinical examination was unremarkable and neither laboratory investigations nor stool analysis for pathogenic bacteria/protozoa demonstrated any explaining cause. Abdominal ultrasound and contrast-enhanced CT revealed only accelerated peristalsis. As diarrhea persisted, gastro- and colonoscopy were performed which showed endoscopically and histologically distinct villous atrophy in the duodenum and terminal ileum with intraepithelial lymphocytosis and crypt hyperplasia. Results were

typical for celiac disease but transglutaminase antibodies were negative. Nevertheless, a gluten-free diet was implemented. Additionally, AS was stopped because of hypotension. As symptoms disappeared, the patient was discharged and seen for outpatient nutritional counselling.
After 3 months AS therapy was reinitiated. Acute severe diarrhea reoccurred 11 days later. Comprehensive medical examination was repeated, but still being inconclusive except for discovering C. difficile toxin in this second stool analysis, which was treated with metronidazole. A second gastroscopy confirmed villous atrophy of the duodenum. AS was immediately stopped. Without further specific treatment, symptoms improved after 8 days. In addition, gluten-containing food was reinitiated and tolerated well with documented clinical and histological remission of the villous atrophy in the duodenum 5 months later.
Discussion: This case illustrates through AS exposure, stop of AS exposure and re-exposure with AS combined with the clinical and histological findings sprue-like enteropathy as a potential side effect of ARB. This diagnosis is strongly supported by the histological findings and the lack of clinical response to gluten-free diet. The pathogenesis of sprue-like mucosal damage caused by ARB is not completely understood but is considered to be an immune-mediated inflammation[1]. Literature review shows a predominant association with olmesartan, although few case reports with other ARB exist[1-3]. To our knowledge, this is the first case of an association with AS.

Test	Normal value	Results of first referral	Results of second referral
CRP	< 8 mg/l	*15 mg/l*	*10 mg/l*
Hemoglobin	140-180 g/l	151 g/l	161 g/l
Leucocyte count	4.0-10.0 G/l	7.1 G/l	7.3 G/l
Thrombocyte	150-300 G/l	246 G/l	254 G/l
Creatinin	<115 µmol/l	112 µmol/l	108 µmol/l
Sodium	136-144 mmol/l	139 mmol/l	*134 mmol/l*
Potassium	3.6-5.1 mmol/l	3.6 mmol/l	3.9 mmol/l
ALT (GPT)	<55 U/l	45 U/l	33 U/l
Alcaline phosphatase	30-120 U/l	75 U/l	58 U/l
Bilirubin	< 20 µmol/l	17 µmol/l	2 µmol/l
Pancreatic amylasis	< 46 U/l	34 U/l	16 U/l
TSH	0.25 – 4 mIU/l	1.42 mIU/l	1.38 mIU/l
Stool calprotectin	< 50 µg/g	*96 µg/g*	*3990 µg/g*
HIV-1/2 screen	Negative	n.d.	Negative
Transglutaminase IgA	< 7 U/ml	< 7 U/ml	< 7 U/ml
Endomysium IgA	Negative	Negative	Negative
Total Serum IgA	0.7 – 4.1 g/l	2.5 g/l	3.8 g/l
Multiplex-PCR for DNA of Shigella spp., Salmonella spp., Campylobacter jejuni/coli, Plesiom shigelloides, EHEC, ETEC, Vibrio species, Yersinia enterocolitica	Negative	Negative	Negative
PCR for DNA of giardia lamblia and entamoeba histolytica	Negative	Negative	n.d.
PCR for Norovirus RNA	Negative	n.d.	Negative
Clostridioides difficile (Toxin)	Negative	Negative	*Positive*
SARS-Cov-2 PCR	Negative	Negative	Negative

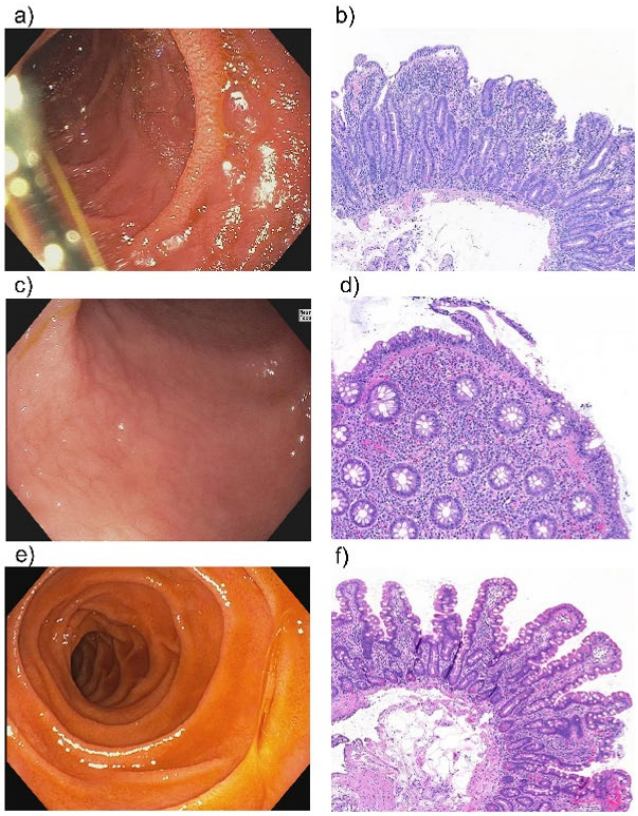

Figure 1: a) endoscopy of the duodenum at first presentation showing severe villous atrophy with mucosal scalloping. b) histological findings of a biopsy taken from the duodenum with distinct villous atrophy with intraepithelial lymphocytosis and crypt hyperplasia. c) endoscopy of the terminal ileum showing severe villous atrophy. d) histology taken from terminal ileum represents distinct villous atrophy and increased lymphoplasmacytic inflammatory infiltrate with cryptitis. e) normal endoscopy findings in the duodenum five months after stopping of AS therapy with complete remission of initial celiac disease like histology f).

P53

Severe drug-induced immune thrombocytopenia

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Learning objectives: Drug-induced immune thrombocytopenia (DITP) is an important differential diagnosis of acute thrombocytopenia. Many drugs have the potential to cause severe thrombocytopenia within hours after a first administration. Symptoms range from an asymptomatic course to clinically relevant bleeding with a potentially fatal outcome. Recognition of the etiology and immediate withdrawal of the offending drug are crucial in the management of DITP.

Case: A 56 year-old female with no medical history was hospitalized with a left lower lobe pneumonia and started an empiric therapy with ceftriaxone and clarithromycin.
A few hours after the first antibiotic administration the patient reported gingival bleeding and epistaxis. Laboratory tests unveiled a severe drop of platelet count from 597 G/L at admission to 4 G/L 46 hours later. We diagnosed a DITP due to either ceftriaxone or clarithromycin and switched to levofloxacin. Because of the bleeding, we administered one unit of platelets.
Thrombocyte count normalised within 48h after discontinuation of the potentially triggering drugs.

Discussion: Thrombocytopenia in DITP is thought to be caused by drug-dependent, platelet-reactive antibodies that recognize neoepitopes on the platelets after drug exposure. After excluding pseudothrombocytopenia, it is important to consider every drug

and even non-drugs as potential candidates for triggering DITP.
In our patient a classical HIT type II was unlikely because of lack of pre-exposure to any heparin and HIT type I is characterized by a mild drop in the platelet count only. Furthermore, in the present case of an acute drop of platelets in the inpatient, one has to consider sepsis, disseminated intravascular coagulation or a rarer thrombotic thrombocytopenic purpura or hemolytic-uremic syndrome as differential diagnoses; we considered them unlikely because of normal leucocyte counts, a normal blood smear but for the thrombocytopenia, elevated fibrinogen counts (4.6 g/L) and a normal creatinine.
We suspect ceftriaxone as the trigger for the acute DITP. Reexposure would confirm the diagnosis, but due to the extreme and clinically relevant thrombocytopenia, one would be reluctant to reexpose the patient. Currently, there are no validated laboratory tests in clinical routine to establish the diagnosis.[3] Withdrawal of the drug in the acute setting, and avoiding the postulated drug culprit in the future are the most important steps in the management of DITP.

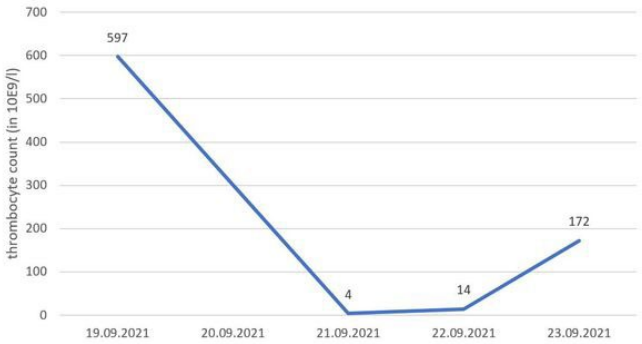

Table 1: thrombocyte count during inpatient treatment

P54

Should "bad news" Be disclosed in person or by telephone? Results of a systematic review and meta-analysis

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Background: Communication of "bad news" (such as a new cancer diagnosis) to patients may have a major impact on their well-being. We investigated differences in psychological distress of breaking bad news in person compared to by telephone in a systematic review and meta-analysis.

Methods: We included all studies that investigated breaking bad news (such as a new cancer diagnosis or genetic risk for life-limiting diseases) in person compared to by telephone in adult patients regardless of diagnosis regarding the association with symptoms of anxiety, depression or PTSD. We systematically searched PubMed, Embase, PsycINFO and CINAHL from the inception of each database to June 1, 2021. We included randomized and non-randomized trials.

Results: We screened 3625 studies and included eleven studies in the qualitative analysis and nine in the meta-analyses, including three randomized controlled trials. Overall, quality of studies was moderate to good. There was no mean difference regarding psychological distress when bad news was disclosed by telephone compared to in person with similar symptom levels of anxiety (3 studies, 285 participants; standardized mean difference [SMD] 0.10 [95% CI -0.15 to 0.35]), depression (3 studies, 248 participants; SMD 0.10 [95% CI -0.30 to 0.49]), and symptom levels of PTSD (2 studies, 171 participants; SMD -0.01 [95% CI -0.48 to 0.36]). Results were similar for satisfaction of care.

Conclusions: We did not find a difference in psychological distress if breaking bad news was done in person or by telephone but there were too few studies to draw more definite conclusions. Future research is needed to understand in which situation a telephone consultation is appropriate to disclose bad news with a patient.

P55

What are barriers and facilitators to mobility of patients hospitalized on an acute medical ward?

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Background: Low mobility during a hospitalization is very common and associated with adverse outcomes. Some interventions could improve mobility under study conditions, but were not broadly implemented. To change practice, barriers and facilitators to mobility in hospital should be addressed. We conducted a systematic literature review of patient-, healthcare professional (HCP)- and environment-/system-related barriers and facilitators to mobility of patients hospitalized on an acute medical ward, to provide a meaningful overview to be used to improve clinical practice.

Methods: We searched Medline (Ovid), Embase (OvidSP), PsychInfo, Web of Science Core Collection, Cochrane CENTRAL, CINHAHL and Google Scholar (inception to October 18, 2021) to identify studies reporting barriers and/or facilitators to mobility of adults hospitalized on an acute medical ward. We applied a deductive and inductive thematic analysis inspired by the Theoretical Domains Framework to classify barriers and facilitators into themes and subthemes relevant for clinical practice.

Results: Among 26 studies (16 qualitative, 7 quantitative, 3 mixed methods), barriers and facilitators were categorized into 10 themes: patient situation, knowledge, beliefs, experiences, intentions, emotions, social influence, role/identity, implementation/organization, environment/resources. Barriers included patient characteristics (e.g., impaired physical status) and symptoms (e.g., pain), HCPs prioritizing other tasks, HCPs labelling patients as "too sick to mobilize", fear of injury, lack of time, lack of clarity about staff responsibility, medical devices, and environment not encouraging mobility (e.g., lack of seats). Facilitators included knowledge of the importance of mobility, HCP skills, interdisciplinarity, clear documentation and unit expectations, encouraging staff, goal individualization, concrete activity program, family/visitor/volunteer support, and availability of equipment/materials for patients and HCPs. Almost all barriers and facilitators might be modified.

Conclusion: This systematic review provides a practical and synthesized overview of patient-, HCP- and environment-/system-related barriers and facilitators to mobility of adults hospitalized on an acute medical ward. This overview can help researchers and clinicians to identify and focus on aspects than can realistically be influenced to improve mobility during an acute medical hospitalization.

P56

When pneumococci wreak havoc

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Learning objectives: Interesting case where Streptococcus pneumoniae was found in an exotic region during a hospitalization.

Case, medical history: A 76 year old patient presented at the emergency department with symptoms of fever, shivering, back pain and vomiting. No Covid-19 anamnesis was present at that time. The patient reported no weight loss and no night sweating.
The clinical examination showed a patient in reduced condition due to the back pain. The blood analysis showed a CRP level of 42mg/l, Leucozytes $10x10^6$/l. Two sets of blood cultures were taken. The performed CT scan ruled an aortic dissection out and showed no signs of pulmonary infiltrates (Figure 1a,b). After incubation time of 12 hours grampositive cocci in chains were seen in Blood Culture. No Endocarditis was seen in TEE. The full body MRI scan showed signs of a septic gonarthritis of the right knee with abscess formations in the Musculus femoralis (Figure 3a,b). The blood cultures showed Streptococcus pneumoniae.

Clinical development: An arhtroscopic lavage with surgical debridement of the Musculus femoralis were performed. We started the antimicrobial therapy with intravenous Penicillin G with

$10x10^6$ IE every six hours for 2 days and changed then to Penicillin $4x10^6$ IE every six hours for 10 days. The patient could be discharged to a rehabilitation in good condition.

Discussion: Streptococcus pneumoniae is a gram-positive, extracellular opportunistic pathogen.
S. pneumoniae are also resistent outside the body. Enviromental studies showed that S.pneumoniae can also be easily cultured from common objects, such as soft toys.
Invasive pneumococcal disease is induced by pro-inflammatory chemokines, cytokines, upregulation of target receptors and damage to the respiratory epithelium caused by viral infektion (e.g. Influenca A) of the upper respiratory tracts.
Muscle abcess, known as pyomyositis is a rare disease. Most common it is due to Staph. aureus. Pyomyositis caused by Streptococcus pneumoniae is distinctly unusual. In the literature only few cases were associated with trauma. Magnetic resonance imaging is the imaging modality of choice, to be able to detect abscess or osteomyelitis as complication. The recommendation is to start early empiric therapy with clindamycin or vancomycin.
In conclusion pyomyositis can be diffucult to diagnosis and St. pneumococcus is a rare cause of this pathology. We treated the patient for cummulative 6 weeks with antibiotics.

P57

Association between tobacco smoking and olfactory function

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Introduction: Tobacco smoking is known to reduce olfactory function. We measured the prevalence of olfactory dysfunction among a population of adult smokers and tested the association between smoking intensity and one measure of olfactory function.

Methods: We consecutively invited 389 tobacco smokers who smoked 5 or more cigarettes per day, participating in a randomized controlled trial that tests electronic nicotine delivery systems (ENDS or e-cigarettes) on the efficacy for smoking cessation to undergo olfactory function testing at the baseline visit. We assessed olfactory function with the "Burghart's Sniffin' Sticks" 16-item Identification test, resulting in an olfactory identification score ranging from 0 to 16. We defined olfactory dysfunction as an olfactory identification score of ≤ 12 points in line with previous literature.
We fitted multivariable regression models to test the association between the olfactory identification score (OIS) or olfactory dysfunction and smoking intensity (number of cigarettes per day [CPD], years of smoking [YOS] and pack-years) adjusted for demographics, substance use other than tobacco and co-morbidities.

Results: Olfactory testing was completed by 376 participants (96.7%). Mean age was 39 (range 18 – 74); 45% identified as women. Participants smoked on average 15 cigarettes per day (standard deviation (SD): 7.1, range 5-60) for a median duration of 18 years and a median of 14 pack-years. Mean OIS was 13.3 (SD: 1.8); 25% had olfactory dysfunction.
Number of CPD (multivariable adjusted coeff: -0.03; 95%CI: -0.05 to -0.00) and pack-years (multivariable adjusted coeff: -0.03; 95%CI: -0.04 to -0.01) were associated with OIS. YOS was not significantly associated with OIS.
Pack-years (OR: 1.03; 95%CI: 1.00 to 1.05) was significantly associated with olfactory dysfunction. Number of CPD and YOS were not significantly associated with olfactory dysfunction among current smokers.

Conclusion: Participants in a smoking cessation trial who smoked at least 5 cigarettes per day, a quarter had olfactory dysfunction at the baseline visit. We will not be able to identify any association between smoking cessation and improved measures of olfactory function until 6-month follow-up, but smoking more cigarettes per day and more pack-years were associated with worse olfactory outcome measures and olfactory dysfunction.

ClinicalTrials.gov Identifier: NCT04617444

P58

Comparison of five different risk scores to predict incident type 2 diabetes in the Swiss HIV cohort study

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Introduction: People living with HIV (PLWH) have a higher risk of type 2 diabetes (T2D) than HIV-negative individuals. In the general population, diabetes risk scores are used to identify persons at risk of developing T2D, but little is known regarding their performance in PLWH. We assessed the capacity of five diabetes risk scores to predict T2D in PLWH.

Methods: Prospective study including all the Swiss HIV cohort study (SHCS) participants followed between 2009 and 2019. Five diabetes risk scores were assessed: FINDRISC versions 1 and 2, Balkau, Swiss Diabetes Association (SDA) and Kraege.

Results: 3853 T2D-free PLWH (78.5% men, 39.9±11.3 years) were included. After a mean follow-up of 5.0 (median 4.8, interquartile range 2.2-7.8) years, 151 participants (3.9%) developed T2D, corresponding to an incidence rate of 7.8 per 1,000 person-years (95% CI: 6.7-9.2). Participants who developed T2D were significantly older (46.4±12.3 vs. 39.6±11.2 years), more frequently obese (18.5% vs. 7.2%), abdominally obese (5.3% vs. 1.5%) and reporting a family history of diabetes (28.5% vs 18.9%) than those who did not have T2D. The AUC for incident T2D ranged from 0.620 (Balkau) to 0.722 (FINDRISC1). Sensitivity ranged between 6.0% (Balkau) and 50.3% (FINDRISC1) and specificity between 81.4% (FINDRISC1) and 98.5% (Balkau). Positive predictive values were all below 20%, while negative predictive values were all above 95%.

Conclusion: In the SHCS, incidence of T2D was high. Diabetes risk scores showed suboptimal positive predictive values but excellent negative predictive value.No score showed clear superiority over others.

P59

Epidemiological trends and outcomes of children, adolescents, and adults hospitalized with inborn errors of metabolism: a population based cohort study

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Introduction: Inborn errors of metabolism (IEMs) are a large class of genetic disorders characterized by disruption of cellular biochemical functions and associated with a high burden of morbidity. Incidences and outcomes of patients hospitalized with IEMs, however, are largely unexplored.

Methods: This was a population-based cohort study using nationwide in-hospital claims data in Switzerland from 2012 to 2020. We investigated incidence rates and hospital-associated outcomes among children (0-9 years), adolescents (10-19 years), and adults (20-39, 40-59, and 60-90) hospitalized with IEMs. Analyses were stratified for type of IEM (Amino acid metabolism disorders [AD], carbohydrate metabolism disorders [CD], fatty acid metabolism disorders [FD]), age, and sex.

Results: We identified 7'430 cases with IEM, of whom 3'707 had AD, 3`224 CD, and 512 FD. Incidence rates per 100`000 person-years of IEM hospitalizations were highest in children across all types of IEM (9.17 for AD, 6.11 for CD, 3.85 for FD) and decreased thereafter until age 40 (3.55 for AD, 2.96 for CD, 0.18 for FD), respectively. Hospitalizations with AD and CD in older adults aged 60-90 years rose again (7.29 for AD, 7.26 for CD), while there was no increase in those with FD (0.31). Absolute differences between male and female patients remained small across all age groups. The overall burden of hospital-associated adverse outcomes was high. While differences between types of IEM were small, patients with AD had

a higher risk of 30-day hospital readmission among children and adolescents, and a higher risk of intensive care unit admission in children and adults above 40 years.

Conclusions: While highest incidence rates of hospitalizations with IEMs were found among children and older adults, the burden of hospital-associated adverse outcomes was excessive across all types of IEM, ages, and sexes.

P60

Gender-specific disease trajectories descry pathogenetic traits in COPD allowing for individualized screening and early intervention

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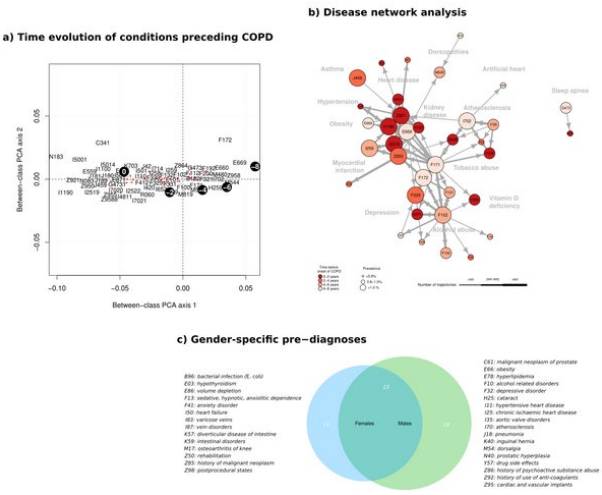
Introduction: Nation-wide hospitalization databases include coded diagnostic information at the level of an entire population over an extended period of time. Key information on comorbidity network and early disease development can be unveiled. Chronic obstructive pulmonary disease (COPD) is an underdiagnosed condition for which it is crucial to identify early disease indicators. The identification of gender-specific conditions preceding the onset of COPD can reveal disease progression patterns allowing for early diagnosis and intervention. Besides well-known risk factors such as tobacco smoking, the appearance of preceding conditions could substantiate the individual risk for the development of COPD. The objective was to investigate the hospitalization history of patients newly diagnosed with COPD and to retrace a gender-specific trajectory of coded entities prior to the onset of COPD.

Methods: A population-wide hospitalization database including information about all hospitalizations in Switzerland between 2002 and 2018 was used. All COPD cases were extracted from the database and comorbidities occurring prior to the onset of COPD identified. Comorbidities significantly over-represented in COPD compared with a 1:1, age- and sex-matched control population were further scrutinized. The longitudinal evolution of the diagnoses preceding COPD were analyzed using between-class principal component analysis and validated using an independent data set.

Results: Between 2002 and 2018, 697'714 hospitalizations with a COPD diagnosis were recorded in Switzerland. Sixty-two diagnoses were significantly over-represented before the initial diagnosis of COPD. These preceding comorbidities included conditions with both well-established and novel link to COPD. Common early pre-conditions included diagnoses of nicotine and alcohol abuse and obesity, followed by cardiovascular diseases (Fig 1). Comorbidities occurring at a later stage close to the onset of COPD included atrial fibrillation, diseases of the genitourinary system and pneumonia. Atherosclerotic heart diseases were more prevalent in males, whereas female-specific pre-conditions included heart failure, hypothyroidism, varicose and intestinal disorders. Disease trajectories could be confirmed using an independent data set.

Conclusions: Gender-specific COPD disease trajectories highlight early indicators and pathogenetic links between COPD and antecedent diseases and could allow for early detection and intervention.



P61

Impact of the COVID-19 pandemic on emergency outpatient consultations and admissions of non-COVID-19 patients (ECCO) – a cross-sectional study

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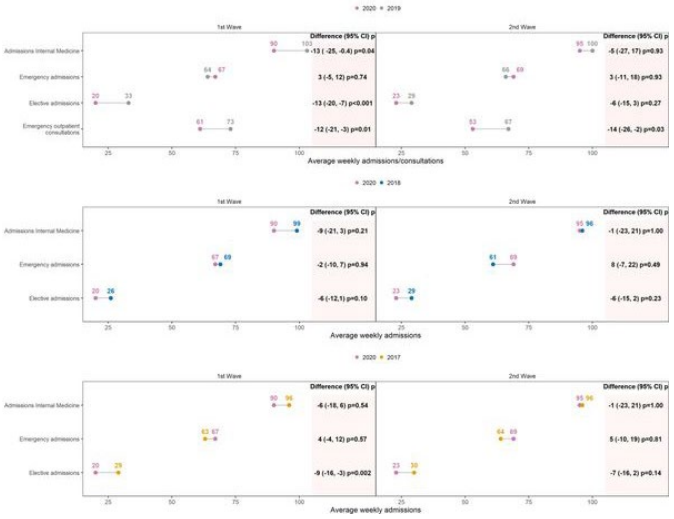
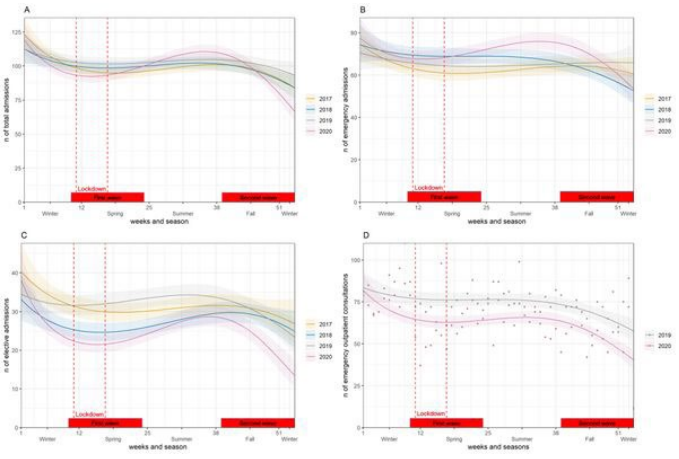
During the first year of the COVID-19 pandemic, healthcare facilities worldwide struggled to provide adequate care for the increasing load of COVID-19 patients while trying to maintain the quality of treatment for all other patients. The aim of this study was to evaluate the shift and the undersupply of non-COVID-19 patients in a hospital medical department in Switzerland.
In this retrospective cross-sectional study, internal medicine admissions from 2017 to 2020, emergency outpatient visits from 2019 to 2020 and COVID-19 admissions in 2020 were analyzed and compared through a regression model. Medicine admissions were also stratified by diagnosis. A questionnaire was used to understand the pandemic experience of local general practitioners, referring hospitals and nursing homes.
Total admissions decreased during the 1st and 2nd wave of the pandemic but increased between the two waves. Elective admissions decreased in 2020 compared to the other years: i.e. they were 1298 (25% of total admissions) in 2020 versus 1692 (31%) in 2019, p = <0.001. Admissions for emergency reasons increased: 3724 (71%) in 2020 versus 3476 (64%) in 2019, p < 0.001. Emergency outpatient consultations decreased in 2020 compared to 2019, 62.77 (14.70), mean (SD), weekly visits in 2020 versus 74.13 (13.98) in 2019, p<0.001.
The majority of general practitioners and heads of referring hospitals also reported a decrease in consultations, especially during the 1st wave of the pandemic. Mental illnesses, anxiety or burn-out were perceived among patients and among staff in general practices and nursing homes.





COVID-19 pandemic negatively affected the care of non-COVID-19 patients, in particular those with chronic illnesses. A shift of health care resources from non-COVID patients to COVID patients was observed. These findings could help institutions to better manage the situation in the future.

P62

Pain medication use in musculoskeletal injuries: disproportionate increase in strong opioid use and treatment costs with wide variation across Swiss cantons

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Introduction: Opioid use in Switzerland has increased over the past years. To date it is unknown what the underlying reasons are. Musculoskeletal injuries are a major contributing factor for chronic pain. The aim of this study was to assess whether opioids are increasingly used for musculoskeletal injuries as an indicator for more liberal opioid prescription practices in Switzerland.

Methods: We assessed pain medication use between 2008 and 2018 for minor and major musculoskeletal injuries in the working population using representative data from the largest accident insurer in Switzerland (SUVA). We calculated annual pain medication use, treatment days, and health care costs for minor and major musculoskeletal injuries. We calculated pain medication use per 1000 injuries by canton and the variation across Swiss cantons using the extremal quotient (EQ, the highest divided by the lowest rate).

Results: In total, 1'930'114 cases with musculoskeletal injuries (minor injuries 591'764 (30.7%), major injuries 1'338'350 (69.3%)) with ≥1 pain medication were analyzed. The proportion of musculoskeletal injuries with pain medication increased by 9.5% between 2008 and 2018. The use of metamizole (+254%), strong opioids (+90.2%), coxibs (+86.2%) was larger compared to other pain medications (paracetamol +28.3%, NSAIDs +3.6%, and weak opioids -5.7%). Strong opioids were increasingly used in minor (+94.9%) and major injuries (+90.0%). Whereas treatment costs per day decreased for most medications, the costs increased for strong opioids (minor injuries +204%, major injuries +33%). Use of strong opioids per 1000 cases varied by a factor of 3.5 for all injuries between Swiss cantons (Figure), for minor injuries by a factor of 3.2 and for major injuries by a factor of 3.9.

Conclusion: We observed a disproportionate increase in the use of metamizole, strong opioids, and coxibs compared to other pain medications. Strong opioids were increasingly used in minor and major injuries indicating a more liberal prescription practice. There was a substantial variation across Swiss cantons and the increased use of strong opioids was associated with increased treatment costs.

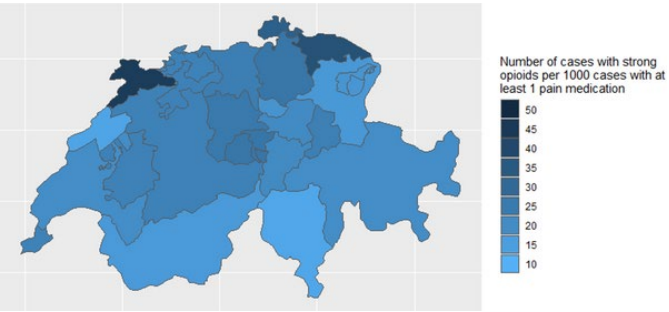

Figure: Strong opioid use per 1000 musculoskeletal injuries per Swiss canton

P63

Patient groups excluded in large lipid-lowering medication trials with cardiovascular outcomes - a systematic review and meta-analysis

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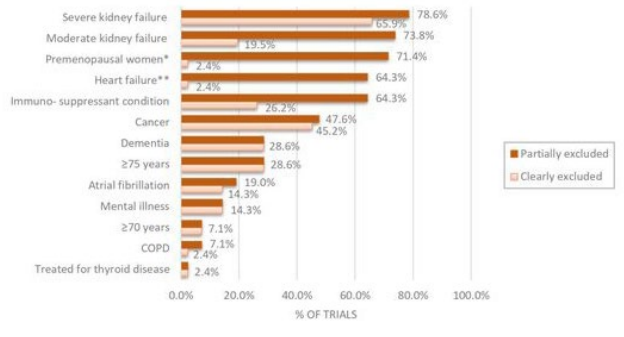
Introduction: Participants in randomized clinical trials (RCTs) might not be representative of the real-world population due to specific exclusion criteria[1,2]. The proportion of older adults, adults with multimorbidity and the exclusion rate of specific groups in RCTs is currently unclear.

Methods: We obtained all trials from the Cholesterol Treatment Trialists Collaboration (CTTC) website and additionally performed a systematic review for large (n≥1000) lipid-lowering RCTs with a 2-year minimum follow-up; defining lipid-lowering trials as trials of statins, ezetimibe and PCSK-9 inhibitors. Multimorbidity was defined as ≥2 chronic diseases and calculated from baseline tables, if unreported. We predefined groups of interest: older adults (≥70 or ≥75 years), women, non-whites, chronic kidney failure (CKD) defined as eGFR <45 ml/min (moderate) or eGFR< 30ml/min (severe), heart failure (HF) according to NYHA classification, immunosuppressant conditions, cancer, dementia, treated thyroid disease, chronic obstructive pulmonary disease (COPD), mental illness, atrial fibrillation, and patients with polypharmacy. For each trial, we extracted the proportions of patients of the predefined groups from baseline tables, as well as of multimorbidity. We then meta-analyzed the prevalence to obtain a pooled estimated with a random-effects model.

Results: We included 42 RCTs (298'605 participants), thereof 32 of the CTTC and 10 from our systematic review. 79%(n=32) of the trials excluded participants with severe and 74%(n=31) those with moderate CKD. 64%(n=27) of the trials excluded participants with moderate to severe HF (ranging from NYHA II-IV), 64%(n=27) those with immunosuppressant conditions, 48%(n=20) those with cancer, 29%(n=12) those with dementia, and 29%(n=12) excluded older adults. The exclusion rates for the remaining groups were <20%. The pooled prevalence was 25%(95%CI 0.0-49%) for participants ≥70y. No trial specifically mentioned multimorbidity or polypharmacy as an inclusion or exclusion criterion. The pooled prevalence of multimorbidity calculated from baseline tables was 51%(95%CI 38-63%). Due to non-reporting, it was not possible to calculate pooled prevalence of other groups or of polypharmacy.

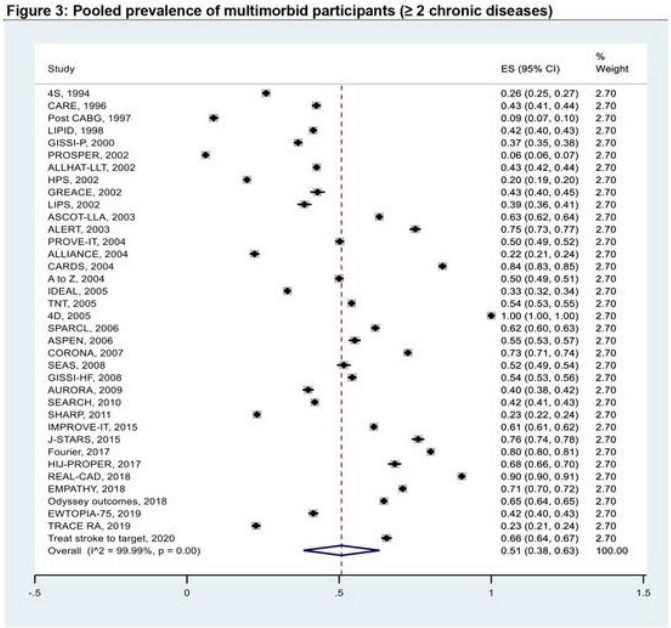
Conclusions: Over half of the trials excluded participants with moderate to severe CKD, HF or immuno-suppressant conditions. Future trials should attempt to minimize exclusion of relevant conditions and emphasize the inclusion of older adults with multimorbidity.

Figure 1: Percentage of RCTs excluding specific predefined groups of interest



Partially excluded: Part of group excluded (e.g. not any HF, but only participants with specific NYHA-stages excluded). Clearly excluded: Whole group defined as exclusion criterion. No trial specifically defined multimorbidity, polypharmacy or non-whites as an exclusion criterion (0.0%; not shown in the graph). *Women: Group of childbearing potential, pregnant or lactating women excluded. n=1 trial excluded all women. ** HF: n=1 excluded all HF, n=2 all HF requiring treatment with digitalis or diuretics, or vasodilators; n=2 all with NYHA II-IV, n=10 all with NYHA III-IV, n=4 if EF<25 or EF<30%, n=1 if "symptomatic" HF or EF <35%, n=1 if "severe" HF, n=1 systolic HF, n=5 decompensated HF

Figure 3: Pooled prevalence of multimorbid participants (≥ 2 chronic diseases)



P64

Persistent symptoms and functional impairment in SARS-CoV-2 positive and negative individuals

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Introduction: Persistent symptoms of SARS-CoV-2 are prevalent several weeks to months following the infection. To date, it is difficult to disentangle the direct from the indirect effects of SARS-CoV-2, including lockdown, social and economic factors. This study aims to characterize the prevalence of symptoms, functional capacity and quality of life at 12 months in outpatient symptomatic individuals tested positive for SARS-CoV-2 compared to individuals tested negative.

Methods: From April 23 to July 27, 2021, individuals tested for SARS-CoV-2 at the outpatient testing center of the Geneva University Hospitals were contacted 12 months after their test date. Only individuals with a laboratory-confirmed test were included in this study. Measurements included the prevalence of COVID-related symptoms, functional capacity and quality of life.

Results: At 12 months, out of the 1,447 included participants (mean age 45.2 years, 61.2% women), an adjusted estimation of 30.3% of persons reported residual mild to moderate symptoms following SARS-CoV-2 infection compared to 13.0% in the control group, with more functional impairment in the SARS-CoV-2 infected group. SARS-CoV-2 infection was associated with the persistence of symptoms and functional impairment overall and in subgroups of women, individuals younger than 50 years, and in individuals with no past medical or psychiatric history.

Conclusion: SARS-CoV-2 infection leads to persistent symptoms over several months including in young healthy individuals, in addition to the pandemic effects, and potentially more than other common respiratory infections. Symptoms impact functional capacity up to 12 months post-infection.

Table 1. Prevalence and number of symptoms in individuals tested positive and individuals tested negative for SARS-CoV-2 at 12 months†*

Symptom	SARS-CoV-2 Positive (n=287)	SARS-CoV-2 Negative (n=1,160)	P-Value
	% (95% CI)	% (95% CI)	
Any symptom	33.4 (31.3-35.5)	6.5 (6.1-6.8)	<0.001
Fatigue	16.0 (14.4-17.5)	3.1 (2.7-3.3)	<0.001
Loss or change in smell	10.0 (8.6-11.5)	1.7 (1.6-1.9)	<0.001
Loss or change in taste	10.3 (7.8-12.8)	1.5 (1.2-1.9)	<0.001
Dyspnea	8.9 (6.6-11.2)	1.1 (0.9-1.3)	<0.001
Headache	9.8 (8.4-11.2)	1.7 (1.5-2.0)	<0.001
Insomnia	8.9 (5.4-12.3)	2.7 (1.6-3.9)	<0.001
Difficulty concentrating/Loss of memory	7.4 (5.8-9.1)	2.5 (2.0-3.0)	<0.001
Mental exhaustion	6.9 (5.0-8.8)	1.4 (1.1-1.7)	<0.001
Paresthesia	5.4 (3.1-7.8)	1.9 (1.5-2.3)	<0.001
Dizziness/Lack of equilibrium	6.4 (4.4-8.5)	1.8 (1.0-2.5)	<0.001
Cough	6.5 (3.4-9.7)	3.2 (1.8-4.6)	0.033
Chest pain	6.0 (2.9-9.2)	4.0 (2.3-5.7)	0.214
Palpitations	3.8 (1.6-6.1)	1.6 (0.6-2.5)	0.032
Myalgia	7.3 (6.2-8.4)	1.7 (1.5-1.9)	<0.001
Arthralgia	2.9 (2.0-3.9)	2.0 (1.7-2.4)	0.050
Digestive symptoms (nausea, vomiting, diarrhea, abdominal pain)	4.0 (3.0-4.9)	1.6 (1.2-2.0)	<0.001
Number of symptoms			
None	67.8 (65.8-69.7)	93.6 (93.2-93.9)	<0.001
1 symptom	10.6 (10.1-11.1)	2.7 (2.6-2.9)	<0.001
2 symptoms	4.8 (4.5-5.0)	1.0 (0.9-1.1)	<0.001
3 symptoms	5.0 (4.7-5.3)	0.9 (0.8-1.0)	<0.001
4 symptoms	2.8 (2.6-3.0)	0.5 (0.4-0.5)	<0.001
5-10 symptoms	7.8 (7.2-8.5)	1.1 (1.1-1.2)	<0.001
≥ 11 symptoms	1.1 (1.0-1.2)	0.1 (0.1-0.1)	<0.001

Table 1. Prevalence and number of symptoms in individuals tested positive and individuals tested negative for SARS-CoV-2 at 12 months

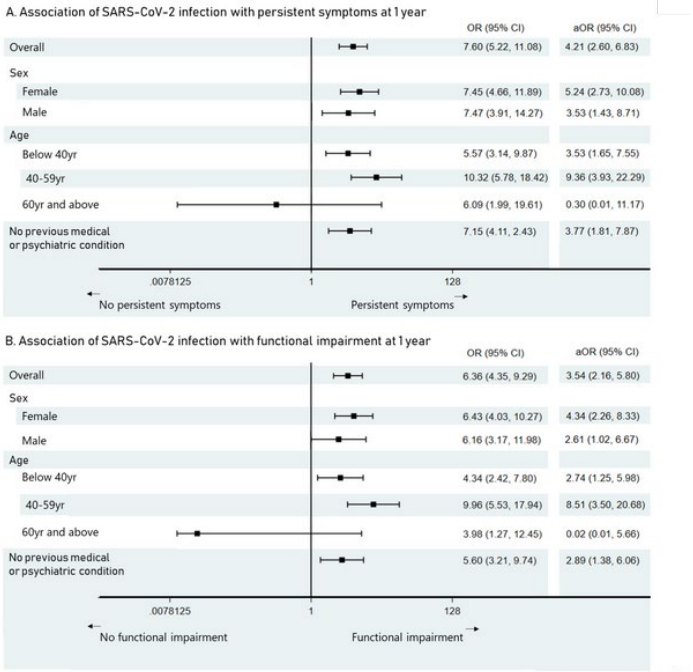

Figure 1. Associations between laboratory-confirmed SARS-CoV-2 infection and the persistence of symptoms and functional impairment at 1 year stratified by sex, age categories, and pre-existing medical conditions (n=1,245)

P65

Regional variation of bariatric surgery in Switzerland. A population-based small area variation analysis

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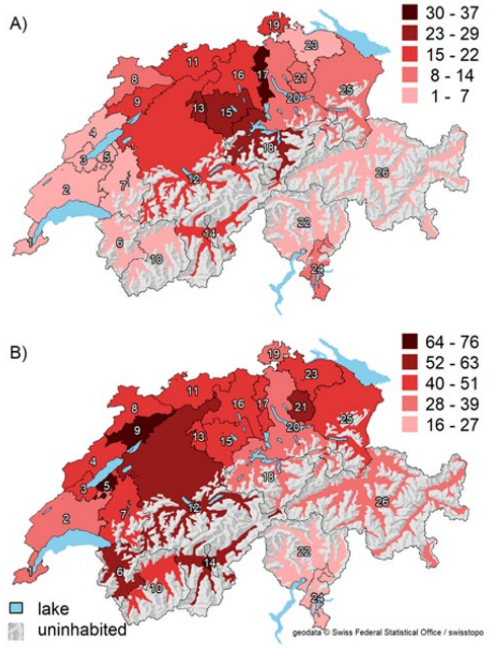
Background: Bariatric surgery – mainly sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB) – is increasingly used in severely obese patients. We assessed the regional variation in bariatric surgery rates in Switzerland and potential determinants for such variation.

Methods: We conducted a population-based analysis using discharge data from all Swiss acute care hospitals from 2013–2018. We derived hospital service areas (HSAs) by analyzing patient flows, calculated age-standardized mean procedure rates and measures of regional variation (extremal quotient [EQ], i.e., the highest divided by the lowest rate, systematic component of variation [SCV], defined as the non-random part of variation). SCV values >5.4 indicate a high, >10 a very high variation. We assessed the determinants of regional variation with multilevel regression models, adjusting for demographics, socioeconomic factors, population health, and number of general surgeons per population.

Results: 23,204 bariatric surgeries were performed in 26 HSAs from 2013-2018. Sleeve gastrectomy rates increased by 10%, gastric bypass rates remained stable during this period. The fully adjusted sleeve gastrectomy and gastric bypass rates varied between 2-31/100,000 and 21-74/100,000 persons across HSAs (Figure). The overall (EQ 2.8, SCV 7.8) and procedure specific regional variation (sleeve gastrectomy EQ 15.6, SCV 42.2; gastric bypass EQ 3.5, SCV 10.2) was high to very high. In multilevel regression, women had a 182% higher bariatric surgery rate. French/Italian language areas had a 39% lower bariatric surgery rate than German speaking areas. Areas with higher proportion of patients with diabetes had a 28% lower overall intervention and a 269% higher sleeve gastrectomy rate. A higher proportion of private/semiprivate insurance was associated with a 24% decrease in overall intervention rates, mainly driven by lower bypass rates. After full adjustment, the substantial part of the variation remained unexplained (overall 40.2%, sleeve gastrectomy 28.6%, gastric bypass 33.8%).

Conclusion: We found a substantial increase in sleeve gastrectomy rates between 2013 and 2018. Regional variation in overall and procedure specific rates was high to very high. Several factors, including female sex, language area, insurance status, and the prevalence of diabetes were associated with procedure rates. 28-40% of the regional procedure variation remained unexplained and most probably represents differing physician practices.

Figure. Fully adjusted map of (A) sleeve gastrectomy and (B) gastric bypass surgery rates across 26 Swiss HSAs



Abbreviation: HSA = hospital service area.

Average predicted procedure rates for each HSA are shown as red-scale categories per 100,000 persons. Adjusted for year, age, sex, language region, Swiss neighborhood index of socioeconomic position (SSEP), insurance status, Swiss citizenship, population density, burden of disease, percentage of diabetes, and the density of general surgeons.

P66

The pandemic toll and post-acute sequelae of SARS-CoV-2 in healthcare workers at a Swiss University Hospital

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Introduction: Healthcare workers have potentially been among the most exposed to SARS-CoV-2 infection as well as the deleterious toll of the pandemic. Very few studies have evaluated so far the COVID-19 direct and indirect effects on healthcare workers. This study aims to differentiate the pandemic toll from post-acute sequelae of SARS-CoV-2 infection in healthcare workers compared to the general population.

Methods: The study was conducted at the Geneva University Hospitals between April 2021 and July 2021, and included all tested staff and all individuals tested for SARS-CoV-2 at the outpatient testing center at the same hospital. The primary outcome was the prevalence of symptoms in healthcare workers compared to the general population, with measures of COVID-related symptoms and functional impairment, using prevalence estimates and multivariable logistic regression models.

Results: The mean age of healthcare workers (n=3,083) was 43.8 years ± 11.0 standard deviation (SD), 72.3% were women. The mean age in the general population group (n=3,556) was 44.4 years (SD, 14.4), 56.5% were women. Healthcare workers suffered mostly from fatigue (25.5%), headache (10.0%), difficulty concentrating/loss of memory (7.9%), exhaustion/burnout (7.1%), insomnia (6.2%), myalgia (6.7%) and arthralgia (6.3%). Regardless of SARS-CoV-2 infection, all symptoms were significantly higher in healthcare workers than the general population. SARS-CoV-2 infection in healthcare workers was associated with loss or change in smell, loss or change in taste, palpitations, dyspnea, difficulty concentrating/loss of memory, fatigue, and headache. Functional impairment was more significant in healthcare workers compared to the general population (aOR 2.28; 1.76-2.96), with a positive association with SARS-CoV-2 infection (aOR 3.81; 2.59-5.60).

