Joint annual meeting 2016

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ABSTRACTBOOK OF THE JOINT ANNUAL MEETING 2016 OF THE SSI | SSHH | SSTMP | SSTTM

Abstracts with posterflash presentation

P03 | Decrease of pneumococcal meningitis associated with introduction of pneumococcal conjugate vaccination in Switzerland

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Background and aims
There is conflicting data whether introduction of pneumococcal conjugate vaccines (PCV) lead to a decrease of pneumococcal meningitis (PM). In Switzerland, PCV7 has been covered by health insurance for all children <2 years since mid 2006 and PCV13 for children <5 years since 2011. We assessed whether there have been changes of PM incidence and serotype distribution in Switzerland.

Methods
Incidence and serotype distribution of PM were obtained from mandatory nationwide laboratory surveillance. Periods from 2004-2006 were considered pre-vaccine, 2007-2010 PCV7 years and 2011-2015 PCV13 years. We calculated X2 tests for trends in proportions and Poisson regression for changes in incidence.

Results
Overall, PM incidence decreased from 0.64/100'000 in 2006 to 0.46/100'000 in 2010 (age-adjusted risk ratio: 0.79, p<0.001) and 0.35/100'000 in 2014 (aRR: 0.77, p<0.001 vs. 2010; aRR: 0.61, p<0.001 vs. 2006). Decreases were observed for most age groups. The proportions of PCV7 and PCV13 serotypes decreased over time (p<0.0001 for both), representing 14.3% and 33.3%, respectively, of PM serotypes in 2015. The incidence of non-PCV13 serotype PM was not different in 2011-2015 from 2005-2006 and from 2007-2010. In 2015, serogroups 15, 19, 6, 3, 8 and 24 were responsible for 80% of all PM. The incidence of penicillin non-susceptible PM was lower in 2011-2015 than 2005-2006 (RR: 0.51, p=0.02) and 2007-2010 (RR: 0.43, p<0.001).

Conclusions
Since introduction of PCV7 and PCV13, incidences of PM overall and of penicillin non-susceptible and vaccine-type PM have decreased. Some non-PCV13 serotypes are emerging causes of meningitis warranting further monitoring.

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P07 | Impact of MALDI-TOF mass spectrometry based identification directly from positive blood cultures on patient management: A randomized trial.

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Objectives
Rapid identification of pathogens directly from positive blood cultures (BC) in combination with an antimicrobial stewardship program (ASP) is associated with improved antibiotic treatment and outcomes. However, there is a lack of prospective randomized studies investigating the effect of rapid identification and ASP separately.

Methods
A total of 425 patients with positive BCs were randomized during a one-year period: (i) MALDI-TOF rapid identification directly from positive BCs versus (ii) conventional processing including subcultures (Figure 1). ASP was identical throughout the study period. Bloodstream infections (BSI) (n=242) and contaminants (n=126) were included and analysed separately.

Results
Baseline characteristics were similarly distributed between the diagnostic groups. Mean time to organism identification was shorter in the MALDI-TOF group (28.2 vs. 49.7 hours, $p<0.001$). Mean time from reporting of gram stain to effective treatment was significantly shorter (3.7 vs. 6.7 hours, $p=0.003$). Rapid identification resulted in improved optimal treatment at 48 hours only in AmpC-producing and non-fermenting bacteria, S. aureus, and Streptococcus/Enterococcus spp. (57 vs. 38%, $p=0.06$, Figure 2). Mean duration of intravenous antimicrobial therapy (13.6 vs. 14.1 days, $p=0.9$) and length of stay (17.7 vs. 20.4 days, $p=0.3$) was comparable. We observed a trend towards a reduced 30-day mortality in the MALDI-TOF group (hazard ratio 0.5, 95% CI 0.3-1.1, $p=0.08$). Rapid identification of contaminations resulted in a shorter duration of intravenous antimicrobial therapy (mean 4.8 vs. 7.5 days, $p=0.04$).

Conclusions
Rapid identification using MALDI-TOF directly from positive BCs provided fast and reliable microbiological results and improved treatment quality in the setting of an established ASP.

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P12 | Influence of time to diagnosis of severe influenza on antibiotic use, length of stay and mortality: a retrospective study

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Background
Timely diagnosis of influenza infection in hospitalized patients might help reduce antibiotic use and, consequently, antibiotic selection pressure during influenza seasons. In this retrospective cohort study, we aimed to evaluate whether time to influenza diagnosis in hospitalized patients with severe influenza is associated with the duration of antibiotic therapy.

Methods
We retrospectively included all hospitalized patients >16 years of age who tested positive for influenza A or B by polymerase chain reaction from respiratory specimens during influenza seasons 2013/2014 or 2014/2015 at the University Hospital Zurich. The primary aim was to assess the association between timing of laboratory-confirmed influenza diagnosis and duration of antibiotic therapy. Secondary outcomes were length of hospital stay, ICU admission, mortality, and duration of isolation precautions. Early diagnosis was defined as laboratory confirmation on the day of or the day after hospital admission and symptom onset, respectively.

Results
126 patients were included (median age 57 years, range 16-93 years; 47.6% females). Timing of influenza diagnosis was not associated with the duration of antibiotic treatment, mortality, ICU admission and the duration of isolation precautions, respectively. However, early influenza diagnosis reduced length of hospital stay (adjusted hazard ratio (95% confidence interval): 0.51 (0.30-0.88), P=0.014). Whereas 75.4% of patients with severe influenza infection were treated with antibiotics, antiviral treatment was only initiated in 59.2%.

Conclusions
Our data indicate that early diagnosis may reduce the length of hospitalization. The duration of antibiotic therapy, mortality, ICU admission and the duration of isolation precautions, however, are unaffected by early influenza diagnosis. Further research that also incorporates the effect of early diagnosis of bacterial pathogens on antibiotic prescribing patterns is warranted

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P16 | A novel HIV-1-based vector that reproduces features of productive and latent HIV-1 infections

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The lack of phenotypic markers to identify in vivo latently HIV-1-infected cells that harbour replication-competent proviruses hampers the progress to understand factors that govern HIV-1 latency. Therefore, we constructed a novel dual fluorescence HIV-1-based vector, containing a constitutively expressed fluorescent reporter gene to identify infected cells and another, driven by the HIV-1 LTR, to distinguish between productive and latent infections. Additionally, the constitutive fluorescent reporter gene cassette is flanked by a pair of genetic insulators, which protect it from position-effect variegation and alleviate promoter interference between the two gene cassettes. We infected Sup-T1 cells with the pseudotyped vector and analysed the various profiles of bulk and clonal cell populations longitudinally. We demonstrated the stability of our system; different variants and inputs of the vector consistently yielded the same infection phenotype and the initial phenotypes of both bulk and clonal cell populations remained the same during long-term culture of up to 12 months. The integration site patterns were similar to those of wild type HIV-1, and we showed the impact of differential integration sites, as well as vector intrinsic factors, on the reversal of silenced HIV-1 LTRs, i.e. an HIV-1 infection-dependent decrease in expression levels of vector-hosting genes and/or mutations in the vector genome correlated with a lower reactivation potential of the silenced HIV-1 LTR. The integration site repertoire of infected cells dwindled during long-term culture, suggesting the influence of integration sites on the selective propagation of certain cell clones. Our system was also responsive to a variety of latency-reversing agents, with the highest response induced with Romidepsin, Panobinostat, and SAHA in combination with TNF. Most latently infected cell clones unresponsive to latency-reversing agents had large deletions within the integrated vector genome, similar to observations in vivo. In summary, we have developed a novel system that enables the identification and separation of cell populations accurately representing productive and latent HIV-1 infections.

P19 | High rates of asymptomatic STIs in patients after primary HIV-1 infection

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The prevalence of asymptomatic sexually transmitted infections (STIs) in patients who presented with a primary HIV-1 infection and received early antiretroviral therapy is unknown. Between June 1st and August 31th 2015 we offered STI screening to all patients from the Zurich Primary HIV-1 Infection Study who attended a clinical visit. Patients were tested for gonorrhea, chlamydia and herpes simplex virus (HSV) by polymerase chain reaction (PCR) and for syphilis by serological assay. In addition, patients presenting with elevated liver enzymes were tested for acute hepatitis C virus (HCV) infection by HCV PCR. All patients were asked to give a first-catch urine specimen and a blood sample. Additional specimens were taken from the throat, rectum and vagina from patients who reported having had oral, anal or vaginal sex. Patients were asked to complete a supplementary questionnaire about sexual behaviour in the preceding three months. Within three months a total of 173 patients attended a clinical visit. Most patients were male (95%), were men who have sex with men (MSM) (85%) and had a suppressed HIV viral load to <50 HIV-1 RNA copies/ml of plasma (90%) at the time-point of STI screening. Of all 173 patients, 45 patients (26%) denied STI screening. Heterosexuals refused STI screening significantly more often compare to MSM (49% versus 20%; p= 0.001). Most frequently self-reported reason for refusing screening was having no sexual contact in the preceding three months (33/45, 73%). Out of all 128 tested patients, 30 (23%) were affected by a STI; 22 patients (73%) being asymptomatic (Table 1). The detected STIs included chlamydia trachomatis (n=17, 52%), gonorrhoea (9, 27%), syphilis (4, 12%), acute HCV infection (2, 6%), and HSV (1, 3%). Three persons had >1 STI.Number of occasional sex-partners, reporting sexual risk behaviour and being MSM was associated with a significant increased risk for acquisition of a STI (Table 1). The favoured anatomical site of asymptomatic presentation was the rectum (n= 13) (Table 2). The number needed to screen to detect one STI in MSM was 4 compared to 19 in heterosexuals. A high rate of STIs was diagnosed in MSM who initially presented with a primary HIV-1 infection and received early antiretroviral therapy. The majority of STIs were asymptomatic. A regular STI screening including asymptomatic individuals should strongly be considered in MSM who report having changing partners or practicing sexually risky behaviour.

Figure 1. Study flowchart.

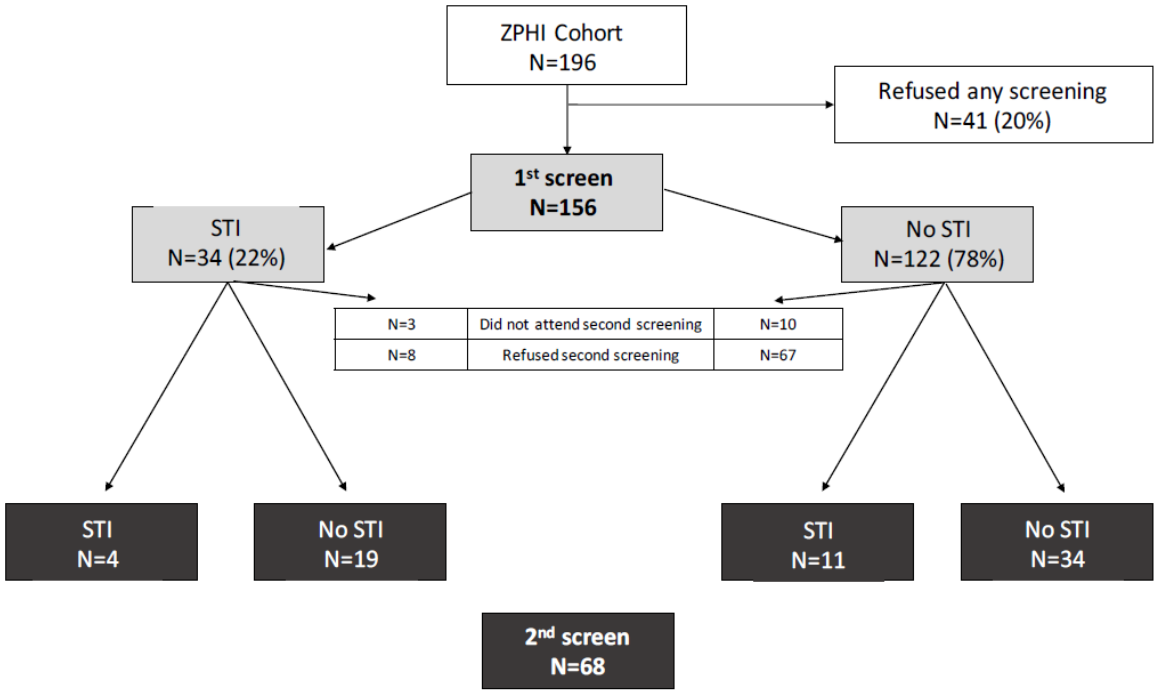

Table 1. Demographic and clinical characteristics of the study population and multivariable analysis.

		Bivariate			Multivariable
		No STI	STI	*P*	Odds Ratio (95% C.I)
n		122	34		
Age (median [IQR])		42.44 [35.26, 47.99]	39.74 [32.43, 43.16]	0.076	0.95 (0.90, 1.00)
Sex (%)	Male	114 (95.8)	29 (96.7)	1	
	Female	5 (4.2)	1 (3.3)		
Ethnicity (%)	White	111 (93.3)	27 (90.0)	0.681	
	Black	1 (0.8)	1 (3.3)		
	Latino	6 (5.0)	2 (6.7)		
	Asian	1 (0.8)	0 (0.0)		
University education (%)	No	99 (81.1)	30 (88.2)	0.478	
	Yes	23 (18.9)	4 (11.8)		
Risk group (%)	MSM	103 (84.4)	33 (97.1)	0.078	Ref.
	HET	19 (15.6)	1 (2.9)		0.48 (0.02, 3.00)
Stable partnership (%)	No	50 (41.3)	18 (52.9)	0.312	Ref.
	Yes	71 (58.7)	16 (47.1)		0.86 (0.33, 2.23)
N of sex partners (median [IQR])		1.50 [1.00, 3.00]	3.50 [2.00, 7.00]	<0.001	1.05 (0.95, 1.15)
Condomless sex (%) [a]	No	100 (82.0)	18 (52.9)	0.001	Ref.
	Yes	22 (18.0)	16 (47.1)		2.92 (1.09, 7.89)
Last CD4 (median [IQR])		686.00 [544.50, 875.50]	588.00 [449.00, 739.50]	0.043	0.92 (0.83, 1.01) [b]
Symptoms (%)	No	112 (91.8)	23 (67.6)	0.001	
	Yes	10 (8.2)	11 (32.4)		1.82 (0.53, 5.85)
Virally suppressed (%)	No	10 (8.6)	1 (3.3)	0.461	
	Yes	106 (91.4)	29 (96.7)		
History of syphilis (%)	No	92 (75.4)	24 (70.6)	0.728	
	Yes	30 (24.6)	10 (29.4)		

[a] with occasional (non-steady) partners [b] as √CD4

Table 2. Detected STIs by site of isolation.

	49 n (%)
Syphilis	9 (18.4)
Gonorrhea throat	3 (6.1)
Gonorrhea rectal	7 (14.3)
Gonorrhea genital	1 (2.0)
Chlamydia throat	5 (10.2)
Chlamydia rectal	19 (38.8)
Chlamydia genital	6 (12.2)
Chlamydia LGV	1 (2.0)
Herpes Simplex Virus	1 (2.0)
Acute Hepatitis C	3 (6.1)

P41 | The impact of HIV associated disorders (HAND) on cART adherence

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Objective
HIV associated neurocognitive disorders (HAND) are defined according to their diagnostic degrees as: asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia (HAD). We aim to investigate whether HIV associated cognitive disorders are associated with lower adherence to the combined antiretroviral treatment (cART).

Design
This is an observational, exploratory, single center cohort study in patients referred to an adherence clinic and to a neuropsychologist for a neurocognitive evaluation.

Methods
Patients' characteristics were retrieved from the Swiss HIV Cohort Study database. A state of the art cognitive assessment was performed by neuropsychologists. Repeated adherence measures were available through electronic monitors stating whether or not a patient was taking cART as prescribed. Implementation was computed as the proportion of patients taking cART as prescribed across time. A Generalized Estimating Equation model adjusted for neurocognitive diagnosis was used to estimate implementation.