Conclusion: Symptoms and functional impairment in healthcare workers are increased compared to the general population, related to the pandemic toll as well as post-acute sequelae of SARS-CoV-2 infection. These findings are of concern, considering the essential role of healthcare workers in caring for all patients including and beyond COVID-19.

Table 1. Estimates of symptoms prevalence and functional impairment in healthcare workers compared to the general poulation, and in SARS-CoV-2 positive and negative healthcare workers

	Healthcare workers (n=3,083)	General population (n=3,556)	P-value	Healthcare workers (n=3,083)		P-value
				SARS-CoV-2 positive (n=1,079)	SARS-CoV-2 negative (n=2,004)	
Symptoms						
Fatigue	25.5 (25.0-26.0)	5.5 (5.3-5.6)	<0.001	32.5 (31.7-3.2)	21.4 (20.9-21.9)	<0.001
Headache	10.0 (9.7-10.3)	3.4 (3.3-3.5)	<0.001	13.3 (12.7-13.9)	7.8 (7.4-8.1)	<0.001
Difficulty concentrating/ Loss of memory	7.9 (7.6-8.2)	2.6 (2.5-2.7)	<0.001	13.4 (12.9-14.0)	4.6 (4.4-4.8)	<0.001
Exhaustion/Burnout	7.1 (6.9-7.4)	1.8 (1.7-1.9)	<0.001	9.2 (8.8-9.6)	6.3 (6.0-6.5)	<0.001
Insomnia	6.2 (6.0-6.4)	1.2 (1.2-1.3)	<0.001	7.8 (7.5-8.2)	5.3 (5.1-5.6)	<0.001
Myalgia	6.7 (6.5-6.9)	2.3 (2.3-2.4)	<0.001	8.9 (8.5-9.4)	6.3 (6.0-6.5)	<0.001
Arthralgia	6.3 (6.1-6.5)	1.4 (1.3-1.4)	<0.001	8.8 (8.3-9.3)	5.5 (5.2-5.8)	<0.001
Dyspnea	5.2 (4.9-5.4)	2.2 (2.1-2.4)	<0.001	12.0 (11.2-12.8)	2.6 (2.4-2.8)	<0.001
Loss or change in smell	7.2 (6.8-7.6)	5.8 (5.5-6.0)	<0.001	17.3 (16.6-17.9)	1.7 (1.5-1.8)	<0.001
Loss or change in taste	4.8 (4.5-5.1)	4.0 (3.8-4.2)	<0.001	12.1 (11.5-12.8)	0.9 (0.8-1.1)	<0.001
Cough	2.8 (2.6-2.9)	1.2 (1.1-1.2)	<0.001	4.5 (4.2-4.8)	1.8 (1.7-1.9)	<0.001
Palpitations	2.3 (2.1-2.5)	0.8 (0.7-0.8)	<0.001	5.1 (4.5-5.7)	0.9 (0.6-1.2)	<0.001
Chest pain	1.3 (1.2-1.5)	0.7 (0.7-0.8)	<0.001	2.2 (1.8-2.6)	1.3 (1.2-1.5)	<0.001
Stress	3.5 (3.4-3.6)	1.3 (1.3-1.4)	<0.001	2.7 (2.5-2.9)	4.2 (4.0-4.4)	<0.001
Functional impairment						
None	79.2 (78.5-79.9)	86.9 (86.2-87.0)	<0.001	57.9 (56.8-59.0)	91.1 (90.6-91.5)	<0.001
Mild	9.9 (9.6-10.2)	7.0 (6.8-7.2)	<0.001	17.1 (16.8-17.4)	4.8 (4.6-5.0)	<0.001
Moderate	7.9 (7.6-8.2)	4.8 (4.6-5.0)	<0.001	17.7 (17.2-18.3)	3.2 (3.0-3.4)	<0.001
Severe	2.9 (2.8-3.1)	1.6 (1.5-1.7)	<0.001	7.2 (6.9-7.6)	0.9 (0.8-1.0)	<0.001

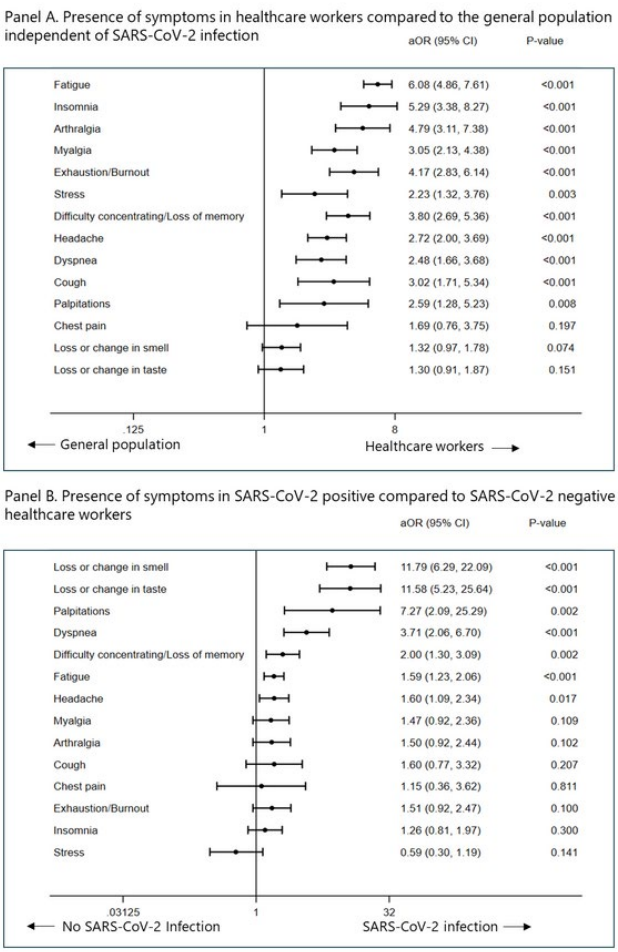

Figure 1. Symptoms prevalence in SARS-CoV-2 infected and non-infected healthcare workers and the general population

P67

Trajectories of SARS-CoV-2 antibodies in health care workers of a cantonal hospital during the first and second pandemic wave

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Introduction: Health Care Workers (HCW) are at highest risk for SARS-CoV-2 infection, baring the general populations' infections risk but additionally being closely exposed during work. Excess seroconversion rates may guide profession-specific interventions to ensure optimal personal protection measurements.

Methods: We investigated the SARS-CoV-2 seroprevalence among HCW during the first and second pandemic wave (spring, summer, and winter 2020/21). Voluntary serological testing was performed by Liaison SARS-CoV-2 S1/S2 IgG (Diasorin, Italy). Potential associations between participant characteristics and seroprevalence were assessed by age and sex adjusted logistic regression models (Stata Vers.17).

Results: A total of 1'350 HCW were included. Seroprevalence among HCW increased over time: during / after the first pandemic wave in April / May and June/July 2020 2.2% (95% CI, 1.4-3.4) and 4.2 (95% CI, 3.0-5.8) tested positive, respectively, in January 2021, 15.6% (95% CI 13.1-18.2) of HCW were seropositive. Stratified by profession and self-reported contact, nursing staff had a significantly higher seroconversion risk than other professions with patient contact and staff without patient contact (Odds ratio 2.17; 95% CI, 1.13-4.17; p=.02). During the observation period, two seropositive individuals experienced a positive SARS-CoV-2 polymerase chain reaction (PCR) test, both 270-275 days after the first positive serology.

Conclusion: Among HCW, nursing staff with frequent and direct prolonged patient contacts had the highest risk of SARS-CoV-2 anti-spike IgG seroconversion. Seropositivity among participants without patient contact mirrors the populations epidemiology. Early targeted interventions among high risk HCW groups are needed for sustained personal protective measurement compliance.

P68

Accuracy and feasibilty of a commercial SARS-CoV-2 Interferon-γ Release Assay (QuantiFERON SARS-CoV-2®) – a preliminary laboratory routine set-up evaluation in hemodialysis patients

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Introduction: The assessment of SARS-CoV-2 specific T cell responses is not established in clinical routine. We evaluated the feasibility and accuracy of a commercial Interferon-γ (IFN-γ) Release Assay (IGRA; QuantiFERON, Qiagen) in hemodialysis (HD) patients.

Methods: 20 HD and 10 healthy control participants were evaluated. IFN-γ secretion in whole blood was evaluated by SARS-CoV-2 IGRA (spike; Ag3) before and after mRNA booster immunization (Spikevax®; HD: double dose). Spike antibodies (Ab) were evaluated in parallel by ABCORA 2 (Inst. of Medical Virology, University of Zurich). Statistical analyses were performed by Prism 9.1.

Results: 19/20 HD participants provided valid results (one indeterminate results). At baseline, 6/19 (32%) HD participants had a negative IFN-γ result (cut-off 0.15 IU/mL). IFN-γ T cell responses increased after booster immunization (p=.02), rendering positive results in all HD. Mean IFN-γ responses were comparable to healthy controls (p=.43). Similarly, a significant increase of anti-spike IgG (S2) was observed (p<.001). Although pre-booster IgG levels were lower in HD participants (p=.006), levels post-boost were comparable to controls (p=.14). Nucleocapsid Ab responses remained negative.

Conclusion: The measurement of a specific T cell response by IFN-γ secretion is feasible. The increase of IFN-γ is paralleled by an increase in IgG Ab after booster immunization, not being different in HD to healthy participants. The clinical relevance remains unknown; further prospective studies are warranted.

P69

BabelDr: a medical speech to sign translation tool

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Introduction: Accessible information has to be offered to linguistic minorities who require it. BabelDr focuses on the accessibility of medical information and aims to automatically translate French triage questions (from «Échelle de tri Suisse») and instructions for linguistic minorities.[1] Nearly 10,000 French medical sentences selected with doctors were manually pre-translated in different languages (Arabic, Farsi, Dari, Tigrinya, Albanian, simple English & Spanish), which ensures reliable and cultural translations. At run time, the BabelDr app allows the doctor to express himself orally. Speech recognition is used to transcribe doctor's interaction. The result is then automatically linked to the closest pre-translated sentences. This suggestion, if validated by the physician, is translated into the language of the patient. The patient replies non-verbally or by pictograms. The app has been used since 2019 at HUG. We describe here how we extend the system to Swiss French Sign Language (LSF-CH), a language spoken by 1,700 people in Switzerland. [2]

Methods: The LSF videos were produced with SigLa, an online platform developed by UNIGE to generate animated virtual avatars using the JASigning technology (Fig. 1). Animations are generated from G-SiGML notation.[3] This code is produced from various linguistic resources, including a glossary that describes individual manual signs with the HamNoSys language (hand movements) and a grammar that models the link between the medical sentences and the corresponding sign language representation. The grammar indicates how manual signs are combined into sequences and adds non-manual elements (eyes gaze, body, etc.). The linguistic description (glossary and grammar) is produced manually from human videos which are used as reference. This description is then used to produce the G-SiGML and avatar videos in a productive way.

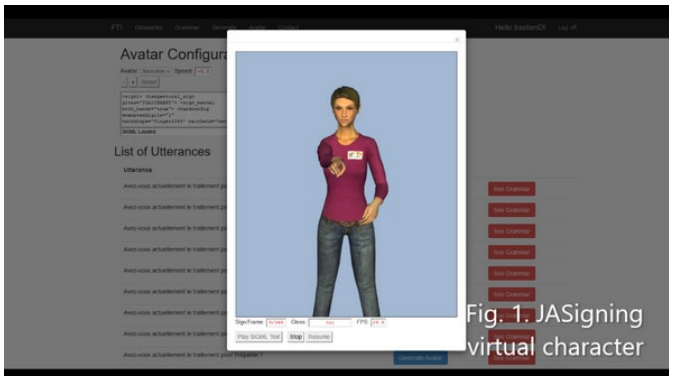

Fig. 1. JASigning virtual character

Results: Results include two unique medical corpora in LSF, one signed by a human interpreter (2,000 reference sentences) and another signed with an avatar (~1 million videos). These corpora are available upon request. Human videos are already integrated in the online BabelDr system.

Conclusion: BabelDr is the first speech to LSF system for medical communication available online. The videos constitute an important resource, which can also be used as reference by LSF interpreters, for different evaluation purposes or for training data-driven systems.

P70

Comparison between nasal and buccal self-swabbing and professional nasopharyngeal/pharyngeal swabbing: a single-centre, prospective, cohort study and survey

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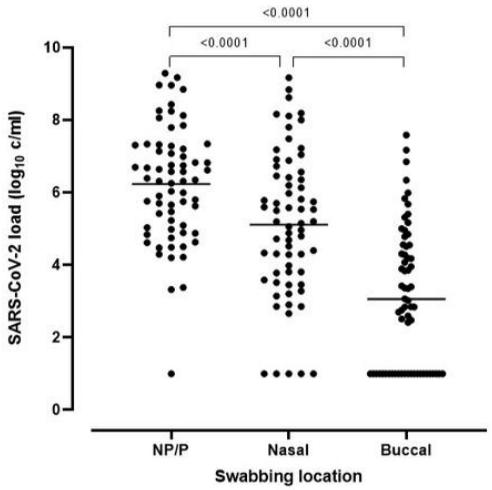
Introduction: Lateral flow assay antigen tests (RDT) are increasingly used for SARS-CoV-2 self-testing. However, sensitivity of RDT in self-collected nasal and mid-turbinate swabs is only about 80%. We aimed (i) to compare SARS-CoV-2 RNA load between self- and professionally collected combined nasopharyngeal/pharyngeal, nasal and buccal swabs and (ii) to assess convenience of sample collection in patients with confirmed or suspected SARS-CoV-2 infection.

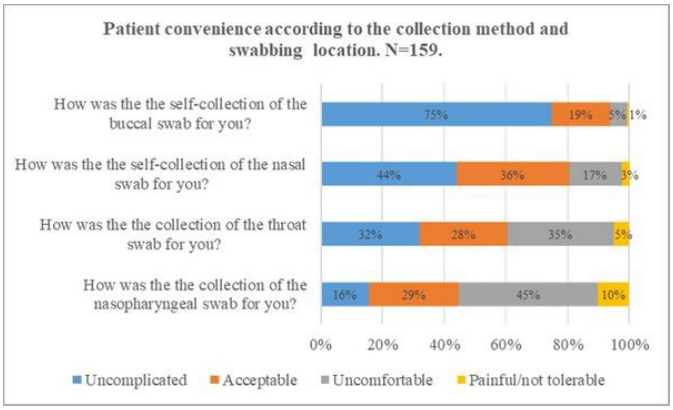
Methods: 159 patients with at least one of the typical symptoms of COVID-19 were prospectively enrolled in a Swiss tertiary hospital between January and November 2021. Written and visual instructions were provided and patients performed a nasal and a separate buccal swab before a professional combined nasopharyngeal/pharyngeal swab was collected. SARS-CoV-2 RNA loads were determined by RT-QNAT targeting the S-gene of SARS-CoV-2. Convenience of the swabbing methods and localizations was evaluated using a questionnaire.

Results: 67/159 (42.1%) patients tested positive for SARS-CoV-2. 64.2% of the patients were male and the median age was 54 years [(interquartile range (IQR) 40 – 63)]. The median SARS-CoV-2 RNA load was 6.3 $\log_{10}$ c/mL (IQR 5.0 – 7.3 $\log_{10}$ c/mL) in the professionally collected nasopharyngeal/pharyngeal swabs, 5.1 $\log_{10}$ c/mL (IQR 3.6 – 6.5 $\log_{10}$ c/mL) and 2.8 $\log_{10}$ c/mL (IQR 1 – 4.5 $\log_{10}$ c/mL) in the self-collected nasal swabs and buccal swabs, respectively (Figure 1). 5/66 (7.5%) and 23/66 (34.8%) of the nasal and buccal swabs respectively were false negative. The majority of patients (69.8%) had never performed a nasal or buccal swab before. Patients' convenience was highest with the buccal swab compared to the nasal or nasopharyngeal/pharyngeal swab (94% vs. 80% vs. 45%) (Figure 2). 145 (91.2%) and 156 (98.1%) patients stated that nasal and buccal self-swabbing respectively was easy to perform. Adherence to instructions was higher in buccal than in nasal self-swabbing (94.3% vs. 80.5%). 136 (85.5%) patients preferred self-swabbing.

Conclusions: SARS-CoV-2 self-testing using RDTs has arisen to one of the cornerstones in the current pandemic. Patients' convenience is highest with the buccal self-swabbing method but this cannot be recommended due to many false negative results. Because viral loads are lower, more sensitive RDTs are mandatory to detect SARS-CoV-2 in self-collected nasal swabs.

Figure 1. SARS-CoV-2 RNA loads according to the collection site. NP/P: professionally collected nasopharyngeal/pharyngeal swab; Nasal: nasal self-swabbing; Buccal: Buccal self-swabbing. SARS-CoV-2 loads below the limit of detection were set to 1 log10 c/mL.





P71

Diagnostics and treatment of acute non-specific low back pain – do physicians follow the guidelines?

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Background: Clinical guidelines for acute non-specific low back pain (LBP) recommend to avoid imaging studies or invasive treatments, and to advise patients to stay active. Despite these recommendations, many patients undergo diagnostic assessments and therapeutic procedures that are not in line with current evidence.

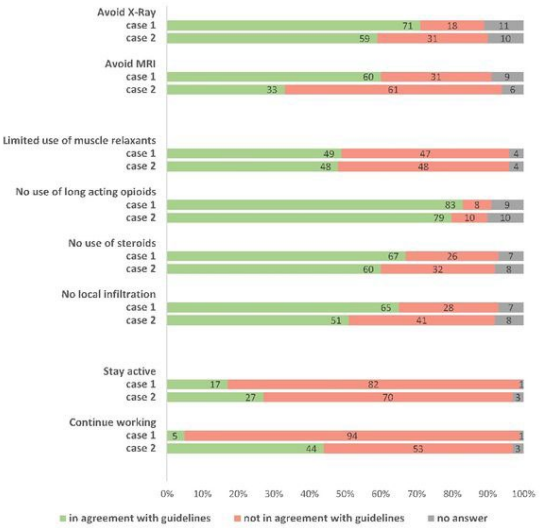
Aim: To assess current clinical practice of Swiss general practitioners (GPs) in the management of patients with acute non-specific LBP.

Methods: Cross-sectional survey using two clinical case vignettes of patients with acute non-specific LBP. The main differences between the vignettes were sex (male vs. female), age (35 vs. 54 years), profession (warehouse clerk vs. IT specialist), pain duration (10 days vs. 3-4 weeks), medical history (none vs. degenerative spine changes and disc protrusion on an MRI 8 years ago), and presence vs. absence of yellow flags.

Results: Of 1,253 GPs who completed the survey, 65% reported to know current clinical guidelines and 79% were aware of the "Swiss Choosing Wisely – Smarter Medicine" recommendations. Although both vignettes presented no red flags or neurological deficits, uncertainty about the likelihood of an underlying disc herniation was high: GPs rated a disc herniation as possible or likely in 40% in vignette 1, and in 54% in vignette 2. In contrast to guideline recommendations, a relevant proportion of GPs requested x-rays (18% and 31%,Figure) or MRI (31% and 61%). Most GPs prescribed NSAIDs, paracetamol, and/or metamizole, and would certify that the patients were unfit to work (94% and 53%). Every second GP prescribed muscle relaxants (47% and 48%) and every third GP prescribed a short course of prednisone (26% and 32%). Spinal infiltration was considered by 28% and 41%. A smaller proportion of GPs used weak opioids (11% and 16%), short- (1% and 2%) and long-acting opioids (8% and 10%). The majority of GPs recommended activity restrictions (82% and 70%) in contrast to guideline recommendations to stay active. A small proportion recommended bed rest/avoidance of any activity (3% and 2%).

Conclusion: Despite awareness of current guidelines recommendations, management of acute non-specific LBP was not in line with them. Although not recommended, a substantial proportion of Swiss GPs considered imaging, medications of unclear benefits (e.g., muscle relaxants, prednisone, long-acting opioids), spinal infiltration, and recommended activity restrictions, that may result in unintended harm to patients.

Figure: Agreement with guidelines in the management of acute non-specific low back pain



P72

Implementation of the first inpatient cardiac rehabilitation program in the canton of Geneva, (SMIR Beau-Séjour)

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Introduction: The absence of an inpatient cardiac rehabilitation center in the canton of Geneva prompted us to develop and implement the first inpatient cardiac rehabilitation program in this canton. The program is integrated in a rehabilitation unit of the Internal Medicine and Rehabilitation Service of Beau-Séjour at HUG.

Methods: To set up this program, we followed the criteria for quality and safety of care for inpatient cardiac rehabilitation dictated by SCPRS (Swiss working group for Cardiovascular, Prevention, Rehabilitation and Sports), and we benchmarked with other inpatient cardiac rehabilitation centers in Switzerland. The have established a financial budget. Training courses for the medical and nursing staff as well as for physiotherapists were organized. A major emphasis was placed on interdisciplinary work as well as on the integration of the patient in his care. Exclusion criteria were clearly defined. A clinical itinerary process was set up as well as a promotion of the program. Process and outcome indicators were defined and monitored every 3 months according to the ANQ (Association National Qualité).Finally a schedule of 3 phases was defined: phase 1 with 6 beds available, phase 2 with 12 beds available and phase 3 with 18 beds available in the cardiac rehabilitation unit.

Results: From November 1, 2020 to September 1, 2021 (end of phase 1), 68 patients were recruited. The average bed filling rate was 70%.The average age of patients was 65 years ± standard deviation (SD) 37.4 and mostly being males (75%). The average time to transfer from acute care to the cardiac rehabilitation unit was 5 days (±SD 3.5). The most common indication for inpatient cardiac rehabilitation was post-myocardial infarction (45%), followed by post-valvular surgery (20%), then chronic heart failure (17%) and post-coronary artery bypass grafting (13%). The complication rate occurring during the program was 5.8%. No deaths occurred during the rehabilitation stay. Quality of life was assessed with the Mac New Heart questionnaire. The average global score of the Mac New Heart on a scale of 1 (1=very limited) to 7 (7=not limited at all), was 4.47 points at admission and 5.54 at discharge.

Conclusion: We confirm the need for an inpatient cardiac rehabilitation center in the Geneva Canton. We validated the launch of phase 2 with 12 available beds, to increase the capacity and offer optimal cardiovascular secondary prevention in this region .

P73

Medical organization and patient safety of a Swiss large venue COVID-19 vaccination site

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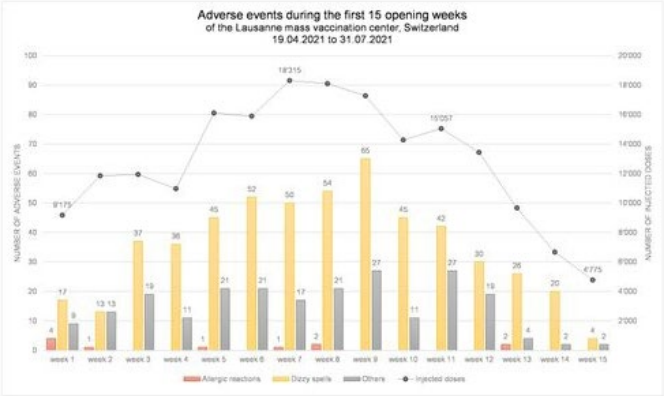
Introduction: The large-scale vaccination against COVID-19 is unprecedented in the era of modern medicine, bringing many logistical and medical challenges. In January 2021, lack of experience about potential adverse events (AE) in mass vaccination centers complicated the planning, organization and sizing of the medical staff. The Lausanne mass vaccination center (Switzerland) was set up in a congress center, aiming to administer over 2'500 injections per day. We expected 4-7 daily benign AEs and one anaphylaxis every 40 days. An internist, an allergist and an emergency physician were on site to best manage AEs in an advanced medical post, with an ambulance available. Herein, we aim to assess patient safety during the first 15 functioning weeks.

Methods: Data were collected in a medical-administrative dataset, including on-site prevaccination assessments, number (frequency) and type of AEs, and description of on-site medical management of vaccination-associated AEs.

Results: During the first 15 weeks, adults showed up for 193'502 injections. After screening questions, 27'872 cases were addressed to advanced prevaccination sorting, of which 2'371 were allocated to a prolonged post-vaccination surveillance. 422 vaccinations were postponed due to: recent SARS-CoV-2 infection 182/422 (43%), relevant allergic conditions 58/422 (14%), fever or active infection 46/422 (11%), obstetrical reasons 20/422 (5%), and other reasons 116/422 (27%). 427 other cases were postponed without prevaccination sorting.
Out of the 192'653 injected doses, 771 situations (0.4%) received medical post-vaccination assessment.The most common condition was dizzy spells (536; 0.3%). 10 patients (0.005%) presented class I or II anaphylactic reactions with one patient transferred to an emergency room for diffuse angioedema, without respiratory nor cardiovascular distress. (Figure 1).

Conclusions: Adequate online and on-site algorithms for prevaccination screening contributed to the successful medical management of this mass vaccination center with only a limited number of AEs. In hindsight, having three doctors on-site to ensure patient safety was not necessary. Yet, mismanagement of a serious adverse event could have been devastating for population willingness towards getting vaccinated, at a time when public concerns were high. This information may be useful for future planning of vaccination center set-ups.



P74

Patient and physician perspectives on statin (dis)continuation in older adults for primary prevention: a mixed-methods study

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Background: Evidence for statin use in primary cardiovascular prevention in older patients is limited. When evidence on risk-benefit profile of a medication is uncertain, using it or not becomes a preference-sensitive decision. Furthermore, data regarding patient and healthcare provider perspectives about statin (dis)continuation are scarce. We assessed patient and physician perspectives on statin (dis)continuation in older adults for primary prevention.

Methods: We used a mixed-methods research design, conducting in parallel focus groups (FGs) with 14 patients and 18 physicians (general practitioners (GPs), internists, cardiologists, neurologists) and a survey among 47 patients. All patients were aged ≥70 years and taking a statin for primary cardiovascular prevention.

Results: Patients were ambivalent towards discontinuing statins; on the one hand fearing adverse cardiovascular events if discontinued, but on the other hand hoping for relief from statin adverse effects and looking forward to taking less medications. In this context, patients relied on their GP for decision-making, although some patients wanted to ultimately make the decision to (dis)continue the statin by themselves. Physician knowledge and beliefs about statin (dis)continuation varied across specialities. Neurologist and cardiologist choice to (dis)continue was mostly based on evidence from statins in secondary prevention or in younger patients, whilst internist and GP choice was more patient-focused. Nevertheless, all physicians emphasized the importance of patient involvement in decision-making. Decision-making regarding statin (dis)continuation was most frequently deferred to GPs, while specialists reported rarely facing this question. GPs reported difficulties, such as a lack of evidence about statin (dis)continuation in this age group or fear of making the patient feel as if they were no longer worthy of treatment, for example because of their older age. GPs and internists were less willing to discontinue a statin prescribed by a specialist.

Conclusion: Physicians emphasized the importance of patient involvement in decision-making. Many patients relied on their GP for decision-making regarding statin (dis)continuation, yet GPs felt unable to offer evidence-based advice. Thus, more evidence on the role of statins in older adults for primary prevention is needed. Moreover, tools to help physicians convey risks and benefits of statin (dis)continuation to patients should be developed.

P75

Patients' preference for participation in medical decision-making secondary analysis of the BEDSIDE-OUTSIDE trial

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Introduction: Patients may prefer different levels of involvement in decision-making regarding their medical care. We investigated associations of patients' decisional control preference (DCP) with their medical knowledge and perceived quality of care during hospitalization.

Methods: This is a secondary analysis of a randomized controlled multicenter trial conducted at medical divisions of three tertiary Swiss hospitals between 2017 and 2019. The primary outcome was patients' subjective average knowledge of their medical care, (rated on a visual analogue scale from 0 to 100). We classified patients as active, collaborative or passive control preference according to the Control Preference Scale.

Results: Among the 761 included patients, those with a passive DCP had a similar subjective average knowledge (points) (81.3 ±19.4) compared to patients with a collaborative DCP (78.7 ±20.3) and active DCP (81.3 ±21.5) (p=0.59). Patients with an active vs. passive DCP reported significant less trust in physicians (adjusted difference, -5.08 points [95% CI, -8.69 to -1.48], p=0.006) and in nurses (adjusted difference, -3.41 points [95% CI, -6.51 to -0.31], p=0.031). Also, patients with an active vs. passive DCP were significantly less satisfied with their hospital stay (adjusted difference, -7.17 points [95% CI, -11.01 to -3.34], p<0.001).

Conclusions: Patients with an active DCP have lower trust in the healthcare team and lower overall satisfaction despite similar medical knowledge. Knowledge of a patients' DCP may help to individualize and improve the patient-physician relationship and increase their satisfaction with medical care.

P76

Predictors of functional recovery and hospital discharge after neurorehabilitation

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Introduction: Several indicators are associated with prognosis in neurorehabilitation. This study aimed to identify predictors of functional recovery and home discharge (HD) among hospitalized patients undergoing a specialized neurorehabilitation program in the University Hospitals of Geneva.

Methods: Observational retrospective study carried out in the neurorehabilitation center. Hospitalized patients admitted to the neu-

rorehabilitation programs from 01.01.2018 to 30.04.2020 were included in the analysis. Clinical data from medical records was automatically extracted. The main outcomes were functional recovery defined as Δ Functional Independence Measure (FIM at discharge - FIM at admission) ≥ 10, or a Montebello rehabilitation factor score (MRFS) ≥ 0.5, together with the rate of HD. Univariate and Multivariate logistic regression models were used to determine factors associated with each of the three outcomes.

Results: Of a total of 701 patients, 47.2% were female, aged of 66.6 ± 17.4 y, with a mean length of stay of 24.8 ± 25.9 days. The most frequent diagnosis was stroke (60.6%). FIM at admission was of 77.8 ± 32.5, with a proportion of 32.1% and 18.1% of patients who presented a Δ FIM ≥ 10 and a Montebello Score ≥ 0.5 by the end of hospitalization, respectively. HD was organized in 75.3% of cases (15.1% institutionalized). According to the Δ FIM, longer length of stay was associated with better recovery (OR: 1.05; 1.04 - 1.06 95% CI; p <0.001), while higher the comorbidities score (CIRS) lowered the chance of presenting Δ FIM ≥10 (OR: 0.96; 0.94, 0.99 95% CI; p = 0.016). Regarding MRFS, each additional day of hospitalization increased recovery by 2%. A higher comorbidity burden was inversely associated with recovery, as one supplementary point in the CIRS lowered by 4% the chance of having a MRFS ≥ 0.5. Being under antidepressants was associated with worse recovery (OR: 0.37; 0.18, 0.79 95% CI; p = 0.010). HD was associated with lower functional status at admission, as well as a higher functionality at discharge. On the other hand, the use of antipsychotics was negatively associated with HD (OR: 0.49; 0.30 - 0.80 95% CI; p = 0.004).

Conclusions: Regarding functionality recovery, longer length of stay was associated with better recovery while higher CIRS lowered the chance of presenting Δ FIM ≥10 and MRFS ≥ 0.5.
HD patients had lower age, and a lower functionality at admission and higher functionality at discharge was associated with HD.

P77

Quality and variation of care for chronic kidney disease in Swiss general practice: a retrospective database study

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Introduction: Large-scale clinical databases can identify gaps in quality of care in real-life practice. In particular, they allow assessing management of conditions subject to specific guidelines such as chronic kidney disease (CKD). Literature about care for CKD is scarce, especially concerning potentially unwarranted variation. With our study, we therefore aimed to investigate quality and variation of CKD care in Swiss general practice using data from the Family medicine Research using Electronic medical records (FIRE) project.

Methods: We defined and evaluated 14 quality indicators (QIs) for CKD care in a retrospective study during 2013–2019. We defined two cohorts of patients aged ≥ 18 years treated by 483 GPs: a *renal function (RF) assessment cohort* consisting of patients affected by diabetes, hypertension or cardiovascular disease (n = 47,201, median age 68 years, 49% female), and a CKD care cohort consisting of patients with laboratory-confirmed CKD (n = 14,654, median age 80 years, 58% female, 82% stage ≥ G3). Within these cohorts, we computed QI achievement rates and explored their determinants by means of mixed-effect logistic regression. Intraclass correlation coefficients (ICCs) were used to express GP-level variation of QI achievement.

Results: We observed the highest QI achievement rate for *withholding non-steroidal anti-inflammatory drug (NSAID) prescription in patients with CKD staged G2–3b* (83%), the lowest for *albuminuria assessment within 18 months of follow-up* (18%). GP-level variation was highest for QIs involving *RF assessment during 18 months of follow-up in patients with diabetes* (ICC 0.31), *cardiovascular disease* (ICC 0.28) and *hypertension* (ICC 0.24). Male patients were more likely to meet QIs involving cardiovascular risk management, stage-dependent completeness of monitoring, and prescription of renin-angiotensin-aldosterone system inhibitors. Diabetes was strongly associated with higher rates of complete CKD monitoring.

Conclusions: Our study found high QI achievement for withholding NSAID use in patients with CKD. High GP-level variation of RF assessment in patients at risk and gaps concerning care of female patients with CKD indicate room for improvement.

P78

Trends and regional variation of carotid endarterectomy and stenting in Switzerland: a population-based small area analysis

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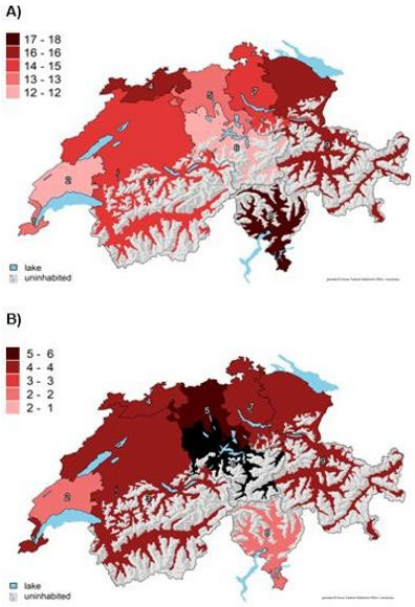
Introduction: Carotid endarterectomy (CEA) and carotid stenting (CAS) are procedures to treat symptomatic severe carotid artery stenosis but significant variation exists for choice of revascularization procedure. We assessed trends and regional variation in CEA/CAS in Switzerland and explored potential determinants of variation.

Methods: We conducted a population-based analysis using patient discharge data from all Swiss acute care hospitals from 2013-2018. We generated hospital service areas (HSAs) by analyzing patient flows and calculated age-/sex-standardized mean procedure rates and measures of regional variation (extremal quotient [EQ] and systematic component of variation [SCV]). We determined the influence on variation with multilevel regression models, adjusting for demographic and socioeconomic factors (language, insurance status), burden of disease, and supply factors (density of interventional radiologists, specialist surgeons, or cardiologists).

Figure: Fully adjusted CEA (A) and CAS (B) rates across 9 Swiss HSAs from 2013 to 2018.



Abbreviation: CEA, carotid endarterectomy; CAS, carotid stenting; HSA, hospital service area.

Average predicted procedures rates for each HSA per 100,000 persons. Adjusted for year, age/sex, language region, insurance status, burden of disease, and density of specialist physician.

Results: Overall, 8015 carotid procedures (6176 CEA and 1839 CAS) were performed in 9 HSAs from 2013-2018. While the mean overall age-/sex-standardized CEA/CAS rates remained stable over time, CEA rates decreased from 16 to 13/100,000 and CAS rates increased from 4 to 5/100,000 persons per year. From 2013-2018, the fully adjusted CEA and CAS rates varied between 12 to 18/100,000 and 3 to 6/100,000 persons across HSAs, respectively (Figure). The regional variation in overall CEA/CAS (EQ 1.3, SCV 0.6) and CEA rates (EQ 1.48, SCV 0.8) was low, with a high variation in CAS (EQ

2.99, SCV 7.15). In multilevel regression, persons aged 70-79 years had a 112% higher overall CEA/CAS procedure rate than those aged 60-69 years (incidence rate ratio [IRR] 2.12, 95% confidence interval [CI] 2.01-2.23), and women had a 65% lower procedure rate (IRR 0.35, 95%CI 0.33-0.37) than men. French/Italian-speaking areas had a 37% lower CAS rate than Swiss German areas (IRR 0.63, 95%CI 0.48-0.83). A higher burden of disease was associated with a 135% higher CEA rate (IRR 2.35, 95%CI 1.09-5.07, per 1 comorbidity per 1000 persons). After full adjustment, 49.9% of the variance in CEA/CAS rates (42.8% in CEA and 15.1% in CAS) remained unexplained.

Conclusions: While CEA rates decreased between 2013 and 2018, CAS rates increased over the same time period in Switzerland. CAS procedures showed a high variation across Swiss regions, which was largely explained by differences in regional demographic and socioeconomic factors.

P79

Admission serum albumin concentrations and response to nutritional therapy in hospitalised patients at malnutrition risk: secondary analysis of a randomised clinical trial Brief title: Admission albumin concentrations and nutritional therapy

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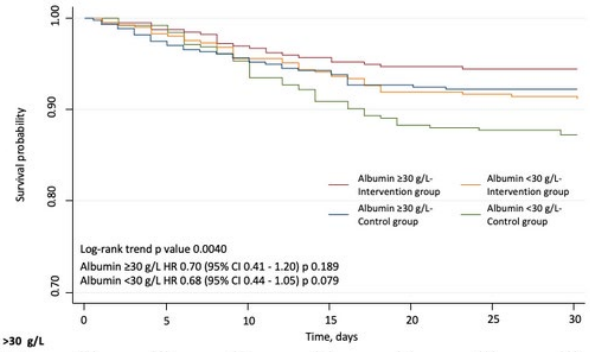
Introduction: Historically, admission serum albumin concentrations have been considered useful biochemical markers for the nutrition assessment. However, there is a lack of randomised trial data investigating whether low albumin concentrations are helpful for identifying patients benefitting from nutritional support.

Methods: This study was a secondary analysis of the EFFORT trial, a Swiss-wide multicentre, randomised controlled trial comparing individualised nutritional support with usual care nutrition in medical inpatients. A total of 1389 of 2028 patients at nutritional risk with available albumin concentrations on admission were included. The primary endpoint was all-cause mortality within 30 and 180 days. Patients were stratified into groups of low or normal albumin based on the albumin cut-off of 30 g/L.

Results: 1389 patients (mean age, 73.1 (SD 3.5) years; 747 (53.8%) men) were included and 676 (48.7%) had low serum albumin concentrations at admission (<30 g/L). Mortality at 180 days was significantly increased in the low albumin group compared with patients with normal albumin concentrations [219/676 (32.4%) vs. 162/713 (22.7%), fully adjusted HR 1.4, 95%CI 1.11 to 1.77, p=0.005]. Effects of nutritional support on 30-day mortality were similar for patients with low vs. normal albumin concentrations compared with patients with normal albumin concentrations (HR 0.68, 95%CI 0.44 to 1.05 vs. HR 0.70, 95%CI 0.41 to 1.20), with no evidence for a subgroup effect (p for interaction=0.97).

Figure 3. Kaplan-Meier Estimate For Time to Death within 30 days for predictive value



Albumin >30 g/L							
Control group	373	362	354	348	341	339	339
Intervention group	340	335	326	323	319	316	316
Albumin <30 g/L							
Control group	326	325	310	293	283	286	284
Intervention group	348	341	330	324	315	314	313

Conclusions: Based on this secondary analysis of a randomised trial, low admission serum albumin concentrations inhospitalised, non-critically ill, medical patients at nutritional risk had prognostic implications and indicated higher mortality risk but were not helpful in selecting patients for nutritional interventions.

P80

Association of CT-based diagnosis of sarcopenia with prognosis and treatment response in patients at risk of malnutrition – a secondary analysis of the EFFORT trial

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Introduction: CT-derived measures of muscle mass may help t identify patients with sarcopenia. We investigated the prognostic significance of CT-derived sarcopenia with nutritional markers, clinical outcomes and response to nutritional support in medical in-patients at nutritional risk.

Methods: Within this secondary analysis of the randomized-controlled EFFORT trial, we investigated associations of CT-based sarcopenia defined as skeletal muscle index (SMI) <41 cm2/m2 in female and <43cm^2/m^2 or <53 cm^2/m^2 in male patients with BMI <25kg/m^2 and ≥25kg/m^2, respectively, at level L3 with different nutritional and clinical outcomes.(1, 2)The primary endpoint was adverse clinical outcome within 30 days of hospital admission.

Results: We included 573 of 2,028 EFFORT patients with available CT scans, of which 68.4% met the CT-based definition of sarcopenia. In multivariate analysis, low SMI correlated with higher nutritional risk based on the nutritional risk screening score (coefficient -0.94 (95%CI -1.87 to -0.01) p=0.049) and lower hand grip strength (coefficient 0.32 (95%CI 0.24 to 0.39) p<0.001). Low SMI was associated with higher risk of adverse clinical outcomes at 30 days (OR 1.59 (95% CI 1.06-2.38), p=0.024) and rehospitalisation (OR 1.86 (95% CI 1.01-3.47), p=0.048). Nutritional support tended to be more effective in reducing mortality in non-sarcopenic patients compared to patients with CT-based sarcopenia (p for interaction 0.058).

Conclusions: Within a population of medical patients at nutritional risk, CT-based sarcopenia correlated well with other nutritional parameters and independently predicted adverse clinical outcomes. Information from CT scans thus may help to better characterize this patient population and may be helpful in guiding therapeutic interventions. The less pronounced response of sarcopenic versus non–sarcopenic patients to individualised nutritional support suggests that successful treatment of advanced malnutrition and cachexia may be more challenging and earlier interventions may be more beneficial.

P81

Association of nutritional risk screening with adverse clinical outcomes in COVID-19 patients: an observational study

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Introduction: Malnutrition is highly prevalent in medical inpatients and may also influence outcomes of patients with Coronavirus disease 2019 (COVID-19). We studied the prognostic implication of nutritional risk as assessed by the Nutritional Risk Screening 2002 (NRS 2002) with regard to adverse clinical outcomes in patients with COVID-19.

Methods: This observational analysis included all consecutive hospitalized adult patients with confirmed COVID-19 at the Cantonal Hospital Aarau (Switzerland) between February 26, 2020 and April 30, 2020 (first wave) and between October 1, 2020 and December 31, 2020 (second wave). The association between admission NRS 2002 with in-hospital mortality, intensive care unit (ICU) and length of hospital stay (LOS) was investigated using multivariable regression analyses.

Results: Our analysis included 305 patients (median age of 66 years, 66.6% male) with a mean NRS of 1.8 ± 1.3 points. Overall, 14.4% (n=44) were admitted to ICU with 7.2% (n=22) needing mechanic ventilation support. Median LOS was 7.0 days (IQR 4.0-13.0) and 14.4% (n=44) died during hospitalization. Compared to patients with low risk for malnutrition (NRS <3 points), patients with mod-

erate (NRS 3-4) or high risk for malnutrition (NRS ≥5) had a significant higher risk for mortality (10.5% vs 22.7% vs 50.0%, p<0.001). This was also confirmed in a regression analysis adjusted for age and comorbidities (Odds ratio of severe malnutrition of 4.85, 95% CI 1.21 to 19.36, p=0.025).

Conclusions: In patients with COVID-19, risk for malnutrition was independently associated with in-hospital mortality. The study of the effects of nutritional treatment in this vulnerable patient population is warranted.

P82

Bleeding risk in elderly patients with venous thromboembolism who would have been excluded from anticoagulation trials

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Introduction: Although elderly patients represent the majority of patients with venous thromboembolism (VTE) and have an increased risk of anticoagulation-related bleeding, such patients are typically excluded from randomized anticoagulation trials. We aimed to determine the proportion of elderly patients who would have been excluded from trial participation and compared the bleeding risk in excluded vs. enrolled patients.

Methods: We studied 991 patients from the SWIss venous Thromboembolism COhort (SWITCO65+), a prospective multicenter cohort study of in- and outpatients aged ≥65 years with acute symptomatic VTE. We identified 12 landmark VTE oral anticoagulation trials from the 8th[1] and updated 9th[2] American College of Chest Physician Guidelines. For each landmark trial, we abstracted the exclusion criteria and applied these criteria to the SWITCO65+ population. We calculated the association between 5 common major exclusion criteria and major bleeding within 36 months using competing risk regression, adjusting for age, sex, and periods of anticoagulation.

Results: A median of 44% (range 20-65%) of elderly patients would have been excluded from participation in 12 landmark trials. Hemodynamic instability, comorbidity, and co-medications were significantly associated with major bleeding (Table). Compared to eligible patients without exclusion criteria, those with 2 and ≥3 exclusion criteria had a 2-fold and 3-fold (Table) increased risk of major bleeding, respectively.

Conclusion: Almost half of older patients with VTE were not eligible for participation in guideline-defining anticoagulation trials. An increasing number of exclusion criteria was associated with an increasing bleeding risk. Thus, whether results from clinical VTE treatment trials can be extrapolated to the elderly remains uncertain and anticoagulation should be used carefully in those patients.

Table: Association between exclusion criteria and major bleeding

Exclusion criteria	Adjusted* SHR (95% CI)
Hemodynamic instability	2.2 (1.1-4.7)
High risk of bleeding	1.3 (0.8-2.1)
Any comorbidity	1.5 (1.1-2.2)
- Active cancer	1.5 (1.0-2.3)
- Chronic liver disease	1.7 (0.5-5.6)
- Cardiovascular disease	1.2 (0.6-2.3)
- Uncontrolled hypertension	0.6 (0.2-2.6)
- History of thrombophilia	0.6 (0.1-4.3)
- Anemia	1.4 (0.8-2.3)
- Thrombocytopenia	1.3 (0.6-2.9)
- Creatinine clearance <30 ml/min	2.2 (1.2-3.9)
Co-medication	1.7 (1.2-2.4)
Invasive treatment	0.8 (0.3-2.1)
Number of exclusion criteria	
0	Reference
1	1.25 (0.80 - 1.95)
2	1.98 (1.22 - 3.19)
≥3	3.09 (1.39 - 6.88)

*Adjusted for age, sex, and periods of anticoagulation

P83

Factors associated with the 30-day health care utilization after discharge from four Swiss General Internal Medicine department: a prospective observational cohort study

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Introduction: Healthcare utilization following a hospital stay is not well known. We aimed to assess the 30-day healthcare utilization of medical adult patients after their discharge from a general internal medicine ward, to assess the factors associated with healthcare utilization.

Methods: All adults consecutively discharge alive from Internal Medical division of 4 secondary and tertiary hospitals in Switzerland, from July 2017 to March 2018, were included in an observational prospective cohort study. They were followed by trained study nurses for up to 30-day, to assess the healthcare utilization: primary care provider (PCP) or specialist consultations, emergency room (ER) visits, nurse visit, and hospitalization. Needs of formal supports were also recorded. Binary outcomes were analyzed by logistic regression adjusted for age and sex.

Results: Of the 934 patients, 733 (78%) had at least one medical visit, 232 (25%) had nurses visit at home, 111 (12%) had new hospital admission and 84 (9%) had ER visit. Only 99 alive patients (11%) had strictly no health care utilization within 30 days. Furthermore, 268 patients (29%) had formal support at their home. Increasing HOSPITAL score, lengths of hospital stay, age or number of comorbid conditions were all associated with an increase in healthcare utilization and needs of non-medical home support services (assist with meal preparation, domestic duties).

Conclusion: The 30-day post discharge is a period of high healthcare utilization. Some parameters of the index hospital stay are useful to predict the post-discharge healthcare needs.

P84

Free triiodothyronine blood levels in malnourished medical inpatients: a secondary analysis of a randomized controlled trial

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Introduction: During acute and chronic illness, the body aims to reduce energy expenditure and catabolism by reducing the deiodination of thyroxine (T4) to triiodothyronine (T3). The level of free T3 (fT3) may be an interesting prognostic marker, particularly in patients at risk for malnutrition. Herein, we investigated fT3 levels in a cohort of malnourished hospitalized patients from a previous trial.

Methods: This is a secondary analysis of the Effect of Early Nutritional Support on Frailty, Functional Outcomes, and Recovery of Malnourished Medical Inpatients Trial (EFFORT), a randomized-controlled Swiss multicenter trial comparing the effects of individualized nutritional support with usual care in adult medical inpatients at nutritional risk. The primary endpoint was 30-day all-cause mortality.

Results: We included 801/2028 (39.48%) patients from the original trial and 492 (61.4 %) patients had low admission fT3 levels (<3.2

pmol/l). fT3 levels showed a significant correlation with loss of appetite [Coefficient -0.28, 95% Confidence interval (95%CI) -0.50 to -0.07, p = 0.01], loss of weight per 10kg (Coefficient 0.78, 95%CI 0.22 to 1.35; p = 0.007) and increase of Albumin levels per 10 g/l (Coefficient 0.64, 95%CI 0.52 to 0.75; p < 0.001). Mortality at 30 days was significantly higher in patients with low vs. normal fT3 levels [64/492 (13.0%) vs. 19/309 (6.2%), adjusted odds ratio 2.19, 95%CI 1.25 to 3.83; p = 0.006]. There was no evidence that patients with low vs. normal fT3 levels would have a different response to nutritional support (p for interaction = 0.451).

Conclusions: In medical inpatients at nutritional risk, low fT3 levels correlated with severity of malnutrition and were a strong predictor for mortality rate and other adverse clinical outcomes, and may help to better risk stratify this population of patients.

Clinical Trial Registration: clinicaltrials.gov as NCT02517476

Keywords: Triiodothyronine, fT3, Mortality, Nutritional risk, Malnutrition, Nutritional support, Randomized trial

P85

High levels of monocytic myeloid-derived suppressor cells are associated with favorable outcome in patients with pneumosepsis and multi-organ failure

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Background: Myeloid derived suppressor cells (MDSCs) are immature myeloid cells with immunosuppressive functions sub-classified into monocytic and polymorphonuclear MDSCs (M-MDSCs and PMN-MDSCs). MDSCs have been associated with poor outcome in sepsis patients. However, since sepsis patients exhibit signs of inflammation and immunosuppression, MDSCs may provide benefit by dampening deleterious inflammation in some patients. To challenge this hypothesis, we measured MDSCs in critically ill sepsis patients with pneumonia and multi-organ dysfunctions and a high likelihood of death.

Methods: We conducted a prospective multi-center observational cohort study in 8 ICUs in Athens and Thessaloniki, Greece, enrolling critically ill patients with pneumosepsis and multi-organ dysfunctions. At study inclusion, blood was collected in lyophilized antibody tubes (Duraclone) designed to detect MDSCs by flow cytometry. Unsupervised clustering of leukocyte populations was performed using FlowSOM. M-MDSCs corresponded to CD11b+ CD14+ CD15-/low CD16- CD33+ CD124-/low HLA-DR-/low cells and PMN-MDSCs to CD11b+ CD14- CD15+ CD16+ CD33- CD124-(low) HLA-DR- cells.

Results: Forty-eight patients were included, of whom 34 died within 90 days. At study inclusion, M-MDSCs and PMN-MDSCs were increased in sepsis patients when compared to healthy subjects (3.07% vs 0.96% and 22% vs 2.1% of leukocytes, respectively; $p < 10^{-4}$). High levels of PMN-MDSCs were associated with secondary infections (p = 0.024) and new sepsis episodes (p = 0.036). M-MDSCs were more abundant in survivors than in patients who died within 28-days (p = 0.028). Stratification of patients according to M-MDSC levels revealed that high levels of M-MDSC were associated with reduced 90-day mortality (high vs low M-MDSCs: 47% vs 84% mortality, p = 0.003, hazard ratio [HR] = 3.2, 95%CI: 1.4-7.2). Combining high M-MDSC levels with low Acute Physiology And Chronic Health Evaluation (APACHE) II score improved patient stratification ($M\text{-}MDSCs^{high}$/$APACHE\ II^{low}$ vs $M\text{-}MDSCs^{low}$/$APACHE\ II^{low}$: 20% vs 80% 90-day mortality, p = 0.0096, HR = 7.2, 95%CI: 1.6-32). M-MDSCs remained correlated with mortality in patients with low APACHE II score in multivariate analyses (p = 0.05, HR = 5.26, 95%CI: 1.0-27.8).

Conclusions: This is the first study to associate high levels of M-MDSCs with improved survival in sepsis patients. Additional investigations will be required to assess whether MDSCs are prognostic and/or theragnostic biomarkers in sepsis.

P86

In-hospital survival paradox in patients with sleep apnea – a nation-wide nested case-control study

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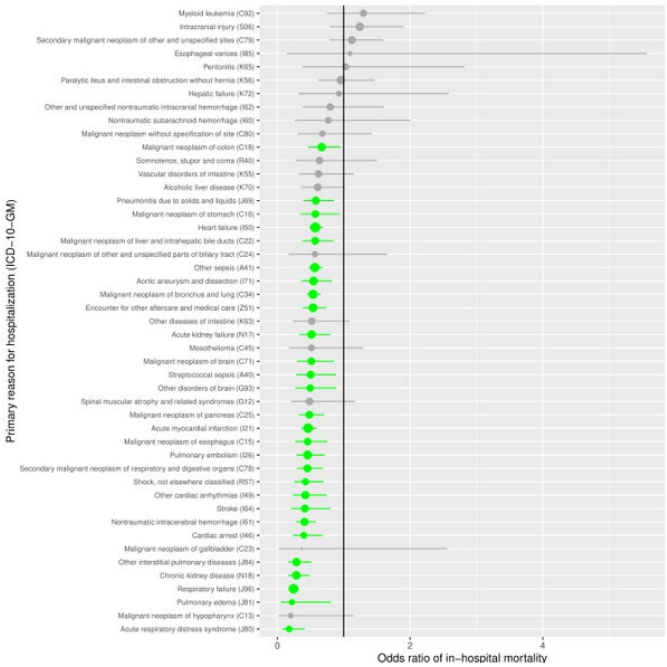
Background: Sleep apnea (SA) is a prevalent disorder characterized by recurrent events of nocturnal apnea disrupting normal sleep and leading to a series of complications when left untreated. SA results in intermittent hypoxia which has an impact on the cardio- and cerebrovascular system. Hospitalized patients with SA typically have a greater burden of comorbidity, a longer length of hospital stay, but may show an improvement of in-hospital mortality compared to patients without diagnosed SA. The reason for this survival benefit is controversial and we aimed to clarify this protective effect in the light of predictive factors including SA-associated comorbidities using a nation-wide hospitalization database.

Material and methods: Data were extracted from a nation-wide hospitalization database provided by the Swiss Federal Office for Statistics. Hospitalized patients with a SA co-diagnosis were extracted from the database together with a 1:1-matched control population without SA.

Results: Overall, 212'581 patients with SA were hospitalized in Switzerland between 2002 and 2018. Compared to the controls, SA cases had a longer median length of hospital stay (7 days; 95% CI: 3 to 15 vs. 4 days; 95% CI: 2 to 10) (p < 0.001) and a higher median number of comorbidities (8 comorbidities; IQR: 5 to 11 vs. 3 comorbidities; IQR: 1 to 6) (p < 0.001). The risk of in-hospital mortality was lower in the SA cases compared to the controls (OR: 0.73; 95% CI: 0.7 to 0.76; p < 0.001). SA was associated with a survival benefit in hospitalizations related to 28 of 47 conditions with the highest rate of in-hospital death (Figure 1). Sixty-three comorbidities were significantly over-represented in SA cases among which obesity, hypertension and anatomic nasal deviations were associated with a significant decrease of in-hospital mortality.

Conclusion: Compared to matched controls, SA was associated with significant and relevant inpatient survival benefit in a number of most deadly conditions. Most comorbidities were correlated with a poorer prognosis, except obesity and hypertension which were associated with an improved in-hospital mortality. Putative mechanisms responsible for the observed phenomenon include the obesity paradox as well as the SA-related beneficial effect of hypoxic preconditioning.



P87

Long-term clinical outcomes in elderly patients with acute venous thromboembolism who have renal impairment

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Introduction: Although both acute venous thromboembolism (VTE) and renal impairment (RI) are more common in the elderly, little is known on the prevalence of RI and long-term prognosis of older patients with VTE who have concomitant RI.

Methods: In a prospective multicenter Swiss cohort, we analyzed 912 patients aged ≥65 years with acute VTE. Using the CKD-EPI formula, we defined three categories of renal function: estimated glomerular filtration rate (eGFR) ≥60ml/min/1.73m^2 (no RI), 30-59ml/min/1.73m^2 (moderate RI), and <30ml/min/1.73m^2 (severe RI). The study outcomes were VTE recurrence, major bleeding, and overall mortality. We examined the association between renal function and clinical outcomes using regression models, adjusting for relevant known confounders and periods of anticoagulation.

Results: Overall, 313 (34%) patients had moderate and 51 (6%) had severe RI. Over a median duration of 29.6 months, 107 patients (12%) had VTE recurrence, 125 (14%) had major bleeding, and 186 (20%) died during follow-up. After adjustment, severe RI was associated with a 2-fold increased risk of major bleeding (sub-hazard ratio [SHR] 2.2, 95%CI 1.1-4.3) compared to no RI, but not with VTE recurrence (SHR 0.6, 95%CI 0.2-1.8) or mortality (hazard ratio [HR] 1.0, 95%CI 0.6-1.9) (Table). Moderate RI was not significantly associated with adverse clinical outcomes.

Conclusions: Older patients with acute VTE had a high prevalence of RI. Patients with severe RI had 2-fold increased long-term risk of major bleeding compared to those with a normal renal function, with a comparable risk of VTE recurrence and mortality. Patients with moderate RI did not carry worse prognosis. The risks and benefits of anticoagulation should be regularly assessed in older patients with acute VTE who have severe RI.

Adverse clinical events	Adjusted SHR* (95% CI)	p-value
VTE recurrence		
eGFR >60ml/min/1.73m^2	Ref.	
eGFR 30-59ml/min/1.73m^2	1.4 (0.9 - 2.0)	0.139
eGFR <30ml/min/1.73m^2	0.6 (0.2 - 1.8)	0.317
	Adjusted SHR† (95% CI)	**p-value**
Major Bleeding		
eGFR >60ml/min/1.73m^2	Ref.	
eGFR 30-59ml/min/1.73m^2	1.5 (1.0 - 2.2)	0.063
eGFR <30ml/min/1.73m^2	2.2 (1.1 - 4.3)	0.019
	Adjusted HR‡ (95% CI)	**p-value**
Overall mortality		
eGFR >60ml/min/1.73m^2	Ref.	
eGFR 30-59ml/min/1.73m^2	0.9 (0.6 - 1.2)	0.429
eGFR <30ml/min/1.73m^2	1.0 (0.6 - 1.9)	0.912

Abbreviations: VTE, venous thromboembolism; SHR, sub-hazard ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

*Adjusted for age, sex, body mass index, provoked/unprovoked VTE, localization of index VTE, history of VTE, active cancer, and periods of anticoagulation as a time-varying covariate.

†Adjusted for age, sex, active cancer, recent major surgery, history of major bleeding, arterial hypertension, diabetes mellitus, chronic heart failure, cerebrovascular disease, chronic liver disease, low physical activity, high risk of falls, anemia, thrombocytopenia, concomitant antiplatelet/non-steroidal anti-inflammatory therapy, and periods of anticoagulation as a time-varying covariate.

‡Adjusted for age, active cancer, diabetes mellitus, physical activity level, systolic blood pressure, anemia, D-dimer, ultra-sensitive troponin, high-sensitive C-reactive protein, and periods of anticoagulation as a time-varying covariate.

Table: Association between renal function and adverse clinical events

P88

Prevalence of micronutrient deficiencies in patients hospitalized with COVID-19: an observational cohort study

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Introduction: COVID-19 has been linked to deficiencies of several micronutrients. We studied the prevalence of deficiencies of nine different micronutrients in a cohort of patients hospitalized with COVID-19 in Switzerland between March and April 2020.

Methods: We measured admission serum/plasma levels of vitamins A, B12, D, and E, as well as folic acid, zinc, selenium, copper, and iodine in 57 consecutively admitted adult patients with confirmed COVID-19 and analyzed prevalence of micronutrient deficiencies and correlations among micronutrient levels. Further, we studied associations of micronutrient levels with severe disease progression, defined as composite endpoint of in-hospital mortality or need for intensive care unit (ICU) treatment.

Results: Overall, 79% (n = 45) of patients had at least one deficient micronutrient level and 37% (n = 21) had ≥3 deficiencies. Most prevalent deficiencies were found for selenium, vitamin D, vitamin A, and zinc (51%, 40%, 39%, and 39%, respectively). There were moderate associations observable between vitamin D and folic acid, vitamin A and selenium, folic acid and selenium, vitamin A and zinc as well as copper with zinc and selenium with correlation coefficients ranging from r = 0.27 to r = 0.42. A negative correlation was found between vitamin A and vitamin B12 (r = - 0.28). Higher levels of folic acid, vitamin A or zinc were associated with a lower risk for a severe progression of COVID-19 (adjusted OR 0.88 (95% CI 0.78 to 0.98, p = 0.02), adjusted OR 0.18 (95% CI 0.05 to 0.69, p = 0.001), adjusted OR 0.73 (95% CI 0.55 to 0.98, p = 0.03), respectively).

Conclusions: We found a high prevalence of micronutrient deficiencies in hospitalized patients with COVID-19, particularly for selenium, vitamin D, vitamin A, and zinc, and an association of deficiencies with adverse clinical outcomes. Whether supplementation of micronutrients is useful for prevention or treatment of COVID-19 warrants further research.

P89

Rapid increase of myeloid-derived suppressor cells and prolonged innate immune dysfunctions in patients with COVID-19

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Objectives: Severe COVID-19 is associated with exuberant inflammation, but long COVID patients show signs of immunosuppression. Polymorphonuclear and monocytic myeloid-derived suppressor cells (PMN-MDSCs, M-MDSCs) are immunosuppressive cells rising during inflammation and infections. We aimed to characterize the dynamic of MDSCs in relation with immune parameters in COVID-19 patients followed for 3 months.

Methods: Fifty-six PCR-confirmed SARS-CoV-2 infected adult patients hospitalized at the Lausanne University Hospital were included in the study. Blood was obtained at study inclusion and 3 months later in 21 patients (14 moderate and 7 severe COVID-19), and from 10 healthy controls. Blood was stimulated with Toll-like receptor (TLR) ligands: lipopolysaccharide (endotoxin), R848 (viral RNA mimic), Pam_3CSK_4 (bacterial lipopeptide) and CpG DNA (microbial DNA mimic). Leukocyte populations and cytokines were analyzed by flow cytometry and unsupervised clustering, mass cytometry, multiplex bead assay and ELISA.

Results: Forty-five patients (80%) had moderate COVID-19, and 11 (20%) severe COVID-19. Two patients (3.5%) died. At hospital admission, PMN-MDSCs and M-MDSCs counts were increased 2-4-

fold in COVID-19 patients when compared to healthy controls (P=0.01-0.03). PMN-MDSCs and M-MDSCs counts were higher in severe than in moderate COVID-19 patients (P<0.005). PMN-MDSCs counts inversely correlated with T cell counts (P=0.025). PMN-MDSCs and M-MDSCs positively correlated with blood levels of epidermal growth factor and hepatocyte growth factor (P=0.01-0.02). M-MDSCs further correlated positively with IL-1β, IL-7, platelet-derived growth factor and vascular endothelial growth factor (P=0.0001-0.03). In whole blood stimulated with TLR ligands, the proportions of TNF and IL-6-producing monocytes and dendritic cells (DCs) were reduced in patients when compared to controls. Three months after COVID-19 diagnosis, PMN-MDSCs and M-MDSCs blood counts were back to normal levels, while the production of cytokines by blood, monocytes and DCs was still largely affected.

Conclusions: PMN-MDSCs and M-MDSCs were elevated and correlated with serum cytokine concentrations and disease severity in COVID-19 patients analyzed at hospitalization. Innate immune blood responses evaluated by cytokine production were impaired in patients, which persisted for up to 3 months. Overall, our results suggest that COVID-19 induces rapid and long-standing innate immune dysregulation.

P90

Steps parameters of elderly patients hospitalized for an acute medical illness in a Swiss University Hospital. A monocentric observational pilot-study

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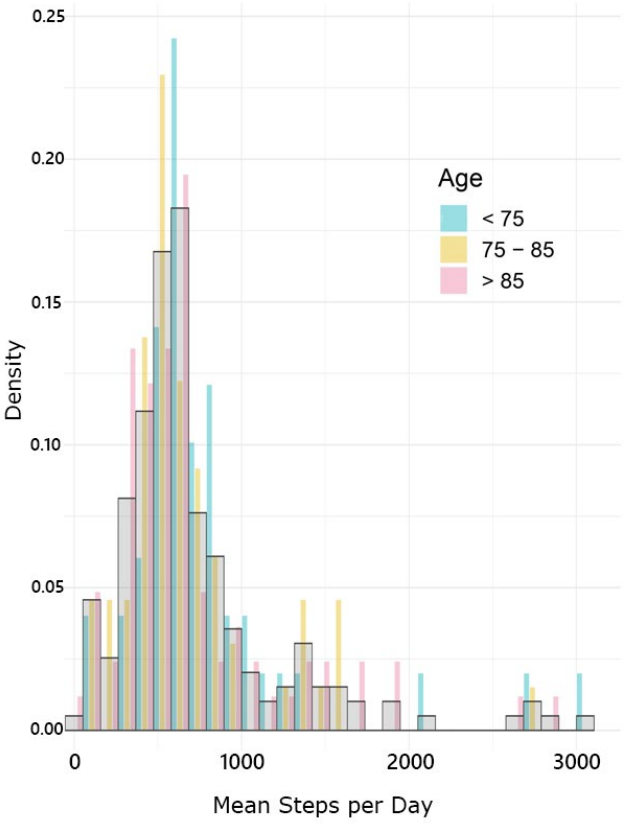
Introduction: Walking is regarded as one of the most effective measures to sustain physical fitness and reduce adverse health events [1]. Still, most elderly patients spend over 80% of their hospitalization time in bed [2]. Objective mobility goals for medical elderly patients hospitalized remain debated. We therefore studied steps parameters of elderly patients hospitalized for an acute illness, to determine goals for future interventional trials and medical practice.



Methods: Observational study conducted from February to November 2018 in a medical ward of the Lausanne university hospital, Switzerland. We measured the step parameters of consecutive medical patients aged ≥65 years admitted for acute medical illness using a wrist accelerometer (Geneactiv). We also collected demographic, somatic, and functional factors.

Results: Overall 187 inpatients had their step parameters (daily step count, walking cadence and bout duration) measured with accelerometers worn for a mean of 3.6 days (SD 3.2). Elderly inpatients (81.5 years (SD 8.5)) walked 603 steps daily [IQR 456, 809], at a cadence of 100 steps/minute [IQR 99-101] with walking bouts of 33 seconds [IQR 27-37] and with 70% of the walking bouts lasting less than 30 seconds. Patients walking ≥600 steps were younger (80.4 years (SD 8.9) vs 82.8 (SD 7.9), p=0.050) and had a longer length of stay (7.8 days (SD 5.1) vs 6.1 days (SD 4.1), p=0.011) than those walking <600 steps. Patients at high risk of bed sores and a functional decline walked less (628 steps (SD 422) vs 807 (SD 568), p=0.016 than those with lower risk of sores.

Conclusions: During a hospitalization for an acute medical illness, patients aged ≥65 years walk a mere 603 steps daily and most of the time for periods of less than 30 seconds. This information should be used to build up future interventional trials or to set mobility goals for patients hospitalized in Swiss hospitals.

P91

The role of admission cortisol levels in patients with disease-related malnutrition: a secondary analysis of a randomized clinical trial

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Introduction: Cortisol is an important anabolic stress hormone which increases appetite and correlates with stress metabolism. Yet, there is a lack of clinical data demonstrating whether cortisol blood levels could add to the malnutrition assessment in medical patients. We therefore studied the association of admission cortisol levels and nutritional parameters, severity of disease and response to nutritional support among medical patients at nutritional risk.

Methods: This is a secondary analysis of the of the Effect of Early Nutritional Support on Frailty, Functional Outcomes, and Recovery of Malnourished Medical Inpatients Trial (EFFORT), a multicenter, randomized-controlled trial that compared individualized nutritional support with usual care nutrition. Theprimary endpoint was 30 days mortalit.

Results: 764 patients (mean age, 73.4 (SD 0.5) years; 413 (54 %) men) were included and 191 (25 %) had cortisol levels in the highest quartile (> 723 nmol/l). Cortisol levels correlated wit higher NRS[Coeff (95%CI)47.73 (24.1 to 71.3); p < 0.001]and loss of appetite[Coeff (95%CI)70.89 (4.8 to 136.9); p = 0.035]. 30 days mortality was significantly increased in the high cortisol group compared to patients with normal cortisol levels (34/191 (17.8%) vs. 48/573 (8.38 %)), fully adjusted OR 2.39, 95%CI 1.44 to 3.98, p=0.001). Effects of nutritional treatment on mortality were more pronounced for patients with high cortisol compared to patients with normal cortisol levels (adjusted OR 0.56, 95%CI 0.24 to 1.33 vs. OR 1.22; 95%CI 0.65 to 2.31) (p interaction = 0.096).

Conclusion: High admission cortisol among medical inpatients at nutritional risk correlated with nutritional parameters, disease severity and predicted response to nutritional support.Cortsiol thus may help to better characterize malnourished patients in the future.

P92

Seasonal influenza vaccination hesitancy in health care workers – are face mask obligations counterproductive?

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Introduction: Health Care Workers (HCW) are in the focus of influenza (FLU) and newly COVID-19 vaccine campaigns. Understanding changes HCW vaccine perceptions will inform future targeted campaigning.

Methods: We conducted an online survey among all HCW of the Solothurner Spitäler AG (soH) on FLU campaign perception and reasons for vaccination after the campaigns in 2019/20 and 20/21. COVID-19 vaccination willingness and in 20/21 reasons to decline FLU vaccination were included. Mandatory face masks for unvaccinated HCW were only instituted in selective high-risk wards before the universal obligation during the COVID-19 pandemic. Descriptive findings are presented.

Results: 2'100 (50.8%) (2019/20) and 2'551 (58.2%) (2020/21) HCW filled in the questionnaire. The majority of vaccinated HCW reported self / relatives' and/or patients' protection as the main motivation for vaccination (91.8 and 91.5% respectively). In 2019/20, 8% reported compulsory mask wearing strategies to be the main individual reason for FLU vaccination, of whom 38.5% refusing a hypothetical COVID-19 vaccine. Conversely, of FLU un-vaccinated HCW in 2020/21, 24.3% reported universal pandemic mask obligations to be a reason not to vaccinate against FLU, 21.5 and 22.8% being unsure or refusing COVID-19 vaccination, respectively. 30% un-vaccinated HCW reported doubts on FLU vaccine safety / efficacy, 28.1 and 33.9%, respectively, being unsure or refusing COVID-19 vaccination. In line with infection control strategies during the pandemic, overall influenza vaccination rates among HCW decreased from 32.3% (19/20), to 29.4% (20/21) and 21.8% (21/22).

Conclusion: Self and patients' protection are the main reasons to get vaccinated. Among unvaccinated HCW, mask wearing obligations may have a negative effect on influenza and possibly future COVID-19 vaccine uptake. Intensified campaigning is warranted during the 22/23 respiratory virus season, with a focus on the supplementary efficacies of vaccinations and facemask protections.

P93

What was on the mind of internal medicine physicians at the end of the first COVID-19 wave?

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Introduction: The first COVID-19 wave (2020), W1, will remain extraordinary because of its pandemicity and the societal upheavals that it caused worldwide. Much is still to be investigated about what front-line physicians experienced personally. Qualitative methodology allows in-depth and vivid description of experiences. In the last weeks of W1, we thus sought to collect narratives of frontline physicians working in a Swiss University Hospital, aiming to identify the content of these experiences.

Methods: During W1, 136 physicians (residents, fellows and senior attending physicians) of the internal medicine division of Lausanne University Hospital (CHUV) took care of circa 600 hospitalized COVID-19 patients. All physicians in this division received invitations to participate in the study. Participants could send testimonials anonymously from April 27 to June 30, 2020, using an online platform specifically developed for the study by the PENbank project team (https://penbankchuv.ch/). Format for testimonials was free. Study material consisted of 14 written narratives, 1 audio-recorded testimonial, and 13 photographs. Data were examined by means of a narrative analysis based on a holistic content approach that considers narratives as a whole and attempts to grasp the overall pattern (nodal points or foci).

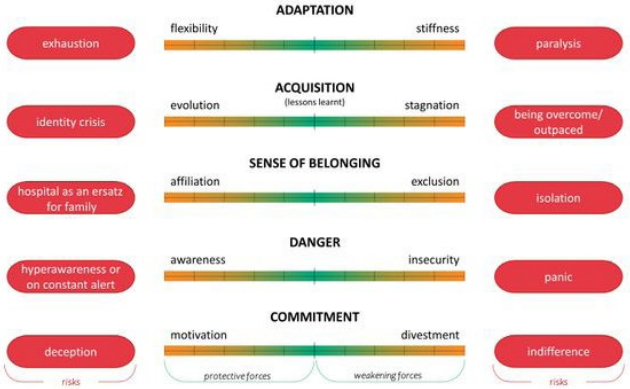
Results: Five foci reflecting how physicians experienced W1 were identified: adaptation (Excerpt 1), acquisition of experiences and knowledge, sense of belonging, danger, and commitment. Participants were positioned on a polarized spectrum with regard to these nodal points (Fig.1): flexibility versus stiffness, evolution versus stagnation, affiliation versus exclusion, awareness versus insecurity, motivation versus divestment.

Conclusions: Polarized modes of physician reactions to the changing work environment and pandemic threats were identified. Our analysis of physician narratives surpasses an observation of possible exhaustion or burnout, deepens the understanding of how physicians experienced the pandemic, both in their professional and private life, and offers insights and clues on how to investigate the impact of the pandemic on well-being and coping capacities. Rather than considering individual and singular experiences or searching for general or collective impacts, these results provide a tool to examine a potential polarization on the spectrum of clinicians' possible reactions and to address specific risks unbalancing an equilibrium.

Excerpt 1

Dear Coronavirus,
It has now been several weeks since you turned the lives of a large part of humanity upside down, and at the level of the CHUV, we have not been spared. You have upset our organization, our scientific beliefs, our economy, our daily family life and above all you have bereaved the lives of so many people [...] And yet, the optimist that I am cannot help but notice the positivity in this crisis: solidarity in my neighborhood, support for hospitals and, strangely enough, we could even say belatedly but also foolishly, recognition for the daily and flawless work of healthcare teams [...] So thank you coronavirus for having shaken up the obvious, thank you for also questioning our economic, spiritual and ecological certainties... in the end I think we needed it a bit.

Figure 1. What was on the mind of internal medicine physicians at the end of the first COVID-19 wave?



The grid shows a spectrum with regard to the 5 foci. The greener the colour, the better the equilibrium. The more orange the colour, the more risk there is of an unbalanced equilibrium, that can reach the extreme polarizations in red.

P94

Barriers and facilitators to deprescribing of cardiovascular medications: a systematic review

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Background: Cardiovascular medications (CVMs) might have potential harms without benefit in some instances (e.g., certain older adults in primary prevention or patients with limited life expectancy). This may warrant *deprescribing*, defined as the process of discontinuing medications which lack benefit or which harms might outweigh benefits. However, the lack of evidence regarding benefits and risks of some CVMs in certain patients and when to initiate deprescribing may lead to insecurity. In this context, the decision to deprescribe a CVM often becomes a preference-sensitive decision, which is influenced by barriers and facilitators experienced by stakeholders involved in decision-making. With this systematic review, we aimed at synthetizing the current knowledge on barriers and facilitators to deprescribing CVMs at the levels of patients, informal caregivers, and healthcare providers (HCPs).

Methods: We searched Ovid/MEDLINE and Embase from January 2003 to November 2021 for studies exploring or assessing patient, informal caregiver and/or HCP barriers and/or facilitators to deprescribing CVMs. Given the topic of this systematic review, we conducted a qualitative rather than a quantitative synthesis of the results. We performed a deductive thematic analysis based on the framework of specific barriers and facilitators to deprescribing CVMs created by Goyal et al.

Results: Main deprescribing barriers for patients, informal caregivers and HCPs included uncertainty due to lack of evidence regarding CVM deprescribing and fear of negative consequences following deprescribing. An important facilitator to deprescribing for patients and HCPs was the occurrence of adverse drug events. Other facilitators for patients were dislike of CVMs or establishment of a deprescribing plan. Necessity and benefit of CVMs were less polarizing, patients and HCPs seeing them as barriers or facilitators equally. HCPs tended to see robust older adults as more likely to benefit from CVMs. However, frail patients were less willing to deprescribe than robust ones. Social influences and patient ambivalence acted both as barriers and facilitators to deprescribing.

Conclusions: We highlight certain differences in patient, informal caregiver and HCP expressed barriers and facilitators to deprescribing CVMs that stress the need for ground discussions about beliefs and preferences of each stakeholder implicated in deprescribing decisions in the context of uncertain risks and benefits.

P95

CaDoBio (calcium dobesilate bioavailability): bioavailability and pharmacokinetics of calcium dobesilate in the nasal mucosal tissue, saliva and blood of treated patients

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SARS-CoV-2 infects endothelial cells through angiotensin-converting enzyme 2 (ACE2) mediated viral entry, while heparan sulfate proteoglycans (HSPGs) provide the first anchoring sites on the cell surface and help the virus make primary contact with host cells.
In severe cases of COVID-19, various cytokines (e.g. IL-2R, IL-6, TNFs) are released, which contribute to the exaggerated immune-mediated cytokine storm and can result in vascular inflammation (endothelialitis), thus promoting vascular hyperpermeability.
Calcium dobesilate (CaD) is a well-established vasoactive and angioprotective drug improving endothelial dysfunction[1].
Additionally, CaD has been shown to have potential antiviral effects [2]. These antiviral effects of CaD are thought to be mediated via its interaction with the heparansulfate (HS) binding site of the viral SARS-CoV-2 spike protein (direct action). Preliminary pre-clinical results using viral pseudotyped particles demonstrated that CaD reduces the uptake of SARS-CoV-2 spike protein in cultured endothelial cells by more than 50% (unpublished data, Haller).
Due to its long experience on the market and its well tolerated safety profile [3], as well as the two-axis rationale to dampen both viral infectivity and endothelial inflammation/dysfunction, CaD could represent an interesting alternative for the treatment of Covid-19 disease.
This is a Phase I, open-label, monocentric project to measure the concentrations of calcium dobesilate in the nasal mucosal tissue, saliva and blood in patients treated with CaD, either already on treatment (N=10), or starting a new treatment (N=4).
Nasal mucosal tissue, saliva and blood samplings have been collected in order to measure its nasal mucosal tissue, oral and plasma concentrations, respectively before first dose, and 4h (peak) and 8h afterwards.
CaD concentrations have been assessed by tandem mass spectrometry.
CaD concentration was measured in the plasma in the micromolar range. CaD was also detected in the saliva and nasal extracts, and this as early as 4h after the first dose, although at much smaller concentrations.
CaD detection in nasal and oral mucosa is a cornerstone for the evaluation of the potential of calcium dobesilate to treat patients diagnosed with Covid-19, as it shows that CaD is able to rapidly reach the nasal mucosal and oral tissues to exert its potential anti-SARS-CoV-2 activity. Further study will now be conducted to assess the in vivo antiviral effect of CaD.

P96

Cardiovascular drug doses in patients with atrial fibrillation – does one size fit all or do we need sex-specific doses?

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Introduction: Women with heart failure (HF) with reduced ejection fraction (EF) had lower risks of mortality or cardiovascular hospitalizations when receiving submaximal doses of beta-blockers (BB) and renin-angiotensin system (RAS) inhibitors. However, optimal doses of BBs and RAS inhibitors in women with atrial fibrillation (AF) are unclear. We investigated sex-specific associations of BB and RAS inhibitor doses with cardiovascular outcomes in patients with AF with and without HF.

Methods: We used data from the prospective BEAT-AF and Swiss-AF cohorts. The outcome was major adverse cardiovascular events (MACE), including death, myocardial infarction, stroke, systemic embolization, and HF-related hospitalization. The predictors of interest were sex, and BB or RAS inhibitor dose, split in categories of 0%, 1-49%, 50-99% or ≥100% (reference) of the maximally recommended dose. We used Cox models adjusted for demographics, comorbidities, and co-medication, and assessed interactions between sex and BB or RAS inhibitor dose.

Results: Among 3,855 patients (28% women), median dose at baseline was 12.5% (IQR 1.3-25%) of the maximum for BBs and 12.5% (IQR 0-50%) for RAS inhibitors. MACE occurred in 1,113 patients over 5-year median follow-up. The distribution of RAS inhibitor and BB doses was similar in women and men. Multivariable Cox models revealed an overall lower hazard of MACE in women, compared to men (HR: 0.80; 95% [95%CI 0.70-0.91]). Compared to the maximum dose, we found a lower hazard of MACE associated with no (HR: 0.75 [95%CI 0.67-0.85]) or low dose of RAS inhibitor (HR 0.83 [95%CI 0.74-0.94]). This association was most pronounced in men in the lowest RAS inhibitor group (interaction p=0.02). Hazard of MACE was lower in women in the two submaximal dose groups of BB (interaction p<0.02; p=0.01) compared to the maximal BB dose.

Conclusions: We found a lower hazard of MACE associated with low-dose or no RAS inhibitor in both men and women. The reason for this could be a lack of benefit of fully dosed RAS inhibitor in patients with AF or it might have resulted from unmeasured confounders, e.g., better left ventricular EF in those without RAS inhibitor. The interaction between female sex and submaximal BB dose was similar to findings for HF with reduced EF. Therefore, dosing of cardiovascular drugs should be carefully evaluated in patients with AF, as sex differences in pharmacokinetics and cardiovascular outcomes have emerged by several studies.

P97

Computer-assisted decisional program reminding the Ottawa ankle rules for radiological assessment of ankle injuries – a before-after study

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Introduction: Ankle injuries are a common cause of emergency department (ED) visits for which x-rays (XR) are the reference standard to differentiate between sprains and fractures[1]. The Ottawa ankle rules (OAR) were designed as a clinical decision aid to minimize unnecessary radiographies[1] with a sensitivity close to 100%[2]. A systematic review has shown a decrease of 30-40% of radiographies when the OAR are applied[2]. The object of the study is to assess the effectiveness of an electronic alert using a pop-up window intervention with a reminder of the OAR in an electronic health record in decreasing the number of ankle and foot XR in the emergency department.

Methods: Study design: quasi-experimental pre-post study (phase 1 and 2) at the ED of the Geneva University Hospital (HUG).

Participants: Adult patients presenting at the ED for an ankle injury. Intervention: e-alert. When a physician orders an ankle XR, a pop-up (Figure 1) window will appear in the electronic health record of the HUG (DPI, Dossier Patient Intégré) with a reminder of the OAR and its pertinence. Physicians then have the choice to order the XR or not. If they decided to order the XR, they will have to document whether the OAR criteria were met.

Outcomes: Proportion of XRs prescribed over the total number of patients consulting for an ankle trauma.

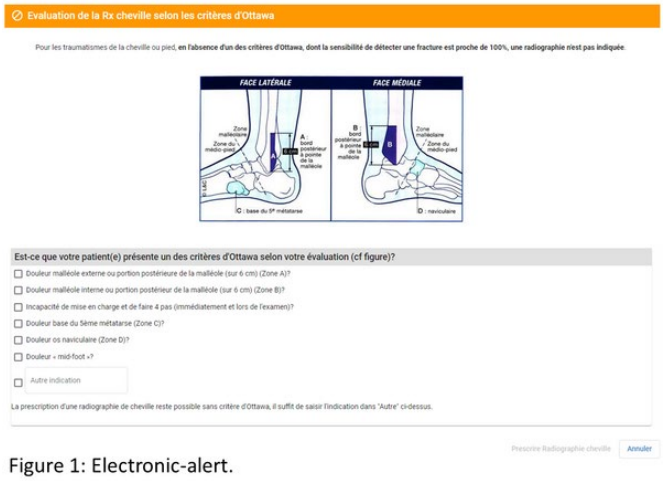
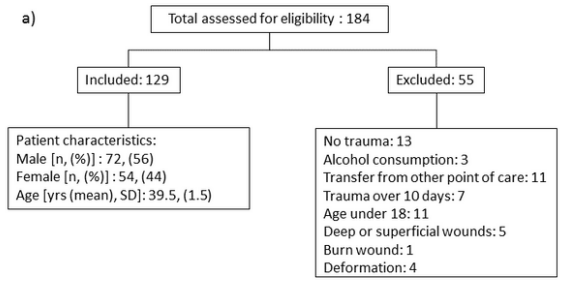


Figure 1: Electronic-alert.



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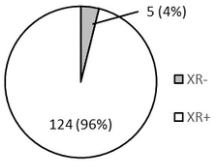

c)

	OAR		
XR	-	+	total
-	4	1	5
+	8	116	124
total	12	117	129

d)

	OAR				
	-		+		
	XR		XR		
ED Fx	-	+	-	+	total
-	4	8	1	86	99
+	0	0	0	30	30
total	4	8	1	116	129

e)

	Follow-up				
	-		+		
	OAR		OAR		
ED Fx	-	+	-	+	total
-	12	85	0	2	99
+	0	6	0	24	30
total	12	91	0	26	129

Figure 2: a) Patient enrollment and characteristics. b) Included patients with X-rays (XR+) and without (XR-). c)Two-way frequency table for presence of Ottawa Ankle Rules (OAR) and X-rays performed (XR). Three-way frequency tables for: d) Presence of fracture presence of fracture at the emergency department (ED Fx), OAR and XR; and e) ED Fx, OAR, presence of fracture at follow-up (Follow-up Fx).

Secondary outcomes: Proportion of prescribed XR that met the OAR criteria, ED length of stay, ED costs, and OAR parameters (sensibility, specificity, negative predictive values).
We will compare outcomes from the period before the implementation of the alert (from November 2021 to January 2022) with patients of the period after the implementation of the alert (from February to April 2022). Patients will be contacted by telephone two weeks after the ED visit to enquire if another radiological procedure was performed as well as whether a fracture was ultimately diagnosed.

Results: (phase 1, preliminary):
We have assessed all patients presenting at the ED with ankle trauma at triage from November 1, 2021 to January 20, 2022. 184 patients were assessed, after exclusion, 129 patients were included (Figure 2a). Of the 124 patients (96%) who had an XR (Fig 2b), only 116 met OAR criteria (Figure 2c). Among those diagnosed with a fracture at the ED (n=30), all had OAR criteria (Figure 2d) and at follow-up all those who have been diagnosed with a fracture in absence of fracture at initial assessment (n=2) also met OAR criteria (Fig 2e).

P98

Factors associated with loneliness in a 75+ years old population in the Canton of Baselland, Switzerland. A cross-sectional survey study

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Introduction: Care for older adults must be redesigned to cope with the needs of the growing older population in the following decades. As loneliness is associated with deteriorating physical and mental health, including increased mortality, it deserves special attention in this age group. We aimed at studying the degree of emotional loneliness, and associated variables, reported by the 75+ community-dwelling citizens in the Canton Baselland in Switzerland.

Methods: Data was acquired with the cross-sectional INSPIRE Population Survey, a paper-and-pencil survey sent to all 75+ community-dwelling adults in Canton Baselland between March and August 2019. The questionnaire was designed to investigate the current and expected needs and preferences of older adults.

Results: The response rate was 30%, with 8846 returned questionnaires. The mean age was 81.82 years old (range 75-111 years), and 51.8% were women. Overall, 43% of respondents (95% CI=41.96-44.05) reported some degree of loneliness. Multivariate analyses showed that the subgroups most likely reporting loneliness were those living without a partner (OR=1.96, 95% CI=1.71-2.24), women (OR=1.41, 95% CI=1.24-1.60), the eldest (OR=1.04, 95% CI=1.03-1.06), and those born outside Switzerland (OR=1.25, 95% CI=1.07-1.45). To have a higher monthly household income (OR=0.59, 95% CI=0.44-0.79 comparing highest vs. lowest incomes), reporting higher degrees of life satisfaction (OR=0.52, 95% CI=0.49-0.56) and functional competence status (OR=0.87, 95% CI=0.82-0.93) appear to have a protective effect.

Conclusions: Our study highlighted that almost half of the sampled adults suffer from emotional loneliness in Canton Baselland. Improving loneliness in this age group could have broad general health benefits, therefore, loneliness should be considered an integral part of the care of older adults especially the most affected, namely those living without a partner, women, and the oldest.

P99

Factors influencing deployment of nursing activities in a new interprofessional organizational model in general practices in the canton of Vaud

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Introduction: To ensure better care coordination and to provide adapted care delivery, a new interprofessional organization in general practitioners' (GP) practices including nurses is being assessed through a pilot implementation study (the Mocca project) in eight GPs' practices in the canton of Vaud. The aim of this study is to evaluate which factors influence the appropriation of the nursing role and deployment of nursing activities in GPs' practices.

Methods: A qualitative observational study was carried out in the eight practices of the Mocca project. Qualitative data came from five interviews with nurses and five interviews with patients, and one focus group with six GPs. Thematic analysis was performed using an inductive approach in order to extract categories and to assemble them in themes and then formulate hypothesis.

Results: Several influencing factors were reported at nursing level as well as GPs and patients' levels. The nurses with diversified previous professional experience mentioned being more comfortable with their new nursing role in primary care. Conversely, when they perceived a lack of experience and knowledge in some specific fields (e.g. addictology, diabetes), nurses encountered difficulties in the appropriation of their role in the patient follow-up activities. At GPs' level, the main barrier for the nursing activities' deployment was the GPs' willingness to refer patients to the nurses for follow-up activities. This willingness highly depended on their previous interprofessional experience, and on the trust in the nursing skills. A strong knowledge of their patients and heavy workload were facilitating factors to refer their patients to the nurses. At patients' level, the main element facilitating the deployment of nursing activities was the patient's acceptance and satisfaction regarding nursing care and follow-up.

Conclusions: The appropriation of the nursing role and deployment of nursing activities,especially follow-up activities for patients with chronic conditions is a complex process. It is not only due to the nurses who have to developed specific experience and knowledge in primary care but also to the GPs and their trust in the wide scope of nursing skills.

P100

General practitioner opinions and practices regarding vaping for smoking cessation

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Introduction: Electronic cigarettes are the most frequently used smoking cessation tool in Switzerland. Many general practitioners (GP) are reluctant to recommend e-cigarettes as they are not as regulated as medications and their relative long-term safety for smoking cessation unclear. Conversely, many GP adopt a harm-reduction approach because vaping is popular, less harmful than smoking and effective for smoking cessation. We sought to describe GP knowledge and practices regarding vaping for smoking cessation in Switzerland. We further aimed at assessing the interest of GP for a decision aid (DA) for smoking cessation. A DA presenting balanced information about e-cigarettes for tobacco cessation could help GPs to discuss the potential benefits, risks and uncertainties of this tool for tobacco cessation, regardless of their personal beliefs.

Methods: We administered questionnaires to GP from the Sentinella practice-based research network in Switzerland. We asked GP if they recommended vaping for smoking cessation, to rank the harm for health on a scale of 0 to 9 (9 = most harmful) of e-cigarettes, conventional cigarettes and nicotine replacement therapy, and about their interest in a DA for the choice of smoking cessation therapy.

Results: Of 170 GP in Sentinella, 70 (41%) completed the survey. Most were men (70%), 66% were aged >50, 74% were from German speaking and 26% from French speaking area. The proportion of GPs who gave a score≥7/9 for perceived harm was 10% for NRTs, 54% for e-cigarettes, and 98% for conventional cigarettes. A minority (31%) recommended e-cigarettes for smoking cessation with regional differences (56% French speaking and 23% German speaking areas). Most GPs (68%) stated they were interested in using a DA.

Conclusion: While most participating GPs estimated e-cigarettes to be less harmful than conventional cigarettes, a minority recommended e-cigarettes for smoking cessation. Most were interested in using a DA for smoking cessation counselling. Future studies should explore the reasons for this reluctance and test interventions enabling patients to get balanced information on smoking cessation therapies.

P101

Monitoring COVID-related daily activity in family medicine practices of the canton of Vaud: results from a cantonal sentinel surveillance system

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Introduction: At the cantonal level, family medicine was initially not captured by the COVID information system, and data about COVID-related activity in this context were scarce apart from national data collected within Sentinella. We aimed to monitor trends of COVID-related activity in family medicine and paediatric practices in the canton of Vaud, in particular deployment of SARS-COV-2 tests and vaccines during the year 2021.

Methods: Family practitioners and paediatricians established in the canton of Vaud were invited to join an ad hoc sentinel surveillance system. Online data collection was based on daily activity reports and monthly questionnaires. In particular, participants categorized daily counts of consultations and phone calls into predefined COVID-related categories.