Results
Forty patients were analyzed, median (IQR) age was 50 (42, 58) years and 25 (62.5%) were male. Ten patients (25%) were without neurocognitive deficits, 6(16%) had ANI, 3 (7.5%) had MND, 3 (7.5%) had HAD and 17 (42.5%) had neurocognitive disorders attributed to other co-morbid conditions (mostly depression). Implementation over 3.5 years showed a significant decline (50% drop) in medication adherence among patients diagnosed with ANI, MND, HAD in comparison with patients who had no deficit or a non-HAND cognitive disorder (implementation stayed approximately stable around 90% during monitoring) (fig1).

Conclusion
Our findings support the hypothesis that HAND is associated with a decrease in cART adherence.

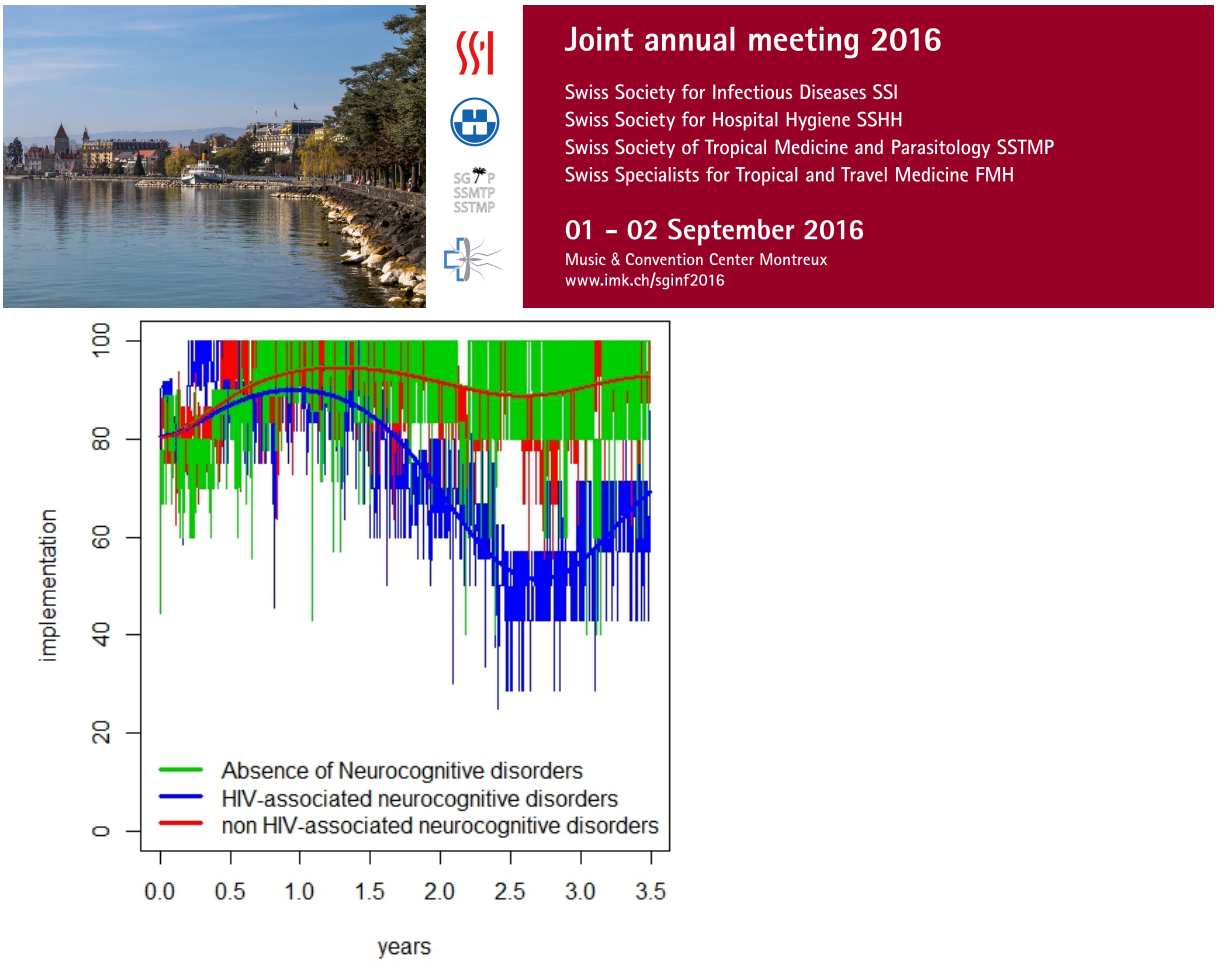

Figure 1 Implementation computed as the proportion of patients taking medication as prescribed over time per neurocognitive group

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P44 | Identifying the etiology of undiagnosed respiratory infections in lung transplant recipients by unbiased metagenomic sequencing

D. Lewandowska [1], P. Schreiber [2], M. Schuurmans [3], B. Ruehe [1], O. Zagordi [1], C. Bayard [2], M. Greiner [2], F. Geissberger [1], R. Capaul [1], A. Zbinden [1], J. Böni [1], C. Benden [3], N. Mueller [2], A. Trkola [1], M. Huber [1]

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Introduction
Despite routine testing for the most common respiratory viruses and bacteria, a considerable portion of post-transplant infections with respiratory symptoms remains of unknown etiology. Using an open metagenomic approach, we re-analyzed respiratory samples from lung transplant patients presenting with symptoms suggestive of an airway infection, but without detection of a viral or microbial etiologic pathogen in routine diagnostic methods.

Methods
For metagenomic sequencing, virus particles were enriched from respiratory swabs, total nucleic acids extracted and amplified randomly. Sequencing libraries were prepared with NexteraXT and sequenced on a MiSeq Illumina (1 x 150 bp). Quality filtered reads were cleaned from non-viral reads by an in-house bioinformatics pipeline and blasted against a database containing > 40'000 viral sequences.

Results
Among 71 participating individuals, 22 (31%) showed no respiratory symptoms up to 15 months after lung transplantation; 47 (66%) developed a total of 60 episodes of respiratory disease of which 28 were of viral and 3 of bacterial origin. In 26 (47%) episodes, no microbial or viral etiology of infection could be determined by routine diagnostics. Analyzing 24 undetermined throat swabs, the metagenomic approach identified a viral etiology in 5 patients (3 Rhinovirus A, 1 Rhinovirus B, 1 Coronavirus HKU infection). Of note, in 2 cases these viruses showed evidence of late amplification in routine PCR but did not fulfil the criteria for positivity. In many samples we detected Torque teno virus (TTV) and Human herpesvirus 7 (HHV-7) reads that were confirmed by specific PCR. While TTV loads increased with immunosuppression both in swabs and blood, HHV-7 remained constantly at low level and was restricted to the respiratory tract.

Conclusions
Our metagenomic approach was able to identify diverse viral pathogens in a single analysis and revealed low-level infections with known respiratory viruses that were not reported in routine screening. The presence of HHV-7 is intriguing and should be investigated in more detail to understand its pathogenetic role. No other potentially disease related viruses were found in the remaining symptomatic lung transplant patients leaving the exact etiology of the condition unclear. Overall, our study highlights the potential of metagenomic sequencing in complex diagnostic situations such as immunocompromised hosts and underlines the need to incorporate this technology in the

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P49 | Secular trends of bloodstream infections during neutropenia in 15,184 hematopoietic stem cell transplants: 13-year results from a European multicenter surveillance study (ONKO-KISS)

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Background
Emerging antibacterial resistance challenges the choice of empiric therapy for bloodstream infections (BSI) in patients undergoing hematopoietic stem cell transplantation (HSCT). Currently, only limited data is available on the epidemiology of BSI pathogens over time, and most evidence comes from retrospective, single-center studies.

Methods
From 2002 to 2014, we investigated changes in the incidence of causative organisms of BSI during neutropenia among adult HSCT recipients from a prospective cohort for infection surveillance in 20 hematologic cancer centers in Germany, Austria and Switzerland (ONKO-KISS).

Results
15,184 HSCT recipients with neutropenia (60.3% allogeneic and 39.7% autologous) developed 2,388 BSIs (incidence, 15.8%). Gram-negative bacterial BSIs increased over time both in patients after allogeneic HSCT (allo-HSCT) and autologous HSCT (auto-HSCT). Among allo-HSCT patients we observed a significant increase in the incidence of BSIs due to Escherichia coli (from 1.1% to 3.8%, $p<0.001$) and due to enterococci (1.8% to 3.3%, $p<0.001$). In contrast, the incidence of BSIs due to coagulase-negative staphylococci decreased in allo- and auto-HSCT patients (8.2% to 6.3% and 7.7% to 2.0% respectively, $p<0.001$). No significant trends were seen for the incidence of BSI due to MRSA, vancomycin-resistant enterococci and ESBL-producing Enterobacteriaceae. The BSI case fatality remained unchanged over the study period (overall 3.1%).

Conclusion
In this large multicenter study, the incidence of gram-negative BSIs among HSCT patients with neutropenia has increased while gram-positive BSIs decreased, possibly by improvements in intravascular catheter care. Prospective surveillance of antimicrobial resistance evolution in gram-negative bacilli may be increasingly important for guiding empiric antibiotic therapy strategies.

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P57 | Clinical presentation and outcome of Dengue in the native and expatriate communities of Dar es Salaam, Tanzania

N Boillat-Blanco [1, 2, 3], B Klaassen [5], L Franco Narvaez [7], Z Mbarack [6], J Samaka [3], T Mlaganile [3], A Mamin [4], B Genton [1, 2, 8], L Kaiser [4], V D'Acremont [2, 8]

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Introduction
Uncontrolled urbanization and human mobility has led to a rapid increase of dengue over the last decade and its geographic distribution is expanding to Africa. Severe dengue has been reported infrequently in Africa suggesting that specific population genetic or environmental characteristics may be protective. We describe the clinical presentation and outcome of dengue during the first documented outbreak in Dar es Salaam, Tanzania, that occurred in both native and expatriate populations. This gives a unique opportunity to study differences in clinical presentation between these two populations.

Methods and Materials
Febrile adult patients with confirmed dengue (NS1 and/or IgM and/or PCR positive) were included between December 2013 and July 2014 in three public clinics and one private clinic. Clinical outcome was assessed by a visit/call at day 7. Association between ethnicity and clinical presentation (in particular dengue warning signs) was assessed using logistic regression adjusted for age, sex and duration of symptoms at inclusion.

Results
After exclusion of 3 patients because of mixed-ethnicity, a total of 431 adult patients with dengue (serotype 2, genotype Cosmopolitan) were included in the study. 185 native Tanzanians were included in the public clinics and 249 patients with different ethnicity in the private clinic. 241 were black (232 Tanzanians and 9 from other African countries) and 190 non-black (125 Europeans/Americans/Australians, 48 Asians/Middle East and 17 white South Africans). 18% had previous dengue exposure (positive IgG) and 3.5% were co-infected with malaria. Black patients were younger (mean 33 vs 42 years) and attended care after a longer duration of symptoms (mean 2.9 vs 2.7 days). Black ethnicity was associated with a higher prevalence of myalgia and arthralgia (aOR, 95%CI): 2.3, 1.5-3.6), and with lower prevalence of rash (0.05, 0.03-0.11). Warning signs, such as hypotension (0.08, 0.01-0.76), mucosal bleed (0.43, 0.20-0.90) and elevated haematocrit (aCoef, 95%CI: -1.9, -3.4- -0.4) were less prevalent in the black population. Severe dengue occurred in 1% of the patients and two patients died.

Conclusions
Although all patients were infected with the same genotype, the clinical presentation differed according to ethnicity. Black patients presented with a lower rate of warning signs, suggesting cross-protection from previous infections by dengue or other endemic flavivirus or protective genetic host factors.

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P58 | Etiologies of acute febrile illness among HIV positive and HIV negative adults attending outpatient clinics in Dar es Salaam, Tanzania

N Boillat-Blanco [1, 2, 3], Z Mbarack [5], J Samaka [3], T Mlaganile [3], T Kazimoto [3], A Mamin [4], B Genton [1, 2, 6], L Kaiser [4], V D'Acremont [2, 6]

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Background
Fever is one of the most frequent reasons of attendance at health facilities. Little is known about etiologies of fever in adults which urge clinicians to overprescribe antimicrobials. We investigated causes of fever in adults attending outpatient clinics in urban Tanzania.

Methods
Consecutive patients ≥18 years with tympanic temperature >38°C were recruited. Detailed medical history and clinical examination were undertaken. Rapid tests for malaria, dengue, typhoid, HIV, Cryptococcus, tuberculosis (Gene-Xpert), Streptococcus A, syphilis and rota/adenovirus were performed, as well as blood cultures, serological analyses. Multiplex PCR was done on nasal swabs and blood. Chest X-rays were performed in patients with clinical pneumonia according to WHO guidelines. Other investigations (urine, stool and CSF cultures, β-D-glucan, immunofluorescence of inducted sputum, urine Histoplama antigen) were done according to algorithms developed beforehand. All final diagnoses were based on pre-defined criteria.

Results
520 patients were recruited between July 2013 and May 2014. 25% were HIV infected. They presented with 720 diagnoses: 35% acute respiratory infection (ARI), 19% dengue, 8% malaria, 6% nasopharyngeal infections, 5% urinary tract infection, 5% other bacterial infections (occult bacteremia, meningitis, rickettsiosis, leptospirosis, arthritis, liver abscess), 4% typhoid, 4% systemic viral infections, 4% gastroenteritis, 1% cryptococcus and 9% unknown. ARI were more frequent among HIV infected compared to HIV negative patients (55% vs 23%; $p<0.001$) while dengue was rarely diagnosed (4% vs 26%; $p<0.001$). HIV modified the distribution of the causes of ARI. While most HIV negative patients presented with upper respiratory tract infection (URTI; 66%) of viral origin, tuberculosis, radiological pneumonia and pneumocystis were frequent among HIV infected patients (89%). The rates of severe sepsis (25 vs 8%) and death (12 vs 3%) were significantly higher in HIV infected patients ($p<0.001$).

Conclusion
These results highlight the need of systematic HIV screening in febrile patients and call for implementation of guidelines integrating HIV status to support clinicians in the management of patients with acute fever. They also show the importance of surveillance of epidemic-prone diseases causing fever, such as dengue, to identify outbreaks timely and avoid unnecessary antibiotic or antimalarial treatment.

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P64 | Campylobacter up, Salmonella down: an analysis of Swiss surveillance data, 1988-2013

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Campylobacter spp. and Salmonella spp. are the two most frequently reported foodborne pathogens in Switzerland. Based on the Epidemics Act, diagnostic laboratories are obligated to report positive cultures from human clinical samples to the Federal Office of Public Health (FOPH). We analysed data from the National Notification System for Infectious Diseases (NNSID) of the years 1988-2013. Data from the Federal Statistical Office on the average resident population of Switzerland were used to calculate notification rates. Campylobacter case notifications more than doubled from 3'127 to 7'499 cases between 1988 and 2013. During the same time period, notified salmonellosis cases decreased from 4'291 to 1'267 cases. In 1995, salmonellosis was replaced by campylobacteriosis as the leading foodborne disease in the Swiss surveillance system. Reports of both pathogens are most frequent during summer months. However, campylobacter case notifications show an additional peak during the winter festive season. For campylobacter, notification rates decreased in children under 5, were stable in 5-9 year-olds and increased in all other age groups between 1988 and 2013. Salmonella notification rates decreased in all age groups.
Many factors can influence notification rates apart from disease incidence: help seeking behaviour of patients, testing and treatment behaviour of physicians, willingness of patients to provide stool samples, laboratory methods used and notification compliance. However, it seems unlikely that changes in one or several of the aforementioned factors would influence Campylobacter and Salmonella case notifications differently. Hence, we assume that the inverse trends observed for the two pathogens indicate changes in disease incidence at population level. Interventions such as the implementation of mandatory screening of layer hens for Salmonella Enteritidis and measures to eradicate positive flocks seem to have been effective in reducing human salmonellosis. New legal microbiological criteria for foodstuff concerning Campylobacter were implemented in 2014. Additional measures are foreseen for 2016. The impact of those interventions on human campylobacteriosis needs to be evaluated in the near future.