Results: Thirty-seven practices contributed regularly to the system over the year. Between March 20th and December 31st 2021, out of 81'407 medical consultations, 4'950 (6.1%) were related to new COVID suspicions as defined by the federal Office of Public Health, and 5'252 (6.4%) otherwise related to COVID. Depending on the week and the practice, between 5.6% and 26.5% of face-to-face consultations were COVID-related. In paediatrics, COVID-related activity corresponded mostly to new COVID suspicions (11.2% of on-site consultations), whereas among general internal medicine specialists and practitioners other COVID topics predominated (9.8% of face-to-face consultations), mainly questions about vaccination. Consultations for persisting COVID-related symptoms were stable at a low level throughout the year, and constituted less than 1% of all consultations. Most practices swabbed patients for SARS-CoV-2 tests, and an increasing proportion performed rapid antigenic tests over the year. In paediatrics, COVID-suspicions were not systematically tested, reflecting general virus circulation in the population. Concerning vaccination, after an initial interest in spring 2021 – when nearly 70% of family medicine practices offered on-site vaccination –, none delivered vaccines at the end of the year.

Conclusions: Throughout 2021, COVID-related consultations constituted an important part of family medicine and paediatric practices' activity in the canton of Vaud. Monitoring COVID-related activity in primary care during a pandemic documents how physicians translate recommendations into practice and provides health authorities with valuable information to guide public health action.

P102

Hypnosis for Long COVID symptoms: preliminary experience in Geneva University Hospitals

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Introduction: A significant proportion of COVID-19 patients present sequelae for several weeks or months after the disease. Symptoms can vary in intensity and severity and often include fatigue, dyspnea, cardiac (e.g. palpitations), neurological (e.g. headache) and psychiatric disorders (e.g. memory loss, lack of concentration, "brain fog"). These post-acute sequelae of SARS-CoV-2 infection are commonly referred to as "Long COVID". It is supposed that "Long COVID" can results as a consequence of a deregulated immune response.[1]
This condition is of public health concern with occupational, economic, and social implications, as people who were previously in good health are often extremely limited in their daily activities, to the point of having to reduce their percentage of work, retrain or apply for social assistance. There is no drug treatment for "Long COVID", instead this complex and proteiform condition requires a multidisciplinary, coordinated management.[2] A medical consulta-

tion dedicated to patients suffering from these symptoms was created at Division ofPrimary CareMedicine at the University Hospitals of Geneva.[3] In this frame, hypnosis is increasingly offered to these patients as an integrative tool for managing common symptoms like dyspnea, chronic pain, sleep problems, and anxiety.
Methods: Retrospective observational study including 10 patients referred to the Consultation of Hypnosis for "Long-COVID" symptoms. Symptoms modifications throughoutthe different hypnotic sessions, as well as patient satisfaction were assessed.

Results: Preliminary data from this small cohort, show that all patients experienced after a few (3-7) hypnotic sessions an improvement of their symptoms, increased comfort and personal empowerment.

Conclusions: The benefits of hypnosis, that "state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion", according to the American Psychiatric Association[4], have been ascertained in different medical disciplines[5]. Our preliminary observations suggest that hypnosis can have its place in the multimodal management strategy of "Long COVID" symptoms.

P103

Optimizing colorectal cancer (CRC) screening through quality circles of primary care physicians (PCP): a cluster randomized controlled trial

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Background: In Switzerland, CRC screening rates are below the recommended levels and few PCPs are aware of their own prescription practice nor offer their patients a choice between colonoscopy and faecal immunochemical test (FOBT) for CRC. We designed a cluster randomized controlled trial in primary care practices in Switzerland in quality circles (QC) of PCPs to test the effect of a multilevel intervention on CRC screening rates.

Methods: We invited QCs of PCPs to take part in a multilevel CRC screening intervention. QCs went through two Plan-Do-Check-Act (PDCA) quality improvement cycles, one year apart, the intervention group started PDCA right away; the control group waited 12 months before beginning the intervention. In the first PDCA cycle, we summarized the evidence for PCPs, gave them communication material enabling shared decision making about CRC screening and asked them to collect data from 40 consecutive patients to measure their current practice. The data collected enabled performance feedbacks with group discussions on their processes of care. We repeated the PDCA cycle in the intervention group after 12 months and compared the intervention group's outcomes to those of the control group when they started the intervention. The main outcome was CRC screening rate (colonoscopy in the last 10 years or FOBT in the last 2 years) 12 months after the start of the intervention among 40 consecutive patients per PCP. Secondary outcome was prescription of at least 1 FOBT among 40 consecutive patients per PCP.

Results: Of the 120 QCs we invited, 12 expressed interest and 9 took part in the study (5 intervention; 4 control). A total of 63 primary care physicians (32 intervention; 31 control) from these QCs collected data on 2114 patients (1132 intervention; 982 control; mean age 61.5, 53% women) 12 months after the start of the trial. In our intention-to-treat analyses, clustered by PCP and QC, the proportion of patients tested for CRC within recommended intervals was 58% (655/1132) in the intervention group and 42% (416/982) in the control group (OR 1.96;95%CI:1.13-3.40). The proportion of PCPs who had at least one patient screened with FOBT was 12 (37.5%) in the intervention group to 11 (35.5%) in the control group (OR 1.05, 95% CI: 0.35-3.55).

Conclusion: A multilevel quality improvement intervention with participatory approaches aimed at optimizing CRC screening in QCs of PCPs significantly increased CRC screening rates at 12 months follow-up.

P104

Pathways to career choice: a qualitative study to enhance a conceptual framework

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Introduction: In the context of efforts to make primary care (PC) a more attractive career option, we previously proposed a conceptual framework integrating various elements impacting career choice during medical school (1). We conducted this qualitative study to confront this hypothetical framework to the narratives about students' real-life experiences of their career choice process with a focus on PC.

Methods: We conducted semi-structured interviews with recent graduates of the Faculty of medicine in Geneva, recruited from a previous cohort study using a purposive sampling strategy to include participants positively inclined towards PC. Interviews were conducted to elicit narratives about paths to current career choices. Data were analysed iteratively by three researchers using an inductive approach; findings were discussed within an expert research team. After 14 interviews (10 females, 4 males), saturation was reached as no further themes were identified.

Results: Two main themes emerged. (1) The dynamic nature of the career choice process was expressed by the participants' image of their future profession evolving from a vague ("idealistic") to a more concrete ("realistic") image, in parallel with changing preferences. Students' priorities were increasingly driven by anticipated future needs, notably work-life balance and personal satisfaction. (2) Pathways to career choice were determined by the level of being committed to a career option, informing decision-making strategies. More committed students tended to use active, purposeful strategies focused on career planning. Less committed students described more passive behaviours such as waiting for opportunities to arise. All students engaged in explorative behaviours with the aim to discover or confirm career interests.

Discussion: Our study explores real-life experiences linked to career decision-making and validates two main elements of our conceptual framework. The "chronosystem" plays an overarching role as students' image of their profession and their own priorities evolve. Our analysis also enhances the hypothesized "trajectories", which are mainly a function of the level of being committed to a career option. Concretely, our findings may stimulate the reflection about how PC curricula may be adapted to students' evolving priorities, what opportunities for exploration of career options could be offered, and how individual career counselling could support students in their career planning process.

P105

Patients with a history of statin-associated muscle symptoms: can we get them back on statins? A systematic review and meta-analysis

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Introduction: Statin-associated muscle symptoms (SAMS) can negatively affect adherence to statins and clinical outcomes, although recent N-of-1 trials found large nocebo effects. The recommendations for the management of SAMS in the guidelines are still based on expert opinion. The aim of the study was to provide stronger evidence on the tolerability and acceptability of different statin-based tested strategies in patients with a history of SAMS.

Methods: We included randomized controlled trials (RCTs) examining adults with a history of SAMS, comparing interventions testing statin-based strategies with a control group. We searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Clinical Trials, Scopus, Clinicaltrials.gov and Proquest databases from inception to April 2021. Outcomes were incidence of SAMS, representing tolerability and treatment discontinuation due to SAMS,

representing acceptability. We pooled results using random-effects meta-analysis, expressing results as odds ratios (OR) for the incidence of SAMS and treatment discontinuation. OR >1 indicates higher incidence of SAMS and higher discontinuation rates in the statin-based treatment group.

Results: We screened 8,330 articles and identified 12 eligible RCTs. 9 trials were included in quantitative synthesis with a total of 1,669 participants in RCTs. There was high diversity in study design, statin dosage, comparators, follow-up duration and outcome assessments. The incidence of SAMS in RCTs ranged from 8.3% to 69.2% in the statin-based group vs. 0% to 79.6% in the control group. The discontinuation rates ranged from 0% to 22% vs. 0% to 25%, respectively. In the meta-analysis the incidence of SAMS was not increased in the statin-based intervention arm compared to the control (OR 1.21, 95% CI 0.92-1.60, p=0.18, figure 1). However, the risk of therapy discontinuation was higher with statin-based strategies (1.46, 95% CI 1.07-2.01, p=0.018, figure 2).

Conclusions: In patients with a history of SAMS, muscle symptoms and treatment discontinuation were common in trials comparing statins and different comparators. Although the risk of SAMS was similar between statin-based strategies vs. controls, more patients discontinued statin therapies over the trial duration compared to non-statin therapies. Although these findings need to be confirmed in larger dedicated trials, patients with a history of SAMS may get rechallenged successfully with statins if clinically indicated.

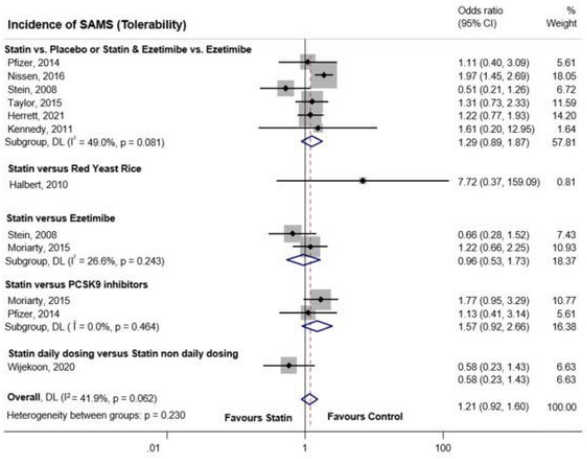

Figure 1: Tolerability expressed as odds ratios experiencing muscle symptoms. An odds ratio >1 indicates higher incidence of muscle symptoms in the statin or higher statin dosing group

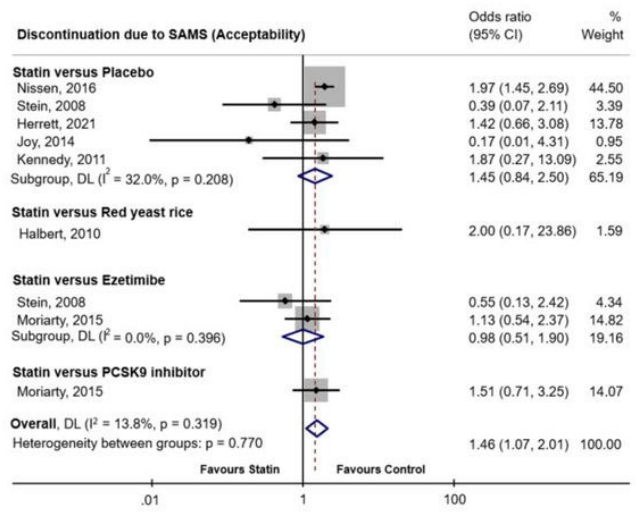

Figure 2: Acceptability expressed as odds of discontinuation due to muscle symptoms. An odds ratio >1 indicates higher discontinuation due to SAMS in the statin or higher statin dosing group

P106

Postgraduate training modules in Swiss general practice – an overview in the cantons in 2021: a project of SAFMED (Swiss Academy of Family Medicine)

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Introduction: Postgraduate training modules in general practice* form the backbone of General Practitioner (GP) training and are of central importance in promoting the choice to become a GP. The coordination of the GP training modules in Switzerland lies with the cantons, is therefore federally structured, and thus extremely heterogeneous regarding the offer, admission requirements, funding, and mentoring. To record the current supply of GP training module posts a survey in the 26 cantons was carried out on behalf of SAFMED, following comparable surveys in 2014 and 2019.

Methods: Data was collected from May to December 2021 by e-mail correspondence and telephone interviews with the responsible cantonal coordinators. Descriptive analysis was carried out using R software.

Results: All cantons currently offer a postgraduate GP training module programme (status December 2021). The canton of Ticino started in October 2021. A total of 285 posts are provided. The median number of posts per canton is 6.5 with a variance of one post (cantons NW and OW) to 45 posts (canton VD). In relative terms, the number of posts per canton varies from 0.4 posts (canton GE) to 12.4 posts (canton AI) per 100,000 inhabitants. An undersupply of posts (demand > supply) is reported in 11 cantons. Since 2019, the number of training module posts has been increased in nine cantons, and five cantons are planning an increase in posts in the near future. In Switzerland, 61% of the costs (= salary of the practice assistants) are covered by the cantons, 31% by the teaching practices themselves and 8% by the hospitals.

Conclusions: Encouragingly, by the end of 2021 all Swiss cantons offer a postgraduate GP training module programme. A substantial increase of 25 training posts has been documented since the year 2019. However, nearly half of the cantonal coordinators report an undersupply of training module posts and the relative supply per number of inhabitants in the cantons varies considerably. Further, the coordination, funding and mentoring of GP training module programmes are organised very heterogeneously across Switzerland. In the light of the promotion of young GPs, it seems mandatory to improve the coordination of the cantonal programmes to optimise their use.

* Deutsch: Praxisassistenz; Französisch: Assistanat au cabinet

P107

Quality and outcome of diabetes care during the COVID-19 pandemic in a primary care setting in Switzerland

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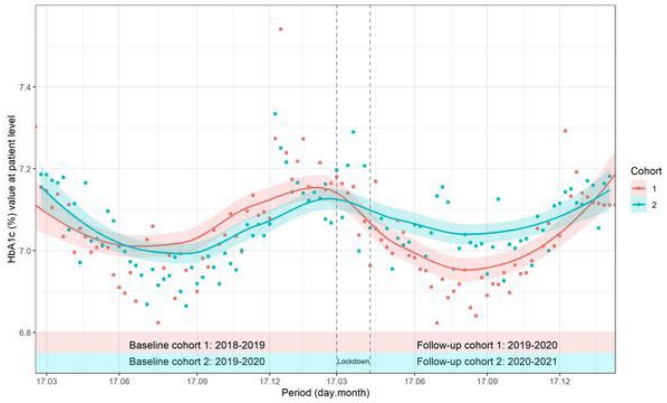
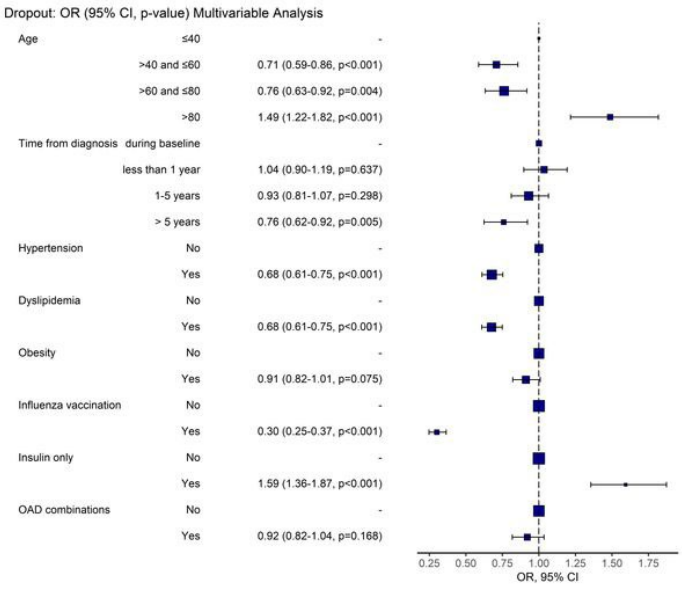
Introduction: During the pandemic, not only COVID-19 infections have an impact on public health but also the management of non-communicable diseases such as diabetes mellitus. Patients may not receive the same quality of care because of the pandemic. The aim of the study was to determine the impact of the pandemic on the quality and outcome of diabetes care.

Methods: This study was a retrospective comparison of two cohorts from the FIRE (Family Medicine ICPC Research Using Electronic Medical Records) database. Adult patients (≥18 years) with adiabetes mellitus and at least one consultation at a general practitioner, between 17.03.2018 and 16.03.2019 (cohort 1) and 17.03.2019 and 16.03.2020 (cohort 2), were included and observed for two years (until 16.03.2020 and 16.03.2021 respectively). Quality indicators and outcomes of diabetes care, at patient and practitioner level, were compared before and during the pandemic. Logistic regression identified patient's risk factors for dropout.

Results: A total of 27,043 patients and 191 practices were included, 23,903 in cohort 1 and 25,092 in cohort 2. The fraction of patients lost to follow-up, attributable to the pandemic, was 28% [95% Confidence Interval: 25%, 30%]. At patient level, the number of prescribed medications and comorbidities increased during the pandemic, compared to the previous year. Regular measurement of weight, Hemoglobin A1c (HbA1c), blood pressure and serum creatinine were less frequent.
At practitioner level, during the pandemic less patients reached the target of aHbA1c value ≤ 7% and a blood pressure value of <140/90mmHg. However, more patients had a LDL-cholesterol value of < 2.6 mmol/l. Although higher HbA1c values were observed after the lockdown, values converged, for both cohorts, to the same level by the end of follow-up (fig. 2).
Factors associated with continuity of care during the pandemic were: patient age between 41 and 80 years; diabetes onset of more than 5 years before the study start; diagnosis of hypertension or dyslipidemia; influenza vaccination during the last year. Risk factors for dropout were: age > 80 years and an insulin only medication regimen (fig. 5).

Conclusion: A considerable drop of quality in diabetes mellitus care could be observed during the pandemic (17.03.2020 - 16.03.2021). However, HbA1c values converged to the same level, for both cohorts, at the end of the observation period. Thus, the long term effect on relevant outcomes was not yet visible.





P108

State of communication between practices and hospitals – a survey among primary care physicians in the canton of Lucerne

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Introduction: Good communication practice and efficient information exchange between providers is vital when it comes to patient safety, effective coordination and continuity of care (Luu et al., 2016; Shahid and Thomas, 2018; Sheehan et al., 2021). The objective of this study was to assess the quality of communication between practices and hospitals in the canton of Lucerne as perceived by local primary care physicians (PCPs).

Methods: A structured questionnaire with 26 questions was the main instrument of this cross-sectional survey, developed through a two-step process. First step was the elaborate literature review to identify concepts and methods. The second step included direct communication with providers, with the aim of confirming the viability of literature findings and identifying additional opportunities of effective provider-to-provider communication. The questionnaire gathered data on demographics and type of practice, quality of communication and types of exchanged information/notifications, among other areas and was electronically distributed by email to 323 locally active PCPs.

Results: A total of 109 completed questionnaires was received from PCPs (56,9% male and 43,1% female), yielding an overall response rate of 34%. Most of the respondents, 43,1% of them, are experienced PCPs who have been practicing for more than 20 years. Although slightly more than half of PCPs were rather or very satisfied with the communication with hospitals, more than 20% of the respondents indicated their dissatisfaction with both the overall communication between their practice and hospitals, and with the communication during patient referrals. On top of that, 46% claim that they are rarely or never informed automatically about their patients being discharged from the hospital. Most respondents (94%) believe that emergency patient admission notifications would be useful, but only 11% receive this information on a regular basis. Regarding reports from the hospital, including admission notifications and discharge summaries, PCPs clearly prefer email as their primary communication channel (97%).

Conclusion: Our study shows that PCPs prefer communication by e-mail and support the implementation of emergency admission notifications when their patients are hospitalized. Applying the knowledge from this study by implementing processes and preferences regarding the contents of information and means of exchange may improve PCPs' experience communicating with hospitals.

P109

A case of severe aphthosis: infection, expression of systemic disease, or separate entity?

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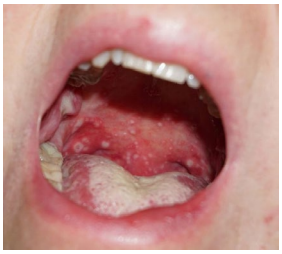
Learning objectives: Enoral aphthae are a common entity, usually responding to symptomatic treatment. In rare cases, severe expression of the disease needs further diagnostic workup to exclude an underlying disease and to determine the appropriate therapy.

Case: A 66-year-old female patient presented with multiple oral aphthae with increasing severity for about 8 weeks. Inpatient admission was necessary because of uncontrolled pain and a poor oral intake. Besides the oral aphthae, gastroduodenoscopy revealed an extensive amount of small ulcers in the whole esophagus. The gastric mucosa as well as vocal folds were free of ulceration, although isolated vaginal ulcers were observed. Laboratory results revealed an elevated CRP (188mg/l) and lymphopenia with no other significant findings.
Further investigations showed no evidence for an autoimmune disease, especially celiac or Crohn's disease. The patient did not fulfill the criteria for Behçet's disease as there were no other skin lesions, no eye lesions and a negative pathergy test. Serology ruled out an infectious genesis by HSV 1+2, VZV, CMV, HIV, Parvovirus B19, HBV

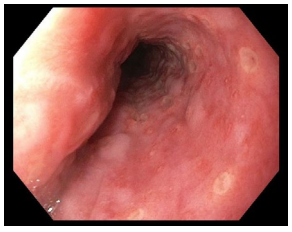
and HCV. Histologically, a nonspecific inflammatory reaction with no signs of infectious etiology, autoimmune bullous dermatosis or lupus erythematosus was seen. Direct immunofluorescence resulted negatively. Chest x-ray, brain MRI, abdominal sonography as well as a gynecological screening did not reveal any evidence for a paraneoplastic etiology.

Besides enteral feeding, pain control and local symptomatic therapy, we started high-dose corticosteroids (1mg/kg), resulting in clinical improvement and healing of the oral ulcerations within 7 days. The patient was discharged and steroids were reduced over 10 weeks. So far, one flare-up has been reported, needing low-dose corticosteroids for 2 weeks.

Discussion: After an extensive work-up to exclude a primary underlying disease, we settled on the diagnosis of complex recurrent aphthosis, which is considered as a separate disease entity. The etiology is unclear and likely multifactorial. First-line therapy recommendation is systemic corticosteroids in combination with topical therapy, although the evidence for a uniformly effective therapy is low. Colchicine and dapsone may be other treatment options. Complex recurrent aphthosis might be a precursor of systemic disease; therefore we highly recommend further monitoring.



Orophharyngeal ulcers in different size



Multiple small esophageal ulcers

P110

A case of shock and elevated procalcitonin revealing an acute calcium-pyrophosphate arthritis

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Learning objective: Calcium Pyrophosphate Deposition Disease (CPPD) is a frequent cause of arthritis, especially in the elderly population, and its variable manifestations can make the diagnosis challenging. Although procalcitonine (PCT) has shown a good predictive value to distinguish bacterial infections from non-infectious inflammatory diseases, its use in rheumatology is still debated.

Case: A 85-year-old female is hospitalized for a non-complicated erysipelas of the right lower limb, presenting with local inflammation, subfebrile state, mild inflammatory syndrome and stage I acute kidney injury. Amoxicillin is initially introduced with good clinical response.
At day 4 the patient mentions lower back pain, becomes febrile (38.6°C) and develops signs of shock (BP 70/28 mmHg, HR 115 bpm). Laboratory findings worsen, showing creatinine 286 µmol/L, CRP 470 mg/L, leucocytes 17.1 G/L, and high PCT 1.37 µg/L (normal < 0.5 µg/L). The source of infection is not identified according to blood and urine cultures, backbone and limb radiographies, abdomen and limb echographies, nor thorax abdomen and pelvis CT-scan. Cardiogenic or obstructive shock are ruled out by echocardiography and there is no element for an anaphylactic cause. Therefore a first hypothesis of septic shock of unknown origin is made and a broad-spectrum antibiotic is introduced (Imipenem). Despite the antibiotic, the patient's clinical and biological status worsens, CRP and leucocytes continue to rise.
Lumbar MRI (Fig. 1) excludes spondylodiscitis and identifies an inflammatory aspect of L5-S1 facets, with joint effusion and synovial contrast enhancement. Finally, the patient develops diffuse polyarthritis (ankles, wrists, metacarpophalangeans and proximal interphalangeans) and dedicated radiographies/echographies confirm a pseudogout flare.
Clinical and biological status improves only after introduction of Prednisone and Colchicine.

Discussion: As described in other cases in literature, we report a case of pyrophosphate microcrystal arthritis presenting with distributive shock and elevated PCT, mimicking a septic shock.
PCT is widely used as a biological marker to rule in a bacterial infection, nevertheless its diagnostic value remains controversial in the rheumatology field. More studies are required to define the appropriate use of procalcitonin in patients affected by an acute inflammatory state of unknown origin, mostly when a microcrystal arthritis is considered in the differential diagnosis.

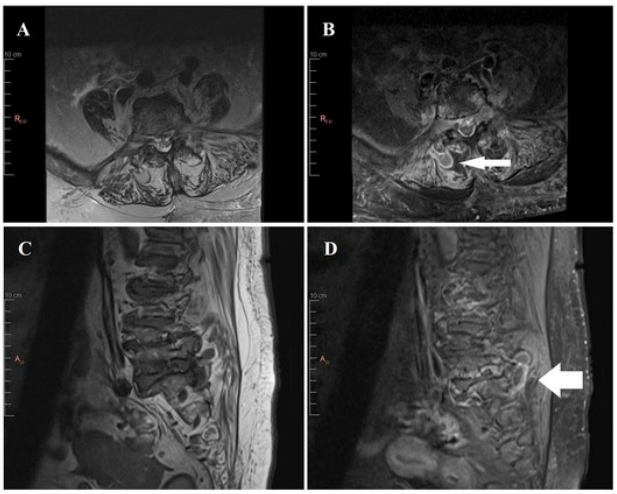

Figure 1.
T2-weighted (A) and fat-saturated constrast-enhanced T1-weighet (B) magnetic resonance images demonstrating joint effusion at the right L5-S1 facet joint (thin arrow).
T1-weighted (C) and fat-saturated constrast-enhanced T1-weighet (D) magnetic resonance images demonstrating synovial contrast enhancement at the right L5-S1 facet joint (bold arrow).

P111

A new mutation PUS1 R144Q defines a distinct anemia phenotype

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Learning objectives: To recognize a syndromic pattern of myopathy, lactic acidosis, and sideroblastic anemia as a distinct cause of anemia, and to discuss its clinical implications.

Case: Two siblings, brother and sister, of Syrian descent presented in our outpatient clinic in December 2020. Offspring of consanguineous marriage, they were born small for gestational age and reported progressive exercise intolerance since childhood. The 27-year-old male patient was diagnosed in Lebanon at the age of 20 years with sideroblastic anemia and thereafter regularly transfused with a total of 500 units of packed red blood cells. They both presented with short stature and no dysmorphic signs. Medical history of the extended family was inconspicuous. Laboratory investigation showed profound hypochromic, normocytic anemia. Ferritin values were elevated (8235 µg/L) in the heavily-transfused brother only. Blood lactate was elevated (maximal 21 mmol/L). Further analyses in the sicker male patient showed ring sideroblasts in the bone marrow and liver fibrosis. Based on the clinical and laboratory findings as well as on the consanguinity, genes of a syndrome called myopathy, lactic acidosis and sideroblastic anemia (MLASA) were analysed. The sequencing of PUS1 revealed a novel homozygous c.431G>A; p.(Arg144Gln) mutation. Both parents as well as 2 siblings carry the mutation in the heterozygous form, one sibling carries the wild type sequence. A favorable course of iron chelation was achieved in the male patient with daily subcutaneous application of deferoxamine over 12 hours via a pump system.

Discussion: Mutations in PUS1 characterize the rare autosomal recessive disease MLASA1. PUS1 is coding for pseudouridylate syn-

thase 1 which is a cytosolic and mitochondrial-expressed enzyme that converts uridine into pseudouridine in several transfer RNA (tRNA) positions, stabilizing the tRNA and increasing the efficiency of protein synthesis. The novel mutation R144Q described here lies in the highly conserved catalytic site of the enzyme[1,2], where another pathogenic mutation R144W has been described [2]. There exists no cure and no treatment. Courses of vitamin B6 or coenzyme Q10 were of no benefit in our patients. Nonetheless, recognizing the constellation of symptoms to adequately test for the specific genetic anomalies is essential to offer the right counseling and assess the hereditary risk in the family's offspring.

P112

A rare case of Herpes zoster-associated dermatomyositis

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Learning objectives: Herpes zoster (HZ) is an infectious disease caused by reactivation of a latent infection with Varicella zoster virus (VZV) in immunocompromised patients, after a primary infection seen in early childhood with remaining of VZV in the spinal ganglions. Diagnosis is usually made clinically, but can be assisted by serologic testing in selected cases. HZ most commonly causes a herpetiform dermatitis following one or more unilateral dermatomes. In rare cases, VZV reactivation can affect other organ systems, e.g. the central nervous system.

Case: A 66 years old male patient presented to the emergency room with acute right sided immobilising inguinal pain. Three days prior he had already been assessed by a family practitioner for a recent-onset painful rash on the right anterior thigh, which was clinically diagnosed as HZ and treated empirically with oral acyclovir. Upon presentation, the patient was febrile with a reduction of muscular strength of the right hip flexors (M2), decreased adductor and patellar reflexes without sensitive impairment. Locally, a rash extending over the L2 dermatome of the anterior thigh was noted. An MRI scan revealed diffuse hyperintensity of the right sided hip flexors with accompanying lymphadenopathia, compatible with myositis without signs of infectious arthritis (Figure 1). Blood analyses revealed significant elevation of inflammatory parameters (Table 1). Liquor analysis showed no signs of infectious radiculitis. A serologic analysis later revealed positivity of anti-VZV IgG and borderline positivity of anti-VZV IgA, but not IgM. Under continuation of systemic treatment with acyclovir as well as sufficient analgesic treatment the patient gradually recovered regaining motor function and mobility and was dismissed from hospital care after 8 days. A telephonic follow-up after 16 days revealed a pain-free, full-mobile patient with no signs of residual exanthema.

Discussion: In the present case, besides the compelling clinical picture, diagnosis of HZ was supported by serologic findings, including highly positive VZV-IgG and borderline VZV-IgA, compatible with VZV reactivation. While VZV reactivation is known to cause an exanthema following a dermatome, only few cases of VZV/HZ-associated (dermato-)myositis affecting the locomotor system and the skin have been reported, proven in this case by an affliction of the motor and sensory branch of L2 spinal nerve.

Table 1: Initial laboratory values and serologic results. *values >100 indicate immunity.

Parameter	Unit	Upper normal limit	Value upon presentation
Total leukocyte count	G/L	10.5	13.5
Lymphocytes	G/L	4.8	0.7
Monocytes	G/L	0.9	1.4
Neutrophils	G/L	7	11.3
Eosinophils	G/L	0.4	0.01
Platelet count	G/L	350	267
C-reactive protein	mg/L	10	183
VZV IgG	IU/L	N/A	**1084***
VZV IgA	Titer	<20	20
VZV IgM	Titer	<20	<20

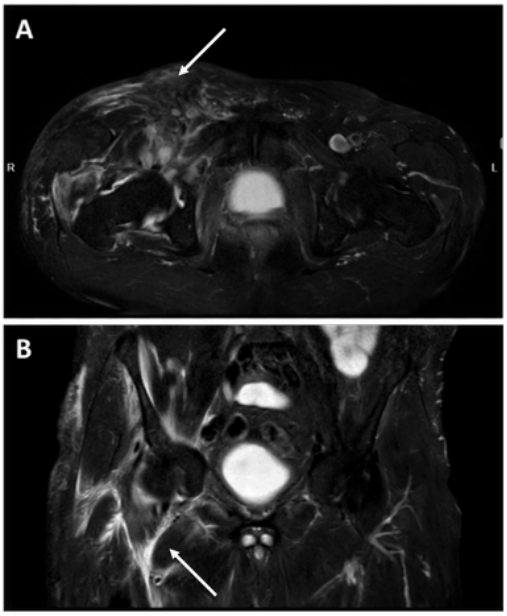

Figure 1: Axial STIR (A) and coronal DIXON T2 (B) MRI sequences hip both sides.

P113

A rare cause of intrahepatic cholestasis

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Learning objectives:

- Autosomal dominant polycystic kidney disease (ADPKD) is a multisystemic and common congenital disorder with a variety of extrarenal organic manifestations. The liver is commonly affected by cysts. Less common is a condition affecting the bile duct system associated with ADPKD.
- Caroli disease is a rare condition characterized by multifocal, segmental dilation of large intrahepatic bile ducts.

Case: A 76-year-old woman with an autosomal dominant polycystic kidney disease (ADPKD) and kidney transplantation 25 years ago was hospitalized because of sepsis due to infection in the urinary tract. C-reactive protein was highly elevated (254 mg/L) and urinalysis was pathological. On admission hyperbilirubinemia (61 µmol/L), elevated cholestatic enzymes (ALP 311 U/L, GGT 804 U/L) and slightly elevated transaminases (AST, ALT) were attributed to sepsis. A cholecystectomy had been performed years ago. Despite antibiotic treatment in line with resistance, liver enzymes and cholestatic enzymes remained elevated. Further diagnostic workup showed first in ultrasound and then in the CT scan intrahepatic cholestasis and atrophy of the left liver lobe with multiple parenchymal cysts. MRCP finally led to the diagnosis of Caroli disease (figure 1).

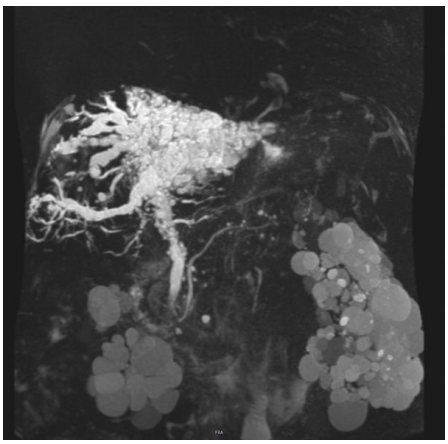

Figure 1: MR scan showing segmental dilation of intrahepatic bile ducts

Discussion: Caroli disease is a rare congenital disorder, which leads to multifocal segmental intrahepatic bile duct ectasia. The bile duct system of the left liver lobe is affected predominantly. Stasis of the bile leads to recurrent cholangitis and choledocholithiasis. The disease is commonly diagnosed during adolescence and patients present with recurrent episodes of cholangitis. Moreover, the risk of cholangiocellular carcinoma is elevated. The treatment is mainly symptomatically up to (partial) liver resection. In our case, the patient received a double pigtail stent to overcome a stenosis of the common hepatic duct.
Caroli disease is transmitted in autosomal recessive manner and is frequently seen with autosomal recessive polycystic kidney disease (ARPKD) as the same gene is involved. However, rare cases has been described in patients with ADPKD.

P114

A rare cause of lymph node swelling, fever and marked hyperhydration: Unicentric Castleman disease

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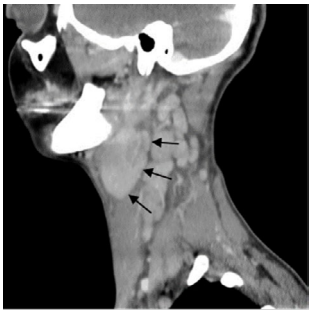
Learning objective: To ascertain considering Unicentric Castleman disease (UCD) when seeing a patient with regional lymph node swelling with co-existing features such as fever, fluid accumulation and blood count changes.

Case: A 35-year-old, otherwise healthy female initially presented to the ENT clinic with a non-painful swelling of the right cervical lymph node and compromised general condition. Inflammation markers appeared significantly elevated, moreover anemia and thrombocytopenia were detected. CT scan showed cervical lymphadenopathy with the most significant manifestation in Level II on the right side and no pathological thoracic or abdominal findings. Initially the otolaryngologists performed a fine needle biopsy which showed no infectious aspect as all microbiological and serological results were negative.
During the postinterventional follow-up the patient developed erythema of her neck which was interpreted as erysipelas and consequently treated with antibiotics. Via CT scan a possible abscess formation was excluded. After completion of antibiotic administration fever was ongoing. Meanwhile the patient developed severe peripheral edema, pleural effusions and a weight gain of 16 kg which prompted the transferral to the internal medical department for further diagnostics. The intravenous administration of fluids alone did not sufficiently explain the massive oedemas of the lower limbs. Regarding the pleural effusion the patient remained asymptomatic. Apart from the negative testing for infectious diseases the blood cultures also remained without pathogen detection. Due to the ongoing inflammation and fever of unknown origin it was decided to perform an excision of the affected lymph node. After the procedure the fever abruptly ended. The histological result presented the diagnosis of an HHV-8 negative, plasma cell-rich UCD. A PET-CT scan showed no residual lesions or other indications for malignancy.

Discussion: In patients with lymphadenopathy and further constitutional symptoms like fever and fatigue, fluid accumulation, anemia and thrombocytopenia UCD as a potential diagnosis should be taken into account and – instead of a Fine Needle Aspirate – an excision of the lymph node should be performed. Our case demonstrates the importance of early histologic confirmation in cases of unclear lymphadenopathy to avoid recurrent radiation exposure from CT examinations (our patient had 3 CT-Scans and 1 PET-CT).



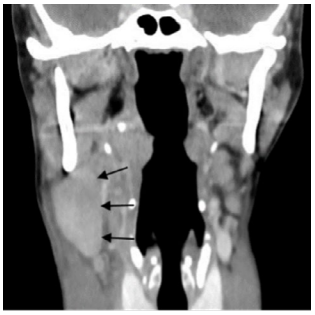


Fig. 1 & 2: CT scan

P115

Acute liver failure caused by traditional herbal medicine

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Learning objective: Acute liver failure (ALF) may be caused by use of traditional herbal medicine.

Case: A 55-year-old Asian man with no pre-existing disease presented with indolent jaundice since three weeks. The patient's history revealed oral intake of seven traditional phytotherapeutics *(Huang Lian, Huang Qin, Huang Bo, Zhi Zi, Sheng Qi, Mai Dong,Xuan Sheng)* during the preceding four months in order to strengthen his immune system. In addition, to treat recent febrile diarrhea, he had been taking oral cefixime for five days. Physical examination showed a generalised icterus, tenderness of the upper right abdomen and encephalopathy I°. Laboratory analysis showed ALF (INR 3.7, factor V 28%, bilirubin 667 µmol/l, ASAT 1118 U/l); ammonia levels proved slightly elevated (74 µmol/l). Initially, the lucid, sane patient refused listing for liver transplantation. Hepatoprotective therapy with acetylcysteine, vitamin K and lactulose was established. Extensive laboratory testing for underlying causes (autoimmune or acute viral hepatitis A-E, primary biliary cirrhosis, acute EBV, CMV, HSV or HIV infection, brucellosis, leptospirosis, vasculitis and Wilson's disease) was normal. Intake of acetaminophen or mushrooms was credibly negated. In abdominal sonography there was no pathologic finding. Transjugular hepatic biopsy showed (sub)acute cholestatic hepatitis without signs of fibrosis. Overall, we saw no explanation for the ALF except for the phytotherapeutics. Interaction with cefixime is arguable, yet jaundice beginning two weeks prior to antibiotic use suggested a separate cause. After deterioration requiring intensive care therapy the patient agreed to a liver transplantation, which was conducted due to urgent listing, as contra-indications were ruled out.

Discussion: ALF is associated with high mortality. In Western countries it is most frequently caused by drug-induced liver injury, mostly acetaminophen intoxication. While occasional interactions of the widely used herbal medicine with probable toxic effect are reported, literature on complications of traditional medicine remains rare. In our case a variety of possible causes for ALF could be ruled out, leaving toxicity of the herbal products the most probable trigger. Some of them are known to affect the CYP pathway and/or to have caused liver damage in other cases. The case stresses the importance of inquiry after herbal medicine when it comes to ALF and the necessity of larger studies assessing its safety.

P116

Amoebic liver abscess: diagnosis and management

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Learning objectives: In the case of acute upper abdominal pain in combination with elevated inflammatory values and a positive travel history, an amoebic abscess must be considered as a differential diagnosis. Detection of a trophozoite from aspirated pus is rarely successful. Differential diagnoses such as bacterial infection, echinococcal cysts, hepatocellular carcinoma, gallbladder empyema, and typhoid fever must be considered.

Case: We report the case of a 65-year-old man who presented to the emergency department with acute right upper abdominal pain and fever. Laboratory analysis showed markedly elevated leukocytes and C-reactive protein, indicative of acute infection, and mildly elevated transaminases. Sonography showed two inhomogeneous liver lesions. Computed tomography confirmed these lesions, but hepatocellular carcinoma was not assumed in the absence of cirrhotic changes. In the absence of eosinophilia, an echinococcal cyst was not assumed and empiric antibiotics with piperacillin/tazobactam were started. In case of a positive travel history (stay in Thailand two years ago), amoebic serology was performed, but in case of a low probability, therapy with metronidazole was not started.
As clinical condition did not improve and inflammatory parameters increased, a abcess drainage was inserted. In addition, the patient's respiratory condition worsened, and the inflammatory parameters continued to increase. Pulmonary embolism and acute coronary syndrome were excluded. At the same time, the amoeba antibodies (ELISA) from serology, as well as the Entamoeba histolytica

DNA from the puncture showed positive. Broad-spectrum bacterial PCR was negative. Cytology of the punctate did not detect trophozoites. Under antibiotic treatment with metronidazole, the inflammatory parameters regressed rapidly, as did the clinical symptoms.
Discussion: Amoebiasis is widespread, about 10% of the world population is infected, 50 million are invasive, of which about 100,000 die per year (1). In our latitudes, invasive amebiasis must be considered if there is a positive travel history, upper abdominal pain, and liver abscess formation. Outbreak can also occur months to years after the onset of infection. Complications of invasive Amoebiasis include rupture into the pleural space or pericardium. Direct detection of trophoicites from the punctate is usually difficult.
Therapy includes metronidazole against the trophozoites, and follow-up with paramycin to clear the cysts.

P117

Approach to a complicated case of hyperthyroidism

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Learning objectives: The term thyroiditis indicates several clinical disorders characterized by inflammation of the thyroid gland, which can result in either a hypothyroidism or an unregulated release of preformed thyroid hormones leading to hyperthyroidism. The underlying cause is often unclear; a multidisciplinary approach is needed.

Case: A 55-years-old patient was referred to our outpatient clinic for evaluation of clinical and biochemical primary hyperthyroidism.
The patient had a history of multiple thyroid nodes, severe autoimmune hepatitis and associated aplastic anemia and was treated with immunosuppressive medications such as prednisone, anti-thymocyte globulin and cyclosporine. One month before symptoms onset, she received an inactivated influenza vaccine followed by influenza-like illness for 3 days. At the diagnosis of hyperthyroidism, she was treated with decreasing cyclosporine doses and was in remission with regard to hepatitis and aplastic anemia.
The patient complained about tachycardia, nervousness and weight loss. The clinical examination showed no tenderness in the thyroid area. In the laboratory analysis fT4 and fT3 were increased (62.7pmol/l and 30.8pmol/l, respectively) while TSH was suppressed. Anti-TSH-Receptor- and Anti-TPO-Antibodies were negative. In a thyroid ultrasound, performed 1 month before symptoms onset as follow-up assessment, a normal size thyroid gland was documented with multiple thyroid nodes. A thyroid scintigraphy with ^{99m}Tc pertechnetate showed a low tracer uptake (0.3%) with no signs of autonomy, consistent with the diagnosis of a thyroiditis. A spontaneous symptoms improvement and remission of fT4- and fT3-levels was observed within three weeks.
Given that no other causes could be identified, we concluded that the thyroiditis is most likely part of the general autoimmune context, cyclosporine-induced or caused by the influenza vaccine (both rarely described in the literature).

Discussion:
1. Thyroiditis can present without classical clinical inflammation signs, like pain or tenderness in the thyroid area.
2. In the context of the history of the patient an autoimmune thyroid disorder (Grave's disease) or a thyroiditis has to be considered with different therapeutical consequences. Since the accuracy of the thyroid antibodies is not 100% the timely performance of the Technetium scintigraphy offers a significant help.

P118

Awareness of cognitive biases during a pandemic is especially important

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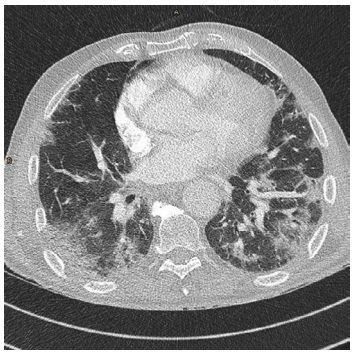
Learning objectives:

- In times of high prevalence of a disease, it is important to avoid cognitive biases
- Availability bias and premature closing

Case: A 75-year-old man presented to our emergency department with pain in both wrists for a month. Laboratory showed elevated liver enzymes, lactate dehydrogenase, and CRP. Radiography of the hands and liver sonography were unremarkable. Due to additional reported general muscle weakness, CK was measured and was very high (5580 U/l). Electromyography of the deltoid muscle and total body MRI supported the presence of myositis. Finally, the myositis panel with positivity for anti-Jo-1 antibody led to the diagnosis of anti-synthetase syndrome (AS).
Three months earlier, during Covid-19 pandemic, he presented with a 3-week history of dry cough and has been hospitalized in another clinic for hypoxic respiratory failure supposed to have COVID-19 (Figure 1). But repeated diagnostic testing for SARS-CoV-2 (PCR, serologic antibodies) were negative. Nevertheless, he received a standard treatment with dexamethasone and antibiotics for ten days and went for rehabilitation. One month later, short-term follow up showed persistent subpleural parenchymal opacities and further diagnostic tests for interstitial lung disease (ILD) showed normal ANA and ANCA. A follow up was arranged three months later, but in the meantime, AS was diagnosed at our institution. Retrospectively, the first hospitalisation was already a manifestation of AS with the diffuse ILD.
It took almost four months from the first onset of symptoms to the final diagnosis and accurate treatment initiation.

Discussion: Cognitive biases play a significant role in the COVID-19 pandemic. This case demonstrates that the cognitive shortcut of cough, hypoxic respiratory failure and pulmonary opacities led to the diagnosis of COVID-19 pneumonia due to the high prevalence at that time. This is known as an availability bias. Not having a positive test result despite repetitive testing should render the clinician suspicions for an alternative diagnosis, for example other diffuse ILD. This is well known as the premature closing bias. This case highlights the importance of being aware of cognitive errors especially during pandemics when other diagnosis is in general more likely. The diagnosis of AS could have been made earlier.



[Figure 1. Chest CT scan on first admission showing consolidations and ground-glass opacities predominantly subpleural and in the lower lobes.]

P119

Cancer is sometimes a bat

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Learning objective: Historically in X-rays pulmonary tularaemia presented with infiltrates and hilar adenopathy. With CT scans being widely available now, findings closely resembling those of pulmonary malignancy.

Cases: We present two cases of pulmonary tularaemia with distinctly different routes of presentation. Both patients were suspected to suffer from metastasised pulmonary cancer until PCR confirmed the presence of F tularensis (Francisella tularensis).
The first case concerns a 63-year-old Swiss male who presented to a peripheral Austrian hospital with a 5 day history of fever and cough. After initial diagnosis of pneumonia and treatment with antibiotics, his condition did not improve. A CT scan of the chest showed highly suspicious lesions for lung cancer in the right upper lobe with lymph node involvement. A PET CT confirmed metabolic activity of the lesions. Biopsies obtained via EBUS-TBNA (transbronchial needle aspiration) and thoracoscopy showed inflammation, but no indication of malignancy. Upon further questioning,

the patient reported that he had been clearing up dead bats in the course of renovations of his holiday home in Austria. A PCR of the biopsies was positive for F tularensis. The patient was treated with Gentamicin and Doxycycline and remains well in 4 month follow-up.
The second case describes a 48-year-old Syrian man who was referred by his GP after a CT scan, which was obtained due to persistent fever and cough. The CT scan showed a suspicious nodule with involvement of the visceral pleura and lymph node enlargement (Figure 1 A&B). Metabolic activity was confirmed by PET CT (Figure 1 C). EBUS-TBNA and thoracoscopic biopsy showed inflammation, but no malignant tissue. PCR of the obtained tissue was positive for F tularensis.

Discussion: Tularaemia is a zoonotic disease most prevalent in the northern hemisphere. In Europe, the number of cases is approximately 800 annually. In general, the incidence is lower in central and southern Europe. In the past decades, data show a migration of F tularensis to western Austria and successively Switzerland.

With advanced imaging techniques the radiological findings often resemble those of pulmonary neoplasia. The subsequently necessary procedures cause considerable stress for the patients as well as the health care system.
When completing the work-up of a suspected pulmonary malignancy pulmonary tularaemia should be considered a primary differential diagnosis.

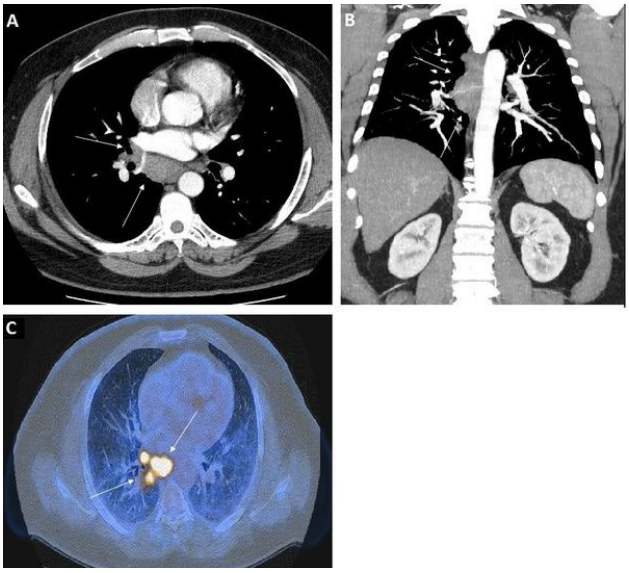

Figure 1

P120

Cardiogenic shock – an endocrine emergency?

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Learning objective: Pheochromocytoma is a rare neuroendocrine tumour with a diverse clinical presentation. Cardiomyopathy due to catecholamine hypersecretion is a potentially life-threatening complication.

Case report: A 56 years old man was referred to our emergency department with cardiogenic shock. He did not take any drugs and his medical history only included a thalassaemia as well a severe depression. Some days before admission, the patient had received his first SARS-CoV-2 vaccination. Laboratory parameters revealed a severe lactate acidosis as well as evidence of multi-organ failure. Echocardiography revealed a severely depressed left ventricular ejection fraction (LVEF) of 10%. Cardiac MRI did not reveal evidence of a specific heart failure etiology. The myocardium appeared fully viable despite massive troponin release. Under heart failure therapy, LVEF improved to 31%.
Diagnostic review of the initially not available external CT scan revealed a tumour in the surroundings of the upper pole of the right kidney. Therefore, plasma metanephrines were analysed and an abdominal MRI was performed showing a large (6 x 7,5 x 6cm) tumour originating from the right adrenal gland. A few hours after the MRI, the patient's situation deteriorated: Alternating hypo- and hypertensive crisis as well as ventricular tachycardia occurred. Since the suspected pheochromocytoma crisis could not be stabilized, an emergency adrenalectomy was performed without preoperative alpha-blockade. Histological analysis confirmed a pheochromocytoma. After surgery, the patient recovered rapidly and LVEF normalized.

Discussion: The various and often unspecific symptoms combined with the rare incidence of pheochromocytoma makes its clinical recognition challenging. If pheochromocytoma is diagnosed, a mostly laparoscopic resection is the first-line therapy. Intraoperative manipulation of the tumour can elicit hypertensive crises due to sudden release of catecholamines. Therefore, preoperative alpha-blockade is currently still recommended, although some studies question this general recommendation.
Pheochromocytoma crisis remains a very rare endocrine emergency associated with significant mortality. Diagnosis should be considered, especially in case of unexplained cardiomyopathy, multi-organ dysfunction, severe hypotension or cardiogenic shock.

P121

COVID-19-vaccination-failure and Good's syndrome

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Learning objectives: Good's syndrome is a rare entity, defined by Thymoma and acquired immunodeficiency. In the case presented, the vaccination failure may provide insights into the B-cell dependent antibody response in a patient with Good's syndrome.

Case: A 56-year-old female presented to the emergency unit with cough, fever and dyspnoea, 17days after she had been tested positive for SARS-CoV-2-RNA. She was vaccinated twice with Spikevax ® (mRNA-SARS-CoV-2-vaccine by Moderna) 8 months earlier. Generally, she is reported to be healthy but had noticed a weight loss during the past weeks. A test for SARS-CoV-2-specific IgG- and IgM- antibodies (Ab) yielded negative results, a CT-scan showed COVID-19-typical opacities in all lobes and as an additional finding a tumoral growth in the anterior mediastinum (size 8 x 10 x 6 cm). The patient was treated with monoclonal antibodies (REGEN-COV Casivirimab/Indevimab) and Dexamethasone during her 9 days of oxygen treatment. The course of disease was favourable, and the patient was discharged after 11 days. The guided CT scan biopsy of the mediastinal mass confirmed an A / AB-Type Thymoma.
Blood test after 4 weeks revealed positivity for SARS-CoV-2-Spike-Ab, yet no SARS-CoV-2-Nucleocapside-Ab were detected. An absence of B-lymphocytes a CD4+- T –cell-lymphopenia with reduced CD4+/CD8+ T cell ratio was identified. Serum levels of IgG-, IgA- and IgM- were low. Overall, these findings associated with Thymoma allow the diagnosis of Good's syndrome.

Discussion: Goods' syndrome is a very rare disorder, characterised by the presence of thymoma associated with hypogammaglobulinemia, CD4+-T-cell-deficiency, reduced B cell count or even the absence of B cells. Lately, several cases have been reported on patients diagnosed with Good's syndrome and affected by the SARS-CoV-2, some of them with fatal outcome. To our knowledge this is the first case report on a patient with vaccination failure due to Goods' syndrome. The acquired immunodeficiency abrogates humoral vaccine response, similarly to B-cell depleting therapies with anti-CD 20 antibodies or Bruton tyrosine kinase inhibitors. The absence of B-cells and CD4+-T-cells which is characteristic for Goods' syndrome, may play a key role in the lacking seroconversion after immunization.

P122

Diagnosis of Giant Cell Arteritis with ultrasound: a case report

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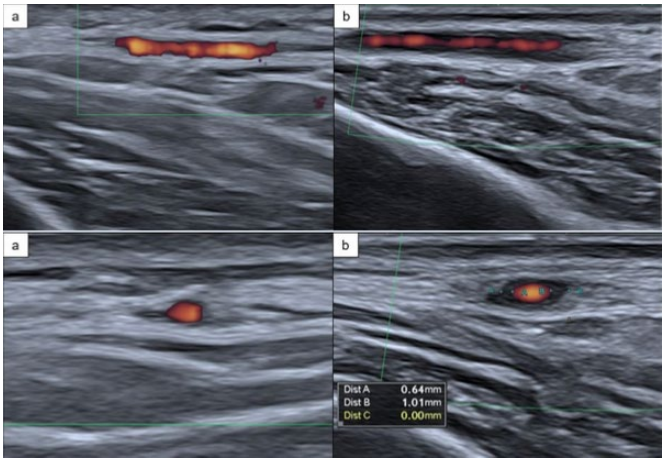
Learning objective: Ultrasound is increasingly being used for diagnostic and therapeutic purposes in internal medicine. The sonographic diagnosis of Giant Cell Arteritis (GCA) has favourable performance characteristics and performance by internists in acute care settings is feasible.

Case: A 67-year old female was referred to the emergency department by her ophthalmologist with diplopia and a frontal headache. Retinoscopy and measurement of intraocular pressure showed no significant abnormalities and posterior circulation stroke was suspected.
The patient described fatigue, aching of the jaw with myalgias of the proximal upper and lower extremity muscles as well as scalp tenderness. Clinical examination revealed vertical diplopia and tenderness over the temples. Laboratory findings showed an elevated C-Reactive Protein and a highly accelerated erythrocyte sedimentation rate. Magnetic resonance imaging of the head demonstrated no signs of a stroke, neuritis or tumor. Specific sequences for evaluation of GCA were not performed.
Given the clinical suspicion of GCA, we performed a doppler sonography of the temporal arteries using a Canon Aplio i700 with a high frequency i18LX5 probe. Both temporal arteries showed hypoechogenic, irregular vessel walls that were thickened up to 1 mm (halo sign). On compression the flow ceased but the thickened walls were still visible (compression sign).
Given the constellation, we diagnosed a GCA and started high dose steroids. Three days after admission the patient was discharged with almost complete remission of symptoms for further outpatient follow-up.



Halo sign: temporal artery of a healthy proband (a), and the female with GCA (b).

Discussion: The simultaneous trends of improving resolution and portability of devices have led to ultrasound having an important role in initial diagnosis and therapy which has the potential to reduce time to diagnosis, length of stay and more costly, elaborate or invasive procedures. In keeping with international guidelines, we recommend ultrasound of the temporal arteries as a first-line diagnostic tool if clinical evaluation and laboratory findings are suggestive of GCA. If a halo and compression sign is detected by the doppler ultrasound, the diagnosis of GCA can be made without further examination, as we show in this case report. We support the adoption of ultrasound for the diagnosis of GCA in acute care settings and recommend its adoption as a routine part in the clinical practice.

P123

Discitis caused by *Helicobacter cinaedi* in an immunocompetent host

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Learning objectives: In Switzerland *Helicobacter cinaedi* is a rare pathogen and as an enterohepatic species mainly causes bacteraemia, cellulitis and gastroenteritis. Singular case-reports have described vertebral osteomyelitis caused by *H. cinaedi*. Due to its fastidious nature, this organism poses a diagnostic challenge. A possible route of transmission is contact to farm animals and rodents.

Case: A 62-year-old man from Kosovo presented with chronic lower back pain, radiating to both groins, which had intensified three days prior to consultation. Past medical history included several analgesic infiltrations of the lumbar spine, the last dating back more than a year. Review of systems revealed no fever or further symptoms of infection. Travel history revealed journeys to the Balkans on a yearly base. The only reported animal contact was to poultry. Physical examination revealed paravertebral muscle tenderness in the lumbar region. Laboratory tests showed normal white blood cell count and markedly elevated C-reactive protein (CRP). Magnet resonance imaging (MRI) was consistent with osteoarthritis of vertebrae L1-L2. Analgesic therapy was initiated and the patient was discharged. Due to persistent pain and elevated CRP, MRI of the lumbar spine was repeated three weeks after discharge, which now revealed discitis L1/L2 with paravertebral abscesses. Blood cultures and abscess material did not grow any microorganisms. Nor did *M. tuberculosis* complex PCR testing yield a positive result. Serologic tests for *B. henselae*, brucellosis and *C. burnetii* were negative. Serial echocardiographic imaging was negative for endocardial involvement. After performing open biopsy, eubacterial PCR revealed *H. cinaedi* DNA fragments while cultures remained negative. Enteral bacterial translocation was suspected, although endoscopic examination was negative. Intravenous antibiotic treatment with ertapenem was established for six weeks with improvement in CRP level and symptoms.

Discussion: *H. cinaedi* is known for causing bacteraemia in the immunocompromised host. Cases of vertebral osteomyelitis with *H. cinaedi* have previously been described. Its rarity and slow pathogen growth on conventional media present the physician with a diagnostic challenge, especially in the oligosymptomatic, immunocompetent host. *H. cinaedi* should be considered in the immunocompetent host, if strong suspicion of bacterial caused discitis persists in the absence of cultural pathogen detection.

P124

Epitheloid angiosarcoma of the thyroid (TAS): an unexpected autopsy finding

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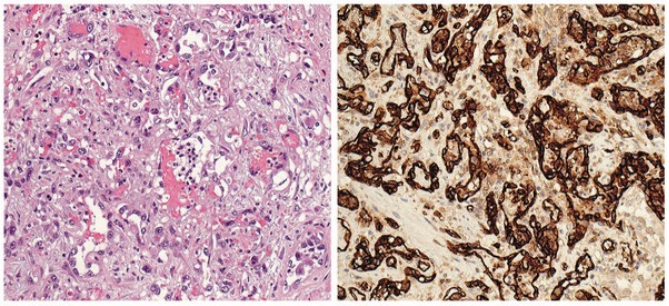
Learning objectives: Thyroid angiosarcoma (TAS) is a very rare, highly aggressive malignant vascular tumor, mainly seen in the Alpine regions. It accounts for up to 16% of all malignant thyroid tumors in Switzerland, Austria and Northern Italy most possibly due to the iodine deficiency in these areas, which leads to chronic multinodular goiter. The clinical manifestations are non-specific and vary depending on its size, extension and presence of metastases.

Case: An 83-year-old patient was referred to the emergency room due to weakness, loss of appetite and weight, hemoptysis and diarrhea for over a month. The clinical examination showed enlarged cervical lymph nodes on the left side and bilateral rales in the lung auscultation. Our differential diagnosis included malignant (metastases, primary lung cancer, lymphoma), infectious (viral, bacterial, fungal) and autoimmune (vasculitis, sarcoidosis) diseases. We conducted an intensive work-up to identify the underlying cause:

Laboratory tests	Hyponatraemia, anemia, increased inflammatory parameters
ABG (room air)	Severe acute partial respiratory failure
SARS-CoV-2 PCR	Negative
Sputum sample (TBC)	Negative
CT Thorax	DD septic embolism or lymphoproliferative disease, enlarged mediastinalandhilar lymph nodes, multinodular goiter
Bronchoscopy	Fresh blood endotracheal/endobronchial; no active bleeding, significant lung parenchyma changes
- Cytology	No malignant cells
Vasculitis-Screening (MPO,PR3, ANCA)	Negative
Thyroid ultrasound	Volume min. 100 mL, large nodular conglomerate in the left thyroid lobe, enlarged, rounded, hypoechoic lymph nodes
CTheadand neck	No additional masses or intracranial tumor manifestations

We organized a lymph node biopsy and initiated an empiric antibiotic therapy (Co-Amoxicillin) to cover a possible pulmonary infection. A rapid deterioration resulted to death of respiratory failure 10 days after admission. The autopsy confirmed an epithelia primary angiosarcoma of the thyroid with extensive metastasis including tumour embolisms and haemorrhages in all lung lobes and multiple lymph node metastases.

Epitheloid angiosarcoma in the thyroid gland



HE (200x) CD31 immunostaining (400x)

Discussion: There is no established consensus on the therapeutical approach of TAS. Early radical surgery is considered the first-choice treatment in cases of removable tumor.Complementary radiation and/or chemotherapy may also be effective. Nevertheless, its rapid spread, high recurrence rate and non-specific clinical presentation contribute to a fatal course with most patients dying within six months after diagnosis. Therefore, raising awareness about primary TAS is vital to enable alertness in our differential diagnosis, provide early recognition and help guide an individualized treatment plan.

P125

Fever of unknown origin, immunosuppression and vascular event: think about Neoehrlichiosis!

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Case: A 65-year-old woman (patient 1) and a 59-year old man (patient 2) were referred to our hospital because of fever of unknown origin (FUO).Patient 1 had rheumatoid arthritis treated with Rituximab(Rtx) and Leflunomid, patient 2 a history of hairy cell leukemia treated with Rtx-containing-chemotherapy and splenectomy. A history of tick bites was not evident.At presentation both patients were febrile and had chills.Patient 1 presented with a thrombophlebitis of the right leg, patient 2 developed a deep vein thrombosis of the left leg. Both patients had leukocytosis, elevated CRP and slightly elevated liver enzymes. Recurrence of the rheumatic and oncological disease, respectively, was excluded. The cause of FUO remained open despite intensive diagnostics. Because of hepatomegaly and elevated liver enzymes patient 1 received a liver biopsy, showing phagocytosis of red blood cells and activation of macrophages (figure 1). The triad of immunosuppression, fever and vascular event lead finally to the diagnosis. Infection with Candidatus Neoehrlichia mikurensis (CNM) was confirmed by positive PCR in peripheral blood.Doxycycline was started for 6 weeks and switched to Rifampicin in patient 1 because of side effects. Both patients had full recovery after the start of therapy.

Discussion: CNM is the causative agent of neoehrlichiosis and is transmitted via tick-bites.CNM has a prevalence between 3.5-8% in ticks collected around Zürich1.Its diagnosis remains challenging since CNM does not grow in routine blood culture.Up to date only about 100 cases of human CNM infection have been described worldwide2.Known risk factors associated with disease severity are splenectomy,malignant or autoimmune clonal B-cell disease and anti-B cell therapy2,as in our patients. Only recently CNM could be cultivated in human endothelial cells3.The endotheliotropism could explain the frequent association of CNM infection with vascular events2.To our knowledge this is the first histopathological study of liver tissue in CNM infection with evidence of hemophagocytosis. This data rise the question if symptomatic CNM infection might be in part related to host inflammatory and immune responses4.

Learning objectives: CNM is a recently identified intracellular bacterium that cannot be identified in standard blood cultures.
The triad of fever, vascular events and immunosuppression(especially anti CD20 therapies like Rtx)should prompt to search for CNM also in the absence of recalled tick-bites.

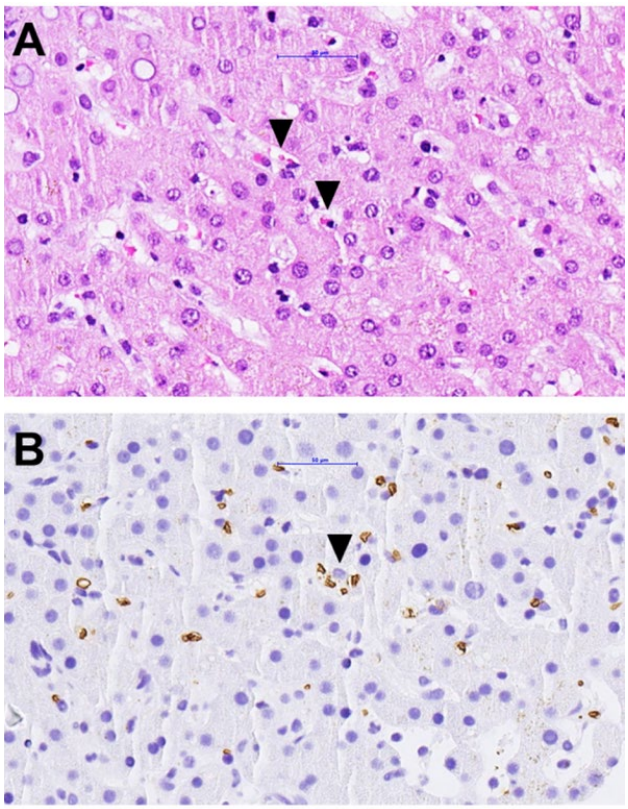

Figure 1. Liver Biopsy, 40x magnification, stained with hematoxylin and eosin (panel A) as well as immunohistochemical staining for Glut-1 (panel B, brown stain denotes positive reaction in erythrocytes). The arrow heads point to erythrocytes and fragmented erythrocytes undergoing phagocytosis / hemophagocytosis within the body of macrophages in the Disse' space

P126

Graves` disease caused by SARS-CoV-2 infection

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Learning objective(s): While acute lung injury represents the most severe form of COVID-19 we must note that other organs, including the thyroid gland, may be directly or indirectly affected by SARS-CoV-2. The acute inflammatory response seems to trigger an immunological response causing Graves` disease.

Case: We report the case of a 54-year-old woman who presented at the emergency room suffering from weakness, dyspnea and palpitations. In the last 2 months she lost 6 kg of weight despite normal appetite. In addition, she complained of a progressive action tremor lasting for three weeks. Two months ago, she was tested positive for Sars-Cov-2 and suffered a mild course of COVID-19, not requiring hospitalization.
Clinical examination showed mild tachycardia, high frequency tremor of the lower extremities and hyperreflexia. Thyroid function tests revealed thyrotoxicosis with a low serum TSH concentration (<0,01 mU/L) and elevated levels of free thyroid hormones (FT4 59,2 pmol/l and FT3 28.7 pmol/l). Additionally, thyrotropin receptor antibodies (TRAb) were positive (4.04 IU/L). Concluding Graves 'disease[BL1] , treatment was started with carbimazol and propranolol resulting in quick improvement of the symptomatology[BL2] .

Discussion: The number of published case reports on different autoimmune diseases, possibly triggered by an infection with Sars-CoV-2, is constantly increasing. Guillain-Barré- Syndrome, autoimmune hemolytic anemia and autoimmune thrombocytopenic purpura present most of the cases. In respect to the thyroid gland, cases of autoimmune mediated Graves 'disease as well as inflammation driven forms of thyroiditis are reported. The thyroid tissue is characterized by one of the highest densities of Angiotensin converting enzyme 2 (ACE2) in the human body. In respect to Sars-CoV-2, ACE2 functions as the host cell receptor for this virus. It is therefore well possible that different thyroid pathologies are triggered by a tissue specific infection with Sars-CoV-2. The T cell system plays an important role in graves 'disease and together with interleukin 6 is also one of the immunological main players in COVID-19. Furthermore viral infections are frequently cited as a major environmental factor involved in the pathogenesis of autoimmune thyroid diseases.
Therefore physicians should be aware of the possible relation between an infection with SARS-CoV-2 and thyroid dysfunctions and consider testing according to symptoms.

P127

Heart rate in a pacemaker patient below programmed base rate: an error in pacemaker function?

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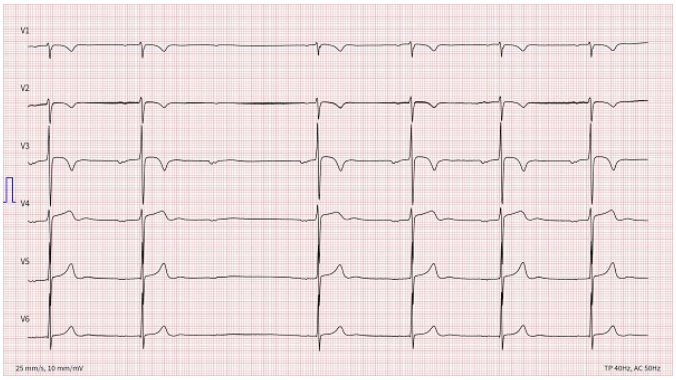
Learning objective: In cardiac pacemaker (PM) therapy, heart rate (HR) below programmed base rate can occur despite normal device function (AV or rate hysteresis, automatic threshold testing, "sleep mode") or due to device malfunction (technical problem with generator or leads, electromagnetic interference).

Case: A 67-year-old male patient presented for routine PM follow-up three months after dual chamber PM implantation because of sick sinus syndrome (SSS). The PM was programmed at a base rate of 40 bpm (corresponding to an interval of 1500 ms). In the resting ECG (*image*), an atrial bradycardia (HR 41 bpm) with Wenckebach behaviour and a ventricular pause of 2.84 s (2840 ms) were visible. Chest radiography showed proper position of the two PM leads. The patient was completely asymptomatic and reported good physical performance during sports.

Discussion: In cardiac pacemaker patients, excessive ventricular stimulation is associated with a 2.6-fold risk of hospitalisation due to decompensated heart failure, an increased risk of atrial fibrillation, developing left ventricular systolic dysfunction, left atrial dilation, and premature battery depletion. Therefore, in patients with primary sinus node dysfunction and intact atrioventricular (AV) conduction, reduction of unnecessary ventricular pacing with algorithms to promote intrinsic ventricular activation is reasonable. AV hysteresis is a concept that allows a PM to work mainly in a "functional" AAI mode (atrial pacing and sensing) with switching to DDD mode (both atrial and ventricular pacing and sensing), if AV conduction deteriorates. AAI mode will then be activated again after a certain amount of cycles with normal AV conduction. In the case presented above, AV hysteresis with programmed maximum pause for ventricular activity of three seconds was the cause of the ECG findings. Signs for activated AV hysteresis are the current pacing mode (in our case AAI<=>DDD). In doubt, interrogating with a PM programmer can reveal the status of AV hysteresis. Other reasons for HR below programmed base rate in a PM patient with normal device function are rate hysteresis (algorithm to allow prolongation of sensed intervals to reduce pacing), during automatic pacing threshold testing, or in "sleep mode" (reduction of base rate during the night). Functional issues or actual device malfunction (technical problem with generator or pacing leads, electromagnetic interference) can also result in HR below programmed base rate.



P128

How to diagnose tick-borne encephalitis (TBE) in vaccinated patients

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Learning objectives: Switzerland is an endemic area for TBE viruses. With vaccination, there is an effective protection option, as the therapy is purely symptomatic and only in 70%, patients notice the tick bite. In vaccinated patients, however, TBE serology in serum is inconclusive. Measurement of NS1-antibodies can be useful to confirm the diagnosis.

Case: We report a case of a 78-year-old patient presenting to our emergency department with fever since 4 days. Other symptoms were absent. Personal history includes coronary heart disease and treated hepatitis C. Laboratory findings revealed mild leukocytosis and normal CRP. A CT scan of the brain were without any pathological findings. According to his relatives, the patient seemed slowed down and tired. The neurological examination showed impaired short-term memory in the sense of a mild encephalopathy. Serological tests for tick-borne encephalitis (TBE) were positive (IgG >24,0, IgM >7,6 MOC). The cerebrospinal fluid revealed a mild pleocytosis (54/µl, a disrupted blood brain barrier but no intrathecal synthesis of immunglobulin). The patient was fully vaccinated for TBE nine years before. The detection of non-structural protein 1-antibodies (NS1) in the vaccinated patient confirmed the diagnosis of an acute tick-borne encephalitis.

Discussion: TBE is an infectious disease caused by the TBE virus from the flavivirus group. TBE viruses are mainly transmitted by ticks. Often there is a bimodal fever course. Neurological deficits in the sense of consciousness disturbance, balance disorders, ataxia, paralysis of cranial nerves or extremities are possible. An isolated meningitis occurs in 50%, meningoencephalitis in 40% and meningoencephalomyelitis in 10% respectively. There is no causal therapy available, permanent neurological damage has been described and the mortality is 2%. The detection of TBE specific IgM antibodies 2-4 weeks after the infection leads to the diagnosis but the interpretation in vaccinated individuals remains difficult (1). In Switzerland there are two vaccines (FSME-Immun™ and Encepur™). It is believed that NS1-antibodies, an antibody against a viral protein, is not present in the vaccine preparation. That's why the presence of NS1-antibodies can distinguish between vaccination and infection (1). This can be very helpful in diagnosing acute TBE from vaccinated condition.

P129

Investigating a dilatation of the common biliary duct? Watch out for morphine!

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Learning objectives: To consider morphine-induced cholestasis as a differential of common bile duct (CBD) dilatation in order to avoid unnecessary and likely harmful work-up.

Case: A 89-year-old female was hospitalized for a methicillin-susceptible Staphylococcus aureus bacteremia, with meningitis and spondylodiscitis. After an initial antibiotic regimen with ceftriaxone and amoxicillin, imipenem was started. Morphine 5mg q4h was started for cervical pain on Day 4. The fever and C-reactive protein decreased and blood cultures became sterile on Day 5. Meanwhile, the patient known for cholecystectomy displayed once admission cholestasis with Gamma-GT (GGT) and Alkalin phosphatase (ALP) 1.5 and 1.7 times the upper limit of normal (ULN), respectively. An abdominal ultrasound showed CBD dilatation and wall thickening suspicious for cholangitis, but there was no abdominal pain. From Day 6, ALP and GGT increased even further, to 7.6 and 30 times the ULN, respectively, with normal coagulation tests. Viral serology was negative. An abdominal scan described a tissue-like protrusion in the descending duodenum and a doubling of the CBD diameter, however now without signs of cholangitis. Endoscopic retrograde cholangiopancreatography confirmed the CBD dilatation with constriction of the sphincter of Oddi (SO), with no suspicious lesion, suspected of morphine use. The image observed on the scan might have been due to a benign bulging papilla. The cholestasis improved rapidly with decreased doses of morphine.

Discussion: This case is illustrative of CBD dilatation and cholestasis caused by permanent contraction of the SO in a context of morphine use. If there are more common causes of cholestasis like mechanical obstruction, sepsis, heart failure and parenteral nutrition, functional obstruction of CBD must not be ignored. It has been shown that morphine, even if a single dose is administrated 30 minutes before a scan, may induce constriction of the SO and produce an image suspicious for mechanical CBD obstruction. Other opioids like pethidine have no such effect, nor does tramadol. Physicians should keep in mind the possibility of a morphine-induced spasm of the SO that may mimic mechanical obstruction as the cause of CBD dilatation. Indeed, this can avoid unnecessary, invasive and risk-related CBD exploration in older aged patients. Finally, knowledge of the entity may allow for a prompt change in treatment and observable rapid improvement cholestasis, as in our patient.

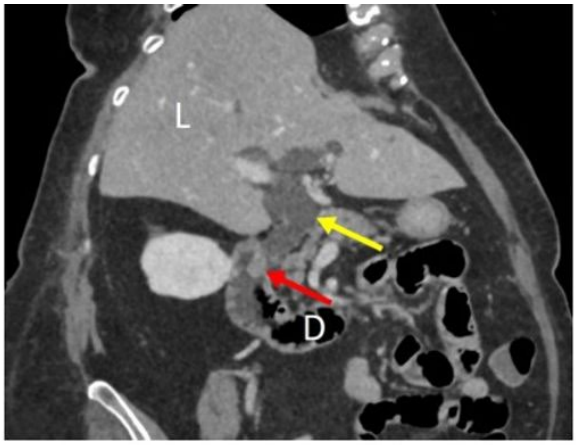

Figure: Coronal oblique reconstruction of contrast enhanced abdominal computed tomography scan of 89-year-old female patient shows significantly dilated common bile duct (yellow arrow). The major duodenal papilla had a nodular aspect (red arrow), and an ampullary tumor was included in the differential diagnosis. L = liver; D = duodenum.

P130

It is not always an (SARS-CoV-2) infection when new infiltrates appear on computed tomography scan during antibiotic treatment

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Learning objective: We report a case of a 77-year old patient who presented with bilateral pneumonia and was subsequently diagnosed with daptomycin induced acute eosinophilic pneumonia (AEP). Non-infectious causes mimicking bacterial or viral pneumonia should be considered including drug reactions such as AEP or DRESS.

Case: A 77-year-old patient presented to the hospital with chest pain, mainly in the left shoulder and aggravated by deep inspiration, dyspnea on exertion and fever. Due to recurrent prosthetic joint infections he was receiving daptomycin for the past 3 weeks administered in an outpatient clinic. Clinical examination was significant for bibasal inspiratory crackles. Laboratory studies revealed a new leucocytosis, slightly elevated eosinophils ($0.4x10^9$/l) [OMF1] and an elevated CRP (168mg/l) but normal procalcitonin. A chest CT scan showed multifocal sub-pleural infiltrates in both lungs, predominantly in the left upper lobe.
Bronchoscopy with bronchoalveolar lavage (BAL) was performed and yielded no evidence of infection but a significant eosinophilia. Pulmonary function tests revealed a moderately reduced CO-diffusion capacity (DLCO) and a mild restrictive pattern.

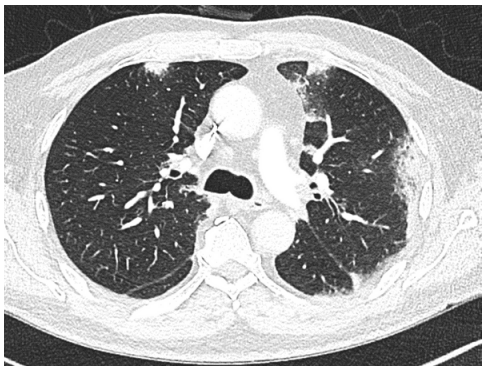

Figure 1: Computed tomography scan with multifocal sub-pleural infiltrates

A drug-induced acute eosinophilic pneumonia (AEP) was diagnosed and the antibiotic treatment switched to vancomycin. Subsequently, clinical symptoms improved, the inflammatory markers normalised and imaging studies showed a complete resolution of the opacities.

Discussion: Drug-induced AEP is a rarely documented but well known side effect of certain drugs such as daptomycin, gemcitabine, infliximab or venlafaxine. Our case demonstrated the typical symptoms and findings of an AEP. However, the differential diagnosis (e.g. opportunistic infection, pulmonary embolism, vasculitis, cryptogenic organising pneumonia) is broad. In our case, diffuse ground glass opacities in the CT scan (mainly localised in the periphery of the lung), a restrictive pattern in the pulmonary function test with a reduced DLCO and a slightly elevated eosinophilic count were characteristic for an AEP as was the eosinophilia in the BAL. A positive dechallenge test with complete resolution of symptoms, inflammation and pulmonary consolidations supported the diagnosis of daptomycin induced AEP.

Diagnostic criteria of a drug induced acute eosinophilic pneumonitis (FDA)

- Concurrent exposure to the drug (e.g. daptomycin)
- Fever
- Dyspnoea with oxygen requirement
- New infiltrates on chest imaging
- BAL with >25% of eosinophils
- Clinical improvement following daptomycin withdrawal

P131

Landscapers' at risk – potentially leathal occupational water exposure

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Learning points: Leptospirosis is a rarely occurring infectious disease in Switzerland, probably underdiagnosed because of unspecific clinical presentation and self-limiting disease. Nevertheless life-threatening presentations may occur. Relevant exposure risks are recreational or occupational water exposure. Therefore, patient history remains the mainstay of any diagnostic and therapeutic interventions.

Case description: A 24-year-old male patient presented with headache, fever, chills, progressive myalgia and minor dysuria one week after the first SARS-CoV-2 mRNA vaccination. The headache persisted since vaccination, the other symptoms for three days. The clinical examination was unremarkable apart from fever (38.5°C), increased pain by head and leg inclination, but without meningism. Laboratory evaluations revealed normal leucocyte counts, elevated C-reactive protein, transaminases and creatine kinase levels, and a slightly impaired renal function (glomerular filtration rate eGFR 72 mL/'/1.73m^2). A lumbar puncture revealed 9 cells/mL and was otherwise unremarkable.
Further patients' history exploration revealed a relevant occupational open water exposure five days prior to the symptoms' onset. Serological examinations and polymerase chain reaction for leptospirosis and Hantavirus were performed. Awaiting the results, the patient developed a progressive pulmonary-renal syndrome (Morbus Weill) with haemoptysis and renal insufficiency (eGFR 18 ml/'/1.73m^2). He was transferred to intensive care and antibiotic treatment with ceftriaxon was initiated.
Leptospira spp. were detected by PCR in blood, urine and liquor. Serological analysis showed a strong increase in anti-Leptosira spp. antibodies during the course of infection. The patient recovered within the next days to weeks without sequelae. Further serological evaluation of his colleague from work who had the same water exposure was negative.

Discussion: Leptosirosis is a rare disease entity in Switzerland. Being a zoonosis, Leptospira spp. reside in the renal tubuli of the hosts, mainly small rodents. Reported human cases in Switzerland remain stable over the years, and are related to exposure with contaminated water. Because of its self-limiting nature and unspecific clinical presentation, leptospirosis may be significantly underdiagnosed. If a potential immunologic interference of the mRNA vaccination has contributed to the life threatening clinical course remains speculative.

P132

Long-term blended-care nutritional therapy for weight management and type-2 diabetes

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Learning objectives: The objective was to assess the efficacy and feasibility of long-term nutritional therapy for an outpatient with obesity and Type-2-diabetes in a blended-care setting, using face-to-face, telephone, and app-delivered care. In particular, the adaptation of the type of care based on the patient's life circumstances and stages of salutogenesis over several years was analyzed.

Case: The patient (male, age=41, BMI=31, HbA1c=6.2%) started nutritional therapy for weight management and glycemic control in January 2016. The patient had a sedentary occupation with frequent business trips, impeding his ability to attend face-to-face counseling sessions. Key therapy targets were weight and HbA1c reduction, adoption of healthy eating habits (in particular, reduction of carbohydrate intake and changes in consumed carbohydrates), as well as medication reduction (insulin and statins). Interactions with the therapist occured as follows in the first year: 4 face-to-face sessions, 1 telephone session, and 5 extended periods of app-delivered care. After one year, the patient had reduced his weight by 13 kg and his HbA1c to 5,6%, and was able to stop using statins. As evidenced by the photo-based food log in the app, his consumption of foods rich in carbohydrates had decreased substantially. Knowing that the relapse risk is high after initial successes, therapy was continued via the app (e.g. via chat) with less intensity over five years. The patient's key medical parameters remained stable, insulin therapy ceased; replaced with metformin, and he reported a reduced burden of disease. He reported that remote care-delivery was crucial for his long-term adherence as it fitted his life circumstances.

Discussion: Low levels of adherence hamper the success of nutritional therapy, especially over long treatment periods. As evidenced by the reported case and several studies [1,2], blended-care can be employed as a viable means to keep patients in therapy and prevent relapse through easy access to nutritional care and high integrability into patients' (diverse) life circumstances.

P133

Nausea, vomiting and occult blood test positivity as manifestation of gastric MALT lymphoma induced by Helicobacter pylori – a case report

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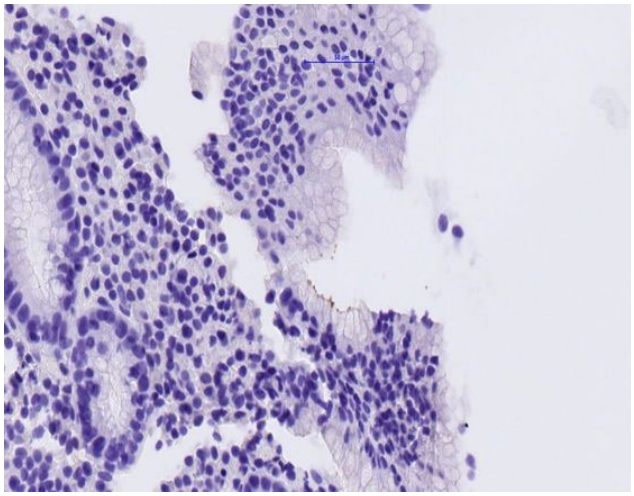
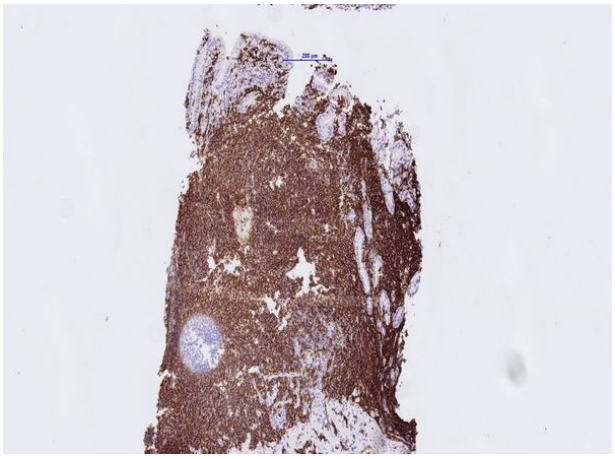
Learning objectives: A colonization by helicobacter pylori can induce a gastric MALT lymphoma.

Case: A 71 year-old female patient referred by her general practitioner, following 3 consecutives positives results of her occult blood tests done in May 2021. For the past few weeks,she, also, had developed additional symptoms such as nausea and vomiting episodes without describing any transit's disorder, nor noticing melena or hematochezia in her faeces.
The patient was hemodynamically stable and afebrile.
The clinical observation was normal: her abdomen was depressible and painless upon palpation with BH present in all quadrants.
Laborating finding showed a hemoglobin's level at 140g/L, there wasn't any inflammatory syndrom. The esophagogastroscopy reveals a hiatal hernia, multiple erosions next to the antrum of the stomach, as well as whitish spots in the esophagus. The colonosocpy showed a hyperplasic rectal polyp.
Multiples biopsies were taken and sent to histopathology. The H. pylori stain confirms the presence of helicobacter bacteria in the stomach. Immunohistochemistry's markings highlight dense lymphocytic infiltrate of B-cell origin.
Complementary investigations were requested. An extension assessment by thoraco-abdomino-pelvis CT is then carried out, it showed a thickening of the stomach's walls with associated mesenteric adenopathy and excluded the presence of lesions dissemination or metastasis. Also the biology's marking for lymphoma : Beta-2-microglobuline was normal (1.46, VN 1.09-2.53).



H. Pylori Immunohistochemistry highlights : Helicobacter bacteria



CD20 Immunohistochemistry highlights lymphocytic infiltrate of B-cell origin

Discussion: HP bacteria was eradicated with a concomitant treatment of 2 antibiotics for 2 weeks (amoxicillin, clarithromycin) along with an PPI for one month (esomeprazole).
A control of H. pylori antigens in stools came back negative. Clinically she improved and endoscopic control will be performed soon. Many studies have highlighted the role of HP's infection in the development of not only gastric's adenocarcinomas, but also gastric MALT lymphoma. Therefore, the diagnosis is based on histological examination, considering that the stomach mucous membrane does not present any lymphoid tissue. The first line of treatment is based on HP eradication, gastric MALT being a rare neoplasia responding on antibiotic treatment. Endoscopic surveillance is important for the follow-up of the patients.

P134

Never say never

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Learning objectives:
- Tubal ligation failure can occur at any time, including in 40+-old women
- There is an increased risk of ectopic pregnancy in case of tubal ligation failure
- Premature closure bias can be very harmful in an emergency setting

Case report: We report the case of a 42-years old woman who was admitted in our emergency room for a low abdominal pain. The pain started very suddenly, was very sharp, and of suspubic location. At the triage, the patient was oriented as a degree 3 emergency to our ambulatory emercency ward, where most people can wait at least one hour before seeing a physician (on a first arrived, first served basis) and are treated as outpatients, going back home the same day.
Because she reported a very strong pain, scored as 10/10 on a visual analogic scale, the nurse asked us to evaluate her immediately after her admission.
When we initially evaluated her, she was hemodynamically stable. The physical examination showed a mild abdominal enlargement which was confirmed by the patient as unusual. The suspubic region was clearly peritonitic. A spontaneous intraperitoneal bleeding was suspected and CT scan was immediately done before we could process the blood sample for betaHCG or collect urines for a point-of-care pregnancy test. In the meantime we called our visceral surgery specialists for an emergent evaluation. They immediately dismissed the hypothesis of an ectopic pregnancy, as the patient had a laparoscopic tubal sterilization about ten years before and was deemed to old to get pregnant.
The CT-scan showed a moderate quantity of intraperitoneal blood and signs of active bleeding. The bleeding was most likely of tubar origin.
Less than our hour after her admission, the patient developped an hemorragic shock, then pulseless cardiac activity. She was successfully ressuscitaded and tranferred to the operating theater. A laparoscopy showed a large amount of blood, and an bleeding ectopic pregnancy. The surgical intervention was a success.
Discussion: Our case put into lignt that although they are rare, tubal ligation failures can occur years after the procedure. Here we review major etiologies of this condition. In case of tubar ligation failure, the risk of an ectopic pregnancy – a life-threatening complication - is high. Acute lower abdominal pain in women under 50 years-old should always be considered as potential ectopic pregnancy. This case illustrates how premature diagnosis closure could have been harmful.

P135

Orbitopathy - not always endocrine-related

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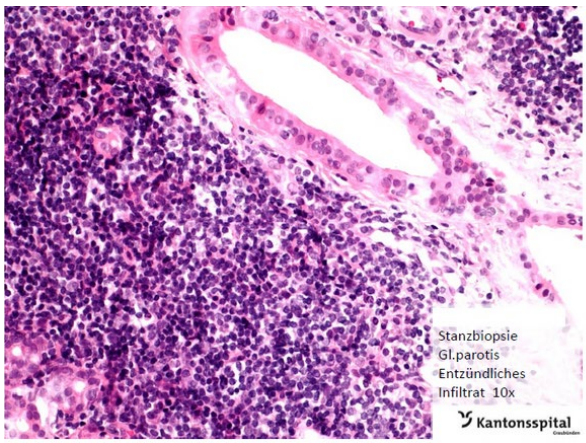
Learning objective: Exophthalmos is not always endocrine-related. Especially in case of normal thyroid function tests the differential diagnosis should be extended. IgG4-related disease (IgG4-RD) mimics many inflammatory, infectious or neoplastic conditions. Consideration of IgG4-RD as a differential diagnosis is important, since organ damage and mortality can be reduced with therapy.

Case: An 86-year-old woman suffered from distorted vision for 6 months, proptosis of the eyeballs, as well as increasing nodular changes of both lacrimal glands. One year earlier biopsies of cervical lymph nodes and salivary glands showed a chronic lymphofollicular infiltrate without detection of malignant cells. A tentative diagnosis of Sjögren's syndrome was made. Further, a goiter with an inhomogeneous hypoechoic parenchyma was observed. Based on the assumption of coexisting Sjögren's syndrome and endocrine orbitopathy, the patient was referred to an endocrinologist.
Endocrine evaluation showed no clinical or laboratory evidence of Graves' disease as an indication of endocrine-related orbitopathy. Thus, other inflammatory or lymphoproliferative diseases have to be considered as a potential cause of the orbitopathy. The combination of dacryoadenitis, sialadenitis and cervical lymphadenopathy lead to the suspicion of IgG4-RD. Protein electrophoresis showed an elevated IgG4. Histologic findings from new biopsies finally led to the diagnosis of IgG4-RD with evident involvement of the lacrimal and salivary glands (known as Mikulicz Syndrome) and the orbital tissue with extraocular muscle enlargement.