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P83 | Systematic review of the level of compliance of health workers in Africa to the results of malaria rapid diagnostic tests

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Introduction
Malaria Rapid Diagnostic Tests (mRDTs) have been recommended by WHO to improve the quality of management of fever cases and reduce unnecessary antimalarial prescription, hence slowing down the development of parasite resistance. Nevertheless, the availability of mRDTs can only have full impact if health workers trust results and stop giving antimalarials when the test result is negative. We performed a systematic review of the level of compliance of health workers with mRDTs' results and influencing factors in Africa, and analysed whether this level changed over time.

Methods and materials
Studies were searched in 4 electronic databases (Medline, Embase, Web of Science and Cochrane) from January 2003 to Mai 2015. Studies on clinical management of at least 50 participants of any age having an mRDT performed at any health care level of urban or rural settings were selected. Data extracted were: study year and design, type of health facility, geographical setting, malaria prevalence, age groups, number of patients receiving antimalarials despite a negative mRDT result and total number of negative patients. The outcome measure was the proportion of patients prescribed an antimalarial treatment despite a negative mRDT result (mPNP).

Results
Of the 189 full text article selected, 29 studies conducted between 2005 and 2012 in 9 African countries were included. The mPNP was 16% (IQR 4%-36%). This proportion was lower in pilot implementation (14%, IQR 3-27%) and large scale (14%, IQR 2-29%) than in randomized studies (23%, IQR 6-48%). Except in drug shops, compliance improved over time, especially for large scale implementation studies (R2=0.64). Community health workers had better compliance (4%, IQR 1-16%) than those working in health centers (24%, IQR 3-39%), hospitals (35%, IQR 25-44%) and drug shops (44%, IQR 23-48%). No correlation was found between malaria prevalence and level of compliance. All studies with baseline survey and/or control group, except one, showed a reduction of antimalarial prescription due to the introduction of mRDT (overall median reduction of 74%, IQR 46-94%).

Conclusions
These results show that compliance of health workers with mRDT results in Africa was good, with overall less than one among six negative patients treated. The lower the level of care was the better the compliance, except in drug shops. A trend toward improvement over time was observed, especially in large scale implementation of mRDTs.

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P67 | Determinants of the effectiveness of mass dog vaccination to eliminate rabies in African cities.

J Zinsstag [1, 8], M Lechenne [1, 8], M Laager [1, 8], M Mindekem [2], S Naïssengar [3], A Oussigéré [3], K Bidjeh [3], G Rives [1, 8], J Tessier [1, 8], DM Moto [2], IO Alfaroukh [3], Y Muthiani [1, 8], A Traoré [4], J Hattendorf [1, 8], A Lepelltier [5], H Bourhy [5], L Dacheux [5], T Stadler [6, 7]

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After polio, dog transmitted rabies is one of the most promising viral diseases that can be targeted for elimination. Two consecutive dog mass vaccination campaigns, co-funded by the Chadian government and external donors in 2012 and 2013 were sufficient to interrupt transmission for more than two years in N'Djaména, the capital city of Chad. A deterministic dog-human rabies transmission model, fitted to routine weekly data on rabid dogs and exposed human cases demonstrated the elimination and was confirmed by a a phylo-dynamic estimation of the reproductive number from dog related rabies virus (RAV) genetic sequences. Similar small scale mass vaccinations in Bamako did not reach a sufficient coverage to interrupt transmission. The low coverage in Bamako has been assessed by a novel mixed method effectiveness model showing that the lack of information by households was a main factor of poor vaccination coverage in the study area. Our results show that dog rabies can be eliminated in African cities with currently available dog vaccines provided communities are well informed and engaged.

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P72 | Recent travelling to tropical or subtropical countries reduces the risk to suffer from travellers' diarrhoea in consecutive trips

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Introduction
Travellers' diarrhoea is one of the most common health problems in travellers, accounting for one third of medical visits after travel (1). Preventive measures like "cook it, boil it, peel it or leave it" appear to have little effect on the incidence of travellers' diarrhoea (2). Potential risk factors including the effect of previous travel on the risk of developing diarrhoea on subsequent trips was analyzed in this study.

Material and methods
Travellers presenting for pre-travel advice at two Swiss travel clinics before travelling to South Asia (India, Bhutan, Nepal, Sri Lanka) were enrolled. A questionnaire was filled in before and immediately after travelling, An univariate and multivariate logistic regression analysis was done to assess for travel-related risk factors for developing travellers' diarrhoea.

Results
For 178 travellers, questionnaires before and after travelling were available. Overall, the incidence of travellers' diarrhoea was 38.2% (95% CI 31.4-45.5%). Travelling to India or Nepal, length of stay of > 3 weeks and staying in a hotel as compared to a private home/guest house were associated with an increased risk for travellers' diarrhoea. Having travelled to a high risk destination for travellers' diarrhoea within the past 12 months before the current trip was associated with a significantly decreased risk (OR 0.16, p=0.002). Eating behaviour did not influence the risk for travellers' diarrhoea.

Conclusions
Travellers' diarrhoea is a common health problem in travellers to the Indian subcontinent. Having travelled to a high risk area for travellers' diarrhoea 12 months prior to the current trip was associated with a significantly reduced risk to suffer from diarrhoea. Travelling is known to alter the gut microbiome (3). Furthermore, travellers who suffer from travellers' diarrhoea were shown to have a lower diversity in their gut microbiome prior to the trip than travellers who did remained healthy (4). The results indicate that travelling might have a lasting effect on the gut microbiome, influencing the susceptibility for developing travellers' diarrhoea.

P77 | Surveillance of the invasive Asian tiger mosquito (Aedes albopictus) in Switzerland

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The spread of invasive mosquito species able to transmit human diseases alongside increasing habitat suitability due to global warming and returning travellers from disease endemic countries pose an emerging public health threat to Europe. In Switzerland, there are at least three invasive mosquito species of which the Asian tiger mosquito, Aedes albopictus, is of particular concern because it is a vector competent for over 20 viruses including Zika, chikungunya and dengue. In 2003 the Asian tiger mosquito appeared for the first time in the Canton of Ticino. Since then the mosquito has continuously extended its range in Ticino and since 2013 the mosquito has been found repeatedly introduced north of the Alps. In this presentation, we will give an overview of the latest data from the national monitoring and control efforts in reducing the spread of the Asian tiger mosquito and discuss the results with a view to the risk of emerging vector-borne diseases in Switzerland.

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P98 | Can we interpret hand hygiene compliance data over time?

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Background
Hand hygiene (HH) is the most important intervention to reduce nosocomial infections. Its promotion by direct observation and feedback as well as educational campaigns is widely performed. However, little is known about the long-term impact of these measures. We analyzed the effects of our hospital-wide interventions 2007-2015.

Methods
HH compliance (HHC) was monitored yearly. We evaluated HHC dynamics by profession, ward and indication as well as the effect of specific interventions: Hospital-wide poster campaigns, educational events and individual team instructions for under-performing wards. Odds ratios (OR) were calculated from mixed-effects logistic regression with robust standard errors, adjusted for ward as random effect and indication and calendar year as fixed effects.

Results
Overall, 12`459 HH indications were observed on 37 individual wards. HHC for nurses improved from 59.0% to 78.8% (OR 1.12 per year, 95% CI 1.07-1.17), HHC for physicians from 63.1% to 68.0% (OR 1.02, 0.97-1.07) (Fig. 1a). Hand disinfections without indication, measured between 2013 and 2015, significantly increased in physicians (OR 1.81, 1.07–3.56), but not in nurses (OR 1.13, 0.85–1.49). Hospital-wide campaigns significantly improved HHC (OR 1.29, 1.10–1.51). Due to substantial year-to-year variations, the HHC performance on an individual ward was not predictive for the subsequent year (autocorrelation rho=0.02; Fig. 1b). There were a few wards with consistently superior and inferior HHC with a trend for lower HHC in larger wards. Additional team instructions of wards with HHC <65% significantly improved rates in the following year (OR 3.30, 2.10–5.20), but were not more effective than simple feedback of HHC results. For reliable comparisons of HHC between wards in a given year and between years on a given ward, a high number of observations is needed: For a presumptive HHC of 60%, 70% and 80%, respectively, 369, 323 and 246 observations per ward and year are required to achieve a CI +/-5%.

Conclusions
Yearly monitoring and individual feedback for every ward together with educational campaigns significantly improved HHC. The increasing rate of hand disinfections without indication underlines growing awareness, but also lacking knowledge, calling for targeted interventions. The reliable comparison of wards is strongly limited by the high number of observations needed. Electronic tools allowing personalized real-time feedback may further improve HHC.

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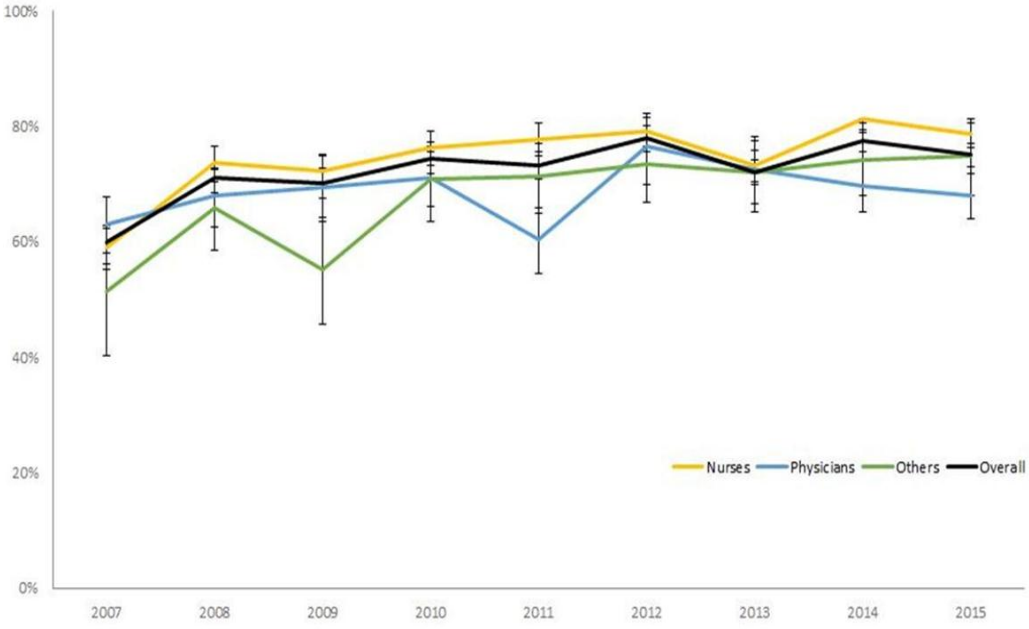

Figure 1a

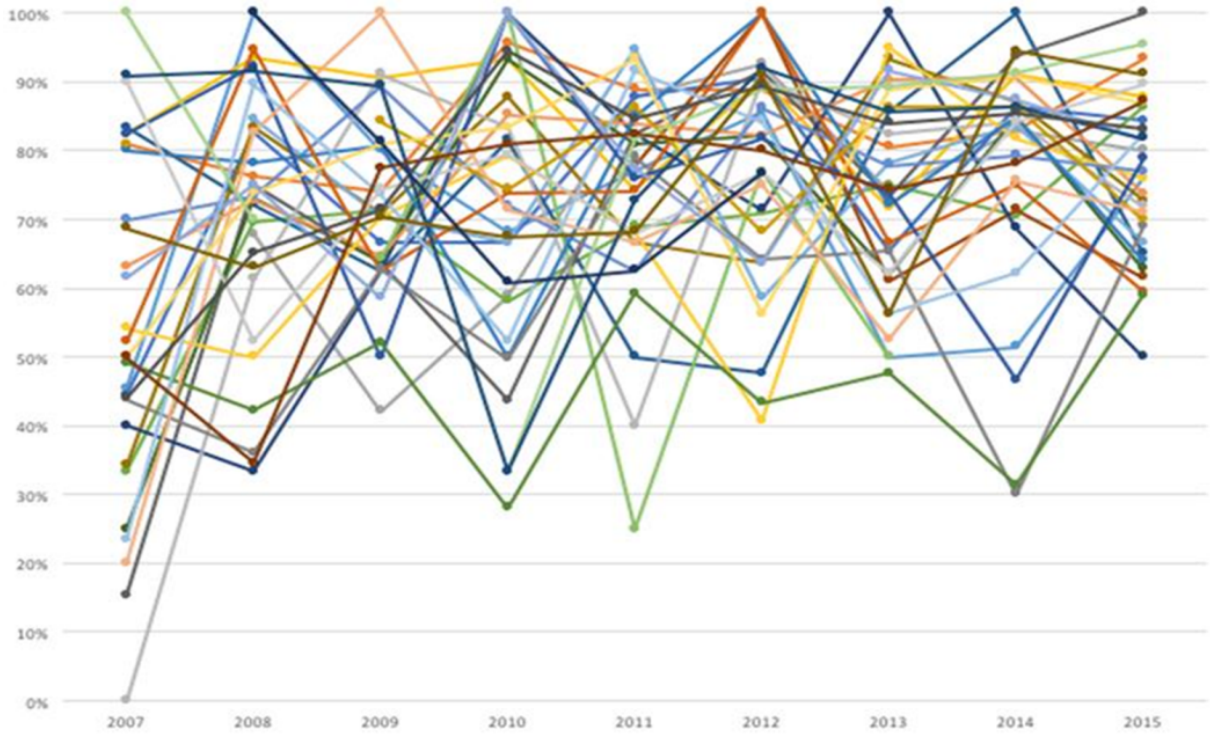

Figure 1b

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P105 | Massnahmen und Resultate nach einer Häufung orthopädischer postoperativer Wundinfekte

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Ausgangslage
Nach Meldung einer Häufung von postoperativen Wundinfekten (SSI) durch die ärztliche Leitung der Orthopädie erfolgten Abklärungen und Interventionen durch die Spitalhygiene in Zusammenarbeit mit den involvierten Bereichen.

Ziel
Beschreibung des Vorgehens, der eingeleiteten Massnahmen, deren Umsetzung und Resultate. Methoden: Falldefinitionen gemäss den CDC-Kriterien, Erstellen einer epidemiologischen Kurve und deskriptive Analyse der infizierten Patienten. Evaluation der Adhärenz der infektpräventiven Massnahmen (Workshops mit den involvierten Berufsgruppen über die Adhärenz mit den bekannten Massnahmen, Festlegen der Interventionen, deren Umsetzung sowie standardisierte Beobachtungen im OP).

Resultate
Ende März 2015 fanden sich am Spital Herisau über einen Zeitraum von 18 Monaten insgesamt 13 SSI bei rund 750 orthopädischen Eingriffe pro Jahr. Basierend auf den Resultaten des ersten Workshops im März 2015 wurden folgende Massnahmen festgelegt: Korrekte Durchführung Haarentfernung, Vermeidung von Störungen/Lärm im OP (Abgabe von Telefonen, Vermeiden von unnötigen Besuchen und Gesprächen im OP) und Definition eines Ablaufs der Einführung neuer Mitarbeitenden im OP. Der Wechsel der Durchführung der Hautdesinfektion von der OP-Pflege zu den Operateuren erfolgte bereits vor dem ersten Workshop. Die Mitte Mai 2015 durchgeführten standardisierten Beobachtungen im OP (5 verschiedene Eingriffe) mit Feedback an die involvierten Bereiche zeigten keine Auffälligkeiten bzgl. Haarentfernung, chirurgischer Händedesinfektion, Verabreichung der Antibiotikaprophylaxe sowie Adhärenz mit der hygienischen Händedesinfektion beim OP-Personal. Das präoperative Team-Time-Out erfolgte in 4/5 Operationen, währen der Operation wurden die Türen durchschnittlich 10 Mal/h geöffnet. Bezüglich Lärm/Störungen im OP war gemäss den Operateuren bereits eine deutliche Besserung eingetreten. Im weiteren Verlauf waren die SSI rückläufig und treten bisher nur noch sporadisch auf. Die Durchführung der Hautdesinfektion erfolgt nun nach Schulung und Erstellung einer Handlungsanweisung wieder durch die Pflege im OP.

Konklusion
Mit einem strukturierten Vorgehen unter Miteinbezug aller involvierten Berufsgruppen konnten rasch Massnahmen definiert und umgesetzt werden. Weitere Beobachtungen im OP zur Überprüfung der anhaltenden Wirkung sind vorgesehen. Inwieweit die Intervention als Ganzes oder die Einzelmassnahmen einen kausalen Einfluss auf diese Verbesserung haben, bleibt offen.

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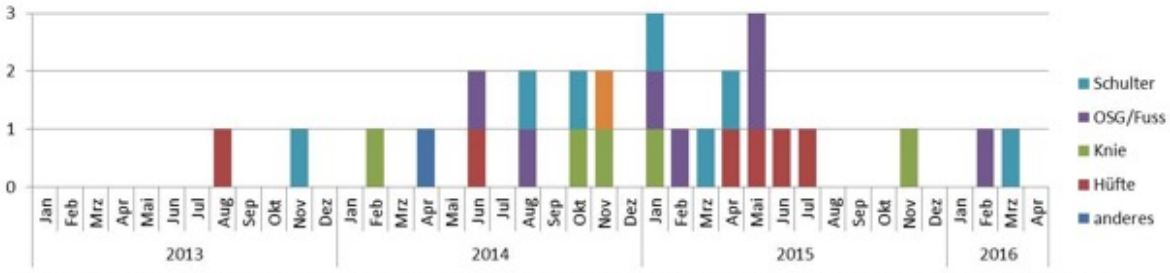

Abbildung: Epidemiologische Kurve der postoperativen Wundinfekte auf der orthopädischen Abteilung im Erfassungszeitraum aufgeschlüsselt nach betroffener anatomischer Region und Monat der Index-Operation.

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P109 | The role of a surveillance program for successfully introducing peripherally inserted central catheters (PICC): a 2-year observational study in an academic hospital

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Background
In our hospital a previous attempt to introduce peripherally inserted central catheters (PICC) was aborted after an unsystematic approach, seemingly accompanied by high rates of complications. The goal of this interdisciplinary project was to introduce PICCs in an academic hospital embedded in a surveillance program for infectious and non-infectious outcomes.

Methods
We prospectively collected data for this surveillance study from all patients who underwent PICC insertion starting January 1, 2014 and had the catheter removed by December 31, 2015 at our 950-bed academic hospital (Bern University Hospital, Switzerland). Infectious complications were defined according to CDC/NHSN criteria. PICCs were restricted to oncology and infectious disease patients and were followed irrespective of the management setting (inpatient, outpatient or intermittently hospitalized after insertion). An interdisciplinary team reviewed the outcomes on a routine basis.

Results
One hundred thirty-five PICCs were inserted in 124 patients, the majority being oncology patients (n=107, 86.3%). Indications for PICC insertions included: chemotherapy (n=97, 71.9%), antibiotic therapy (n=24, 17.8%), total parenteral nutrition (n=8, 5.9%), blood product transfusion (n=4, 3.0%) and palliative care (n=2, 1.5%). During a total of 10'402 catheter-days (median dwell time 62 days), five CLABSI (including one mucosal barrier injury laboratory-confirmed bloodstream infection, MBI-LCBI) and two exit-site infections occurred, yielding an incidence rate of 0.48 and 0.19 infections per 1000 catheter-days, respectively. Incidence rates were 0.67/1000 catheter-days (n=7) for radiologically documented deep venous thrombosis, 0.96 (n=10) for tip dislocation, and 0.67 (n=7) for catheter occlusion. Seventeen catheters (12.6%) were removed because of a complication.

Conclusion
We successfully introduced PICCs in an academic hospital by implementing a systematic surveillance program for complications. Both infectious and non-infectious complications were rare. Infection prevention specialists should be actively involved during the introduction of new intravascular devices in order to provide quality indicators and assure patient safety.

Abstracts of the posters

P01 | Prospective, randomized comparison of one- versus two-stage bursectomy for moderate to severe septic bursitis

I Uçkay [1], E von Dach [1], BA Lipsky [1], D Lew [1]

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Aim
The optimal surgical approach for patients hospitalized for moderate to severe septic bursitis is not known, and there have been no randomized trials of one-stage compared with two-stage (bursectomy, followed by closure in a second procedure) approach. Thus, we performed a prospective, non-blinded, randomized study of adult patients hospitalized for an open bursectomy.

Methods
Patients were randomized 1:1 to a one-stage vs. a two-stage surgical approach. All patients received postsurgical oral antibiotic therapy for 7 days. These are the final results of the prospective study registered at ClinicalTrials (NCT01406652).

Results
Among 164 enrolled patients, 130 had bursitis of the elbow and 34 of the patella. The surgical approach used was one-stage in79and two-stage in85. The two groups were balanced with regards to sex, age, causative pathogens, levels of serum inflammatory markers, co-morbidities, and cause of bursitis. Overall, there were22 treatment failures: 8/79(10%) in the one-stage arm and 14/85 (16%) in the two-stage arm (Pearson-χ2-test; p=0.23). Recurrent infection was caused by the same pathogen a total of 7 patients (4%), and by a different pathogen in 5 episodes (3%). The incidence of infection recurrence was not significantly different between those in the one- vs. two-stage arms (6/79 vs. 8/85; χ2-test: p=0.68). In contrast, outcomes were better in the one- vs. two-stage arms for wound dehiscence (2/79 [3%] vs. 10/85[12%]; p=0.02), median length of hospital stay (4.5 vs. 6 days), nurses' workload (605 vs. 1055 points) and total costs (6881 vs. 11,178 Swiss francs) (all p<0.01).

Conclusions
For adult patients with moderate to severe septic bursitis requiring hospital admission, bursectomy with primary closure, together with 7 days of systemic antibiotic therapy, was safe, resource-saving and effective. Using a two-stage approach did not reduce the risk of infectious recurrence, and may be associated with a higher rate of wound dehiscence than the one-stage approach.

P02 | Should native septic joint arthritis be considered as immediate emergency?

I Uçkay [1], N Lauper [1], BA Lipsky [1], D Lew [1]

[1] Hôpitaux Universitaires Genève, Geneva, Switzerland

Aim
Acute native joint septic arthritis is generally considered an emergency, requiring immediate drainage within hours, often during night shifts. However, there are few data supporting the need for this degree of urgency.

Methods
We performed a retrospective review of adult patients seen in our medical center from 1997-2015 with culture-proven arthritis, specifically examining the epidemiology of sequelae, and the association of these sequelae with the surgical delay.

Results
Of 204 septic arthritis episodes, 46 (23%) involved interdigital hand and foot joints. The large joints included the knee (n=67), shoulder (48), hip (22), ankle (8), acromio-clavicular (5), elbow (4), wrist (3), and sterno-clavicular (1) regions. All patients underwent surgical drainage and received targeted systemic antibiotic therapy. Sequelae of varying severity occurred in 83 patients (41%): recurrences (n=15); secondary arthrosis (30); pain (9), Girdlestone procedure (9); arthrodesis (9); amputation (8); stiffness (8); and, algodystrophia (2). By multivariate Cox regression analysis the following factors did not predict sequeleae: age; treatment with corticosteroids; pre-existing clinical or radiological arthropathy; total duration of antibiotic therapy; location or type of joint; and, the number of surgical interventions. Similarly, there was no influence on sequelae of the number of days of pre-hospitalization arthritis symptoms (odds ratio 1.0, 95% confidence interval 1.0-1.0) and the hours spent in the emergency room (OR 1.0, 0.9-1.2). Specifically, joint lavage done within 6 hours of presentation yielded the same functional outcome as lavage done between 6-12 hours, 12-24 hours, or >24 hours.

Conclusions
Our data suggest that in the absence of clinical sepsis, immediate joint drainage does not reduce the risk of sequelae in patients with septic arthritis.

P04 | Longer Term Safety of Tenofovir Alafenamide in Renal Impairment

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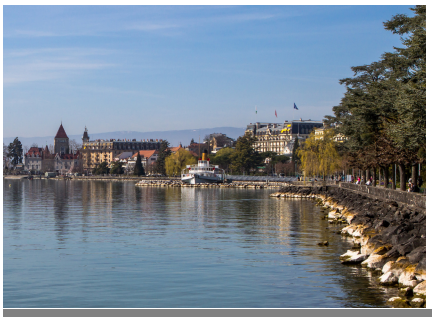
Background
Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that results in 91% lower plasma TFV levels compared to tenofovir disoproxil fumarate (TDF). Switch to a once-daily single-tablet regimen of elvitegravir, cobicistat, emtricitabine, and TAF (E/C/F/TAF) in HIV-1 infected patients with eGFRCG (Cockcroft-Gault) 30 to 69 mL/min was shown to be effective and safe through 48 weeks. Here, we report Week 96 results.

Methods
Virologically-suppressed adults with stable eGFRCG of 30 to 69 mL/min had their treatment switched to open-label E/C/F/TAF. The primary endpoint was the change from baseline in glomerular filtration rate estimated using various formulas at 24 weeks. Week 96 efficacy and safety data are described, including tests of renal function and bone mineral density (BMD).

Results
Of 242 subjects enrolled, mean age was 58 years (range: 24 – 82), 18% Black, 39% hypertension, 14% diabetes, and 65% were taking TDF-containing regimens prior to switch. Through Week 96, no change in median eGFRCG was observed. Five patients (2.0%) with baseline eGFR <50 mL/min discontinued study drug for decreased creatinine clearance, none had evidence of proximal renal tubulopathy and all had comorbidities. Subjects who received TDF at baseline had significant improvements in eGFRCKD-EPI cysC, as well as proteinuria, albuminuria, and tubular proteinuria to levels seen with non-TDF regimens (Figure 1). For subjects who received TDF at baseline, both hip and spine BMD increased significantly (mean % changes from baseline +2.22 and +2.83, respectively, $p<0.001$), and for subjects not receiving TDF at baseline, hip but not spine BMD increased significantly (mean % changes from baseline +1.08, $p=0.039$, and +0.59, $p=0.094$, respectively). 88% maintained HIV-1 RNA <50 copies/mL based on Missing = Failure analysis.

Conclusions
Through 96 weeks, switch to E/C/F/TAF was associated with no change in eGFRCG. Proteinuria, albuminuria and BMD significantly improved. These data support the efficacy and safety of once daily E/C/F/TAF in HIV+ patients with eGFR 30-69 mL/min without dose adjustment.



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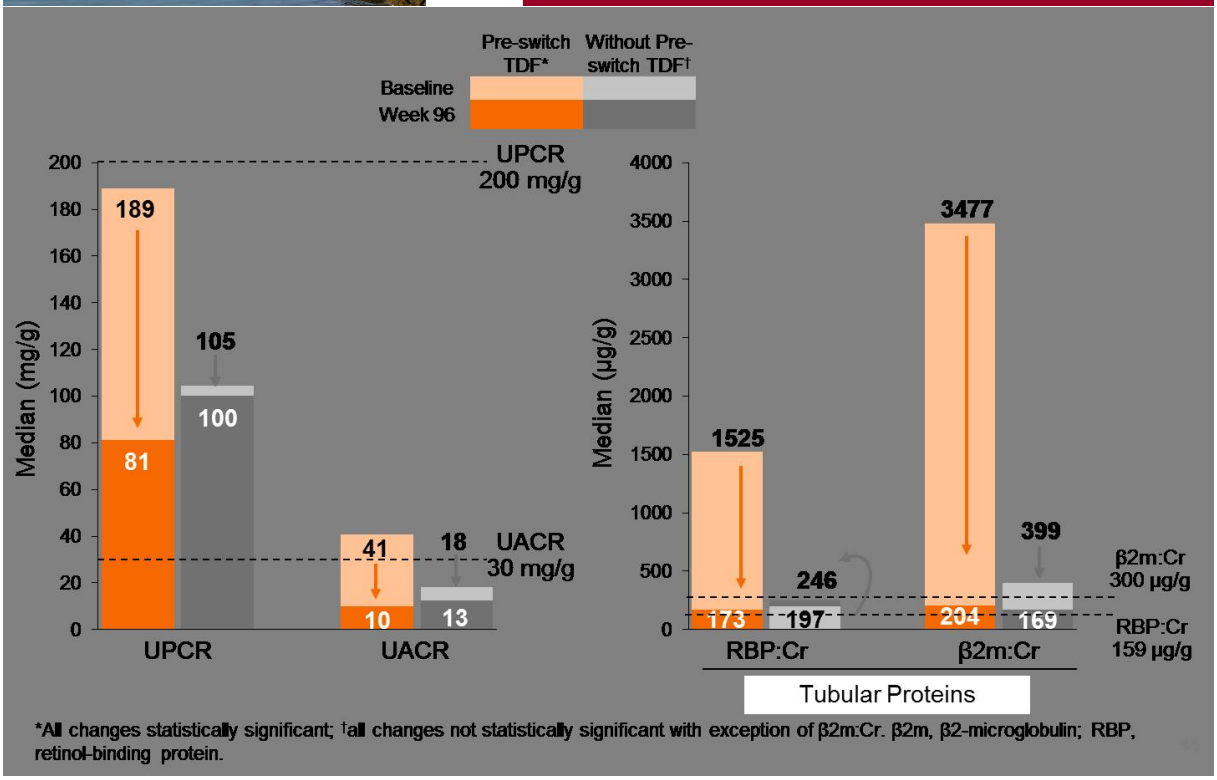

*All changes statistically significant; †all changes not statistically significant with exception of β2m:Cr. β2m, β2-microglobulin; RBP, retinol-binding protein.

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P05 | AIDS defining opportunistic infections (ADOIs) at unusually high CD4 counts below 500/µl: Is HIV the only problem? A chart review of the Swiss HIV Cohort Study (SHCS)

V Gisler [1], M Simsek [1], J Nemeth [2], T Doco Lecompte [3], L Merz [4], M Stöckle [5], P Schmid [6], E Bernasconi [7], C Fux [8], R Weber [2], A Calmy [3], M Cavassini [4], H Furrer [1]

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Background
AIDS defining opportunistic infections (ADOIs), a commonly used endpoint in studies, occur typically, but not exclusively below an ADOI specific CD4 cell threshold. In the Swiss HIV Cohort Study (SHCS), a preceding analysis of ADOIs occurring at CD4 counts above 500/µl showed that these ADOIs were mainly caused by immunodeficiencies in addition to chronic HIV-infection itself (Gisler V et al, J Int AIDS Soc 2014;17). We evaluated whether, this is also true for ADOIs at relatively high CD4 counts below 500/µl.

Methods
Excluding tuberculosis and recurrent bacterial pneumonia, we conducted a chart review of 94 cases of ADOIs in the SHCS, which had occurred at CD4 counts less than 500 µl/l, but above the upper adjacent value in classical box-plot CD4 cell distribution (75. percentile plus 3/2 interquartile range). We assessed whether i) the ADOI fulfilled the SHCS diagnostic criteria and whether ii) HIV-infection was the only ADOI causing condition using predefined etiological categories.