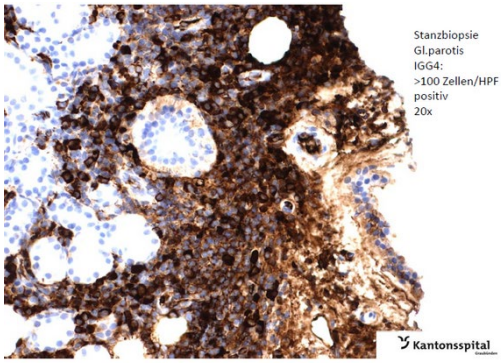


Image 1&2 Punch biopsy glandula parotis: Infiltrates in the lobules and the periductal tissue with stromal fibrosis.

Discussion: The coexistence of exophthalmos and goiter was suggestive of endocrine orbitopathy in the context of Graves' disease. Endocrine orbitopathy is the most common cause of inflammation of the orbit (40-60% of all inflammatory orbitopathies) (1,2). Since only 1-2% of patients with endocrine orbitopathy have normal thyroid tests and TSH-receptor antibodies below threshold, diagnosis of an endocrine orbitopathy without thyroid dysfunction is always based on the exclusion of other diseases (2). Important differential diagnoses are idiopathic orbital inflammation, infections, systemic diseases, neoplasia, or vasculopathies. Accurate diagnosis is important because IgG4-RD can be treated with glucocorticoids, which can reduce severe organ damage and mortality (3)

P136

Patient-derived tumor organoids for personalized medicine in a rare case of hepatocellular carcinoma with neuroendocrine differentiation

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Learning objective: Primary liver carcinomas with concurrent hepatocellular and neuroendocrine tumor components in the same liver lesion are very rare, usually being associated with an aggressive tumor phenotype and poor overall prognosis. As these tumors are exceedingly rare, there is no published evidence to guide drug selection. In this case report we describe the generation of tumor organoids that retain the key characteristics of the originating tumor. These organoids were then used in drug screens to identify the most promising treatment option.

Case: We report the case of a 74-year-old man with a very rare subtype of hepatocellular carcinoma with neuroendocrine differentiation (HCC-NED). The patient presented with a tumor in the liver, which was surgically removed in curative intent. Histopathological work-up of the tumor revealed poorly differentiated hepatocellular carcinoma (Edmondson-Steiner grade IV) with diffuse expression of the neuroendocrine markers synaptophysin and chromogranin. Three months after resection, multifocal recurrence of the HCC-NED was observed. In the meantime, tumor organoids have been generated from the resected HCC-NED and extensively characterized. Sensitivity to drugs approved for the treatment of HCC or neuroendocrine carcinomas was tested in vitro. Based on their in vitro efficacy, etoposide and carboplatin were used as first line palliative combination treatment. Because genomic analysis revealed a NTRK1-mutation of unknown significance (kinase domain) and tumor organoids were sensitive to entrectinib, a pan-TRK inhibitor, the patient received entrectinib as second line therapy. After only two weeks, treatment had to be discontinued due to deterioration of the patient's general condition.

Discussion: We describe a rare case of a patient with HCC-NED. The rapid establishment of patient-derived tumor organoids allowed in vitro drug testing. Unfortunately, the drugs could not prevent the rapid tumor progression. We can only speculate about the reasons for treatment failure of etoposide and carboplatin. On the one hand, the organoid model lacks the tumor stroma, which might influence the response to treatments. On the other hand, drug concentrations in the patient's tumor might have been too low, or the tumor might have developed rapid resistance in vivo. Nevertheless, the report provides a first proof-of-principle for using organoids for personalized medicine in these rare primary liver cancers.

P137

POEMS syndrome: usually an odyssey

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Learning objective:

- POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes) is a rare paraneoplastic syndrome due to an underlying plasma cell disorder.
- Screening for a plasma cell disorder is critical in the diagnostic work-up of progressive inflammatory demyelinating polyradiculoneuropathy.
- A delay in diagnosis is common and results in severe, irreversible neurological disability.
- The complex syndrome necessitates multidisciplinary collaboration to diagnose and manage the diverse disease aspects effectively.

Case: A 63-year-old patient presented with progressive symmetric polyneuropathy and acrocyanosis since one month. The neurophysiology showed a typical pattern seen within the Guillain Barré syndrome, the presumptive diagnosis, with sensory and motor demyelinating polyneuropathy, especially of the distal, lower extremities. Examination of the cerebrospinal fluid showed an «albumino-cytologic dissociation» with increased protein without pleocytosis. Due to progression of the paralysis an intravenous immunoglobulin therapy was applied. The patient was discharged to rehabilitation where his condition deteriorated with rapid progression of the tetraparesis and he was readmitted.

TABLE 1 Criteria for the diagnosis of POEMS syndrome[a]

Mandatory major criteria	1. Polyneuropathy (typically demyelinating)
	2. Monoclonal plasma cell-proliferative disorder (almost always λ)
Other major criteria (one required)	3. Castleman disease[a]
	4. Sclerotic bone lesions
	5. Vascular endothelial growth factor elevation
Minor criteria	6. Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy)
	7. Extravascular volume overload (edema, pleural effusion, or ascites)
	8. Endocrinopathy (adrenal, thyroid,[b] pituitary, gonadal, parathyroid, pancreatic[b])
	9. Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails)
	10. Papilledema
	11. Thrombocytosis/polycythemia[c]
Other symptoms and signs	Clubbing, weight loss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses, diarrhea, low vitamin B_{12} values

Dispenzieri A. POEMS Syndrome: 2019 Update on diagnosis, risk-stratification and management. *AM J Hematol.* 2019: 94:812-827.

Plasmapheresis showed a slight improvement. Back in rehabilitation tetraparesis worsened, at the third admission extravascular volume overload, hyperpigmentation, nail clubbing, thrombocytosis and hypothyroidism appeared. An atypical chronic inflammatory demyelinating polyneuropathy (CIDP) or POEMS syndrome were discussed. On the PET-CT scan multiple lytic and FDG-avid bone lesions were detected. Vascular endothelial growth factor (VEGF) concentration was increased. Serum protein electrophoresis showed a paraproteinemia type IgG Lambda. The bone marrow and targeted bone lesion biopsy showed a monoclonal plasma-cell infiltration fitting with POEMS syndrome. The main lesion was irradiated and a systemic antineoplastic treatment with lenalidomide, dexamethasone and daratumumab was established. With continued therapy the neurological deficits slowly improved, VEGF and the M-protein gradient normalized.

Discussion: The diagnosis of POEMS syndrome remains a challenge, despite the existence of internationally recognized diagnostic criteria (table 1). A good history and physical examination followed by appropriate testing, most notably radiography, VEGF and a bone marrow examination, can differentiate this syndrome from other conditions like CIDP.

P138

Polymicrobial infection of the spine and central nervous system

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Learning objectives: The majority of spinal infections are caused by haematogenous spread of bacteria. Direct extension from a contiguous soft tissue focus is uncommon. Growth of the anaerobic bacteria, *parvimonas micra* from spinal biopsies, as a cause of spondylodiscitis, is very rare. Even rarer is the finding of *parvimonas micra*, concomitant with *actinomyces funkei* in the in cerebrospinal fluid (CSF). The additional growth of *prevotella nigrescens* in a blood culture raised suspicion of an intestinal infection focus.

Case: A 40-year-old male presented with a several week history of progressive pain in the sacral region, and a few days of headache and chills. Physical exam revealed pain on percussion in the sacral region and mild neck stiffness. Laboratory findings showed leukocytosis with 14.5 G/l and an increased CRP 348 mg/l. Spondylodiscitis at L5-S1 and signs of meningitis with diffuse inflammatory reaction of the subarachnoid space were evident on MRI. The CSF was purulent with a pleocytosis of 8400 cells/ul (88% polymorphonuclear leukocytes) and a high protein of 1900 mg/l. Gram stain of the CSF revealed gram positive cocci and gram negative bacilli. Empiric antibiotic treatment with ceftriaxone and vancomycin was initiated. Percutaneous CT-guided biopsy of L5-S1 was performed the following day. CSF culture grew *actinomyces funkei* and *parvimonas micras*.Culture of theL5-S1 biospy sample was positive for *parvimonas micras*. One blood culture was positive for *prevotella nigrescens*. On review of the medical records it became evident that the patient had undergone several endoscopies and a laparotomy to extract foreign bodies from the colon. Diagnostic colonoscopy was therefore performed which revealed suppurative ulcerative lesions in the rectum and rectosigmoid. MRI of the pelvis demonstrated a fistula between the inflamed rectosigmoid and L5-S1. Due to its small size the fistula was managed conservatively with ceftriaxone and metronidazole for at least six weeks. The lumbar pain and general condition of the patient improved within days. Follow-up MRI after six weeks of treatment is still pending.

Discussion: Polymicrobial infection with anaerobic bacteria of the spine and central nervous system (CNS) in an immunocompetent patient is extremely rare. A comprehensive history combined with an extended focus search guided by the isolated pathogens led to the diagnosis of a fistula between the recto sigmoid and L5-S1 as focus of the infection.

P139

Posphatidylethanol (PEth) biomarker as a new opportunity to treat alcohol dependence with denial or minimization of consumption?

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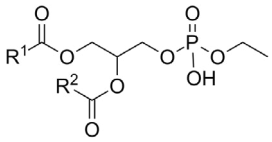

PEth

Learning objectives: To know and use a precise, direct marker for alcohol to treat alcohol dependent patients denying or minimizing their consumption.

Case: A 63 year old patient known for a hepatic cirrhosis with treated hepatocarcinoma is referred for alcohol treatment. Needing an hepatic transplantation, he requires 3 to 6 months of abstinence. He also suffers from depression and fluctuating hepatic encephalopathy. In this context, he came on each visit reporting a complete cessation of alcohol. Still evidence of daily alcohol use existed as shown by clinical signs (facial erythema, alcohol fetor) and elevated phosphatidylethanol dosage (300 microgram/L).
After 6 months of statu quo, avoiding too hard confrontations with the patient, I tried to create a better clinical relationship in order to allow a discussion about the alcohol consumption, using the PEth results as a reminder of the reality. We figured out that the inabilty of the patient to speak was maybe related to the shame and culpability to be unable to abstain, even if his life was in danger. Therefore and according with the patient, we prescribed disulfiram in order to prevent alcohol consumption, on the basis of a controlled delivery in pharmacy. The patient agreed, went 3 times a week to the pharmacy, had a diminished PEth after 4 weeks (53 microgram per liter) and after 8 weeks a negative result (< 20).

Discussion: PEth is a direct alcohol metabolite, reflecting the last weeks consumption of ethanol with better performance (sensitivity 86%, specificity 100% if no contamination)[1]than older markers (gamma-GT, transaminases, carbohydrates deficient transferrin CDT). It is convenient to take at the office with a capillary blood sample that can be sent by post as dried blood spot. It was used for a long time in legal medicine but is emerging in clinical settings. This objective and reliable test is especially useful in case of denial or minimization, in order to avoid confronting each other about the interpretation of formerly used unspecific markers. In order for this tool to be beneficial, it is necessary to create an atmosphere of trust, before discussing its realization at a proper moment. In case of discrepancy between the history and the result, we suggest an alternance of confrontation to this specific test and the gentle development of the alcohol talk. When used for clinical and not legal purposes, it is refunded by the LAMal since end of 2019 (price 110.- FS, code 1683.10).

P140

Septic arthritis or crystal arthropathy?

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Learning objectives: Septic arthritis is often an acute febrile illness, which can affect one or more joints. Hematogenous seeding from elsewhere is the primary source. Predisposing factors include trauma and joint alterations. The clinical presentation can be very similar to a crystal arthropathy. As treatment of the two entities differs importantly, from steroids to antibiotics, it is essential to differentiate the cause of inflammation.

Case: A 74-year-old woman presented to her family doctor with acute pain, swelling and impaired movement in both wrists, and a short episode of fever. The patient was clinically stable. C-reactive-protein (CRP) was elevated at 214 mg/l. Diagnostic aspirate from the left wrist revealed 43.000 cells/ul (67 % polynuclear leukocytes). Microscopy showed multiple crystals, crystal arthropathy was suspected, and oral prednisolone was initiated. The patient re-

turned to the emergency room three days later with persistent symptoms. Diagnostic aspiration of both wrists was performed. The white cell count had raised to 167.000 cells/ul (89 % polynuclear) on the left and to 108.000 cells/ul on the right side. Microscopy again revealed crystals, and the gram stain showed no bacteria. Given that crystal arthropathy remained the most likely diagnosis, therapy was escalated to intra-articular injection of steroids. Although the patient improved over the next 48 hours, symptom resolution was not complete and inflammatory parameters remained high. By then, culture of the joint aspirates from both wrists revealed Haemophilus influenzae. Septic arthritis was diagnosed, therapy with amoxicillin/clavulanate was initiated and arthroscopic joint lavage was performed. Intraoperative findings showed synovitis without pus. Afterwards symptoms and CRP improved rapidly. After eight days, therapy was switched to oral co-trimoxazole for further 14 days. Chest x-ray and echocardiography showed no evidence of endocarditis or septic seeding. Blood cultures remained negative. Further history revealed a recent sinusitis, which may have been the possible source.

Discussion: Septic arthritis with *Haemophilus influenzae* in adults is rare. In the presented case, the likely predisposing factor was an underlying crystal arthropathy. Septic arthritis should be suspected in adults who have joint pain and high cell counts, even when afebrile and clinically stable. A negative gram stain cannot rule out a septic arthritis, therefore, cultures must be obtained.

P141

Severe cardiac involvement in a young adult with multisystemic inflammatory syndrom after COVID-19

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Results of conducted laboratory findings

Haematological parameters	10.09.2021	11.09.2021	12.09.2021	13.09.2021	14.09.2021	15.09.2021	16.09.2021	Reference
WBC (white blood cells)	19.2 G/l	11.91 G/l	14.86 G/l	16.78 G/l	25.05 G/l	25.35 G/l	16.43 G/l	3.0-9.6 G/l
Lymphoctyes	0.1 G/l	1.18 G/l	1.04 G/l	1.31 G/l	1.78 G/l	2.94 G/l	2.58 G/l	1.50-4.00 G/l
CRP	283 mg/l	81 mg/l	43 mg/l	28 mg/l	x	16 mg/l	10 mg/l	<5 mg/l
Procalcitonin	2.51 ng/ml	0.73 ng/ml	0.36 ng/ml	x	x	x	x	<0.5 ng/ml
Platelets	37 G/l	42 G/l	62 G/l	87 G/l	179 G/l	261 G/l	255 G/l	150-400 G/l
Creatinine	184 qmol/l	72 qmol/l	64µmol/l	62 µmol/l	x	64 µmol/l	68 µmol/l	64-111 µmol/l
Troponin-I high sensitive	572 ng/l	x	213 ng/l	x	133 ng/l	x	x	< 34 ng/l
Myoglobin	x	x	35 µg/l	x	72 µg/l	x	x	<140 µg/l
CK	x	x	<7 U/l	x	24 U/l	x	x	<200 U/l
NT-pro-BNP	8719 ng/l	x	x	x	x	x	x	< 300 ng/l
D-dimer	2.25 mg/l	x	x	x	x	x	x	<0.5 mg/l

Learning objectives: Multisystemic inflammatory syndrome (MIS) associated with COVID-19 is less well recognized in adults (MIS-A) compared to MIS in children (MIS-C). Definition includes patients ≥ 21 years with fever (≥38.0 C) combined with 3 clinical criteria of which at least one is primary: severe cardiac illness or rash with non-purulent conjunctivitis. Secondary criteria are neurological symptoms, gastrointestinal symptoms, shock or hypotension and thrombocytopenia. Additionally evidence of SARS-CoV-2 infection and elevated inflammatory markers.

Case: An otherwise healthy 25-year-old man was referred to our emergency department because of persistent fever, nonspecific general symptoms and increased inflammatory parameters. His family doctor had prescribed him antibiotics 2 days before to treat a bacterial superinfection pneumonia 15 days after he was diagnosed with a COVID-19 infection. Clinical examination of this unvaccinated patient revealed a refractory shock. Laboratory results showed high inflammatory parameters, thrombocytopenia, elevated D-dimer level, acute kidney injury and elevated cardiac biomarkers. Computer tomography showed signs of acute heart failure without evidence for a pneumonia. In transthoracic echocardiography (TTE), the LVEF was 40% with diffuse hypokinesia. The patient was transferred to the ICU for further treatment including heart failure therapy and systemic corticosteroids. Seven days after admission, the patient had recovered well and was discharged. After 1 month of cardiac rehabilitation, the patient showed full recovery with a normal LVEF in the TTE. In summary, we treated a young adult with severe cardiac disease with marked systemic inflammation due to a COVID-19 infection, and complete convalescence after a prolonged course of the disease.

Discussion: MIS-A associated with COVID-19 is a rare and emerging syndrome. One of the main challenges is to distinguish it from the COVID-19 infection itself with impact both on acute and long-term treatment. There is need for clear guidance in terms of the acute medication concept (including immunoglobulins, corticosteroids and other immunomodulatory agents), as well as long-term management.
The pathophysiological mechanism of MIS-A is based on a cytokine storm with severe inflammation, coagulopathy and multiorgan failure with cardiac involvement in the post-acute COVID-19 phase.
Further research is warranted to determine if COVID-19 vaccination protects against MIS-A.

P142

Severe neutropenia – what can also be behind it?

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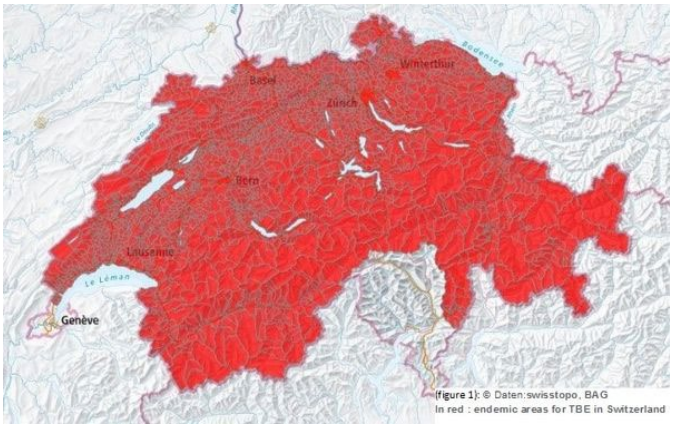
Learning objectives: We present a typical case with Tick borne encephalitis (TBE) Meningitis with a two-phase course to raise awareness about an infectious disease with increasing prevalence in central Europe.

Case: *Initial Phase:*A 26 year old woman without pre-existing conditions presents with a five day history of severe myalgia especially in the thighs and predominantly at night, as well as light flu-like symptoms. She reported a tick bite 4 weeks ago after a walk in the south German countryside. No erythema migrans had been observed. Vital parameters and physical examination were normal. Blood analysis showed a leucopenia (1.9 G/l), severe neutropenia (0.45 G/l) and thrombocytopenia (124 G/l), without additional information from a differential blood count. Thinking of an infectious cause of disease we checked for viral pathogens (HIV, Hepatitis A-E, CMV, EBV, TBE and SARS-CoV-2) as well Borrelia serology. All of these tests were negative. Within one week regular out-patient tests documented a spontaneous recovery of the patient's symptoms and blood count abnormalities.
Neurological Phase: 8 days later the patient started to feel unwell again, this time with fever up to 40°C, headache, photo- and phonophobia and mild nausea, so she presented once more in our emergency ward. Clinical investigation showed new neck stiffness but no disorientation or focal neurological signs. Blood and urine analysis were normal. A cMRI did not show any abnormalities. Analysis from a liquor puncture showed pleocytosis. We repeated TBE serology which now showed seroconversion with positive IgG (1407 kU/l ; ref: >150) and positive IgM (not further quantified). These results confirmed TBE meningitis. After a 10-day-hospitalisation with supportive treatment the patient did not develop complications and was discharged home.

Discussion: Incidence of TBE cases in Switzerland are rising because of climate change. Almost all of CH is now considered an endemic area for TBE (fig. 1). For this reason it is important to be aware of the typical biphasic course of this disease. Leuco-, thrombo-,neutropenia and myalgia are frequently reported during the first phase of TBE. If clinical suspicion is present, then a negative TBE serology should be repeated a few days later, to establish diagnosis.
There is no specific treatment for TBE and so, when walking in the countryside, preventive measures are recommended. Additionally, since the 1970s, highly effective vaccines have been available.



(figure 1): © Daten: swisstopo, BAG
In red : endemic areas for TBE in Switzerland

P143

Should we perform percutaneous angioplasty for arterial stenosis in single-functioning kidney? Case report of an efficient procedure

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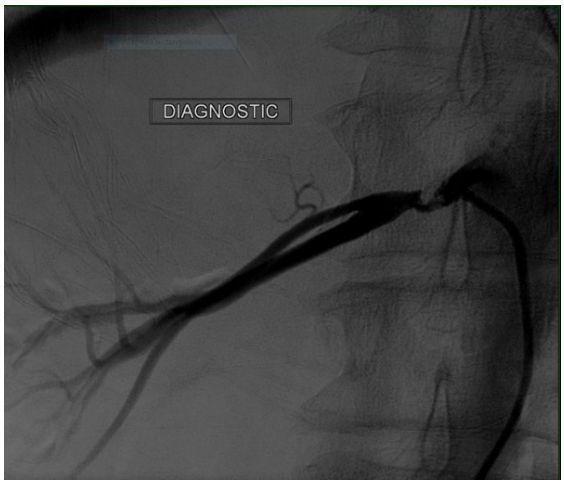
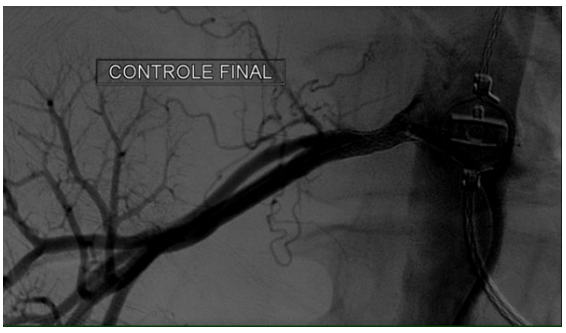
Learning objectives: Renal stenosis should always be looked for in refractory arterial hypertension. Current recommendations show similar outcomes in best medical treatment (BMT) vs Percutaneous transluminal renal angioplasty (PTRA) and BMT is preferred in most cases. PTRA should be considered in patients with acute progressive renal failure despite adequate medical treatment, as outcomes can be remarkably improved.

Case: We describe the case of a 66-year-old patient, with history chronic renal insufficiency hospitalized for acute pulmonary oedema-and pre-renal acute on chronic renal failure in context of hypertensive crisis. Despote supportive therapy, the patient showed rapid deteriotation with recurrent flash pulmonary oedema necessitating oro-tracheal intubation, acute anuric RF with severe hyperkaliemia and acidosis. Hemodynamically significant bilateral arterial stenosis (> 60%) and a single-functioning right kidney were discovered. Because of persistent degradation of renal function, severe electrolyte disturbances and uncontrolled blood pressure despite BMT, renal arteriography was performed, with successful stenting of an ostial stenosis of the right arteria (Figures 1a and 1b). The clinical evolution of the patient was spectacular with possible extubation the next day and normalisation of blood pressure, metabolic and electrolytes disturbance and renal function in 5 days.





Discussion: Hemodynamically significant renal arteria stenosis a narrowing of 50 to 70% of the lumen of the renal arteria. PTRA in patients with RF is still debated, as BMT might show similar long-term outcomes even with severe stenosis (i.e > 70%), though most studies have not been done in acute settings of decompensation1,2. Current recommendations from the American College Cardiology (ACC) and American Heart Association (AHA) states that all patients benefit from BMT citing level 1A evidence, but there is no recommendation for PTRA in acute setting of RF1. Some show a benefice of PTRA with reduced risk of death in specific groups, such as those presenting with flash pulmonary oedema, refractory hypertension and RF. Patients with a unique functioning kidney also benefit from PTRA as compared to BMT3. As a conclusion, PTRA should be considered in specific subgroups like our patient, with rapid progressive acute renal injury and possible normalization of renal function after angioplasty and updated specific guidelines for such subgroups could be beneficial in the future.

P144

Spontaneous nosocomial *Proteus mirabilis* meningitis in an HIV-infected adult patient

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Learning objectives: Gram-negative bacillary meningitis remains a rare occurrence, even in patients with advanced HIV. We report a case of spontaneous healthcare associated *Proteus mirabilis* meningitis in an immunocompromised individual. This is one of four known cases found in existing literature, the second such case in an advanced HIV patient.

Context: Centre Hospital Kabinda (CHK) is a MSF (Médecins Sans Frontières) centre providing free healthcare for HIV patients in Kinshasa, Democratic Republic of Congo. It is a 40-bed facility with intensive care capacity of 6 beds. The patient cohort is advanced HIV patients. The hospital is equipped with a microbiology laboratory since August 2021, previously all samples were referred to a local private laboratory. Widespread bacterial resistance is extensive, for both community and nosocomial infections.

Case: A 23-year-old female was hospitalised in CHK for ongoing weight loss, chronic abdominal pain and vomiting 9 months after initiation of treatment for TB meningitis. Hospitalisation was complicated by healthcare associated gram-negative bacillary meningitis on day 18. Blood and cerebrospinal fluid cultures confirmed *Proteus mirabilis*. Antibiotic susceptibility testing showed extended spectrum beta-lactamase resistant to common antibiotics, and sensitive to Piperacilline/Tazobactam and Meropenem. Despite initiation of high dose Meropenem (2g every 8 hours) by intravenous infusion, she did not improve and died after 4 days of treatment.

Discussion: This case report highlights the importance of microbiological identification of pathogens in resource limited settings. Gram negative bacillary meningitis does not present with pleocytosis in advanced HIV patients, a negative lumbar puncture cannot exclude this diagnosis. Access to clinical bacteriology in resource limited settings is essential to avoid over-use of antibiotics to which there is already resistance. It further plays an essential role in public health by identifying antibiotic susceptibilities. Infection prevention and control measures must be reinforced in order to protect patients from such avoidable hospital acquired infections.

P145

Subdural empyema following odontogenic infection in an elderly adult: case report about a rare case with a rare pathogen (Campylobacter rectus) and multidisciplinary favorable hospital outcome

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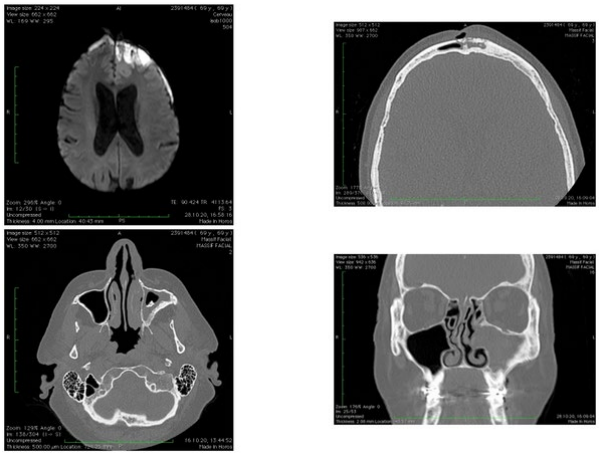
Learning objectives: Potential complications secondary to odontogenic infections or sinusitis include subdural empyema. Disorder of consciousness and/or motor deficiency in these situations have to make us think of this major complication.

Case: A 79-year-old woman, with several comorbidities presented to her GP in early 10/2020 with diagnosis of left dental abscess and acute sinusitis with forehead midline purulent discharge. Local drainage and prescription of antibiotics (ciprofloxacin) were initiated. Facial CT done on the 16/10/2020 revealed acute left diffuse sinusitis with peri-odontal abscess. A culture was done from the frontal sinus discharge on the 20/10/2020 and revealed Streptococcus anginosus and CNS. Her health condition declined and she was hospitalized on the 28/10/2020 with increased headaches, facial

pain, fall at home, vomiting, right lower limb paresia and dehydration without fever or stiff neck.
The initial management was rehydration, facial CT, cerebral MRI, 1rst maxillo-facial operation (3 teeth avulsions, antrotomy, closure of maxillary fistula), and empirical antibiotic (meropenem). After multidisciplinary evaluation (neurosurgery, ENT, oro-maxillary, neuroradiology, ID, IM, ICU), decision is made to proceed to a 2nd operation with bi-frontal craniotomy on the 31/10/2020 for subdural empyema secondary to odontogenic sinusitis. Local cultures revealed several aerobic and anaerobic bacterias including Campylobacter rectus.
After successfull recovery, the patient had worsening consciousness (GCS 8/15). New cerebral MRI motivated a 3rd operation with fronto-temporal craniotomy on the 05/11/2020. Thereafter, her status improved and permitted a return home on the 20/11/2020 with ambulatory antimicrobial therapy to complete 6 weeks. 2 follow-up consultations with cerebral MRI were done on the 02/12/2020 and 05/03/2021 with favorable outcome.

Discussion: This case is a miracle despite the initial survival prognosis estimated to be less than 50 % according to disorder of consciousness and motor deficiency at initial presentation.
This case is outstanding by several aspects:
1. A rare case following frontal sinusitis secondary to odontogenic maxillary abscess in an elderly woman.
2. A rare pathogen (Campylobacter rectus) amongst other typical pathogens (aerobic and anaerobic streptococci). Only one case report has associated this bacteria with subdural empyema.
3. Multidisciplinary approach is the only way to solve this potentially fatal situation.



P146

Tired, incontinent and unsteady on the feet

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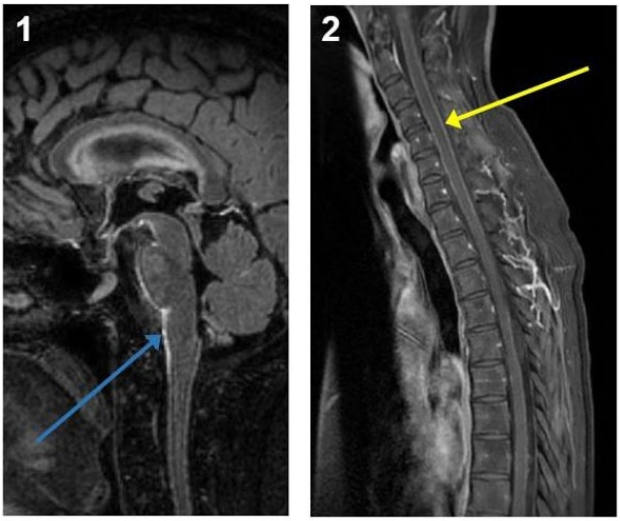
Learning objectives:
- Thorough medical history and precise clinical examination are essential for an effective diagnostic workup.
- Progressive gait disorder and bladder dysfunction should also raise suspicion of an infectious central nervous system disorder.

Case: In January 2022, a 61-year-old woman was hospitalised after her health state deteriorated over more than a year. She has suffered from fatigue, weight loss, a progressive gait disorder, neuropathic facial pain, nocturnal abdominal pain and urge incontinence. During hospitalisation, gait disorder and bladder dysfunction were the predominant symptoms. The patient had several tick bites over the past years without noticing any consecutive erythema.

Physical examination revealed a left side accentuated spastic paraparesis, symmetrical hyperreflexia, bilateral positive Babinski sign, dysmetric finger-nose and ataxic heel-knee tests.
Magnetic resonance imaging demonstrated a leptomeningeal contrast enhancement (see pictures 1 and 2) and cerebellar, pontine and white matter lesions. Cerebrospinal fluid (CSF) from lumbar puncture had a pleocytosis (14 cells/µL), increased protein (5.14 g/L), lactate and ferritin and reduced glucose.
Our main differential diagnoses included chronic tuberculosis, sarcoidosis, cerebral vasculitis, neuroborreliosis, paraneoplastic disorders and meningeosis carcinomatosa.



Picture 1 and 2 Pathological pial contrast-enhancement on the surface of the brainstem (blue arrow) and along the spinal cord (yellow arrow)

Screening for cancer, vitamin B12 deficiency, autoimmune and infectious diseases was inconspicuous except positive test results for *Borrelia burgdorferi* antibodies in serum and cerebrospinal fluid with an increased IgG CSF/serum antibody index of > 5.18 (norm <2). This index together with the long course of disease let us make the diagnosis of a late neuroborreliosis. Fortunately, already within 3 days after treatment initiation with ceftriaxone the patient reported to be more alert.

Discussion: Precise clinical examination and thorough medical history were indispensable to raise suspicion of neuroborreliosis and accordingly choosing the adequate diagnostic tests. The patient's predominant clinical features (spastic-ataxic paraparesis, progressive gait disorder, bladder dysfunction) are described for late neuroborreliosis. Nevertheless, as a clear antecedent manifestation of Lyme borreliosis was absent, diagnostic workup was tricky and the enigma of the health deterioration could only be solved thanks to an interdisciplinary teamwork.

P147

Transmission of Haemophilus influenzae in hospitalized patients in a shared room

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Learning objectives: We describe a sequence of three respiratory tract infections by Heamophilus influenzae (H. influenzae) among patients hospitalized in the same room.

Cases: A 74-year-old man was admitted with a 7-day history of productive cough and dyspnea. The patient was subfebrile, mildly hypoxemic and presented ubiquitous pulmonary wheezing. Blood test showed mild leukocytosis of 11.1x10^9/l and CRP of 115.1 mg/l. The chest x-ray showed perihilar infiltrate on the right side. The patient was diagnosed with community-acquired pneumonia and started on Piperacillin/Tazobactam. However, because of negative procalcitonin and a suspicion of viral origin, the antibiotics were stopped the next day and the patient was continued on inhalations, prednisone per os and oxygen supplementation. Later, H. influenzae was identified in sputum, while blood cultures remained negative.
The patient presented clear clinical improvement, administration of further antibiotics was judged unnecessary and he recovered within 13 days. 7 days after this patient, a 67-year-old man, hospitalized in the same room for cardiorenal syndrome for 9 days, developed a productive cough, dyspnea and impaired consciousness, with an increase of leukocytes and CRP. Chest x-ray demonstrated a possible new infiltrate and H. influenzae was isolated from sputum. All of the blood cultures (4) were positive for Staphylococcus

aureus due to an infected intravenous catheter. Given the clinical picture, piperacillin/tazobactam was administered empirically and was later switched to cefuroxime intravenously and finally to oral amoxicillin/clavulanic acid. 4 days after the second case, another patient, a 69-year-old man, hospitalized in the shared room for over 50 days due to postoperative complications of a graft for abdominal aortic aneurysm, presented productive cough, fever and dyspnea, with increased CRP (241 mg/l). H. influenzae was isolated from sputum and blood cultures were negative. He recovered within 10-days on cefuroxime therapy.
Discussion: Current guidelines don't recommend to isolate patients with H. influenzae pneumonia in one-bed hospital rooms and state that standard precautions are sufficient to avoid nosocomial transmission. Our cases rise the question if the current recommendations should be modified and patients at risk isolated at least until the antibacterial treatment reduces the bacterial load and leads to an improvement in clinical symptoms.

P148

Trench foot during peacetime: when an old war disease reappears among homeless people in Switzerland

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Learning objectives:
- Clinical: identifying this rare disease, which affects mostly the homeless exposed to wet cold weather
- Public health: warning authorities and charities that shelters offering proper hygienic conditions combined with homeless outreach programs are essential during winter and not only when it is freezing.

Case: On December 28th, in Geneva, while it was raining almost continuously, an officer in charge of a marketplace finds a man in his 40s, lying on the street. His clothes are completely wet, he refuses all help. He is known to be homeless and to drink alcohol. He is referred to the emergency room.
Status: Temp: 35.8°C. Both feet are white and cyanotic, with a visible limit above the malleolus, no pedal nor posterior tibial pulse. No pain nor sensation in both feet under the ankle; complete bilateral motor deficit.
Angiology: bilateral thrombotic occlusion of the tibial arteries, no flow under the malleolar area.
Biology: ethanolemia: 85.1mmol/l ; CPK 3924 U/l
Social: He comes from Morocco, has lived in Switzerland for 10 years. He lost his residence permit two years ago after he separated from his wife, and became homeless. He no longer has health insurance.
Evolution: On Dec 29thhe presents a tonic-clonic seizure, probably due to alcohol withdrawal. According to orthopaedic surgeons and angiologists: no possibility of spontaneous or therapeutic revascularisation, a mid-tibia amputation of both leg is indicated, high risk of gangrene.The patient initially refuses, but finally submits to a bilateral surgical amputation on Jan 5th. Enterobacter cloacae Complex is found in the wound and treated. He is referred to an orthopaedic rehabilitation unit two weeks later. Simultaneously, legal and social procedures are initiated, in order to obtain a residence permit and a health insurance.

Discussion: In Switzerland, the homeless are often invisible, unlike in other European towns. Therefore the most vulnerable of them, like migrants or people with alcohol problems, escape the radar and put their health at high risk.
Trench foot was described during the French Invasion in Russia in 1812, and 75000 soldiers died from this during the First World War. This injury is cause by exposure to temperatures just above freezing, combined with moisture and results in a vasoneuropathy, inducing necrosis. It is often complicated by infection. Homelessness, alcoholism and migration are contributing factors. Homeless outreach programs are the best prevention.

P149

Unexpected souvenir from Sweden

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Learning points: Nontuberculous mycobacteria (NTM) may be a cause for pulmonary consolidations resembling pulmonary malignancies. Repetitive positive NTM culture results in conjunction with compatible radiological findings, and systemic or pulmonary symptoms are needed to fulfil the diagnostic criteria for pulmonary NTM infection after the exclusion of alternative aetiology.*Mycobacterium malmoense* is a rare cause of NTM infections; we report the fifths case in Switzerland.

Case description: A 82-year-old male presented with a loss of appetite, weight loss (6 kg/6 months). Fever or cough were not present. The initial clinical examination was unremarkable; laboratory abnormalities were limited to an elevated C reactive protein level. A thoracic X-ray and CT scan revealed a consolidation of 7x4x-5.5cm in the upper right lobe with calcifications, a bilateral hilar lymphadenopathy with sluggish calcifications, and additionally multiple small calcified nodules in both lungs, the latter already been present 10 years before. Although the patients' lesions were suggestive for a malignancy, a biopsy by bronchoscopy and cytology of the bronchoalveolar lavage (BAL) fluid showed no signs of malignancy or inflammation, possibly flawed by a sampling error. Two months later the microbiological cultures of the BAL grew *Mycobacterium malmoense*. Persistent growth was confirmed by an independent BAL sample. An antimycobacterial treatment with rifampicin, ethambutol and clarithromycin was initiated. By that time, the patient reported increasing fatigue and moderately productive cough. Over the first 6 months on treatment the patients' performance improved, the cough subsided. A first sputum culture control after 3 months showed no mycobacterial growth. The patient reported to have spent his holidays for the last decades mainly in Southern Sweden, although he did not stay for a prolonged period in Malmö.

Discussion: Most *M.malmoense* cases are reported in Northern Europe and Scotland. The geographical epidemiological predominance in Northern countries is still not understood. As all NTM, *M. malmoense* mainly causes pulmonary infections in structurally altered lungs. Rare manifestations include soft tissue or joint infections, and cervical lymphadenopathy in children. Poor correlations between in vitro resistance testing and clinical treatment outcomes were reported. The recommended effective treatment consists of rifampicin, ethambutol and clarithromycin for up to 2 years.

P150

Valsalva maneuver-induced pneumothorax and pneumomediastinum in a COVID-19 patient with ARDS. An (astonishingly) unusual complication

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Learning objectives: To raise awareness of the risk of pneumothorax and related complications in COVID-19 pneumonia.
To discuss pneumothorax predisposing factors, and possible means of prevention.

Case: A healthy man in his 60ies was hospitalized for hypoxemic respiratory failure due to COVID-19. The patient was admitted in the COVID-19 Intermediate Care Unit of the Division of General Internal Medicine, Geneva University Hospitals, to benefit from non-invasive ventilatory support (respiratory assistance with continuous positive airway pressure and high flow nasal cannula) with sessions of prone position. He was treated with dexamethasone (6 mg qd), tocilizumab (600 mg on day 2 and 3 of his admission) and the anti-SARS-CoV-2 monoclonal antibodies casivirimab/imdevimab. Clinical course was favorable, with gradual reduction of supplemental oxygen from day 8. On day 14, the patient displayed a drastic oxygen saturation drop during straining defecation. Chest X-ray showed a 4 cm left pneumothorax. Pleural drainage with a large bore chest tube was rapidly performed. In spite of that, the patient developed a progressive respiratory failure and mechanical

ventilation had to be used. A chest CT showed a large left basal pneumatocele, a pneumomediastinum and new right sided lobal and bilateral segmental pulmonary embolism. Despite appropriate treatment, his general status worsened and the patient eventually died.

Discussion: The incidence of COVID-19-related pneumothorax ranges from 0.3% to 23%.[1] Histologic studies show diffused alveolar damage; these lesions could, in turn, weaken the pulmonary parenchyma and predispose to pneumothorax.[2,3]. The extensive use of non-invasive and invasive ventilation are likely to play a role in pneumothorax development[4,5,6]. Apart from optimization of ventilation parameters to minimize barotrauma, there is nothing that can be done to minimize these predisposing causes. In our case, the temporal relationship between straining defecation and pneumothorax formation point to Valsalva maneuver as the trigger to this complication. Given the increased frequency of pneumothorax in COVID-19 patients - a population that is prone to constipation (because of opioid use and prolonged bed rest) - it is astonishing that this complication has never been described before. We believe that particular care should be taken to prevent and treat constipation in hospitalized COVID-19 patients, as a simple mean to prevent an ominous complication.

P151

Wide-complex tachycardia: differential diagnosis and unusual approach to confirm origin of tachycardia

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Learning objective: Wide-complex tachycardia (WCT) is defined as tachycardia (> 100 bpm) with a wide QRS complex (≥ 0.12 s). Origin can be both ventricular and supraventricular as well as due to ventricular pacing. Conventional concepts to distinguish the origin of WCT are atrioventricular (AV) dissociation, capture and fusions beats and several electrocardiogram (ECG) algorithms. In patients with a dual chamber pacemaker, real time intracardiac electrogram (EGM) dependably discriminates origin of WCT.

Case: A 90-year-old male patient presented in our emergency department with recurrent episodes of dizziness for three days. Clinical examination revealed stable hemodynamic situation with blood pressure of 139/89 mmHg. ECG (*image 1*) showed episodes of WCT with heart rate of 168 bpm during WCT. In the ECG, AV dissociation (*) was clearly visible in lead V1 during WCT, indicating ventricular tachycardia (VT) as the cause of WCT. Additional interrogation of the implanted dual chamber pacemaker confirmed AV dissociation (*image 2).* No electrolyte disorder was present. After intravenous treatment with amiodarone, episodes of WCT as well as dizziness ceased.

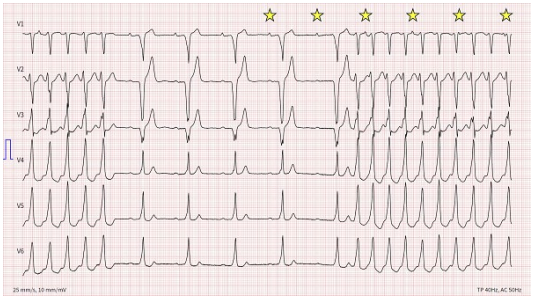

Image 1: ECG with AV dissociation (indicating P waves).*

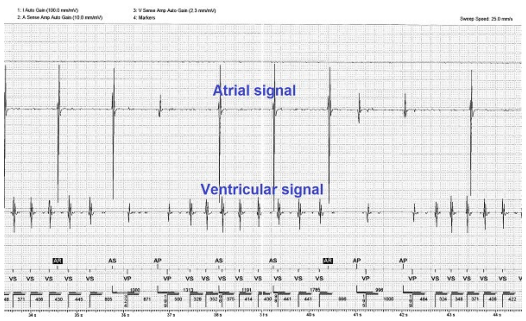

Image 2: EGM showing AV dissociation.

Discussion: Differential diagnosis of WCT is VT, supraventricular tachycardia with widened QRS complex due to aberration (fixed or functional bundle branch block), pre-excitation or intraventricular conduction delay caused by medication (e.g. flecainide), electrolyte disorders (e.g. hyperkalemia) or cardiomyopathies (e.g. left ventricular hypertrophy or dilation), and ventricular pacing by a pacemaker (e.g. pacemaker-mediated tachycardia or ventricular stimulation forced by sensing of an atrial tachycardia up to the maximum tracking rate). Hemodynamic situation does not allow to discriminate ventricular from supraventricular origin. History of coronary artery disease increases pretest probability for VT to 90-95%. Conventional concepts to distinguish the origin of WCT are AV dissociation (AV ratio < 1 or ventriculoatrial (VA) block with VA rate > 1, challenging if dual tachycardia is present), capture and fusions beats which reliably indicate VT if present. Moreover, several ECG algorithms exist to distinguish the origin of WCT as for example proposed by Brugada et al. (Circulation 1991). In patients with implanted dual chamber pacemaker, real time intracardiac EGM is easily accessed by a pacemaker programmer, which dependably discriminates origin of WCT.

P152

A roadmap to competency: pilot testing a family medicine clerkship logbook

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Introduction: The longitudinal family medicine (FM) curriculum at the Faculty of Medicine in Geneva is part of the effort to increase the attractivity of FM careers. Based on a conceptual framework (1), we identified priorities for curriculum improvement, including the development of a competency logbook for the three FM clerkships (in years 2, 4 and 6 of medical school). This process was accelerated in spring 2021, as students expressed a need for guidance regarding the acquisition of competencies due to disruptions in their curriculum because of the COVID-19 pandemic. Here, we describe the development of the pilot logbook and present avenues for the future.

Methods: The logbook was developed through an iterative group-based process and based on the PROFILES learning objectives (2). First, we reviewed the list of Entrustable Professional Activities (EPAs) and Situations as a Starting Point (SSPs) to include those applicable to FM. A group of experienced FM teachers then selected the most relevant competencies and SSPs from the list. These were combined in a grid to be used to track students' activities during clerkships. A small group of students tested a preliminary version of the tool and provided feedback for the development of the final version, to be pilot tested among all students during academic year 2021-2022.

Results: The final logbook has two versions: one for general internal medicine and one for paediatrics. It contains 18 (general internal medicine) or 16 (paediatrics) categories of common situations, presented in table format along with EPAs. The logbook's appendix details the most relevant competencies related to each EPA. At the start of the clerkship, students are encouraged to use it to identify clinical situations to be experienced and to define the appropriate level of supervision for each relevant EPA.

Discussion: The competency logbook's pilot version is a result of the ongoing development of our FM curriculum adapted to students' needs. It is currently being pilot tested. Evaluation will focus on the tool's uptake by students and will inform its further development and implementation. This pilot project will also serve as a base for the development of a longitudinal competency roadmap covering the three FM clerkships, with the aim to reinforce the continuity between clerkships by highlighting the progression of students' competencies and to contribute to clerkship quality by facilitating communication between students and supervisors.