Results
see uploaded graph (word-document)

Conclusion
More than half of the ADOIs occurring at relatively high CD4 counts below 500/µl are caused by the HIV-infection itself (42.6%) or by unmasking IRIS (12.8%). Nevertheless, a substantial part of ADOIs not fulfilling diagnostic criteria (13.8%) or caused by other immunodeficiencies (21.3%) - especially candida-esophagitis - should prompt caution, if ADOIs are used as study endpoints.

Results / Table: *Cases of ADOIs occurring in patients with CD4 counts <500/µl, but above the upper adjacent value in the classical box-plot CD4 cell distribution. For each case of 10 different ADOIs, the most likely explanation is given after an in depth chart review using predefined etiologic categories. Chronic HIV infection is the most likely explanation in the biggest part of cases.*

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			Reason for ADOIs					
ADOI	*Lower CD4-threshold*	*Total*	*Chronic HIV-infection*	*Unmasking IRIS*	*HIV-primo-Infection*	*Other immuno-deficiency*	*Unstable CD4 cells*	*Wrong ADOI diagnosis*
Candida-Esophagitis	350/µl	37 (39.4%)	16		2	18		1
Chronic mucocutanous HSV-infection	250/µl	11 (11.7%)	4			1		6
CMV-disease other than retinitis	200/µl	10 (10.6%)	3	3			2	2
PCP	250/µl	8 (8.5%)	7	1				
Disseminated MAC-disease	100/µl	8 (8.5%)	1	5			1	1
Cryptosporidiosis	200/µl	6 (6.4%)	3					3
PML	250/µl	5 (5.3%)	3				2	
Toxoplasma-encephalitis	200/µl	4 (4.3%)	2				2	
CMV-retinitis	150/µl	4 (4.3%)	1	2		1		
Cryptococcal meningitis	150/µl	1 (1.1%)		1				
Total		94 (100%)	40 (42.6%)	12 (12.8%)	2 (2.1%)	20 (21.3%)	7 (7.4%)	13 (13.8%)

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P06 | An emerging infection: Infective endocarditis after Transcatheter Aortic Valve Implantation (TAVI): A case series

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Background
TAVI is increasingly used to treat aortic valve stenosis in elderly and polymorbid patients not qualifying for valve surgery. In parallel, infective endocarditis associated with TAVI (TAVIE) is emerging, a so far not well described complication. From 11/15 to 04/16 we observed a cluster of four TAVIE cases. We describe clinical presentation and management.

Methods
An 84-year old woman presented with left heart failure and prosthetic hip pain three weeks after TAVI. Hip arthrocentesis and blood cultures (BC) grew Enterococcus faecium. Transesophageal echocardiography (TEE) showed no abscess or vegetation. High-dose i.v. daptomycin (10mg/kg) was initiated due to amoxicillin and high-level gentamicin resistance. The prosthetic hip was debrided and retained. After 16 days BC were still positive, cardiac surgery formally indicated, but denied by the patient. She died. A 91-year old man presented with fever and weakness four weeks after TAVI and pacemaker implantation. BC continuously grew E. faecalis. TEE showed no vegetation or abscess. Due to the patient's wish and age a conservative therapy with i.v. amoxicillin and ceftriaxone (no gentamicin due to eGFR <30ml/min) for six weeks is ongoing. Three months after TAVI, a 77-year old man needed a post-dilatation due to severe paravalvular insufficiency. Two months later he presented with fever and multilevel spondylodiscitis. BC grew oxacillin-resistant Staphylococcus epidermidis and TEE showed a paraprosthetic abscess with fistula to the left atrium. I.v. vancomycin and gentamicin were initiated and biological aortic and mitral valve replacement and patch reconstruction performed. Postoperatively i.v. vancomycin and oral rifampin were administered for 6 weeks. The patient cured. An 81-year old woman presented with weakness one month after a dental intervention and 42 months after TAVI. BC grew Streptococcus oralis (penicillin MIC 0.03mg/l). TEE showed an aortic ring abscess. I.v. penicillin was started and TAVI replaced by a biological valve. Postoperatively i.v. penicillin was continued for six weeks. The patient cured.

Conclusions
TAVIE is a life threatening complication in the elderly. Local valve complications are frequent and the need for surgical treatment is high. Possibly due to groin catheterization enterococci seem to play a relevant role, reason why amoxicillin/clavulanic acid should be considered as antimicrobial prophylaxis rather than s a first or second generation cephalosporin.

P08 | First case of Legionella cincinnatiensis septic arthritis – case report and review of the literature.

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Background
Legionella spp. are a common cause of community-acquired pneumonia. Extrapulmonary manifestations are rare. L. cincinnatiensis has only been implicated in half a dozen cases worldwide. We herein describe the first case of L. cincinnatiensis septic arthritis in a 90-year old lady and review previous cases of septic arthritis caused by other Legionella spp.

Material/methods
Broad-range bacterial PCR and sequencing targeting the 16S rRNA gene was performed when routine cultures were negative. Colonies grown on Legionella selective media were identified as L. cincinnatiensis using DNA sequencing of the macrophage infectivity potentiator (mip) gene.

Results
A 90-year old lady with a past medical history of mild chronic renal failure presented to our hospital with a three-week history of left wrist pain, which was not relieved by three intraarticular corticosteroid injections administered for presumed chondrocalcinosis. Physical examination on admission was consistent with left septic wrist arthritis and an ulnar subcutaneous abscess. After immediate surgical incision of the abscess combined with open joint lavage antibiotic treatment with amoxicillin/clavulanic acid was administered. Two days later a second surgical intervention was necessary. Abundant gram-negative bacilli were observed on gram stain of intraoperative specimens, whereas routine culture was negative. However, broad-range bacterial PCR was positive for L. cincinnatiensis/ longbeachae. Finally, bacteria growing from the subcutaneous abscess on selective media were identified as L. cincinnatiensis. Antibiotic treatment was switched to azithromycin for a total duration of three weeks. Six weeks later, the patient had fully recovered. She denied any recent travel, gardening, swimming or respiratory symptoms prior to pain onset. We speculate that the Legionella infection might have been caused by inoculation during previous repetitive joint injections. Previously, seven cases of septic arthritis with Legionella spp. other than cincinnatiensis have been published with the majority of patients being immunosuppressed.

Conclusions
To our knowledge, this is the first case of L. cincinnatiensis septic arthritis. Our case illustrates the need for a high index of suspicion of infection with unusual/fastidious organisms when symptoms are suggestive of septic arthritis in patients who do not respond to standard treatment.

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P09 | A randomized, double-blind comparison of tenofovir alafenamide vs tenofovir disoproxil fumarate, each co-formulated with elvitegravir, cobicistat, and emtricitabine (E/C/F) for initial HIV-1 treatment: week 96 results

J Fehr [1], HJ Furrer [2], M Cavassini [3], D Wohl [4], S Oka [5], N Clumeck [6], A. Clarke [7], M Das [8], H Rovini [9], M Fordyce [8]

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Objectives
Two international, randomized, double blinded, phase 3 trials in distinct regions directly compared tenofovir alafenamide (TAF) vs tenofovir disoproxil fumarate (TDF), each co formulated with elvitegravir/cobicistat/emtricitabine (E/C/F). At Week 48, E/C/F/TAF met the primary objective of non inferior efficacy with improved renal and bone secondary safety endpoints compared to E/C/F/TDF. We describe longer term follow up of efficacy, safety, and tolerability endpoints through Week 96.

Methods
Antiretroviral therapy (ART) naïve participants were randomized 1:1 to receive E/C/F/TAF (TAF) or E/C/F/TDF (TDF). Week 96 viral suppression (HIV 1 RNA < 50 c/mL) by FDA snapshot analysis, pre defined bone and renal safety, and tolerability endpoints are reported.

Results
1,733 subjects were randomized and treated: 15% women, 43% non white, 23% HIV-1 RNA>100,000 c/mL. Median baseline characteristics: age 34 years, CD4 count 405 cells/µL, and HIV-1 RNA 4.58 log10c/mL. At week 96 virologic suppression (HIV 1 RNA < 50 c/mL) was 86.6% (TAF) and 85.2% (TDF), (difference 1.5%; 95%CI [1.8, 4.8%], p=0.36). Viral outcomes did not vary by age, sex, race, geography, or baseline CD4/HIV-1 RNA. Mean [SD]% decrease in BMD was significantly less in the TAF group for both lumbar spine (0.96 [3.72] vs 2.79 [3.92], p< 0.001) and total hip 0.67 (3.89) vs 3.28 (3.97), p< 0.001. As shown in Table 1, renal safety endpoints favored TAF. There were greater increases in lipids in the TAF arm vs TDF but no difference in rate of initiation of lipid-modifying agents (TAF: 3.8% vs TDF: 4.4%). There were no cases of renal tubulopathy in the TAF arm vs 2 on TDF, including 1 that led to discontinuation.

Conclusion
Through Week 96, rates of virologic suppression were high and similarly maintained in both the TAF and TDF groups. E/C/F/TAF continued to have a statistically superior bone and renal safety profile compared to E/C/F/TDF. These longer term data support the use of E/C/F/TAF as a safe, well tolerated, and durable regimen for initial and ongoing HIV 1 treatment.

Table 1: Renal Safety Endpoints

Median (Q1,Q3) Percent Change from Baseline (unless otherwise noted)	E/C/F/TAF	E/C/F/TDF	Significancee
eGFR Cockcroft Gault (mL/min) (change from baseline)	-2.0 (- 12.4, 9.4)	-7.5 (- 17.4, 2.9)	p <.0001
Urine Protein/Cr	-9.1 (- 39.6,36.0)	16.2 (-22.5, 81.5)	p <.0001
Urine Albumin/Cr	-5.2 (-35.7, 30.1)	4.9 (-32.7, 60.0)	p <.0001
β- 2 Microglobulin/Cr	- 32.1 (-61.0, 4.2)	33.5 (-27.8 , 230.7)	p <.0001
Retinol Binding Protein/Cr	13.8 (-18.8, 66.1)	74.2 (10.4, 192.3)	p <.0001

P10 | Immunglobulin attenuate streptokinase-mediated virulence in necrotizing fasciitis by Streptococcus disgalactiae subspecies equisimilis

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[1] Universitätsspital Zürich, Zürich, Switzerland

Streptococcus dysgalactiae subsp. equisimilis (SDSE or Group C and G Streptococcus) causes a wide spectrum of human diseases ranging from superficial to invasive infections, particularly in patients with underlying chronic disease or immunodeficiency. Invasive streptococcal infections such as necrotizing fasciitis (NF) have predominantly been associated with group A Streptococcus (GAS or S. pyogenes or), however recent studies show SDSE as an emerging cause of serious disease, making improved understanding of SDSE virulence essential. We observed a fulminant case of NF caused by SDSE. Virulence factors expression profiling revealed striking differences between this clinical SDSE NF-isolate and a well characterised clinical GAS NF-isolate (GAS M1T1 5448), despite the similarities of clinical manifestations. The SDSE NF-isolate produced extremely high levels of streptokinase, mediating fibrinolysis and therefore important for bacterial escape from the site of infection; the patient lacked of streptokinase-blocking antibodies. Passive immunotherapy with exogenous commercial pooled human intravenous immunoglobulin (Ex-IgGs) efficiently blocked streptokinase-mediated fibrinolysis caused by bacterial supernatants in human blood ex vivo. Confirming an important role of streptokinase in SDSE virulence, we found that a streptokinase-deficient mutant of the clinical isolate lost virulence in a murine NF-model. Likewise, clinical severity in the murine NF-model was equally attenuated by administration of Ex-IgGs. In conclusion our data support a major role of streptokinase in SDSE-associated invasive infection, linking susceptibility to lack of endogenous streptokinase-blocking antibodies and providing a rationale for Ex-IgGs therapy as a potentially useful adjunction to antibiotics.

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P11 | Pharmacokinetic-pharmacodynamic (PK-PD) of emtricitabine/tenofovir alafenamide (F/TAF) demonstrated wide exposure range associated with clinical safety

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Background
Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that has been co-formulated with emtricitabine (F) into a fixed-dose combination tablet (F/TAF) as an N(t)RTI backbone. We conducted a randomized, double-blind, active-controlled study in virologically-suppressed HIV-1 infected patients receiving tenofovir disoproxil fumarate (TDF)-containing regimens to evaluate the efficacy and safety of switching from F/TDF to F/TAF vs continuing F/TDF while remaining on the same third agent. Study drugs were taken without regard to food.

Methods
Patients were randomized 1:1 to switch to F/TAF or continue F/TDF while remaining on the same third agent. The TAF and TFV PK area under the curve over dosing interval (AUCtau) and maximum concentration (Cmax) were estimated via population PK analysis. The safety endpoints for PK-PD analysis were selected: gastrointestinal (GI) adverse event (diarrhea, nausea, vomiting, abdominal pain), change in hip and spine bone mineral density (BMD), and change in selected lipid parameters. Subjects were grouped into quartile subgroups based on TAF and TFV exposures for evaluation of exposure-safety trends.

Results
663 patients were randomized and treated (F/TAF 333 vs F/TDF 330). Drug-related serious adverse events were rare (0 vs 0.3%). Drug discontinuation due to adverse events (AEs) was low (2.1% vs 0.9%). In F/TAF-treated patients, TAF and TFV PK exposures were available for 292 and 328 subjects, respectively. No trends in GI AEs were observed across wide range of TAF exposures (Table 1). Similarly, no trends with TFV exposures were noted. The changes in BMD (hip and spine) and fasting lipids at Week 48 were comparable across TAF and TFV exposure quartiles, with no trends noted.

Conclusions
These data demonstrate that TAF is well tolerated with no trends of safety signal across wide ranges of TAF exposures in virologically suppressed HIV-1 infected patients.

Table 1

Quartile range of TAF AUC_{tau} (ng*h/mL)	**1Q (30.3 to 87.6)**	**2Q (87.6 to 129.5)**	**3Q (129.8 to 173.1)**	**4Q (173.8 to 466.7)**
Diarrhea	13.7%	8.2%	9.6%	4.1%
Nausea	6.8%	2.7%	6.8%	1.4%
Vomiting	4.1%	1.4%	4.1%	4.1%
GI and abdominal pain	6.8%	1.4%	0%	6.8%
Hip BMD % change, mean (SD)	1.14 % (2.323)	1.38% (3.055)	1.31% (2.283)	0.81% (3.196)
Spine BMD % change, mean (SD)	1.28 % (3.398)	1.56% (2.994)	2.00% (3.113)	1.34% (3.319)
Change in total cholesterol, mean (SD)	11.9 mg/dL (38.35)	13.7 mg/dL (34.43)	12.6 mg/dL (27.89)	12.0 mg/dL (29.28)

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P13 | Patient satisfaction in an outpatient parenteral antimicrobial therapy (OPAT) unit practising predominantly self-administration of antibiotics with elastomeric pumps

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Background
Outpatient parenteral antibiotic therapy (OPAT) by self-administration has several advantages. It leaves more autonomy to the patient, discharge from hospital can be more easily organized and treatment costs are lower. Self-administration of antibiotics using elastomeric pumps has become the most frequently used treatment modality at the OPAT unit of the University Hospital of Lausanne. Questions remain however how comfortable patients feel using this mode of treatment.

Methods
A questionnaire was proposed to all patients treated at the OPAT unit between June 2014 and December 2015. The questionnaire included 14 multiple choice questions and 7 open questions.

Results
The questionnaire was distributed to 188 patients and 109 questionnaires were returned. Mean age of the responders was 58 years, 71 patients (65%) were men. 69 patients (63%) were treated by self-administration, 21 patients (19%) attended the OPAT unit on a daily basis, and 19 patients (17%) received their antibiotics by home health care nurses. Elastomeric pumps were used for 81 patients (74%). A non-significantly larger proportion of patients treated by home health care nurses (63%) said to have had no fear before starting treatment than patients treated at the OPAT unit (33%, $p = 0.059$) or patients treated by self-administration (42%, $p = 0.10$). 15 patients (22%) treated by self-administration feared to have problems manipulating the elastomeric pumps. In the end overall satisfaction of the patients was very high with 87% giving the highest rating to this multiple choice question. Highest ssatisfaction was more frequent in patients self-administering antibiotics using elastomeric pumps than in patients treated at the OPAT unit (93% vs 76%, $p = 0.025$) and patients treated by home health care nurses (93% vs 79%, $p = 0.020$). Patients self-administering antibiotics attributed particularly high scores to the professionalism of the nurses and doctors and the explanations received.

Conclusions
Satisfaction was high in all patients treated by OPAT. Patients treated by self-administration using elastomeric pumps responded with even higher scores to several questions than the patients treated at the OPAT unit or by home health care nurses. This shows that some patients are eager to take over responsibility of their treatment. Patients' capacity to appropriate themselves the responsibility of care should not be underestimated by the health professionals.

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P14 | Hepatitis C and the Risk of Non-Liver-Related Morbidity and Mortality in HIV+ Persons

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Background
HCV infection has been associated with increased non-liver-related morbidity and mortality; however studies have yielded inconsistent results.

Methods
The incidence of clinical events in four HCV-seropositive groups (untreated spontaneously cleared/detectable HCV-RNA, treated with/without sustained virologic response (SVR)) and matched HCV-seronegative Swiss HIV Cohort Study (SHCS) participants from 08/1994 to 12/2014 were studied. We compared HCV-seropositive to HCV–seronegative patients and aviremic to replicating HCV infection. Poisson regression was used to assess differences across these groups (see footnote in Figure).

Results
We included 2503 HCV-seropositive individuals, 540 with cleared HCV infection, 1294 untreated viremic, 345 treated with SVR, 281 treated without SVR, and 2503 HCV-seronegative controls. After a mean follow-up of 8.2 years, we observed 107/18 (HCV-seropositive/HCV-seronegative) liver events, 41/14 kidney diseases, 230/121 osteoporosis/fracture, 114/129 cardiovascular events, 162/126 HIV CDC B/C events, 106/10 liver-related deaths and 227/218 non-liver-related deaths. Adjusted incidence rate ratios for the HCV-negative and different HCV-seropositive groups are shown in the Figure. Compared to HIV-monoinfected controls, HCV-seropositive groups combined had an increased risk of liver disease (IRR 6.29 [95% CI 3.52-11.22]), liver-related death (8.24 [3.61-18.83]), kidney events (2.43 [1.11-5.33]) and osteoporosis/fracture (1.43 [1.03-2.01]). No evidence for an association with increased risk was found for cardiovascular diseases, HIV CDC B/C events and non-liver-related death. Among HCV-seropositive individuals, those with replicating HCV infection had an increased risk of liver-related events compared to aviremic participants (untreated viremic vs cleared 2.84 [1.36-5.89]; non-SVR vs SVR 6.74 [1.36-5.89]) and liver-related death (untreated viremic vs cleared 2.10 [0.99-4.47]; non-SVR vs SVR 3.36 [1.37-8.21]). Non-liver-related diseases and death did not significantly differ between HCV viremic vs aviremic patients.

Conclusion
While incidence for non liver-related death and cardiovascular events was not elevated, HCV exposure was associated with an increased risk of kidney disease and osteoporosis. This risk did not seem to be dependent of persistent HCV replication.

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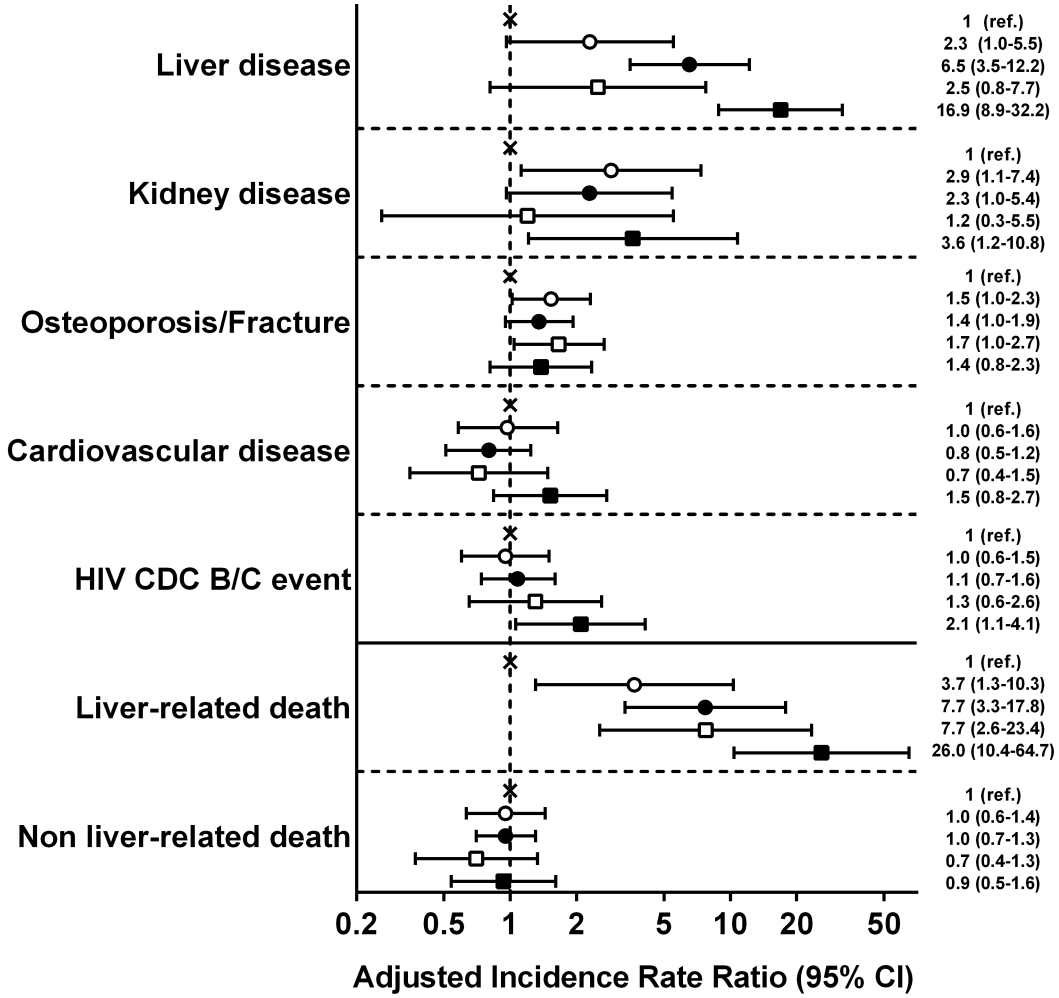

Nested case-control design within the Swiss HIV Cohort Study. Results from Poisson regression of incidence-density-matched HCV seropositve and -negative pairs adjusted for HIV transmission category, age, HIV-1 RNA, smoking, alcohol use, active injection drug use, duration of HIV and HCV-infection.

- × HCV seronegative

HCV seropositive:

- ○ No Tx, HCV-RNA neg.
- ● No Tx, HCV-RNA pos.
- □ Tx, SVR
- ■ Tx, no SVR

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P15 | Tenofovir alafenamide in HIV-infected patients with TDF-associated renal toxicity: A single centre experience

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Introduction
Tenofovir disoproxil fumarate (TDF) use is associated with the development of renal toxicity and loss in bone mineral density. Tenofovir alafenamide (TAF) is a new prodrug with lower renal and bone toxicity. We aimed to assess virological efficacy and renal safety of TAF plus emtricitabine (F/TAF) in patients with previous contraindications to TDF.

Methods
Single-center, retrospective analysis of SHCS participants who started F/TAF in the framework of a compassionate use program. Laboratory assessments included HIV and hepatitis B [HBV] (where applicable) viral loads [VL], renal function (inorganic phosphate [Pi] and creatinine [C] in serum and urine, urinary protein to creatinine ratio [UPCR]) and bone mineral density (BMD).

Results
F/TAF was started in 7 patients since January 2015 because of TDF-related Fanconi-syndrome (n= 2) or proximal renal tubulopathy (n= 5). Two patients had osteoporosis, two osteopenia. Alternative antiretroviral therapy (ART) could not be prescribed because of acquired drug resistance (n=3), HBV coinfection (n=2), previous side effects or HLA-B*5701 positivity (n=4). At baseline, all patients had a suppressed HIV-VL, median CD4 T cell count was 582/ l (range 85-1056/ l). Third agents were PI (n=1), NNRTI (n=1) and INSTI (n=2), or combined regimens (n=3). Median estimated glomerular filtration rate (eGFR) at baseline was 58 ml/min (range 30-80 ml/min), median Pi-excretion fraction (FE-Pi) was 26% (range 15-51%), median UPCR was 59mg/mmol (range 0- 91mg/mmol). Follow-up data was available for 5 patients; median follow-up time was 1.3 months (range 0.9-9.27 months). There were no adverse events attributed to F/TAF therapy. All patients maintained HIV-VL suppression during follow-up. HBV replication remained undetectable in one patient (prior treatment with entecavir); in another patient without previous HBV-active ART HBV VL decreased from 9.39 log to 3.07 log at last follow up visit. At last contact, the median change in eGFR was 2ml/min (range 0-30ml/min), change in UPCR was -32.5mg/mmol (range -18 to -47mg/mmol) and FE-Pi 0% (range -9-+5%).

Conclusion
In patients with previous contraindications to TDF, F/TAF was well tolerated with improvement of renal tubulopathy and stable glomerular function. F/TAF is a valuable alternative antiviral drug, particularly in HIV-infected patients with limited treatment options due to renal toxicity, osteoporosis and/or co-infection with HBV.

P17 | Highly sensitive droplet digital PCR to quantify the HIV-1 latent reservoir

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The latent reservoir of the human immunodeficiency virus type 1 (HIV-1) is the major hurdle in curing HIV-1. It is established early after infection and maintained by the integration of viral DNA that mostly stays transcriptionally silent in long-lived cells on antiretroviral therapy (ART). The measurement of the HIV-1 latent reservoir in human peripheral blood mononuclear cells (PBMCs) in patients on ART is challenging, since the reservoir is relatively small. We developed a highly sensitive assay for the measurement of total intracellular HIV-1 DNA based on the RainDrop digital PCR system, which allows absolute quantification of genomic DNA by separating one sample into a large number of picoliter-sized droplets and carrying out a PCR reaction within each droplet. We established and validated a multiplex PCR protocol by measuring HIV-1 pol in a highly conserved region and CCR5, a single copy gene to determine the input cell number. The optimization procedures included comparisons of different DNA extraction protocols, PCR conditions, primer and fluorescent probes design variations. Finally, we achieved a very sensitive limit of detection of 20 HIV-1 DNA copies per 106 million genomic equivalents for the evaluation of 3 µg DNA per reaction (~450,000 cells). Furthermore, in comparison with a well established qPCR HIV-1 DNA assay the droplet digital PCR assay shows similar accuracy and higher sensitivity. Thus, droplet digital PCR is an attractive tool to measure HIV-1 DNA with high sensitivity that will improve monitoring of patients on ART.

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P18 | Infectious Complications after Transplantation from Donors with Circulatory Determination of Death – a Case-Control Study

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Background
Since re-introduction of donation after circulatory determination of death (DCD) in 2011, a total of 47 Maastricht III donors were recruited at our institution. To date little is known on the incidence of infectious disease (ID) after DCD transplantation. ID events were compared between patients with organs from DCD donors and DBD donors (Donation after Brain determination of Death).

Methods
A case-control design matched a case DCD patient with two control DBD patients transplanted with the same organ immediately before and after the case patient. The goal of a 1:4 case-control matching could not be achieved for all patients, due to overlapping patients. ID events were systematically collected during the first year after transplant. Follow-up observation time was one year. Organs allocated to other centers were not considered.

Results
32 cases were matched to 89 controls (kidney (N=20), liver (N=8) lung (N=4). Incidence of proven bacterial infections (PI) (HR 2.0, 95% CI 1.3-3.2, p=0.003) was higher in recipients of a DCD organ. This difference was driven by the kidney group (2.4, 1.4-4.2, p=0.003). For lung and liver, the limited case numbers only allowed to observe a trend toward significance. Dominant pathogens were E. coli (27.9% of PI) for kidney recipients and Enterococcus spp. for liver (36.3% of all PI) as well as lung (15.3% of all PI) transplant recipients. Main sites of infection were the urinary tract in kidney (80.2%), bacteremia and liver infections (each 24%) in liver and respiratory tract infections (48.7%) in lung recipients. No difference was observed for neither viral nor fungal infections. One-year graft function did not differ between cases and controls.

Conclusions
Causes for the higher incidence of bacterial ID events remain to be determined, but did not affect graft function or mortality at one year. Potential causes could be the higher rate of delayed graft function after DCD kidney transplantation, or the warm ischemia time of the donor predisposing for bacterial colonization of the graft.

P20 | Antibiotics for Preventing Recurrent Urinary Tract Infection: A Meta-Analysis

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Background
The scientific literature on randomized controlled trials (RCT) for antibiotic prophylaxis of recurrent urinary tract infections (RUTI) has not been screened systematically in more than 10 years.

Methods
We used the search terms “recurrent”, “UTI”, “prophylaxis”, “antibiotic”, and “RCT” among others. We screened MEDLINE, EMBASE, the Cochrane Library, clinicaltrials.gov and reference lists of retrieved articles. We considered any published RCT in adults where antibiotics were used as RUTI prophylaxis. From the selected articles we extracted data on RUTI episodes in both comparators (antibiotic vs. antibiotic or placebo). For statistical analyses, we used the random effects model and expressed the results as risk ratios (RR) with 95% confidence intervals (CI).

Results
We included 23 RCTs in this meta-analysis. Summarizing the 11 placebo-controlled (PC) studies, the risk ratio for developing UTI was 0.15 (95% CI 0.08 – 0.29); the corresponding overall risk reduction was 55% (NNT 1.81, 95% CI 1.67-2.17). After 2004, a single RCT, comparing fosfomycin to placebo, was conducted and revealed an absolute UTI risk reduction of 68% (NNT 1.54). The 5 RCTs that remained after excluding cinoxacin (n=6), an obsolete antibiotic, showed similar results (risk reduction 61%, NNT 1.64, RR 0.11 (0.07-0.17)]. For PC studies, overall study quality was low and the funnel plot indicated potential publication bias. In the nine head-to-head trials of different prophylactic antibiotics, nitrofurantoin was the single most common comparator [to norfloxacin (3 studies), cefaclor (1) or trimethoprim (TMP) / sulfamethoxazole and trimethoprim combination (SMZ / TMP) (3)]; there was no significant treatment difference [RR 1.01 (0.74-1.37)]. Four studies compared trimethoprim (± sulfamethoxazole) to other antibiotics [RR 1.34 (0.89-2.03)] and three compared norfloxacin to others [RR 0.86 (0.43-1.70)]. One RCT compared continuous versus post-coital ciprofloxacin and found no difference either [RR 1.39 (0.24-8.07)]. Three studies compared continuous to intermittent antibiotic prophylaxis. Due to its particular design, one study could not be co-analyzed with others.