P153

Defining entrustable professional activities for postgraduate training in general internal medicine: a national consensus study

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Introduction: Entrustable Professional Activities (EPAs) are observable tasks that are regular parts of a physician's daily clinical work. Before being permitted to accomplish these tasks independently, trainee doctors must gain their supervisors' trust. Defining the list of EPAs that should be mastered by the end of postgraduate training (PGT) is critical to setting clear expectations about autonomous practice. We aimed to define EPAs relevant for PGT in General Internal Medicine (GIM) at a national level.

Methods: A total of 248 EPAs were drawn from a systematic literature review and 4 focus groups discussions. EPAs were formulated according to published best-practices and organized into 6 domains (Care of adult population; Care of patients with special needs; Care coordination and communication; Management and Leadership; Quality of care/educational & research activities; Miscellaneous). We used a modified RAND appropriateness method to evaluate and rate the relevance of the proposed EPAs to ambulatory and/or hospital training, and the maximum level of entrustment expected from trainees at the end of PGT. Ratings were made on a 9-point likert scale. Relevance was categorized as high (median (med) 7-9), low (med 1-3) or uncertain (med 4-6) or disagreement (1/3 of ratings 1-3 and 7-9).

Results: 28 internists with several years' experience as clinical supervisors were invited to the first round of individual rating (10 women, 12 from ambulatory practice, from the German (12), French (13) and Italian speaking region (3)) and 11 agreed to participate to a second expert panel meeting. 225/248 (90%) EPAs were deemed high-priority for PGT in GIM. 174 (77%) were considered relevant to both training tracks, 18 (8%) for the hospital track and 27 (12%) to the ambulatory track. 62% of EPAs were ranked with very-high priority (median score 8.5-9) for both training tracks. Low-ranked EPAs related to pregnancy, newborn or child care. 198 (88%) EPAs were considered to require a maximal level of entrustment (ability to supervise) at the end of PGT. Results could be further classified in 5 domains, 28 EPAs and 225 specifications.

Conclusions: This study provides a list of 28 EPAs and 225 specifications for PGT in GIM, using a national consensus process and a scientific approach. The results of this study will provide a solid foundation for structuring the future PGT programs in GIM in Switzerland. It also provides to trainees and supervisors a common reference for assessment.

P154

Reinforcing interprofessional education in the pregraduate curriculum of the Medical Faculty of the University of Lausanne, quite a challenge

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Introduction: The Medical Faculty of the University of Lausanne mandated the Department of Family Medicine of Unisanté to reinforce interprofessional education in the pregraduate curriculum.
Interprofessional education occurs "when two or more professions learn with, from and about each other to improve collaboration and the quality of care"[1].
Until 2020, all medical students participated at 1 ½ days of interprofessional education in the 1rst master year with nursing, physiotherapy, midwife and radiology technician students.
Method: We started by mapping the medical curricula for courses on interprofessional competencies.
We although learned about interprofessional education by reading and discovering different medical curricula in Switzerland and abroad.
Now, we introduce new courses in interprofessional competencies throughout the curriculum.

Results: The mapping confirmed that the only interprofessional education to which all the students are exposed, is the 1 ½ days in the first master year. They are few interprofessional optional courses.
Since 2020, our 2nd bachelor year students observe interprofessional interactions during a 1/2 day at a family practice office and during a day with the "Centre medico-social" and return a reflexive work. They get some theory on interprofessional competencies during a lector.
During the 3rd bachelor year, 8 medical students have the opportunity to present their bachelor thesis with 8-10 nursing students.
We are building an 8 hours practical exercises day, during the 3rd bachelor year for all medical students with nurse, physiotherapy, midwife and radiology technician students starting this fall.
During the 2nd master year, the students have 2 hours ex-cathedra teaching on interprofessional competencies.
Finally, they all do a shadowing experience with a reflexive work during the practical month at the office of a family doctor.

Conclusion: Interprofessional education is implemented at the medical faculty with the support of the medical dean.
The main obstacles are the difficulty to change the existing curriculum, to adapt our curriculum to the one of other medical professional schools and to have enough competent teachers.
The main critique is that not all courses are truly interprofessional, as some are taught only with medical students.
We encounter a lot of enthusiasm of the faculty but although of the other medical professional schools and are building an interprofessional education through the whole curriculum.

P155

Teaching patterns and scripts: a qualitative study

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Introduction: Clinical teachers use both clinical and teaching scripts[1]when supervising students in their daily practice. Teaching scripts result from the knowledge of medicine and patients, of context, teaching and learners. Contrary to clinical scripts, little is known about the development of teaching scripts. The aim of the study was to explore how the different dimensions of teaching scripts interact with each other and whether they vary according to clinical teachers' level of teaching experience and professional background.

Methods: A purposeful sample of twenty clinical teachers from different disciplines and levels of teaching experiences were invited to conduct a videotaped clinical supervision with a simulated resident about a patient presenting with subacute low abdominal pain. The session was followed by a semi-structured and a stimulated recall interview. Both were transcribed and analysed using deductive and inductive approaches.

Results: According to their working context, participants' approach to the supervisory role differed - teaching in the emergencies meant little time and high prioritization while supervising patients admitted on the ward or in the ambulatory setting gave them more time and allowed a larger focus on differential diagnosis and management. They usually categorised learners according to their level of experience and the fact that they had or not worked with them before. They used such categorisation to judge the degree of autonomy and reliability of the learner. Knowledge of patients was embedded in all dimensions but more visible when participants taught the clinical reasoning process. Regarding knowledge of teaching, we distinguished four clear teaching patterns in terms of teaching intentions, learning culture and clinical reasoning approach: simple (pedagogical framework) and flexible (teaching approach), simple and fixed, complex and fixed and complex and flexible. Others were defined as "in transition" as they still were in development. Participants' work setting, prior clinical and teaching training, reflective and analytical skills as well as their ability to enrich their pedagogical framework with other influences seemed to determine the development of these patterns.

Conclusion: The results of this study sheds light on what faculty development programs should focus on depending on participants' teaching patterns in order to help them acquire both rich and flexible approaches to teaching in a clinical context.

P156

Ultrasonography in Internal Medicine (USIM) – educational concept

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Learning objective: To enumerate internal medicine point-of-care-ultrasonography (POCUS) requirements and propose a structured learning process to achieve them.

Description: POCUS is a valuable tool for the internist. Its field of application is large and extensive, ranging from free fluid detection to echo-guided procedures.[1] The conditions to obtain a Swiss POCUS certification have been established in 2018, and include a minimum of one hundred POCUS exams in each given pre-specified domain (e.g. emergency ultrasonography, focused thoracic ultrasonography), of whom at least one-half under the supervision of a certified Swiss POCUS tutor. Since 2022 POCUS certification has been integrated in the postgraduate formation program of general internal medicine. In the near future, every aspirant to the internal medicine specialization will be required to fulfil the criteria for the obtainment of POCUS certification on basics of emergency ultrasonography.[2] This includes ability to detect abdominal and pleural free fluid, perform venous compression and abdominal aorta ultrasonography, among others. Achievement of POCUS competences is a demanding process and requires rigorous training. This training includes an initiation phase, followed by a practical training period of supervised images' acquisition.[3] Supervision by experts is crucial for mastering the essential skills for a secure use of POCUS. Although supervisors are available, they are unquestionably not enough to meet training needs in French-speaking part of Switzerland.

Discussion: Here we illustrate the educational concept of our institution, targeting every internal medicine doctor at the beginning of their residence. After an e-learning and practical hands-on course on healthy subjects and internal medicine inpatients, residents are attributed to a certified POCUS tutor. Training slots are scheduled for direct supervision on patient or simulator. Indirect remote supervision is encouraged by means of a secured electronical logbook. This will maintain a high level of proficiency and promotes growth of tomorrow's supervisors.

P157

Understanding factors and reasons for non-participation of patients with diabetic kidney disease to a medication adherence program: a mixed methods study

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Introduction: An interprofessional medication adherence intervention (PANDIA-IRIS study) led by pharmacists, combining motivational interviewing and electronically monitored (EM) feedback was introduced to all consecutive patients with diabetic kidney disease (eGFR ≤60 ml/min/1.73m2) visiting their nephrologist or diabetologist in a University outpatient setting. About 73% (202/275) eligible patients declined to participate; factors and reasons for refusal were investigated.

Methods: 1) Coded sociodemographic and clinical variables were collected retrospectively in patients' medical records for those having signed the general consent form (CGF) and compared to the included patients.
2) Patients having refused the adherence program were invited for a qualitative semi-structured interview until data saturation. Verbatim transcription and inductive coding were performed by two investigators until consensus.

Results: Patients who refused to participate were older (mean age 68 yrs. 95% CI 66-70, SD: 11) than those who accepted (64 yrs. 95% CI 61-67, SD: 10), p=0.02. More women vs. men refused participation: 38/45 women (84%) vs. 85/135 men (63%), p=0.007. Time since diabetes diagnosis was longer in patients who refused vs. those who accepted (median 15 yrs. IQR 7-23 vs. 9 yrs. IQR 4-16, p=0.002). Main reasons for non-participation were: no perceived need, patients did not agree to use EM and the study design was perceived as a burden. Patients who refused described a well-established medication routine and perceived that the program could have been beneficial if introduced earlier in their therapeutic journey. Other barriers that emerged: a difficult relationship with healthcare providers, a lack of awareness of the pharmacist's role in supporting adherence and a negative perception of clinical research.
On the other side, included patients found the EM feedback useful to prevent forgetfulness and support medication literacy and motivation; they were also reassured by the interprofessional intervention.

Conclusions: Investigating factors and reasons for non-participation in a study helps tailoring intervention designs to the needs of polypharmacy patients. There is an urgent need to advocate interprofessional outpatient collaborations between physicians, pharmacists and nurses to support medication adherence in patients with diabetic kidney disease.

P158

A framework to use electronic health record metadata to visualize the past medical history of patients

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Introduction: In clinical practice time and cognitive focus are two of the most limited resources. Visits are short and often it is not possible to extend the anamnesis far beyond the current medical issue at hand. In preparation of a visit, clinicians therefore often consult the EHR (electronic health record) to reconstruct a clinical narrative as an actionable basis for communication and decision [1]. This process of data aggregation and integration using an EHR is tiering and error prone [2], but it makes for a crucial part of the work as an internist today.

Method: We hypothesize, that the most challenging part of building a clinical narrative is to retrieve temporal relations between different pieces of data. EHR systems use list views to visualize reports and other information, leaving it to the clinician read and interpret the metadata, e.g. date, besides extracting the content of the document per se [3].
Github.com offers an interesting approach to visualizing temporal metadata: changes to a repository are visualized as a mini calendar with a color spectrum encoding the count of changes per day. We have translated this concept for EHR metadata (Figure 1). A prototype is available: octameter.ch/ehr_metadata

Result: A day is visualized as a small box and weeks are grouped into seven boxes in a row. The color of a box encodes metadata available for that day (e.g. report, ECG, x-ray). For easy identification, color codes for hospital departments can be used. Pinpoints with specific icons for selected report categories further aid in identification (Figure 2). Clicking on the boxes/pinpoints opens up the corresponding report.

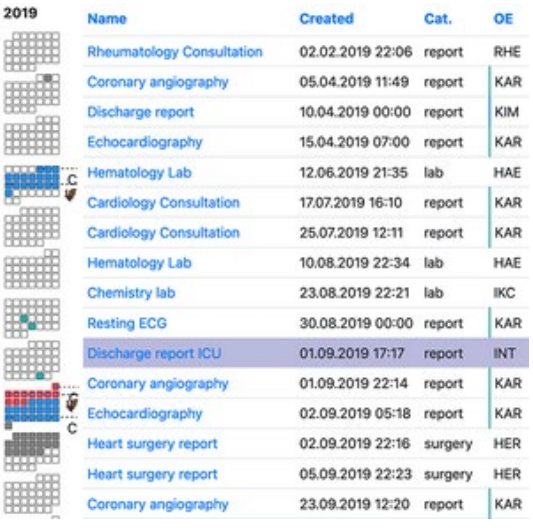

Figure 1: Calendar view next to a contrived report list

Discussion: This concept is easy to understand and could be helpful during EHR information search. Temporal relations in the data can easily be explored. User preferences could be added to control the level of detail to avoid cognitive overload. The risk of a filter-bubble and resulting biases must be kept in mind. Integrated into an EHR our concept could help clinicians to construct the clinical narrative more quickly, reduce their mental load and maybe even increase their work satisfaction. In the context of the upcoming national electronic patient record in Switzerland this is of special interest.

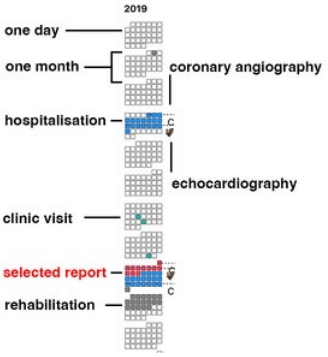

Figure 2: The bat signifies an echocardiography, C represents a coronary angiography, blue and gray are hospitalizations, a red border marks the selected report

P159

Assisted teleconsultation in an outpatient pharmacy: results of a pilot study in Geneva

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Introduction: Assisted teleconsultation (ATC) is the act of telemedicine involving on one side a patient in the presence of a healthcare professional (HP), and the expert HP on the other side. ATC in outpatient pharmacy may be an alternative to the emergency room for patients with a semi-urgent medical problem[1]. It might avoid emergency consultations with a low urgency degree while limiting the cost and optimizing patients' trajectories.
HUG@home is both an application for secured teleconsultations developed in the Geneva University Hospitals (HUG) in 2019 and an ATC on-call service for healthcare partners initially to support home nursing[2]. Between October 2020 and June 2021, Pharma24 and HUG conducted a pilot study on ATC with HUG@home in an outpatient pharmacy.

Methods: After pharmacist's evaluation and triage, ATC in a private room was proposed to patients consulting at Pharma24 for a semi-urgent medical problem. Psychiatric consultations were excluded. ATC took place between the patient assisted by the pharmacist and a senior resident of the Primary Care Division of the HUG. Prospective data on patients, consultation reasons, ATC duration, patient's orientation and pharmacist' satisfaction were collected by pharmacists and physicians for each consecutive consultation.

Results: Thirty-nine consultations took place, 12 with video and 27 with telephone. Patients' median age was 37 years (IQR 26-50), 59% were women. Near half of the consultations (19) happened during the week-end. 28 (72%) consultations ended with a prescription, 9 (22%) with recommendations and 2 (6%) with an emergency care referral. Without ATC, 33 (87%) patients would have consulted a doctor for their problem, 24 (61%) in an emergency room. Pharmacists' satisfaction on the medical management was very high, and moderate on the technical side. 15 (41%) consultations concerned ORL, ophthalmologic and dermatologic systems. Mean ATC duration (including administrative time) was 22.4 minutes (IC95% 18.6-26.1). A preliminary cost-effectiveness evaluation estimated a saving of 100 to 165 CHF per consultation preventing an emergency room visit.

Conclusion: A young population with semi-urgent medical problems can be managed in the pharmacy using ATC with a primary care doctor. With 171 pharmacies in the Geneva canton, this innovative project has a potential of extension to offer an alternative to an emergency room visit. Financial, technical and training aspects should be optimized in the future.

P160

Do patients have communication preferences during a videoconsultation?

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Introduction: Teleconsultation can influence health behaviours through changes in the form and content of physician-patient communication.To avoid negative impact on doctor-patient communication, experts in clinical communication have issued recommendations for video consultation.However, these recommendations have never been validated by real patients. The aim of our study was to explore patients' preferences regarding doctors' behaviours in video consultation as well as the socio-demographic factors influencing their choice.

Methods: We conducted an exploratory study in both private and public medical centers and emergency services in Geneva in 2021. Patients in the waiting room were invited to watch videos displaying variations of doctor communication behaviors during video consultation and indicate which one they preferred. The videos featured 6 specific physician video communication behaviours with 2 variations for each:
1) Camera framing: face vs face and bust
2) Gaze orientation: towards camera vs towards screen and camera
3) Social phase: related to connexion quality or not
4) Privacy reminder regarding the online platform and environment: with or without
5) Pauses after physicians' statements: usual length / longer pauses
6) Empathy: with or without increased non-verbal expression.

Results: 417 patients watched three different videotaped standardized encounters illustrating specific video consultation behaviours (two variations each). A majority of patients preferred framing with both face and bust (50.7%) versus face alone (21.8%).They valued eye gazing towards the camera (42.9%) versus eye gazing shifting between screen and camera (13%).Social phase related to connection quality was praised (43.1% vs 17.1%) as well as the privacy reminder regarding the online platform and environment (80.8% vs 6.5%). Patients preferred short rather than long pauses after physician's statements (63.9 vs 14.9%) as well as expressive rather neutral non-verbal behaviour when associated with verbal empathy (46.7% vs 17.6%).The percentage of patients indicating no preference varied between 12.6% (privacy reminder) and 43.1% (eye gazing).

Conclusion: Our results confirm that patients prefer the use of the video specific communication behaviors recommended by experts, with the exception of shifting eye gazing and long pauses after physician's statements. These recommendations, if confirmed by other studies, should be more consistently taught during medical training.

P161

Has telemedicine come to fruition? Patients' and physicians' perceptions and preferences regarding telemedicine

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Introduction: The SARS-Cov2 pandemic boosted the use of telemedicine for both COVID-infected patients as well as for patients with acute or chronic disease. The aim of our study was to evaluate both patient and physician perceptions, preferences, and acceptability regarding the use of the different modalities of telemedicine for various health problems.

Methods: We conducted a cross-sectional survey in Geneva in 2021. Patients in waiting rooms of both private and public medical centers and emergency services were invited to answer an online questionnaire, while physicians working in private and public settings were asked to answer a similar questionnaire by email. The questionnaire focused on digital literacy, acceptability, preferences, as well as barriers and facilitators concerning a variety of telemedicine modalities for different health concerns.

Results: 570 patients (55% women) and 543 physicians participated (42% women, 40% physicians working in private practice and 60% physicians employed by public institutions). After face-to-face consultations, most patients preferred the telephone to other modalities for health issues such as simple medical advice (65%), discussion of clinical parameters (61%), acute or chronic problems (55% and 60%), and psychological support (57%).They valued emails for communication of blood tests (56%) and renewal of medication (49%). Half of patients considered video to be acceptable for psychological support. A large majority of physicians considered the phone to be an acceptable modality for all the issues mentioned above (85% to 94%). Emails and videos were considered to be acceptable for follow-up of patients with chronic diseases (53% and 54%) and provision of simple advice (51% and 48%). 65% of physicians would use video for psychological support. Patients' mains reasons for using telemedicine were lack of traveling (72%) and saving time (56%). Disadvantages were lack of physical examination (60%), technical problems (43%), and unsuitability (43%). Physicians feared the potential negative impact of telemedicine on the therapeutic relationship and insisted on the need for a facilitated access and a user-friendly format of online platforms.

Conclusion: The use of telemedicine has increased since the pandemic but both doctors and patients continue to prefer face-to-face consultations. Telephone remains more acceptable than video in most medical situations.

P162

Survey-based evaluation of an innovative speech-enabled translator in emergency settings: a Phase II cohort study

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Introduction: Healthcare systems worldwide are increasingly confronted with migrant patients and associated language barriers, leading to a potential decrease in the quality of care in hospitals especially in emergency departments.[1] The gold standard is to use a professional interpreter during consultations, but this solution can be difficult in emergency settings where time is of the essence.[2] With modern technology, automatic translation tools such as Google Translate are available, but they are not precise enough for use in the medical context.[3] Our objective is to evaluate satisfaction of the technical features and the perceived efficacy of an innovative speech-enabled, fixed phrase translation tool called "BabelDr" in an emergency department.

Methods: We conducted a phase II cohort study using a survey-based design to assess patient and physician satisfaction and perceived efficacy of the technical features of the tool in real life situations. Thirty of 42 eligible allophone patients visiting an outpatient emergency unit (mean age, 38.2 [standard deviation, 16.49] years; 53.3% (n=16) were male) were included. Selected patients had no understanding of the French language. Physicians were assigned if they did not have a common language with the patients.

Results: Regarding satisfaction, 90% (n=27) of patients and 86.6% (n=26) of physicians had a positive impression of the translation tool. In addition, 90% (n=27) of patients felt able to tell the physician why they came to the emergency room and 93.3% (n=28) expressed that they understood the tool's translations. Forty percent (n=12) of patients also stated that they would not have preferred to use an interpreter during the consultation. Regarding the perceived efficacy, 93.3% (n=28) of physicians affirmed that they could understand the patient's health problem and 80% (n=24) were able to make a diagnosis. A significant positive association (P<0.05) was observed between physicians' appreciation of the different features of the tool and their overall satisfaction.

Conclusion: Our study suggests that the fixed-phrase translation system BabelDr is suited for diagnostic interviews in an emergency context and a valid alternative when no interpreter is available and time is at the essence.

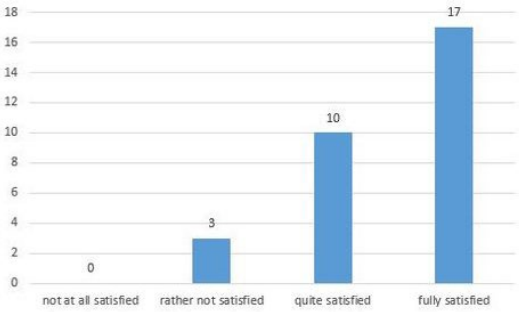

Figure 1. Distribution of patients (n=30) for the question: "How satisfied are you with this translation tool?"

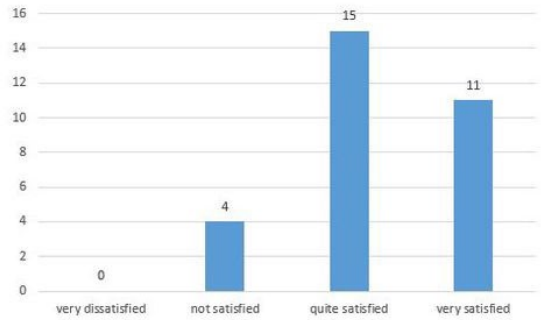

Figure 2. Distribution of doctors (n=30) for the question: "Concerning the use of this software, would you say that you are...?"

Société conviée SSPTC: Présentations de posters / Gastgesellschaft SGKPT: Posterpräsentationen

P163

Cardiovascular therapy and in-hospital mortality in patients with severe COVID-19: a Swiss cohort study

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has a significant impact on mortality in patients with COVID-19 and cardiovascualr comorbidities: the exposition sequences and dosage of cardiovascular medications still remain controversial.

Methods: Logistic regression models adjusted for potential confounders were used to assess the associations of use (i.e., pre-hospital use, in-hospital use) and modifications in exposure (i.e., discontinuation on admission, initiation during hospitalization) to eight common cardiovascular therapies.

Results: Of 838 inpatients with COVID-19, 468 (55.8%) were exposed to cardiovascular therapies before hospitalization, 779 (92.5%) had at least one of their cardiovascular drug prescriptions modified, 453 (54.1%) were male, and 152 (18.1%) died before discharge. The mean age was 66.5 ± 17.6 years. Overall, no cardiovascular therapy used before the hospitalization was associated with the risk of in-hospital death after accounting for potential confounders. During the hospitalization, the use of diuretics (adjusted odds ratio (aOR) 2.59 [1.68-3.98], p<0.001) was associated with an increase, and the use of agents acting on the renin-angiotensin system (aOR 0.39 [0.23-0.64], p<0.001) and lipid-lowering agents (aOR 0.41 [0.24-0.68], p=0.001) were associated with a reduction in the odds of in-hospital death, respectively. Exposure modifications associated with decreased survival were the discontinuation of an agent acting on the renin-angiotensin system (aOR 4.42 [2.08-9.37], p<0.001), a β-blocking agent (aOR 5.44 [1.16-25.46], p=0.031), a lipid-modifying agent (aOR 3.26 [1.42-7.50], p=0.005) or an anticoagulant (aOR 5.85 [1.25-27.27], p=0.025), and the initiation of a diuretic (aOR 5.19 [2.98-9.03], p<0.001) and an antiarrhythmic (aOR 6.62 [2.07-21.15], p<0.001). Exposure modification associated with improved survival was the initiation of an agent acting on the renin-angiotensin system (aOR 0.17 [0.03-0.82], p=0.028).

Conclusions: In hospitalized patients with COVID-19, there was no detrimental association of the pre-hospital use of any cardiovascular medication category and these therapies should be continued as is recommended. Agents acting on the renin-angiotensin system and lipid-modifying agents tend to benefit in patients with COVID-19. Regular cardiovascular medications could be continued in hospitalized patients with COVID-19.

P164

Daptomycin population pharmacokinetics and dosing nomogram in patients at Swiss university hospitals

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Introduction: Daptomycin is an antibiotic used in the treatment of infections with gram-positive bacteria [1]. This lipopeptide exhibits dose-linear pharmacokinetics and is primarily eliminated unchanged via the kidneys. Treatment efficacy correlates with the ratio of area under the curve (AUC) over minimum inhibitory concentration (MIC), and thus varies with the targeted organism's sensitivity to the drug [2]. An AUC/MIC > 800 is considered bactericidal, whereas 400 < AUC/MIC ≤ 800 is bacteriostatic. To minimize the risk of rhabdomyolysis, it is preferable to keep trough level C24h < 24 mg/L [3]. A posteriori dose adjustment in the form of therapeutic drug monitoring (TDM) is commonplace to optimize efficacy and prevent toxicity. Pharmacometric models can be used for initial (a priori) dose finding but involve specialist knowledge often not readily available at point-of-care. Dosing nomograms would be a solution to shorten time to target attainment.

Methods: We performed a retrospective study of inpatients receiving routine TDM of their daptomycin treatment at the University Hospital Basel (UHBS) and Lausanne University Hospital (CHUV). Included covariates were demographic data, chemistry and hematology results, infection specific data (type, site, organism, MIC when available) and clinical outcome at time of discharge from hospital. Patient data were used to build a population-based pharmacokinetic model with NONMEM (Icon Development Solutions, Ellicott City, MD, USA) and to generate dosing nomograms (Figure).

Results: A total of 58 patients were included (n=31 at UHBS, n=27 at CHUV), providing a total of 174 samples. The final model was a one-compartment model with linear elimination (volume of distribution (Vd) 15.90 L (inter-individual variability (IIV): 40%) and clearance (CL) 0.79 L/h (IIV: 33%)). Influential covariates on clearance were serum albumin concentration and renal function (as estimated by the Cockcroft-Gault equation). Dosing nomograms were generated by simulating concentration profiles at steady state for a broad range of doses (2-14 mg/kg) and computing AUC 0-24h for typical patients at serum albumin levels of 20 g/L or 35 g/L.

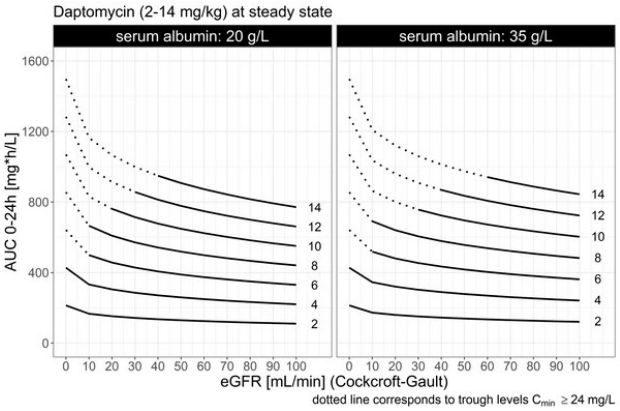

Figure - Daptomycin dosing nomograms for typical patients

Conclusions: Since daptomycin is given mostly in critically ill patients, timely and precise dose recommendations are needed. Dosing nomograms can help make informed decisions for optimizing initial dosage, pending therapeutic monitoring when appropriate.

P165

Development of an assay by liquid chromatography coupled to tandem mass spectrometry for thiopurines drugs in whole blood and application for their therapeutic drug monitoring

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Context: The cytotoxic and immunosuppressive thiopurine drugs, namely 6-Thioguanine nucleotide (6-TG) and the 6-Methyl-mercaptopurine (6-MMP), are mainly used in acute lymphocytic leukemia, disorders of immune regulation and inflammatory bowel disease. Quantification methods for their Therapeutic Drug Monitoring are usually reported in various blood matrices, but barely with Dried Blood Spots (DBS). Moreover, comparisons between thiopurines quantification in blood and DBS are scarce.

Objective: We performed a cross-validation between a well-established external assay and our newly developed, optimized, and fully FDA-validated method to verify their agreement. In parallel, we evaluated the correlations between concentrations of 6-TG and

6-MMP determined in blood collected on EDTA, versus on heparin with 0.02% (m/v) dithiothreitol (Hep-DTT), and versus DBS.

Methods: We applied linear regression and Bland-Altman test to thiopurine levels obtained from 34 patient samples. A total <15ml blood was collected for laboratory quality control purposes and analytical methods validation. The DBS was obtained by spotting 20 µl of the EDTA sample on a Whatman FTA DMPK-B Card. Hematocrit and red blood cell were measured from EDTA-blood to normalize the thiopurines levels according to Dervieux et al[1].

Results: All patient samples were found to lie within the validated range of the assay (5-2'000 ng/ml for 6-TG, and 50-20'000 ng/ml for 6-MMP). A good correlation between EDTA and hep-DTT results could be observed (slope 0.98, r^2=0.93 and 1.01, r^2=0.92, for 6-TG and 6-MMP respectively). Despite a good correlation between DBS and EDTA samples (r^2> 0.95), a significant bias is observed for 6-TG and 6-MMP with a slope of 0.61 and 0.74, respectively. Similar correlation and bias are found for hep-DTT samples.

Conclusion: We demonstrated that the 10 ml collecting tubes of heparin with DTT prepared by the external laboratory and used so far can be conveniently replaced by standard 2.6 ml EDTA tubes. Our LC-MS/MS method for 6-TG and 6-MMP quantification in whole blood improves the convenience for both patients and health care personnel. Alternately, DBS compared to both blood anticoagulant matrices provide lower thiopurines levels. At this stage, the method for DBS quantification must be considered with caution and only as under investigation. Thiopurines DBS stability and potential adsorption on the solid support of DBS card will be further investigated.

P166

Equilibrium renin-angiotensin-aldosterone system profiles in newly diagnosed hypertensive patients after intermediate dose treatment with four different blood pressure lowering medications

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Background: Renin-angiotensin-aldosterone system (RAAS) molecules are important for blood pressure (BP) regulation. BP medications, such as Angiotensin converting enzyme inhibitors (ACEi) and Angiotensin receptor blockers (ARB) directly target the RAAS, while calcium channel blockers (CCB) or hydrochlorothiazide (HCT) have indirect effects. We investigated the effect of these four drugs on concentrations of aldosterone and 10 different RAAS peptides.

Methods: In this randomized open-label parallel group study, patients with treatment-naïve arterial hypertension were randomized to monotherapy with either perindopril (ACEi), olmesartan (ARB), amlopidine (CCB) or HCT. Equilibrium concentrations of aldosterone and 10 RAAS peptides were quantified in plasma using LC-MS/MS before the start of treatment (0wk) and both pre- and 4 hours post drug intake after 4wks of once daily treatment with an intermediate dose.

Results: 72 participants successfully finished the 4wk treatment period (ACEi n=18, ARB n=17, CCB n=20, HCT n=17). Compared to before treatment, ACEi significantly increased Ang1-10 and Ang2-10 concentrations, decreased the Ang1-8/1-10 ratio (marker of ACE activity) and increased combined Ang1-10 and Ang1-8 concentrations (marker for renin activity), whilst ARB treatment significantly increased Ang1-10 and Ang1-8 concentrations. Four weeks of CCB intake had no significant effect on pre-dose RAAS molecule concentrations, but caused a significant acute increase of the renin activity and Ang1-10, Ang1-8 and Ang1-5 concentrations 4h after intake. Four weeks of treatment with HCT increased renin activity, Ang1-10, Ang1-8, Ang3-8 and aldosterone concentrations. Concentrations of the remaining smaller RAAS peptides remained below the limit of quantification in more than 50% of the subjects. No statistically significant associations were found between changes in the 4wk RAAS molecule concentrations and BP response, however, some RAAS molecules showed changes associated with participants who had a ≥10 mmHg decrease in systolic BP.

Conclusion: ACEi and ARB both affected the upper part of the RAAS cascade and increased renin activity, Ang1-10, Ang1-8 and Ang 2-10 concentrations. CCB and HCT had indirect effects on RAAS peptide concentrations due to activated renin feedback. The Ang1-8/Ang1-10 ratio was a strong indicator for ACEi-intake and could serve as a marker for treatment adherence e.g. in patients with difficult to control hypertension.

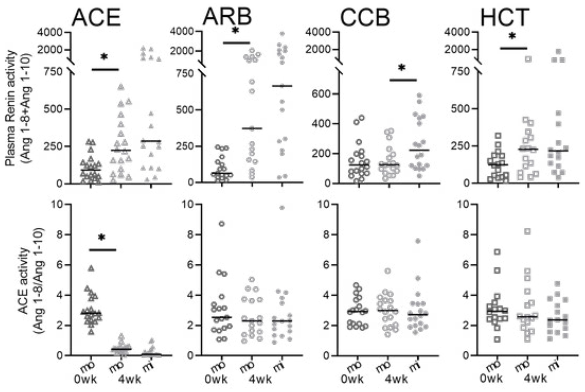

Figure 1. The renin activity (sum of Ang 1-10 and 1-8) and ACE activity (ratio of 1-8/1-10) in patients with newly diagnosed arterial hypertension before (0wk; morning) and after four weeks of daily treatment (4wk; pre-dose/morning and postdose (4hrs)) with either an ACE-inhibitor (ACE), an angiotensin receptor blocker (ARB), a calcium channel blocker (CCB), or a diuretic (hydrochlorothiazide, HCT).

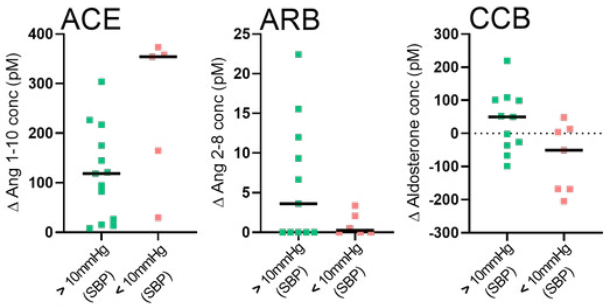

Figure 2. Differences in concentrations (Ang1-10, Ang 2-8 and Aldosterone, respectively) between 0wks (morning) and 4wks (morning) of daily treatment with ACEi, ARB and CCB (respectively) vs. the ABPM SBP response of above or below 10mmHg

P167

Machine learning for the prediction of drug induced liver Injury patterns

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Introduction: Drug induced liver injury (DILI) is one of the most common reasons (32%) for the withdrawal of drugs from the market [1]. Due to the overall infrequent occurrence of DILI (13.9 ± 2.4 per 100,000 patients) this severe adverse effect is often first noticed when the drug is already on the market [2]. With the predictions from machine learning (ML) models, hepatotoxicity and their injury patterns may be anticipated before pre-clinical studies and therefore be used to inform drug discovery and development. They can also help assess DILI potential of novel drugs in clinical settings.

Methods: We used several ML paradigms (Random Forest (RF), Support Vector Machine (SVM), k-nearest neighbor (kNN), and decision tree induction (DTI)) to differentiate between hepatotoxic and non-hepatotoxic substances obtained from LiverTox [3] based on physio-chemical properties (descriptors). Endpoints for the ML models were overall DILI potential and specific injury *patterns.*

Results: For overall DILI classification, RF performed best (balanced accuracy of 0.71 for all substances and 0.73 for the substances that have a known injury pattern). Injury patterns were predicted best by kNN and SVM models, though their predictive power was weak (0.32, and 0.26, respectively; **Table 1**). Surface descriptors were the most informative attributes (**Figure 1**), most commonly: atom type electro topological state, extended topochemical atom, ring count, and charged partial surface area, indicating membrane permeability and lipophilicity are the strongest determinants of DILI potential.

Machine learning for the prediction of DILI

	balanced accuracy					macro f1-score				
Dataset	kNN	RF	DT	log Reg	SVM	kNN	RF	DT	log Reg	SVM
TOX	0.65	0.71	0.64	0.61	0.62	0.65	0.71	0.63	0.61	0.62
TOX2	0.71	0.73	0.58	0.65	0.63	0.71	0.73	0.55	0.65	0.63
PAT_S	0.24	0.25	0.23	0.24	0.18	0.19	0.26	0.17	0.23	0.19
PAT_nS	0.22 (0.2171)	0.22 (0.2240)	0.15	0.21	0.22 (0.2243)	0.23	0.25	0.13	0.21	0.24
PAT2_S	0.32	0.25	0.22	0.24	0.17	0.27	0.26	0.18	0.23	0.16
PAT2_nS	0.23	0.22	0.17	0.24	0.26	0.24	0.23	0.16	0.24	0.27

Table 1: Overview of the different models (TOX: overall hepatotoxicity, PAT: injury patterns) and their metrics. Marked in green are the best values for the different models built from the corresponding dataset.

Conclusions: Overall DILI can be predicted with simple ML models solely from physiochemical properties derived from their structures. This allows risk assessment for novel drugs and in virtual screenings. Models of injury patterns performed considerably worse, most likely due to small training data sets. With the further addition of data, the models can improve their predictivity.

Machine learning for the prediction of DILI

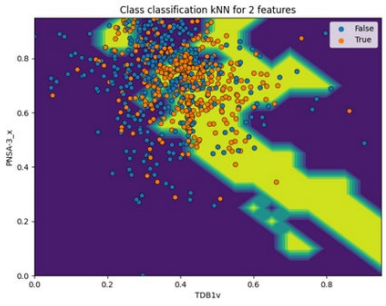

Figure 1: Visualisation of the two most expressive physio-chemical descriptors used in a kNN model of overall hepatoxic potential (k=11). Features are ranked by the relative explained variance each descriptor contributes to the final model [4].

Conflicts of interest: None to declare.

Keywords: Machine Learning, Drug induced liver injury, Hepatotoxicity, Quantitative structure-activity relationship

P168

Network analysis of drug-disease and target-disease interactions in COVID-19

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Introduction: The number of chronic conditions and prescribed drugs increase with age [1], with the most common indications being cardiovascular disorders (esp. arterial hypertension), and diabetes [2]. In the current pandemic of COVID-19, several comorbidities were identified as risk factors for severe courses/ death. Drugs used to treat pre-existing chronic conditions may not only interact with other drugs, but also influence the course of disease (drug-disease interactions, DDSI). This is also true on the molecular target level, at which drugs may interact (target-disease interactions, TDSIs). Therefore, the aim of this study was to analyze the DDSIs and TDSIs with regards to severity of COVID-19 using a network analysis approach.

Methods: We used network analysis to compare drugs and drug combinations COVID-19 patients (n=505) received before and on the day of admission to the Insel Hospital Group Switzerland (February to November 2020) with respect to disease severity. Drugs were mapped to their molecular target(s) and their location.

Results: The main nodes and edges were mainly identical between the severity cohorts, however, the network of the severe cohort had a higher heterogeneity. The diuretic and cardiovascular drugs had a higher percentage in severe COVID-19. Noteworthy is the greater share of patients with diabetes and cardiac comorbidities in the non-severe cohort, particularly when treated with dipeptidyl peptidase-4 inhibitors (DPP4i). In addition, antipsychotics in combination with other drugs were more common in the severely ill. At target level, we observed that the target location might have an influence on the disease progression in severe (A) vs. non-severe (B) COVID-19 (Fig. 1).

Conclusion: Even though we identified significant differences between groups, some drugs were mainly predictive for severity of the comorbidity. A possible protective effect of DPP4i is plausible on pathophysiological grounds [3, 4] but the study situation is ambiguous [5-10]. Possibly, the protective effect depends on comorbidity combinations. The importance of the target location could potentially be attributed to disruption of functional membrane micro-domains (lipid rafts), which in turn could decrease viral entry into the cell and thus disease severity. Therefore, TDSIs might also be induced by changes in cell membrane structure, and not only direct target interaction. However, this needs to be investigated in further studies.

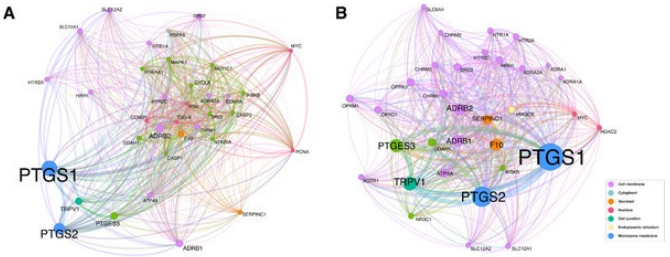

Fig. 1

P169

Population pharmacokinetic modelling to characterize the effect of chronic kidney disease on tenofovir exposure after tenofovir alafenamide administration

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Introduction: Tenofovir alafenamide (TAF) is gradually replacing tenofovir disoproxil fumarate, both prodrugs of tenofovir (TFV), in HIV prevention and treatment due to its better tolerability. There is thus a need of describing TFV pharmacokinetics (PK) and its variability in people living with HIV (PLWH) under TAF in a real-life setting. This project aims to characterize TFV exposure in PLWH receiving TAF, while specifically assessing the impact of chronic kidney disease (CKD).

Methods: We conducted a population PK analysis with NONMEM® on 877 TFV and 100 TAF concentrations measured in 569 PLWH. A stepwise procedure allowed identifying the models that best fit first TAF and TFV data simultaneously, and then exclusively TFV data. We integrated directly cobicistat coadministration (in patients receiving TAF 10 mg) as a covariate affecting TAF relative bioavailability. Other potential demographic and clinical covariates were tested for significance. Model-based simulations allowed comparing TFV trough concentrations (C_{min}) in patients having various levels of renal failure.

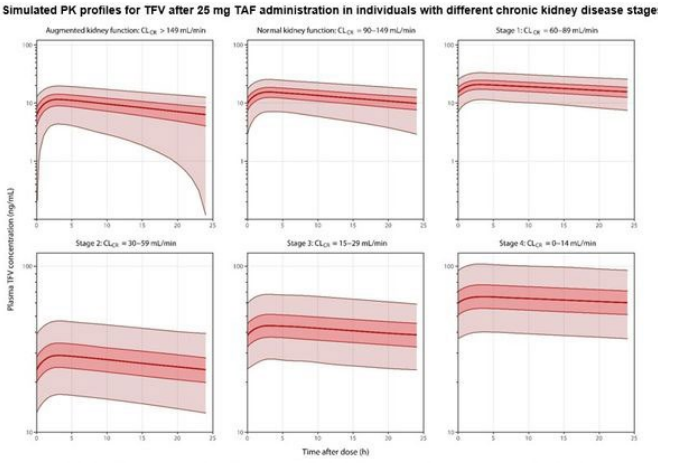

Figure 1: Red solid lines represent the 2.5%, 25%, 50% (median), 75% and 97.5% percentiles. The dark red surfaces are the corresponding 50% prediction intervals of the simulated data, and the light red surfaces are the 95% prediction intervals.

Results: A one-compartment model for TAF, with first order-absorption and elimination through complete conversion into TFV, and an additional compartment with linear elimation for TFV best described TAF and TFV data. This model, assuming a fixed absorption rate constant of 2 h^{-1} for TAF, was consistent with almost immediate conversion of TAF into TFV. An identical description of TFV PK was deduced from TFV data alone. TFV parameter estimates of the base PK model with variability (CV%) were an increase in TAF bioavailability by 106% (34%) under cobicistat, a volume of distribution of 2660 L, and a clearance of 39.9 L/h. Only creatinine clearance (CL_{CR}, calculated according to Cockcroft & Gault equation) appeared to have a clinically relevant impact on TFV clearance. Model-based simulations (Figure 1) revealed a 294% and 515% increase of median TFV C_{min} in patients with CL_{CR} of 15-29 mL/min, and 0-14 mL/min, respectively, compared to patients with normal renal function (CL_{CR}= 90-149 mL/min). Conversely, patients with augmented renal function (CL_{CR}> 149 mL/min) had a 36% decrease of median TFV C_{min}.

Conclusion: CL_{CR} significantly affects TFV exposure after TAF administration in PLWH. Dosage adaptation in PLWH with CKD seems thus warranted; model-derived recommendations regarding TAF dosing intervals need to be validated in a prospective study.

P170

Population pharmacokinetics of bictegravir: a pharmacometric-based analysis in a real-life setting

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Introduction: Bictegravir is a novel integrase strand-transfer inhibitor available as fixed-dose combination with tenofovir alafenamide and emtricitabine, currently recommended as initial first-line treatment in naïve-HIV-infected patients or as an antiretroviral replacement therapy in virologically suppressed patients. Bictegravir pharmacokinetics (PK) has not been described in real-life settings yet. The aim of this study was to characterize bictegravir PK in patients living with HIV, taking into account covariates that might affect its disposition, to guide clinicians in the interpretation of bictegravir plasma levels measured for therapeutic drug monitoring (TDM).

Methods: Patients included in the analyses were followed within the frame of the TDM program at the CHUV between June 2019 and October 2020, with plasma concentrations obtained during follow-up visits. A population PK model was developed with a nonlinear mixed-effect approach (Monolix®) by comparing several model structures, and sequentially testing interindividual variability (IIV) on the PK parameters as well as different error models for the residual unexplained variability (RUV). Age, gender, bodyweight, creatinine clearance, albumin, total bilirubin, pregnancy, and relevant co-medications were tested for significance as potential covariates influencing bictegravir PK, using a stepwise approach.

Results: A total of 319 steady-state plasma concentrations from 264 individuals were available for analysis. Two participants were pregnant, and 3% and 1% of the enrolled patients received one or more CYP3A4 inhibitor and inducer, respectively, at the time of TDM. A one-compartment model with first-order absorption and elimination best characterized drug disposition, with IIV assigned to drug clearance and RUV depicted by a proportional error model. None of the tested covariates appeared to significantly affect bictegravir PK. Final parameters estimates were a clearance of 0.47 L/h with an IIV of 29%, and a volume of distribution of 12 L. The absorption rate constant was fixed at 2 h^{-1} owing to the paucity of data collected right after drug intake.

Conclusion: Prediction ranges are useful to support the interpretation of bictegravir TDM. Considering the safety profile and rather large therapeutic margin of bictegravir, TDM appears essentially relevant in cases of suspicion of poor compliance, suspect strong drug-drug interaction or peculiar clinical condition such as pregnancy or liver failure.