P21 | Antimicrobial activity of Lactobacillus salivarius and Lactobacillus fermentum against Staphylococcus aureus

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Recent reports increasing on the probiotic properties of lactobacilli for combating other pathogens but limited data on the antibacterial activity of Lactobacillus salivarius against Staphylococcus aureus are available. We studied the antibacterial activity of two oral lactobacilli isolates in co-culture with different strains of S. aureus using planktonic and biofilm assays, and cell-free supernatant (CFS) assays. We found that both lactobacilli strains - sequenced as L. salivarius CNU1334 and Lactobacillus fermentum CNU1969 - significantly killed S. aureus cells whereas growth of lactobacilli was not affected. Using growth killing curves and a colony biofilm assay, killing effect of L. salivarius was strong in co-culture with planktonic (100%, log 8.6 reduction) and biofilm S. aureus cells (log 6.3 reduction). In L. fermentum killing effect was only seen against planktonic cells (log 2.1 reduction). Killing of S. aureus was independent on accumulation of H2O2 but the effect significantly decreased with cell-free supernatant with pH neutralization from 100% to 34% and 29%, respectively. Additional killing effects was seen when CFS was heat-treated implicating an additional inhibition by secreted proteins. Using 2D Gel electrophoresis and MALDI-Tof/ToF MS to identify proteins with antibacterial activity we found several proteins such as a peptidoglycan binding proteins with a Lysin Motif (LysM) domain. Further studies are needed to determine if one of these secreted proteins proves his killing potency, which would have great impact in the fight against S. aureus infections.

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P22 | Implementing Antimicrobial Stewardship: One Size does not fit all

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Background
Antimicrobial Stewardship Programs (ASP) reduce antimicrobial use, costs, side effects and not at least pressure on selection of resistant bacteria. In our 700-bed tertiary hospital we have guidelines on antimicrobial use, restrictions on some antimicrobials, and an ID consultation service but beyond that not yet a formal antimicrobial stewardship program. Aim Planning to implement a hospital-wide ASP we aimed to get baseline data on the quality of antimicrobial prescriptions, the factors leading to inappropriate antimicrobial use and the adherence to our local guidelines.

Methods
On three wards (two surgical disciplines (department A and B) and one medical (department C) a senior infectious diseases physician reviewed the charts of all hospitalized patients during 6 months twice weekly. Antibiotic prescriptions were stated as appropriate or inappropriate according to our local guidelines or, in case of no existing or applicable guideline, according to infectious disease physician judgment. Recommendations were communicated in short written form.

Results
2752 charts were reviewed between November 2015 and April 2016. Prescription of antimicrobials was found in 1241 (45.1%), corresponding to 704 different patients. Antimicrobial treatment was stated inappropriate in 32.5% (Department A), 49.2% (Department B) and 26.3% (Department C). According to preliminary analysis leading cause for inappropriateness was different in the 3 clinics: In Department A it was mainly a prescription of inappropriate broad spectrum antibiotics (69,6%), in Department B it was prolonged postoperative prophylaxis or no infection at all (76.7%). In Department B most of the inappropriate antimicrobial prescriptions (73.5%) were covered by our local guidelines, while 50% of those in Department A were judged as too complex to be fitted in a guideline. While Department B and C showed no improvement during the intervention, improvement was seen in Department A.

Conclusion
We found a substantial amount of inappropriate antimicrobial prescriptions in all departments, and therefore much room for improvement. The factors leading to inappropriateness of antimicrobial use seem to be very different, therefore we think antibiotic stewardship has to be tailored to the specific requirements of each department e.g. support by ID visits in Department A and intensive teaching and insistence to apply existing guidelines in Department B.

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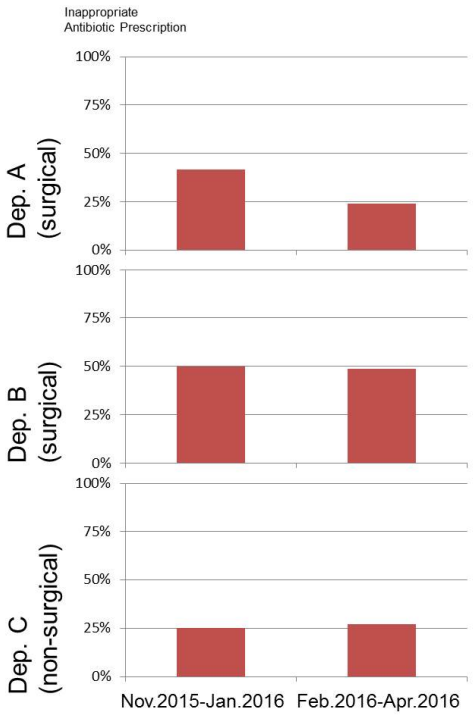

Figure: Rate of inappropriate antibiotic prescription in two surgical and one non-surgical department comparing the first three months period with the second

P23 | How long do we need to hold cultures in bone and joint infections to isolate Propionibacterium acnes?

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Background
Propionibacterium acnes is able to cause invasive infections such as osteomyelitis or implant-associated infections. To diagnose P. acnes as the causing pathogen a cultivation time up to 10-14 days is recommended, which the risk for cultivation a skin contaminant. We retrospectively analyzed whether shortening cultivation time to 7 days is a viable option in bone and joint infections.

Methods
We included cases with at least one positive sample with P. acnes being hospitalized at the orthopedic clinic Balgrist in Zurich, Switzerland between 2006 and 2015. We recorded various clinical and microbiological data in particular time to positivity for different cultivation methods. We defined an infection when at least 2 samples were positive.

Results
Median time to first positive sample with P. acnes in 380 samples was 6 days (95% CI 6-7). Grouping into 70 cases with infections and 47 without an infections, median time to first positive sample was faster in infected cases (5 days, 95% confidence interval [CI] 4-5; versus 9 days, 95% CI 7-10; $p<0.0001$). Stopping cultures at day 7, we would have misdiagnosed 15 patients (21.4%) with an infection. In tissue biopsies, thioglycolate broth incubated for 10 days showed best sensitivity (66.3%) with decreased specificity of 79.1%. Resuscitation was not influenced by transportation time (median 10.4 hour).

Conclusion
In patients with a high prevalence of P. acnes infections we do not recommend to shorten cultivation time to 7 days. Growth was not influenced by transportation time indicating that P. acnes survive in the biofilm.

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P24 | Long-term impact of late-onset cytomegalovirus replication on chronic lung allograft dysfunction and mortality in lung transplant recipients receiving antiviral prophylaxis

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Background
Cytomegalovirus (CMV) disease has been associated with the development of chronic lung allograft dysfunction (CLAD) after lung transplantation. However, the relevance of asymptomatic CMV viremia occurring after the discontinuation of antiviral prophylaxis (late-onset CMV replication) on the development of CLAD is not fully understood. We aimed to assess the long-term clinical impact of asymptomatic CMV replication in a cohort of lung transplant recipients receiving universal antiviral prophylaxis.

Methods
We performed a single-center study including all patients who underwent lung transplantation between 2004 and 2014. Patients received valganciclovir prophylaxis for 3 to 6 months (according to CMV serostatus risk of the donor [D] and recipient [R]), followed by monitoring of CMV replication by PCR during the first year post transplant. CLAD was defined according to ISHLT definitions. Risk factors for the development of CLAD and for mortality were assessed by univariate and multivariate Cox models. A lineal regression model was used to evaluate the influence of CMV replication in the evolution of FEV1.

Results
Overall, 69 patients were included. CMV serostatus was D-/R- in 13 (19%) patients, D-/R+ in 17 (25%) patients, D+/R+ in 27 (39%) patients and D+/R- in 12 (17%) patients. Overall, 34/69 (49%) patients developed at least one episode of asymptomatic CMV replication and 8/69 (11.5%) patients developed CMV disease. Median duration of CMV replication in viremic patients was 57.5 days. After a median follow-up of 3.69 years, 25/69 (36%) patients developed CLAD and 14/69 (20%) patients died. In the univariate cox analysis, bacterial pneumonia was associated with a higher incidence of CLAD (HR 2.58, p=0.06), but asymptomatic CMV replication (HR 1.36, p=0.45), CMV disease (HR 1.00, p=0.99), and duration of CMV replication (HR 1.00, p=0.76) were not (Figure 1). In the multivariate model, bacterial pneumonia remained associated with CLAD (HR 2.73, p=0.04). In the mixed model of linear regression, we did not observe a correlation between CMV replication and a significant decline of FEV1 (estimate -0.162, CI 95% [-0.498 to 0.170], p=0.35). CMV replication was not associated with a higher mortality (HR 0.75, p=0.62).

Conclusion
In this cohort of lung transplant recipients receiving antiviral universal prophylaxis, asymptomatic CMV replication did not influence long-term allograft lung function and patient survival. These results suggest that the use of universal prophylaxis is protective against the indirect effects of CMV, irrespective of the development of late-onset CMV replication.

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P25 | Missed Opportunities for HIV diagnosis: data from patients newly presenting for HIV care at Lausanne University Hospital between 2010 and 2015

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Background
Late presentation to HIV care, defined as patients first presenting for HIV care with a CD4 count <350 cells/mm3, occurs in 49.8% of patients newly enrolled in the Swiss HIV Cohort Study (SHCS). The aim of this study was to describe the characteristics of patients presenting for HIV care at our centre and whether HIV infection could have been diagnosed earlier at our hospital.

Methods
The medical records of all new patients presenting to our HIV outpatient service between 2010 and 2015 were examined retrospectively. For each patient, we recorded demographic characteristics, HIV stage at diagnosis and reason for HIV testing. For each medical visit at our hospital up to five years preceding the diagnosis, we examined whether an HIV test had been indicated according to the 2015 Swiss HIV testing recommendations. If a test was not performed, we considered the visit a missed opportunity (MO).

Results
We analysed records for 201 patients. Mean age at diagnosis was 38±11 years. 103 patients (51%) were male. 106 (52%) were Swiss, European or North American and 66 (33%) were from Sub-Saharan Africa. 122 infections (58%) were acquired heterosexually, 68 (18%) homosexually, 13 (6%) parenterally and in 8 cases (3%) mode of transmission was unknown. Table 1 summarizes the reasons for performing HIV testing in this population. 16 patients (8%) presented with an acute HIV infection, 119 (59%) were late presenters of whom 67 (55%) had advanced disease (CD4 count below 200 cells/mm3). 94 patients (46%) had a least one MO for HIV diagnosis in our hospital during the 5 years before diagnosis of whom 44 (46%) had multiple MOs. MOs were more frequent in patients presenting with an initial CD4 count > 350 cell/mm3 (56% versus 40%, $^{x}2=4.8$, p = 0.03).

Conclusion
We identified a higher proportion of late presenters than previously reported by the SHCS. This could be due to local characteristics of the HIV positive population in Lausanne or underrepresentation of late presenters in the SHCS. 46% of patients had at least one MO at our hospital during the 5 years before diagnosis. MOs were more frequent in patients with CD4 counts >350 cells/mm3, suggesting that HIV testing in these patients should be optimised.

Reasons for performing HIV testing	Number of patients, n (%)
Disease for which the prevalence of HIV is > 0.5%	59 (29)
Epidemiological risk	42 (21)
Symptoms of acute HIV infection	36 (18)
Patient-initiated	28 (14)
AIDS-defining illness	21(10)
Pregnancy	14 (7)
Introduction of immunosuppressive treatment	1 (1)

Table 1: Reasons for performing HIV testing among 201 newly diagnosed HIV patients seen at Lausanne University Hospital between 2010 and 2015.

P26 | Investigating Barriers in HIV-Testing Oncology Patients: The IBITOP Study Phase II

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Background
In November 2013, the Swiss Federal Office of Public Health (FOPH) HIV testing recommendations were updated. For the first time, cancer patients undergoing chemotherapy were listed under indications for HIV testing. Just prior to these recommendations, we performed a study Investigating Barriers In HIV-Testing Oncology Patients (IBITOP I) among oncology physicians and patients at Lausanne University Hospital (LUH)1. In this study, 18% of cancer patients were offered HIV testing although patient acceptance of testing was high (91%). The current study, IBITOP II, examined HIV testing practices following the 2013 FOPH recommendations and physician barriers to testing.

Methods
Between 1st January and 31st October 2015, patients of unknown HIV status newly diagnosed with solid-organ non-AIDS-defining cancers (non-ADCs) referred to LUH Oncology Service, Lausanne, Switzerland, were offered free HIV testing as part of their oncology work-up. The primary endpoints were 1) physician proposition rates for HIV testing and 2) physician reasons for not offering testing.

Results
Of 438 patients of unknown HIV status with a new non-ADC diagnosis, 255 (58%) were offered HIV testing, of whom 42 declined (acceptance rate 213/255, 84%). Excluding 37 patients tested prior to their oncology consultation, 146 patients (of 438, 33%) were not offered testing. The most frequent physician reasons for not testing were: forgetting (35 patients, 24%); patient follow-up elsewhere (25 patients, 17%); no planned chemotherapy (25 patients, 17%); excessive burden of information for the patient (23 patients, 16%); and no time (21 patients, 14%).

Conclusion
This is the first study to shed light on physician reasons for not HIV-testing cancer patients despite national HIV testing recommendations which propose this. Given the physician barriers to testing we observe, testing will not be practised universally among cancer patients. Further, it is possible the HIV testing rate of 58% will be lower outside the context of a study on testing. As HIV-positive status impacts on the medical management of cancer patients, knowledge of HIV status is important. We conclude that opt-out testing in this setting, conducted as part of the baseline oncology work-up, would circumvent physician barriers and optimise testing rates. 1. Merz L et al. Investigating barriers in HIV-testing oncology patients. The IBITOP study: phase I. Journal of the International AIDS Society. 2014;17(4 Suppl 3):19622.

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P27 | Deficiency in sirtuin 2 increases bacterial phagocytosis by macrophages and protects from chronic staphylococcal infection

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Background and aim
Sirtuin 2 (SIRT2) is one of the seven sirtuins that constitute the family of NAD+-dependent histone deacetylases. Sirtuins are at the center of great interest due to their connection with metabolism, age associated diseases, and lifespan. Recent studies, focusing mainly on SIRT1 and SIRT6, suggest that sirtuins impact on immune functions. Our aim was to get insights into the role of SIRT2 on innate immune responses.

Methods
SIRT2 expression was analyzed in cell populations by RT-PCR and by extracting data from web resources. SIRT2 knockout mice were housed in SPF conditions. Thymic and splenic subpopulations were analyzed by FACS. Bone marrow-derived macrophages (BMDMs) and dendritic cells (DCs) and splenocytes were stimulated with a panel of TLR ligands, bacteria, exotoxins and polyclonal activators before measuring intracellular signaling, cytokine production and proliferation. BMDMs were incubated with fluorescent beads and bacteria (E.coli, S.Typhimurium, S.aureus, S.pneumoniae, GBS, N.meningitis) to quantify phagocytosis by flow cytometry or CFU counting. Mice (n=8-16/group) were challenged with LPS, TSST-1, E.coli (i.p.), S.aureus (i.v.) and K.pneumoniae (i.n.).

Results
SIRT2 is the most expressed sirtuin in myeloid cells, with highest levels observed in macrophages and mast cells. SIRT2-/- mice develop normally and express normal proportions and absolute numbers of thymic and splenic immune subpopulations. SIRT2-/- and SIRT2+/+ BMDMs, BMDCs and splenocytes similarly activate intracellular MAPK signaling, produce cytokines and proliferate to microbial ligands and polyclonal activators. SIRT2-/- BMDMs phagocytose inert beads and live bacteria better than SIRT2+/+ BMDMs. In line with these results, SIRT2 deficiency neither sensitizes nor protects mice from endotoxemia, TNF-induced shock, fulminant lethal E.coli peritonitis and non-lethal K.pneumonia pneumonia, but powerfully protects from chronic staphylococcal infection.

Conclusions
SIRT2 deficiency increases bacterial phagocytosis and protects from chronic staphylococcal infection. These data suggest that SIRT2 inhibitors developed for treating metabolic and neurodegenerative diseases may represent adjunctive therapies to treat chronic bacterial infections.