P171

Pregnancy outcomes after maternal exposure to trazodone in pregnancy: preliminary results of a comparative ENTIS cohort study

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Introduction: The Swiss Teratogen Information Service (TIS) is dedicated to providing evidence-based information to health care professionals about medication safety during pregnancy. By collecting data on cases of exposure reported to our service, as well as the outcome of pregnancy or any effects on the child, we contribute to research in the field of teratology. By pooling and analysing data collected by TISes in different countries, we organise studies addressing risks associated with medication poorly characterised regarding reproductive safety. The aim of this study was to assess the risks linked to trazodone exposure during pregnancy for which limited safety data is available.

Methods: This multicentre, observational prospective cohort study compared pregnancy outcomes in women exposed to trazodone in early pregnancy compared to a reference group of women exposed to a SSRI (sertraline, citalopram or escitalopram). Data were collected between 1996 and 2021.

Results: The sample included 221 trazodone and 869 SSRI exposed pregnancies. Exposure to trazodone in the first trimester was not associated with a difference in the risk of major congenital anomalies (trazodone (1/169, 0.6 %), SSRI (18/730, 2.5 %), crude odds ratio 0.2; 95% [confidence interval (CI) 0.03 - 1.8]. The cumulative incidences of live birth were 61 % and 73 % in the trazodone and reference group respectively (HRadj 1.1 [95%CI 0.9-1.3]. Trazodone exposure was not associated with a significantly increased risk of termination of pregnancy (HRadj 1.6 [95%CI 0.9-2.7]) and spontaneous abortion (HRadj 1.4 [95%CI 0.9-2.2]). There was a trend toward a higher preterm birth rate (13.5% versus 8.3%, p = 0.05) and earlier gestational age at birth (median 39 weeks, interquartile range (IQR) 37-40 versus median 39, IQR 38-40, p = 0.03) in the trazodone group compared to the SSRI group. Birthweight (median 3125 g, IQR 2800-3500 versus 3162 g, IQR 2880-3500, p = 0.64) did not differ between the groups.

Conclusions: This study did not reveal a significant difference in the risk of major birth defects after first trimester exposure to trazodone, compared with SSRI exposure. Overall pregnancy outcome after trazodone exposure was similar to that of the reference group. Even though this study is the largest comparative evaluation of teratogenic effects of trazodone so far, its sample size is still limited and the results call for confirmation through further studies.

P172

Queries on medication use during pregnancy: an analysis of data from the Swiss Teratogen Information Service

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Introduction: Limited information on medication safety may result in concerns on how to treat pregnant and breastfeeding patients. The Swiss Teratogen Information Service (STIS) provides information to healthcare professionals about medications during pregnancy and breastfeeding. Our objective was to describe the queries addressed to the STIS over the past two decades.

Methods: The STIS maintains a database of queries likely to provide information on pregnancy outcomes after exposures to various substances. We have initially analysed general characteristics of all queries. Thereafter, we focused on exposures to medications during singleton pregnancies and associated health-related aspects.

Results: From 2000 to 2019, 7148 queries were entered into the database. An increasing number of queries was recorded over the study period, with an average of 357 queries entered into the database per year. Most of the callers were physicians; more specifically, gynaecologists/obstetricians (2389/7148; 33.4%) and psychiatrists (1007/7148; 14.1%). Two-thirds (4747/7148; 66.4%) of the queries addressed drug intake during pregnancy; the next most frequent queries concerned a planned medication in the context of pregnancy (928/7148; 13.0%) or drug use during breastfeeding (873/7148; 12.2%). In more than 50% (3795/7148) of cases, women were treated with more than one drug; a total of 16513 drugs (taken alone or in combination) were identified. The most frequent queries concerned drugs for the nervous system (ATC-group N, n=7042), followed by anti-infectives for systemic use (J, n=1586). Analysis of follow-up information on cases of medication exposure during singleton pregnancies (n=2672) revealed an offspring malformation rate of 4.2%. The organ system most often affected was the musculoskeletal system, followed by the circulatory system; congenital malformations of the nervous system as well as chromosomal abnormalities were seen as well. The three most frequently documented congenital diagnoses were malformations of cardiac septa, the brain and major arteries.

Conclusions: Pregnant women are often in need of (multiple) medications and prescribing physicians require professional counselling in this area. A variety of drugs is mentioned in queries addressed to the STIS, whereby psycholeptics and psychoanaleptics are the most frequent ones. Proper guidelines on their use during pregnancy appear particularly urgent.

P173

Safety, tolerability, pharmacokinetic profile and ex-vivo antitubercular activity of macozinone formulated as spray-dried dispersion (SDD) versus native crystal powder (NCP): single ascending doses, randomized, placebo-controlled, cross-over phase Ia trial in healthy volunteers

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Background: Macozinone (PBTZ169) is a novel benzothiazinone derivative that inhibits arabinose synthesis, thereby compromising the biosynthesis of mycobacterial cell walls. Macozinone administered as NCP was well tolerated in a first phase I trial. A new formulation based on SDD was expected to improve its solubility and oral absorption. The present study aimed at verifying the safety and tolerability of this SDD formulation, estimating its oral bioavailability relative to NCP, and determining its pharmacokinetic profile and *ex vivo* antitubercular activity.

Methods: Healthy males aged 18-48 y were assigned to 4 consecutive panels of 8 subjects, and randomized to receive ascending single doses of macozinone as 10, 20, 40, 80, 160 or 320 mg of the SDD formulation, as 160 or 320 mg of the NCP, or as a matching placebo in a double-blind, cross-over, two-period design.
Standard clinical and laboratory safety tests were assessed for pre- vs post-dose comparisons. Concentrations of macozinone and its metabolites were measured by LC-MS/MS in 14 serial samples over 48 h to determine non-compartmental PK parameters. Antitubercular activity against *M. smegmatis* was assessed in 5 samples over 24h using a resazurin microplate assay.

Results: All 32 enrolled participants completed the study. Adverse events were mild and comparable in all panels, with no difference between formulations and placebo. No dose-response relationship, no trend over time or no clinically relevant abnormalities were detected for vital signs, ECG tracings or standard biochemical and haematological analyses.
The pharmacokinetic profile of both formulations showed dose-linearity, with a fair degree of interindividual variability (CV of 55% in AUC). The median terminal half-life was 12.3-14.5 h following 160 and 320 mg doses for either formulation. Relative bioavailability of NCP compared to the SDD was on average 58%, with a mean Tmax of 0.75-1 h for SDD, and of 0.5 h for NCP. *Ex vivo* growth inhibition of *M. smegmatis* was confirmed for macozinone serum concentrations above 2-5 ng/mL.
Conclusion: Both formulations of macozinone were safe and well tolerated up to single doses of 320 mg. SDD improved exposure by slightly less than 2-fold compared to NCP. *Ex vivo* antimycobacterial activity of macozinone appeared at concentrations in line with the *in vitro* MIC_{99} (1 ng/mL) for *M. smegmatis*, supporting promising prospects for its contribution to the control of multi-resistant mycobacterial infection.

P174

Scombroid poisoning with sudden cardiac arrhythmia: an unusual case report

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Learning objectives: Scombroid fish poisoning is an acute syndrome resulting from consumption of fish containing high levels of histamine (1). Bacteria can produce substantial amounts of histamine in fish kept at temperatures above 4°C (2). The most common symptoms include facial flushing, abdominal pain, diarrhea, headache and palpitations usually starting within an hour after meal.

Case: A 49 years old woman presented to the Emergency Department with a 1-hour history of sudden onset of face redness heat and tachycardia. Co-morbidities included hypothyroidism. She denied any allergies for drugs or food. Thirty minutes after lunch the patient began to feel facial heat with accompanying redness and tachycardia. She did not experience any difficulties in swallowing, throat swelling, chest pain, dyspnea or abdominal discomfort. The patient ate boiled rice and tuna in oil. She presented with a pale red cutaneous discoloration of the face and neck, and some reddish maculae in her décolleté without itching sensations. Cardiac auscultation revealed rhythmic tachycardic tones, without murmurs. Laboratory tests showed mild lymphocytosis of 4.66G/l and blood sugar of 11.1mol/l. ECG reveiled rhythmic narrow complexes tachycardia at around 140bpm consistent with atrial tachycardia. Echocardiography showed structurally and functionally normal heart without signs of myocardial ischemia or infarction. Vagal manoeuvers and subsequent adenosine 6mg were ineffective. Another 12 mg adenosine resulted in a temporary sinus rhythm. Metoprolol 5 mg finally led in a successful conversion in a sinus rhythm and improved symptoms. In depth history revealed, that the tuna can was opened more than one week earlier. The tuna was stored in oil in the refrigerator (temperature 4-6°C). The taste of the fish was bitter and spicy. The diagnosis of scombroid syndrome with histaminosis and rare cardiac symptoms was finally made. Levocetirizin was

administered and further surveillance on the ward was performed. The subsequent clinical course was unremarkable and the patient was discharged after 2 days without sequelae.

Discussion: Toxin-containing fish usually have a peppery or sharp taste (1). The symptoms resolve within 12 to 48 hours if untreated and has no long-term sequelae (3). Only a few reports of cardiac symptoms associated with scombroid poisoning are available. Potential therapeutic options include the Valsalva maneuver, diphenhydramine (4) or beta-blockers as shown in this patient.

P175

Semi-mechanistic pharmacometric analysis to characterize copeptin and aldosterone kinetics and dynamics in response to rehydration treatment for diabetic ketoacidosis (DKA) in children with type 1 diabetes

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Introduction: Diabetic ketoacidosis (DKA) is a frequent complication of type 1 diabetes (T1D), and is characterized by hyperosmolar hypovolemia. The response of water-regulating hormones arginine vasopressin (AVP, antidiuretic hormone) and aldosterone to DKA treatment in children is not well understood. We aimed to characterize the dynamics of the response in copeptin (marker for AVP) and aldosterone secretion to rehydration treatment in paediatric patients with DKA.

Methods: Data originated from a prospective observational multi-centre study including 28 paediatric T1D patients treated for DKA (median 11.5 years of age, weight 35 kg). Serial measurements of the hormone levels were obtained during 72h following start of rehydration treatment. Semi-mechanistic pharmacometric modelling (non-linear mixed effect regression) was used to analyse the kinetic/dynamic relationship of copeptin secretion in response to correction of hyperosmolality, and of aldosterone secretion in response to correction of hypovolemia.

Results: Modeling revealed different sensitivities (dynamic relationships) for osmolality-driven copeptin secretion during the first 72 hours of rehydration, possibly explained by an osmotic shift introduced by hypovolemia. The response of aldosterone secretion to correction of hypovolemia seemed to be delayed. This was well described by an extra upstream turnover compartment, possibly representing chronic upregulation of aldosterone synthase (CYP11B2). Disease-dependent differences in copeptin dynamics, and weight-dependent differences in aldosterone dynamics were additionally observed.

Conclusion: Semi-mechanistic modeling provided novel physiological insights in hormonal water regulation in pediatric patients during DKA treatment. Such pharmacometric approaches have the potential to facilitate development of personalised monitoring and treatment strategies to reduce the risk of further complications.

Société conviée SSPTC: Posters / Gastgesellschaft SGKPT: Poster

P176

N-of-1 tests in routine practice: pharmacological considerations

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Introduction: An "N-of-1 test" is a randomized double-blind multi-period crossover trial conducted on a single patient to assess the efficacy and safety of a specific treatment in chronic or recurrent diseases. Such tests aim to optimize personalized efficacy, safety and resource allocation.
Despite their potential for improving patient management, N-of-1 testing is still barely adopted among the medical community. Most physicians are not familiar with their implementation. Their use requires some organization and a careful evaluation of pharmacological aspects to assess feasibility and choose an appropriate design.

Methods: A systematic literature search was performed, targeting a predefined set of therapeutic agents relevant in general practice. Information on N-of-1 test indications, dosages and design was collected. These data, complemented by pharmacological properties collected from reference sources, were used to establish a list of criteria conditioning the feasibility and to propose an N-of-1 test design for each drug.

Results: Pharmacological criteria conditioning the feasibility of N-of-1 tests have been identified. The treatment must have a rapid onset of action, a reversible effect and a short elimination time, to prevent abandonment due to prolonged tests. The time needed to reach efficacy depends on both the molecule and the disease to be treated. The molecule's formulation must allow for the preparation of a comparator similar in every respect. Double-blind titration is possible, provided that it can be done quickly enough to keep test duration reasonable. Drugs that induce physical dependence with definite withdrawal symptoms are poor candidates for N-of-1 testing (e.g. strong opioids).
Every molecule selected was classified according to suitability for N-of-1 testing. Design recommendations for candidate molecules are deduced from pharmacological principles and literature reports.
Conclusion: N-of-1 tests represent a reference method for "diagnosing the therapeutic response and tolerance" at the individual level, in line with the modern concept of individualized and participatory precision medicine. Tools and services to facilitate N-of-1 testing are needed to promote it in routine practice. This literature review will guide primary care clinicians in requesting N-of-1 tests or including them in their routine practice, suggesting an appropriate design for the main molecules suitable for these tests in well-selected conditions.

P177

Persistent hiccup under opioid treatment: a case report

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Learning objectives: To be aware of the existence of hiccup as a rare but potentially invalidating side effect of opioid treatment, and thus lead to a better recognition of the condition in everyday clinical practice. To know the pharmacological options for the management of persisting hiccup, as recommended by the latest systematic reviews on the subject.

Case: We report on the case of a 64-year-old man diagnosed with advanced renal cancer and painful osteolytic metastases, presenting a history of persistent and invalidating hiccup under opioid treatment. Hiccup was slowly resolving after opioid discontinuation and almost systematically recurring after multiple re-challenges by opioid rotation, showing a strong chronological opiate-hiccup correlation. Different pharmacological treatments have been tried to relieve the patient, and the one showing best results was oral baclofen.

Discussion: Hiccup is a rare and probably underdiagnosed side effect of opioid treatment. We performed a non-systematic review of scientific literature that showed only a handful of reported cases of opioid-related hiccup. Despite the large number of available treatments, the physiopathological mechanisms behind the hiccup reflex are still poorly understood and a lack of scientific evidence exists concerning the optimal management of the condition. In recent systematic reviews, Baclofen comes forth as first line empirical therapy for persistent and intractable hiccups, with gabapentin as an alternative. Knowing the existence of opioid-related hiccup will facilitate its identification in everyday clinical practice, which might be especially relevant in particular clinical contexts such as the palliative care and chronic pain field.

Société conviée SPSG: Posters / Gastgesellschaft SFGG: Poster

P178

Do physicians discuss cardio-pulmonary resuscitation prognosis with hospitalized older patients? An analysis of admission interviews

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Introduction: International standards stipulate that a patient's wishes regarding Cardio-Pulmonary Resuscitation (CPR) have to be elicited when hospitalized. To date, there is little research based on natural data regarding how physicians explain CPR. Our aims are to investigate whether and how physicians and patients discuss CPR prognosis at hospital admission.

Methods: We audio-recorded hospital admission interviews of 51 patients performed by 17 physicians. We used quantitative content analysis to determine whether CPR prognosis was discussed, and who initiated this discussion. We used thematic analysis to investigate how CPR prognosis was discussed.

Results: CPR in general and CPR prognosis specifically were discussed in 43 (84%) and 22 (43%) of the 51 interviews, respectively. Discussion of CPR prognosis was brought up by physicians in 9 cases and by patients in 13 cases. The main themes associated to discussion of CPR prognosis were chances of survival and risk of impairment. Physicians usually highlighted the unpredictability of CPR outcomes ("We don't know what we'll be able to achieve"), were elusive as to providing factual details ("It's a procedure that involves risks") and scarcely referred to the patient's individual prognosis. While patients don't refer to chances of survival, they summon the element of hope in regard to remaining alive ("when there's life there's hope") which, implicitly, displays their understanding of CPR prognosis. Risk of impairment ("becoming a vegetable") is often cited by patients who prefer to eschew CPR.

Conclusions: Although a general discussion about CPR occurred in most interviews, its prognosis was specifically discussed in less than half of them. Yet, explaining CPR is essential for equipping patients to make autonomous decisions about their future care. Our findings highlight the need to improve physicians training to better support patients in making informed decisions.

P179

Mortality in COVID-19 older patients hospitalized in a geriatric ward: Is obesity protective?

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Objective: To investigate the relationship between obesity and 30-day mortality in a cohort of older COVID-19 inpatients.

Methods: Patients included were aged 70 years or more; hospitalized in acute geriatric wards between March and December 2020; with a positive PCR for COVID-19; not candidate to intensive care unit admission. Clinical data were collected from patients electronic medical records. Data on 30-day mortality were retrieved from the hospital administrative database.

Results: Patients included (N=294) were on average 83.4±6.7 years old, 50.7% were women, and 21.7% were obese (BMI>30kg/m2). At 30-day, 85 (28.9%) patients were deceased. Compared to survivors in bivariable analysis, deceased patients were older (84.6±7.6 vs 83.0±6.3 years, P=.059), more frequently with very complex health status (63.5% vs 39.7%, P<.001), but less frequently obese (13.4% vs 24.9%, P=.033) at admission. Over their stay, deceased patients more frequently (all P<.001) developed radiologic signs of COVID-19 (84.7% vs 58.9%), anorexia (84.7% vs 59.8%), hypernatremia (40.0% vs 10.5%), delirium (74.1% vs 30.1%), and need for oxygen (87.1% vs 46.4%) than survivors.
In multivariable analysis that controlled for all markers of poor prognosis identified in bivariable analysis, obese patients remain with 64% (adjOR 0.36, 95%CI 0.14-0.95, P=.038) lower odds to be deceased at 30-day than non-obese patients.
Conclusions: In this population of older COVID-19 inpatients, an inverse association between obesity and 30-day mortality was observed even after adjusting for all already-known markers of poor prognosis. This result challenges previous observations in younger cohorts and would need to be replicated.

Liste des auteurs / Autorenverzeichnis

A
Abbiati, M. P104
Abdolhassani, N. P105
Abdul, F. P46
Abela, I.A. P68
Abolhassani, N. P1
Acerbis, E. P174
Achab, S. P160, P161
Achard, M. P163
Adam, L. P5
Adams, A. P30
Addor, M.-C. P171
Aeberli, D. FM4
Aeberli, J. P42
Aeschbacher, S. P1
Aeschbacher-Germann, M. P2, **P63**
Agoritsas, T. P34, P43, P102
Aigner, F. P118
Aliyeva, F. P4
Allevato-Déléaval, M. P150
Alves Saldanha, S. P169
André, P. P164, P165, P169, P170, P173
Anker, D. FM6
Antonakos, N. P89
Araschmid, L. P33
Arm Vernez, I. P46
Arnold, C. P122
Arsever, S. **FM1,** P134
Arza, A. P145
Arzel, B. P31
Ashikali, E.-M. FM15
Aubert, C.E. FM5, P22, **P55,** P74, P94, P96
Auderset, D. P101
Audétat, M.-C. P155
Auer, R. P11, P18, P23, P24, P57, P100, P103
Aujesky, D. FM4, FM7, FM9, FM10, P1, P7, P14, P49, P55, P63, P65, P78, P80, P82, P87
Auricchio, A. P22, P96

B
Baggio, S. FM6, P46
Bajwa, N. P155, P160, P161
Baldinger, R. P112
Balinari, S. P23
Ballmer, P.E. P112, P115
Bandiera, C. **P157**
Banz, Y. P125
Barbagallo, M. P22
Bardinet, C. P173
Baroffio, A. P104
Barrelet, I. P150
Bart, P.-A. P89
Bassetti, C. P18
Bassetti, S. P10, P15, P75
Bathelt, C. P27
Baty, F. P60, P86
Baud, D. P171
Bauer, D.C. FM4, P5, P63
Baumann, L. P67
Baumgartner, A. **P80**
Baumgartner, C. FM7, FM8, FM9, P36, P39, P49, P96
Baumgartner, P. P85
Baumgartner, R. P172
Baumgartner, C. P14
Baur, F. P27
Bausch, S. **P33**
Beck, K. P15, **P54,** P75
Becker, C. P15, P54, **P75**
Beeler, P.E. P108
Beer, J.H. P1, P22, P96
Beglinger, S. **FM8,** P74
Belkin, M. P4
Bellaoud, Y. P38
Beneyto Afonso, C. **P78, P87**
Beringer, G. **P146**
Berlin, I. P57
Berlin, M. P171
Bernard, S. P3
Bernasconi, E. P44, P58
Bernasconi, L. P88
Bernasconi, M. P70
Berner, A. P20, P42, P43, P150
Bertschinger, M. P137
Bétrisey, S. P1, P2, **FM10**
Beyeler, M. P23
Beyer, S. P124
Bideau, M. P152
Biechele, J. **P142**
Biller-Andorno, N. P103
Bilz, S. P80
Bingisser, R. P4
Bisatz, F. P61
Bizzozzero, T. FM16
Blanc, A.-L. P45
Blatter, R. P15, P75
Blattes, E. P173
Blondet, F. **P58**
Blondon, K. P97
Blum, M.R. FM5, P2, P9, P63, P71, P105,
Boccardi, V. FM12
Bodenmann, P. P26
Bodmer, M. FM9
Boeckel, G. P40
Boesiger, F. P79
Böhm, S. P115
Boillat-Blanco, N. P48
Boland, B. FM5
Bolick, L. P92
Boll, D. P136
Bolliger, D. P51
Bologna, K. P27
Bolt, L. **P49**
Bonati, L.H. P1, P22, P96
Bonvin, R. FM11
Borel, B. P101
Bosia, T. P123
Bosisio, F. FM16
Boss, O. P10
Bosshard, W. FM12
Boudabbous, S. P97
Bouillon, P. P69, P162
Boulet, M.-C. P154
Bourquin, C. P93
Braillard, O. P64, P102, **P159**, P160, P161
Brand, S. P52
Brändle, M. P80, P120, P135
Breakey, N. P122
Breidthardt, T. P4, P51
Bretagne, L. FM8, **FM9**
Bretscher, C. P13, **P79**
Broers, B. FM1, P3, P24
Brüll, S. **P138**
Bruni, F. P70
Brunner, L. **P74**, **P94**
Brunner-Ferber, F. P173
Brunschwig, I. **P42**
Brutsche, M. P57, **P60**, **P86**
Brutus, L. P176
Büchi, A. FM4
Buclin, C. P34
Buclin, T. P164, P165, P169, P170, P171, P173, P176
Bührer, J. **P5**, **P105**
Büla, C. FM12, FM16, FM17, P178, P179
Bulliard, J.-L. P103
Burckhardt, M.-A. P175
Burget, L. P126
Bürgi, J. P68
Bürgin, M. **P13**
Bürgisser, N. P150
Burgstaller, J.M. P77
Burkard, T. P27, P166
Burns, F. P80
Burton, R. P144
Busnel, C. FM15

C
Cagienard, F. P138
Caillon, A. P46
Calandra, T. P85, P89
Calmy, A. P58
Cambet, Y. P46
Cantero, O. P26
Canzoniere, T. P92
Carballo, D. P163
Carron, P.-N. FM17, P73
Castillo, C. **P178**
Castioni, J. P19, P73
Cavassini, M. P58, P170
Cedraschi, C. P72
Ceppi, F. P165
Cerutti, B. FM1
Chappuis, F. P66, P64
Chapuis-Taillard, C. P145
Charmillot, T. **P19**
Chastonay, O. **P26**
Chatzidaki, E. **P124**
Chenaud, C. P66
Chèvre, N. P19
Chiche, J.-D. P89
Chiolero, A. P7, P65, P78
Chocano, P. FM4
Chocano-Bedoya, P. FM6
Choffat, D. **FM7**, P14
Choong, E. P95, **P165**
Christ, E. P117
Christ-Crain, M. P27
Chtioui, H. P165, P173
Ciullini, L. P173
Claessens, Y.-E. FM3
Clair, C. P96
Coen, M. P20, P42, P43, **P102**, P150
Cogliatti, S. P52
Cohidon, C. P12, P99
Cole, S. P173
Collet, T.-H. FM4
Comazzi, R.D. P23, **P24**
Combescure, C. P44
Conen, D. P1, P22, P96
Conte, G. P1
Corley, D.A. P29
Corna, L. FM6
Coslovsky, M. P1
Coto-Llerena, M. P136
Coucke, C. P48
Courlet, P. P169
Courvoisier, D. P34, P64, P66
Coutaz, M. FM11, FM14, P179
Coynel, D. P27
Cullati, S. FM6, P50
Cusini, A. P138, P140

D
Da Costa, B.R. P5
D'Amelio, P. **FM12**
Danier, J. P25
Dao, K. P170, **P171**
Darbellay Farhoumand, P. FM9, P14, **P34**, P49
Da Silva Pereira Clara, J.A. P165
David, B. **P69**
Debray, M.-P. FM3
Decosterd, L.A. P169, P170, P173, P165
Décosterd, L.A. P95
De Geest, S. P98
Delabays, B. **FM2**, P17
De La Harpe, R. **P6**
De La Harpe, R. FM2, P21
Delaloye, R. P136
Del Giovane, C. FM8, FM10, P1, P2, P5, P63, P105
Della Vedova, L. **P110**
De Lucia, S. **P134**
De Marchis, G.M. P1
De Perna, M.L. P174
De Ridder, D. **P31**
Descombes, E. P143
Desfontaine, V. P165, P169
Desgranges, F. P48
Dhaini, S. P98
Dias Poço, R. P72
Diav-Citrin, O. P171
Díaz Hernàndez, L. **P98,** P107
Dicko, A. P144
Diebold, J. P121
Diebold, M. P51
Diethelm, M. P114
Diezi, L. **P176**
Di Gangi, S. P61, P107
Di Silvestro, K. FM14
Diteepeng, T. P22
Djarmouni, R. P159
Dominicé Dao, M. FM1, P160, P161
Donzé, J. P55, P80, P83
Dotta Celio, J. P157
Doubeni, C.A. P29
Dräger, S. **P8**, **P70**
Duarte, D. P157
Ducros, C. P103
Dufey-Teso, A. P20
Dunner, S. P45
Durieux-Paillard, S. **P148**
Durmisi, M. **P91**
Dürst, A.-V. FM12
Duss, S. P18
Duthaler, U. P166
Duval, X. FM3

E
Eggimann, M. **P115**
Ehrenmann, P. **P120**
Ekobena, P. P170, P171
El Bentiri, H. P148
Elbl, C. P61
Eleftheriou, G. P171
El Hakmaoui, F. P99
El Mounaouar, L. P42
Elvert, R.A. **P140**
Erba, A. **P117**
Ercan, C. P136
Erhart, B.-M. P113
Erkman, S. P19
Ernst, D. FM9
Escher, M. **P50**, P177
Escher, R. P53, P111, P122, P125
Essig, M. FM9
Etienne, S. P10, **P32**
Exadaktylos, A.K. P35

F
Falk, A. P121
Fankhauser, H. P145
Fankhauser, M. P23
Fassier, T. FM13, P129, P155
Favrod, C. P73
Favrod-Coune, T. **P139**
Fehlmann, C. P97
Fehr, T. P61, P140
Fellay, J. P6
Feller, M. P1, FM4, P5

Fernandes, S. **FM17**
Fernandez, J.D. P58
Ferrazzini, E.L. P78
Fischer, U. P1, P78
Fischer, R. P107
Flahaut, A. FM6
Fleisch, I. P145
Florin, J. **P65**
Foerster Pidoux, M. P73
Follonier, C. P163
Fournier, S. P6, FM2
Frangos, E. P47
Frank, M. P128
Frei, A. P57
Frick, S. FM9, P153
Fricker-Feer, C. P149
Frigerio, S. P146

G
Gachoud, D. P153
Gallon, J. P136
Gallot Lavallée, F. FM8
Gamio-Veis, R. P137
Garin, N. FM3, FM13, P34, P44, P45
Garnier, A. P73
Gassmann, D. **P158**
Gastaldi, G. P95
Gastens, V. FM5
Gavin, A. P93
Gavinio, R. **P97**
Geigges, M. FM6
Geissbühler, E.R. **P113**
Gemperli, A. P108
Gencer, B. P1, P2, P5, FM10, P63, P105
Genné, D. FM9, P26
George, N. P171
Gerber, T. **P106**
Gerlach, J. P69, P162
Germann, C. P35
Gerrits, E. P109, P141
Gessler, M. P174
Giamarellos-Bourboulis, E.J. P85
Giehl, C. P8
Gilbert, C. **P85**, **P89**
Gillon, J.-Y. P173
Girard, G. P25
Girardin, F.R. **P163**
Glarner, N. P51
Glutz, M. P1
Gold, G. FM14
Gollut-Tanner, S. P20
Gonzalez Rodriguez, E. FM4
Gotta, V. **P175**
Graber, F. **P53**
Graf, C.E. FM12, FM14, FM15, P47, P76
Graf, V. P148
Graup, V. **P119**
Gregoriano, C. P59, **P81**, P88
Gresens, A. P124
Grgičevič, K. **P108**
Griot, S. P80
Grosgurin, O. P42, P156
Gross, S. **P15**, P54, P75
Gruber-Mösenbacher, U. P135
Grünig, V. P57
Gruntz, K. P130
Gualandro, D.M. P4, P51
Guessous, I. P31, P64, P66, P95, P97, P102
Guettinger, E. P24
Guidi, M. P95, P169, **P170**, P173
Günter, A. **P167**
Gürke, L. P51
Gurzeler, G. P13
Gussekloo, J. FM4
Guttinger, E. P100
Güttler, A. P116
Gygli, R. P35

H
Habfast-Robertson, I. **P100**
Hagmann, M. P60
Hakiza, L. FM13
Haller, D.M. P3, P104, P152
Haller, M. FM10
Hammann, F. P164, P167, P168
Handgraaf, S. P163
Hangartner, N. **P61**
Hanna Deschamps, E. **P72**
Harari, A. P85
Haschke, M. P166
Hasse, B. P58
Haueter, R. P113
Häuptle, C. P106
Hauser, P. **P137**
Hauser, R. **P21**
Hauser, S. **P59**, P81
Hautz, W. P44
Haynes, A.G. P7, P65, P78
Heck, S. P53
Heim, M. P136
Heinzer, R. P18
Heinzmann, J. **P39**
Hemett, O.M. P143
Hemkens, L.G. P27
Hempel-Bruder, C. P100
Hennings, E. P1
Henrard, S. FM5
Hentsch, L. P177
Henzen, C. P56, P80
Herrera, B. P159
Herrmann, F.R. FM14, P46, P47, P76, P163
Herzig, J.J. **P116**
Hirsch, H.H. P70
Hoess, C. P80
Hoffman, M. P58
Hoffmann, M. **P67**, **P68**, **P92**, **P131**, P146, **P149**
Hoffstetter-Suillot, L. P143
Hofmeister, J. **FM3**
Holzer, D.T. **P11**
Hösli, P. **P135**
Houegnifiouh, K. P133
Huber, L.C. FM9
Hudelson- Perneger, P. P160
Hudelson- Perneger, P. P161
Hug°, B. P108
Huibers, C. FM5
Hullin, R. P21
Humair, J.-P. P57
Hunziker, S. P15, P54, P75
Huser-Pitteloud, J. P173

I
Imoberdorf, R. P124, P137, P158
Inauen, J. P55
Ionescu, A. P90
Ionita, I. FM15
Ivanyuk, A. P173

J
Jäger, L. **P28**, **P77**
Jakob, J. P24, P57, P100, P103
Janakiram, A.A. P162
Janett-Pellegri, C. FM4
Janggen, M.-A. P103
Jaques, A. **FM11**
Jaunin-Stalder, N. **P154**
Jean, M. FM14
Jeanloz, N. P27
Jejati, H. FM6
Jeker, R. P135
Jeleff, A. P20
Jenkinson, S.P. P18, P23, P24
Jensen, C.D. P29
Jermini-Gianinazzi, I. **P9**, P71
Jirasko, V. P70
John, G. P83
Jones, L. FM16, P132
Joost, S. P31
Joss, I. FM12
Joss, S. P103, P146
Jox, R.J. FM16
Jungo, K.T. FM8
Junod-Perron, N. P20, **P155,** P160, P161

K
Kägi-Braun, N. P13, P79, P80, P84, P91
Kägi, S. P140
Kahlert, C.R. FM6
Kaiser, E. P18
Kaiser, L. P64, P66
Kaiser, N. P63
Kampouri, E. P16
Karakike, E. P85
Karege, G. P150
Kassi, E. P10
Kastner, L. P121
Kaufmann, M. FM6
Kayser, B. P90
Kearney, P.M. FM4
Kern, C. **P164**
Kestenholz, P. P121
Khalife, M. P144
Khanna, N. P123
Kneubühl, A. P147
Knoblauch, C. FM9
Knol, W. FM5, FM8
Kobza, R. P96
Koch, D. P81, P88
Kocher, B. **P14**
Kohler, P. FM6
Kölbener, F. **P122**
Kollmar, O. P136
Kopp, B. P14
Koster, M. P52
Kraege, V. P58, P73, **P93**
Krähenbühl, M. P10
Krähenbühl, S. P164, P166
Krauer, J. P156
Krause, K.-H. P46
Krayenbuhl, M. P145
Krief, H. FM17, P179
Krull, I. P120
Kühne, J. P27
Kühne, M. P1, P22, P96
Kunerl, A. P113
Küng, F. **P166**
Kunz, L. P73
Künzli, N. P142
Kusejko, K. P169
Kutz, A. P59, P81, P88

L
Lacroix, O. FM14
Lafaix, R. P159
Lagrandeur, J. **P179**
Lam, L. P157
Lamy, T. P110
Laurent, C. P104
Lava, S. P48
Le Bloc'h, F. **P45**
Leidi, A. **P156**
Lengsfeld, S. **P27**
Lenherr, C. P68, P131
Lenoir, O. **P118**
Le Roy, D. P89
Leszek, A. P156
Leuppi, J. P75, P15
Leuzinger, K. P70
Levati, S. FM6
Levin, T.R. P29
Lidsky, D. P139
Liechti, F. P39, P55
Lindner, G. P35, P41
Lister, K. P148
Loosli, N. P131
Lopez-Ayala, P. P4
Lorentzen, E. P40
Loretz, N. P54
Lorthe, E. FM6
Lotkowska, O. **P147**
Löwinger, D. P18, **P23,** P24
Luchinger, R. P160, P161
Luciani, M. P22
Ludwig, C. FM15
Luechinger, R. P155
Lurati Buse, G. P51
Lüthi, B.S. **P107, P141**
Luthy, C. P72
Lutz, L. P27
Lyko, C. P105

M
Mach, F. P17, P163
Maeder, M. P60, P101, P120
Maire, M. P18
Maisonneuve, H. P3, P104
Maldonado, R. P125
Malézieux-Picard, A. FM13, **P46**
Mancinetti, M. FM9
Mangana, F. P144
Mani, H. P55
Marfurt, S. P127, P151
Margini, C. **P125**
Marien, S. FM8
Marinoni, C. **P73**
Markun, S. P77
Marques-Vidal, P. FM2, P6, P17, P21, P58, P90, P48
Marti, C. P42, P156
Martin, A. **P16**
Martin, Y. P103
Martinvalet, M. P38, **P129**
Masserey, E. P101
Mastromauro, L. FM15
Matter, M. P136
Matthey, A. P95
Matthys, V. P45
Mattmann, M. P55
Maza, M. **P126**
Mazouri-Karker, S. P159, **P160**, **P161**
Mc Carthy, V.J. FM4
Méan, M. FM7, FM9, P21, P49, P58, P82, P87, P90, P93
Méan, M. P14
Mecocci, P. FM12
Meienberg, A. P10, P27
Meier, C.F. P112
Meier, M.-A. **P136**
Mendes, A. FM14
Mentil, N. P80
Mercier, T. P95, P165
Merlo, C. P108
Messer, J. **P12**
Messi, M. P87
Metry, B. P11
Meyer-Massetti, C. P18
Meynard, A. P152
Meynard, T. P148
Meyre, P.B. P67
Michel, G. FM6
Michel, P. P6
Michou, E. P4
Min, J.-Y. P25
Mirlesse, N. **P47**
Molo, L.Y. P25
Monney, L. FM12
Montet, X. FM3
Monti, M. P48, **P153**
Mooijaart, D. FM4
Moor, B. FM11

Moor, J. **P36**, **P96**
Moradpour, D. P165
Möri, C. P55
Moro, D. FM14
Moschovitis, G. P1, P22, P96
Moser, M. P86
Mosimann, S. FM9
Moutzouri, E. **P1**, P2, FM4, P5, FM10, P63
Mueller, C. P4, P51
Mueller, Y. **P101**
Müggler, S.A. **P127**, **P151**
Mujagic, E. P51
Mulder, F. **P18**, P23
Muller, Y.D. P73
Müller, B. P59, P80, P81, P88
Müller, D. P22, **P62**
Müller, J. P54
Müller, N.A. **P84**
Müller, O. P10, FM2, P6
Muradbegovic, J. P102
Mutal, J. P69
Mwakingwe-Omari, A. P25

N
Nanchen, D. FM2
Nascè, A. **FM13**
Nater, C. P36
Nehme, M. **P64**, **P66**, P102
Nehring, J. P10
Nendaz, M. P20, P50, P155
Netzer, S. **FM4**, P96
Neyer, P. P88
Nguyen, N. P165
Nickel, B. P131
Nickel, C.H. P4
Noirez, L. P48
Norambuena, J. P93
Nowacki, T.M. P40
Nuciforo, S. P136

O
Oberle, J. **FM5**
Olpe, T. P80
O'Mahony, D. FM5, FM8
Osswald, S. P1, P22, P96
Osthoff, M. P8, P33, P70, P130
Osthoff, M.F. P32
Otto, M. P175

P
Paladini, R. P1
Panchaud, A. P23, P171, P172
Panczak, R. P7, P65, P78
Pantaleo, G. P89
Papachristou, A. P4, **P51**
Papadimitriou Olivgeris, M. P48
Parent, T. P110
Parisi, L. **P111**
Pasierski, J. **P114**
Passweg, J. P117
Pavlicek, V. P80
Pawlowska, V. **P48**
Payrard, L. **P83**
Pechère-Bertschi, A. P163
Pedrazzini, B. P154
Pennacchio, F. FM6
Périard, D. P143
Périvier, S. **FM15,** P110
Perneger, T. P50
Perreau, M. P89
Perrig, M. FM9
Peter, U. P109
Pfarrwaller, E. **P104**, **P152**
Pfaundler, N. P65
Pfeifer, P. P23, P24
Pfister, M. P175
Pfister, O. P4
Piscuoglio, S. P136
Piso, R.J. P67, P92, P131
Pistelli, A. P171
Pittet, V. P153
Plate, A. P28
Platon, A. FM3, P44
Podmore, C. **P29**
Poglitsch, M. P166
Poletti, P.-A. FM3
Poortvliet, R.K.E. FM4
Popescu, C. P10
Potin, M. **P145**
Potlukova, E. P10
Prendki, V. FM3, FM13, **P44**, P46
Preynat-Seauve, O. P46
Pruijm, M. P157
Puelacher, C. P4, P51
Puhan, M.A. FM6
Putallaz, P. P179

Q
Quarella, M. P135
Quinn, T.J. FM4

R
Räber, L. P7
Rakovic, D. P14
Rassouli, F. P60
Ravioli, S. **P35**, **P41**
Rayneau, N. P72
Redin, C. P6
Reichenstein, D. P10
Reichlin, T. P1, P96
Rennebaum, F. P37, P40
Reny, J.-L. P14, P34, P43, P49, P102
Ribaux, P. P46
Richardson, J.L. P171
Rieder, A. P152
Righini, M. P82, P87
Riley, M. P25
Rimensberger, C. P9, P71
Rochat, M. **P17**
Rodak Matteuci, R. P113
Rodic, B. P137
Rodondi, N. P1, P2, FM4, FM5, P5, FM6, P7, FM8, FM10, P14, P22, P57, P63, P65, P74, P78, P80, P82, P87, P94, P96, P105
Roger, T. P85, P89
Rohacek, M. P10
Rohn, V. P41
Rohrbasser, A. P11, P103
Roland, S. P121
Rollason, V. P171
Romanens, M. **P30**
Ronga, A. FM16
Roos, J. P56
Rosemann, T. P28, P77
Rosenow, L.R. P112
Rossel, J.-B. FM7
Rossier, C. P45
Roten, C. FM9
Roth-Kleiner, M. P73
Rothuizen, L.E. **P173**
Rottenburger, C. P117
Rousson, V. P171
Roux, X. FM13, P38
Rubli Truchard, E. **FM16**, P178
Rüesch, L. P114
Ruf, M.-T. P131
Ruggiero, C. FM12
Ruthishauser, J. P80

S
Saager, L.V. **P112**
Sader, J. P155
Sailer, C. P27
Salamun, J. **P95**, P97, P134
Sartori, C. P48, P16
Sasaki-Pereira, A. **P20**
Sauter, T. P44
Savigny, E. P150
Schaefer, I. P4, P51
Schäfert, R. P15, P54, P75
Schaffner, T.O. **P25**
Scharf, T. P11, P18, **P103**
Schechtman, S. P171
Scheffler, M. FM3, P129
Schenker, C. **P7**, **P82**
Scherer, F. P50
Schiemann, U. P133
Schindera, S. P80
Schirmann, F. P132
Schmid, M. **P121**
Schneider, M.P. P159, P157
Schnider, A. P76
Schnoz, C. P124
Schoch, O. P86
Schoenenberger, A. FM9
Schoeni, A. P23, P24, P57
Scholtze, D. P119
Scholz, S.M. P62
Schöni, A. P100
Schöning, V. P167, **P168**
Schottinger, J.E. P29
Schrijver, I.T. P85, P89
Schünemann, M. P10, P123
Schütz, P. P13, P15, P59, P75, P79, P80, P81, P84, P88, P91
Schütz Leuthold, M. **P99**
Schwarz, J. P99, P101
Schwenkglenks, M. P1
Seelmann, S. **P10**
Seematter, L. FM17
Seiffge, D. P1
Sekarski, N. P48
Selby, K. P29, P100, P103
Senchyna, A. **P3**
Senn, L. P16
Senn, N. P99
Senn, O. P28, P61, P77
Serratrice, C. **FM14**, P110
Serratrice, J. P34, P102
Seydoux, C. **P143**
Shrestha, S. **P4**
Sidler, M. P127, P151
Siegrist, S. P80
Silva, M. **P76**
Simmen, C. P4
Simões-Wüst, A.P. P172
Sinnecker, T. P1, P22
Siqeca, F. P98
Sommer, J. P104, P152
Soni, J. P25
Sood, R. **P144**
Soret, G. P156
Souchet, C. **P133**
Soysal, S. P136
Spaggiari, D. P173
Spechbach, H. P69, P95, P97, **P162**
Speich, B. P27
Speierer, A. P63, **P2**, **FM6**, FM10
Sperb, R. P126
Spinas, G. P135
Spinewine, A. FM8, P74
Springer, A. P22
Stalder, O. P82, P87
Stanga, Z. P80
Stanojkovic Nardiello, S. P4
Staub, N. P80
Steiger, J. P51
Steiner, L. P51
Steinmetz, M. P27
Sterie, A. P178
Stettler, B. **P130**
Stiefel, F. P93
Stirnemann, J. FM3, FM13, P44
Stoeckli, L.M. P52
Stoekle, M. P58
Stoller, A. P166
Strambo, D. P6
Strasly, I. P69
Strauss, M. P37, P40
Strebel, I. P51
Streit, S. P36
Stringhini, S. FM6
Strombo, D. FM2
Strube, C. P23, P24
Sudano, I. P30
Suenderhauf, C. P164
Suggs, L.S. FM6
Suter-Riniker, F. P67
Sutter, A. **P132**
Szajek, K. P138
Szinnai, G. P175

T
Tal, K. P11, P18, P23, P24, P57, P103
Tancredi, S. FM6
Tanno, A. P70
Tasheva, P. P90
Tepasse, P.-R. P37, P40
Terracciano, L. P136
Tessitore, E. P72, P163
Thalmann, N.F. P62
Théroude, C. P85, P89
Thies, K. P10
Tholomier, A. FM15
Thomann, R. P80
Thorball, C.W. P6
Thoueille, P. P95, **P169**
Tobler, R. P140
Tochtermann, N. P9, P71
Tommasini, F. **P90**
Trachsel, M. P9, **P71**
Trendelenburg, M. P10
Tribolet, P. P80
Trippolini, M.A. P9, P62, P71
Tritschler, T. P82
Tschumi, F. P112
Turk, A. P116, P118, P128
Türkmen, T. **P52**

V
Van der Lely, L. P115
Van der Velpen, V. P166
Van der Wegen, M. P109
Vanetta, C. P22
Vaucher, J. FM2, P6, P17, P21
Vernaz, N. P46
Vesa, D.-V. P141
Vespignani, G. FM12
Viala, B. P48
Vieira Cardoso, D. P97
Vieux, L. P66
Villoz, F. P105
Vocat, A. P173
Vogt, D.R. P27
Voigt, G. P10
Volken, T. FM6
Völkle, M. P81, **P88**
Vollenberg, R. **P37**, **P40**
Vollenweider, P. FM2, FM7, P6, P14, P21, P48, P58
Von Bredow, F. P146
Von Eckardstein, A. P22
Von Garnier, C. P48
Von Rotz, M. P10
Von Wyl, V. FM6
Vosbeck, J. P136
Vuilloud, K. FM12
Vukajlovic, T. P27

W
Wagner, C. FM6
Wagnetz, D. P119
Wälchli, C. **P57**
Waldegg, G. P125
Walo, C. P144
Walther, M. **P123**
Wandeler, G. P58
Warmuth, W. P30
Weber, E. FM9

Weerawardane, T.S. **P150**
Wegner, F. P37, P40
Weiler, S. **P174**
Weiss, L. FM11
Weiss, N. P29
Wenemoser, E. FM9
Wenger, M. P30
Wertli, M. P7, P9, P62, P65, P71, P78
Westendorp, R. FM4
Widmer, N. P45
Wiesner, J. FM1
Wigger, O. P141
Wilde, M. P10
Wildisen, L. FM4
Winterfeld, U. P171, **P172**
Winzeler, B. P27
Wirtz, C. P140
Wolf, L. **P38**
Wolff, T. P51
Wuerzner, G. P157
Wussler, D. P4
Wyss, S. **P109**

X
Xausa, G. **P177**

Y
Yerly, S. P46
Yilmaz, M. **P56**

Z
Zampatti, N. **P128**
Zanchi, A. P157
Zanchi, D. P27
Zebalos Valle, A. **P43**
Zechmann, S. P107
Zekri, D. P38
Zekry, D. FM12, FM13, FM14, P46
Zeller, A. P98, P106, P107
Zerlauth, J.-B. P145
Zermatten, P. FM11
Zhao, W.K. P29
Zimmerli, L. P113, P131, P146
Ziswiler, T. **P22**
Zobel, F. P23, P24
Zulbeari, F. P133

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