P28 | The gut-derived short chain fatty acid propionate mediates anti-inflammatory activity but does not impact on host susceptibility to bacterial and fungal infections in vivo

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Background and aim
Short chain fatty acids (SCFAs) are end products of the fermentation of resistant starches and dietary fiber by intestinal bacteria. Through inhibition of histone deacetylases or signaling via G-protein coupled receptors, SCFAs mediate antioxidative, anticarcinogenic and anti-inflammatory effects. Yet, to which extent SCFAs impact on innate immune responses and infection remains largely unknown. Considering that propionate is one of the most abundantly produced SCFAs, the aim of this study was to get insights into the impact of propionate on innate immune responses in vitro and in vivo.

Methods
Mouse bone marrow-derived macrophages (BMDMs) and dendritic cells (BMDCs) and human whole blood were exposed to propionate (0-2 mM) and stimulated with LPS, Pam3CSK4, CpG ODN, E.coli, S.aureus and C.albicans before measuring cytokine and NO production. Mice (n=8-16/group) were treated with or without propionate (200 mM in drinking water or 1 g/kg i.p. every other day for 21 days) and antibiotics (to deplete the gut flora) before being challenged with LD10 or LD80-100 of LPS, E.coli (i.p.), K.pneumoniae, S.pneumoniae (i.n.), S.aureus and C.albicans (i.v.).

Results
Propionate dose-dependently inhibits cytokine production by BMDMs, human whole blood and PBMCs and NO production by BMDCs without showing any cytotoxic effect. Propionate neither sensitizes nor protects (weight loss, severity index, survival) from endotoxemia, infection and lethal sepsis, even when mice are beforehand depleted of gut microbiota. Propionate reduces anti-Klebsiella and anti-Streptococcus IgG titers in mice surviving pneumoniae. Sera collected from propionate-treated and propionate-untreated mice infected with a sublethal dose of S.pneumoniae similarly protect naive mice from lethal pneumoniae upon transfer. Moreover, propionate-treated mice infected with a sublethal dose of S.pneumoniae are protected from reinfection with a lethal dose of S.pneumoniae.

Conclusions
Despite evident anti-inflammatory properties in vitro, propionate has no significant impact on host susceptibility to primary bacterial and fungal infection and bacterial reinfection. These data support the development of therapies using propionate or directed at the diet or the microbiota for treating non-infectious inflammation-related disorders such as obesity, atherosclerosis, inflammatory bowel diseases, allergy and cancer.

P29 | Which antibiotics reduce intracellular persisting Staphylococcus aureus?

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Staphylococcus aureus infections often develop a chronic course as for example osteomyelitis, are difficult to treat and often relapse despite the fact that most isolated pathogens show a good susceptibility to antibiotics tested in the clinical microbiology laboratories. In this project, we especially considered the versatile characteristic of S. aureus to invade and hide within host cells and to switch to a dormant persister state. We previously showed that the frequency of non-growing persisters increased after exposure to low pH in vitro and also after uptake and survival within host cell lysosomes. Typically S. aureus infections are initially treated with a beta-lactam such as flucloxacillin which is effective only on extracellular bacteria. In order to assess which antibiotic could diminish the intracellular reservoir, we compared different classes of antibiotics and assessed their efficacy in reducing bacteria protected within host cells using an in vitro cell culture assay. We found that flucloxacillin, rifampicin, ciprofloxacin and clindamycin efficiently killed non-protected planktonic bacteria (reflecting the situation encountered during a bloodstream infection) as well as bacteria within a biofilm in vitro within 24 hours. In contrast, none of tested antibiotics, neither given alone or in combination, completely eradicated S. aureus sequestered within host cells over the treatment duration of three days. We found that the antibiotics predominantly killed the fast-growing bacteria, resulting in selection of persisters. The best reduction of intracellular bacteria was achieved using the antibiotic combination of 1mg/ml flucloxacillin, 0.64 µg/ml rifampicin and 4 µg/ml ciprofloxacin (90 % killing, 1 log reduction). In a next step, we will address whether longer treatment duration or other agents which specifically target persisters are efficient in eradicating intracellular reservoirs. These data might then help in finding an optimal treatment strategy for chronic and difficult-to-treat S. aureus infections.

P30 | Immunogenicity of Standard vs. High Dose of Inactivated Influenza Vaccine in Solid Organ Transplant Recipients: a Randomized Controlled Trial

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Background
Although high–dose (HD) influenza vaccine improves protection against influenza in the elderly, the effect among solid organ transplant (SOT) recipients is unknown. We assessed the immunogenicity and safety of HD vs. standard dose (SD) influenza vaccination in SOT recipients.

Methods
SOT recipients were prospectively randomized to receive 15 µg (SD) or 30 µg (HD) of the 2014/15 influenza vaccine. Immunogenicity was evaluated using a hemagglutination inhibition assay (HIA). Vaccine response was defined as a 4-fold increase of the HIA titer for at least one of the 3 viral strains. Geometric mean titers (GMT) and seroprotection rate (SP) (HIA ≥40) were also analyzed. Follow up period was 6 months.

Results
39 patients (30 kidney and 9 liver transplant recipients) received the SD and 40 (33 kidney and 7 liver) the HD influenza vaccination. Baseline characteristics were similar between groups. Rate of systemic adverse events (AEs) to vaccination was similar between groups (23.1% SD and 22.5% HD) and no serious vaccine-related AEs were observed. 28% of patients in the SD group compared to 42.5% in the HD group (p=0.18) responded to vaccination at 2 weeks, with a significant difference observed for the response to influenza B (5.1% vs 22.5%; p=0.026). GMTs at 2 weeks were 97.8 and 138.5 (p=0.26) for H1N1, 147.5 and 198.9 (p=0.17) for H3N2, and 82.1 and 118.0 (p=0.04) for influenza B in SD vs. HD, respectively. Most patients were seroprotected at 6 months (79% for H1N1, 90% for H3N2, and 91% for B) without differences between groups. In univariate analysis, HD vaccine (OR 1.88; p=0.19) was positively associated whereas vaccination during the first 2 years post transplant (OR 0.33; p=0.03) was negatively associated with vaccine response. No biopsy proven rejections after vaccination were observed. Only one patient (in the HD group) developed laboratory-confirmed influenza.

Conclusions
HD influenza vaccine was safe and well tolerated and may increase antibody responses in SOT recipients. If confirmed in a larger population, HD influenza vaccination may become an appropriate strategy to reduce the burden of influenza after SOT.

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P31 | Liver fibrosis in HIV-monoinfected persons with chronic elevated aminotransferase levels

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Background
Chronic alanine aminotransferase elevation (LEE) is frequent among HIV-infected persons without hepatitis B and C coinfection. However, little is known about its clinical significance. We studied the association of LEE and significant liver fibrosis in HIV-monoinfected patients.

Methods
A case control study was performed including patients with LEE without chronic viral hepatitis and matched controls of the Swiss HIV Cohort Study (SHCS). Matching criteria were similar duration of HIV infection and follow-up. Chronic LEE was defined as ALT >50/>35 U/L (males/females) at ≥2 consecutive semi-annual visits. All participants underwent transient elastography (TE) and the two non-invasive fibrosis biomarkers, APRI and FIB-4, were calculated. Significant liver fibrosis was defined as Metavir ≥F2 in TE.

Results
In 94 case patients and 101 controls valid TE, APRI and FIB-4 results were available. Baseline characteristics of cases and controls were as follows: median age 48(cases)/48(controls) yrs (p=0.68); male 72/80% (p=0.20); median CD4 cell count 615/524/µL (p=0.03); on antiretroviral therapy (ART) 98/95% (p=0.64); median ART duration 9.6/8.7 yrs (p=0.17); median BMI 26.1/24.3 kg/m2 (p=0.01). The median TE score was 5.05 kPa (IQR 4.0-7.3 kPa) in cases and 4.6 kPa (3.7-5.8 kPa) in controls. Significant liver fibrosis was present in 24 (25.5%) of cases, and 8 (7.9%) of controls, including cirrhosis (Metavir F4) in 6 (6.4%) cases, and 2 (2.0%) controls. Adjusted logistic regression analyses showed an independent association between LEE and liver fibrosis (OR 3.84 [95% CI 1.57-9.42]). There was a trend but no significant association between liver fibrosis and older age (40-50 yrs 2.00 [0.38-10.54], >50 yrs 2.23 [0.41-12.13], versus <40 yrs), duration of ART exposure (5-9 yrs 1.86 [0.55-6.29], 10-14 yrs 1.05 [0.28-3.96], ≥15 yrs 2.49 [0.66-9.38] versus <5 yrs), obesity (1.87 [0.64-5.45]), and moderate/severe alcohol consumption (1.09 [0.19-6.21]) (Figure). APRI and FIB-4 correlated with TE with Spearman's rho of 0.357 (p<0.001) and 0.240 (p<0.001), respectively.

Conclusion
HIV-monoinfected persons with LEE had a high rate of significant liver fibrosis and cirrhosis. LEE was independently associated with liver fibrosis.

Figure
Unadjusted and adjusted logistic regression analyses of the association of chronic ALT elevation with significant liver fibrosis

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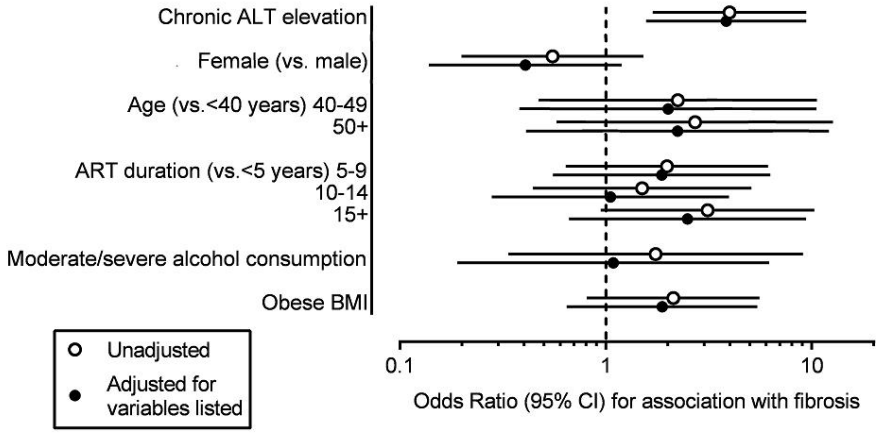

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P32 | Decreased resistance to azithromycin in Gram-negative bacteria in eukaryotic growth medium

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Increasing numbers of multi-drug resistant bacteria pose a growing global health problem, highlighting the importance of prescribing an appropriate antibiotic. Antibiotic susceptibility of clinical strains is routinely assessed using the disc diffusion method on Müller-Hinton (MH) II agar. Gram-negative bacteria are considered to be intrinsically resistant to macrolides and thus also show small inhibition zones on MH II agar; although clinical studies have recently shown that macrolides may have a beneficial effect in patients suffering from Gram-negative infections. Our goal was to find a testing method that better reflects these in vivo findings. Using the nutrient-poor, and thus nutritionally more physiologic eukaryotic cell culture medium Roswell Park Memorial Institute (RPMI) instead of the relatively nutrient-rich MH II agar as the growth medium for antibiotic susceptibility testing, we found the macrolide azithromycin to exhibit larger inhibition zones when tested on certain Gram-negative bacteria. Various clinical strains of P. aeruginosa (n=29), K. pneumoniae (n=27), E. coli (n=24) and E. cloacae (n=26) were tested for their susceptibility to azithromycin. In the group of the Enterobacteriaceae the average inhibition zone increased by 7 mm on RPMI compared to MH agar, but only a small sub-population of P. aeruginosa showed a shift to larger inhibition zones. Of the 20 carbapenemase-positive Gram-negative strains collected at the Institute of Medical Microbiology at the University of Zurich, all Enterobacteriaceae (n=18) showed azithromycin inhibition zones of more than 15 mm on RPMI agar and less than 10 mm on MH II agar. No inhibition zone diameter difference was found for the two carbapenemase-positive P.aeruginosa we tested. No diameter differences between MH II and RPMI agar were found for drug classes other than macrolides. We demonstrated that the inhibition zones of azithromycin significantly increased in both fully susceptible as well as multi-drug resistant Gram-negative bacteria when tested with the disc diffusion method on the physiological RPMI agar. For certain species-drug combinations modified testing conditions may thus better reflect in vivo responses and have the potential to provide an improved predictive power of therapeutic success.

P33 | Evaluating the impact of influenza vaccination on pneumococcal nasopharyngeal colonization in Canadian Hutterite Children.

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Background
Streptococcus pneumoniae (SPN) can cause significant morbidity and mortality. Carriage rates are highest in young children depending on socioeconomic, environmental, and genetic factors. Influenza vaccination has been associated with a reduced risk of pneumonia-related death and hospital admissions in elderly people and a reduced risk of acute otitis media in children. Data on the effect of inactivated trivalent influenza vaccine (ITIV) on upper respiratory tract colonization with SPN are sparse. Our goal was to assess the impact of ITIV on SPN colonization in children during the influenza season and to identify predictors of SPN carriage.

Methods
This was a secondary analysis of prospectively collected data of a cluster-randomized controlled trial in Canadian Hutterite colonies where 947 school-aged children received either ITIV or hepatitis A vaccine as a comparator. The surveillance period started two weeks after the last child had been immunized. Children with symptoms of acute respiratory infections (ARI) were swabbed. We analysed these swabs for SPN using a real-time PCR assay. Covariates previously described as important were pre-defined to be adjusted for in multivariable analysis. We applied a random-effects logistic regression model to account for clustering.

Results
A total of 580 nasopharyngeal swabs were collected from 384 children. Overall, 126 (36%) children had at least one episode of SPN colonization. The proportion of SPN carriage among children < 6 years of age was 52.3% compared to 32.4% and 28.7% among those aged 6-10 years and 11-15 years, respectively. Multivariable analysis showed that children < 6 years (OR 2.8, 95% CI 1.2 to 6.4) were significantly more likely colonized with SPN than children in the age group of 11 to 15 years (Table). ITIV recipients were 1.2 times more likely colonized with SPN than those in the comparator group, however, this was not statistically significant (OR 1.2; 95% CI 0.6-2.4). The odds of being colonized with SPN in children infected with rhinovirus was almost two times the odds of those with no viral detection (OR 1.82; 95% CI 0.8-4.0), but the result was not significant.

Conclusion
ITIV had no protective effect on nasopharyngeal SPN colonization. That children with rhinovirus-associated ARI are more likely colonized with SPN is consistent with previous studies. Concomitant viral respiratory infection may have masked a potential effect of ITIV.

Table. Random-effects logistic regression model to evaluate the effect of various predictors on pneumococcal colonization.

	OR	**95% Confidence interval**
Intervention group (influenza vaccination)	1.2	0.6 - 2.4
Age category < 6 years	2.8	1.2 - 6.4

Age category 6-10 years	1.1	0.5 -	2.6
Female participants	0.9	0.5 -	1.7
Has sibling < 3 years	1.0	0.6 -	1.7
Ln25(OH)vitamin D level	0.8	0.3 -	1.6
Antimicrobial use during present illness	1.1	0.4 -	3.3
Rhinovirus positive	1.8	0.8 -	4.0
Influenza virus positive	1.1	0.6 -	1.9
Respiratory syncytial virus positive	1.2	0.4 -	3.2
Other or multiple viruses positive	0.7	0.3 -	1.9

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P34 | Agreement between nasal mid-turbinate and nasopharyngeal swabs to detect Streptococcus pneumoniae by polymerase chain reaction in children and adults.

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Background and objectives
Polymerase chain reaction (PCR) is a reliable method for detecting S. pneumoniae (SPN) carriage and the nasopharynx is the sampling site recommend by the WHO. Correct sampling from the nasopharynx is uncomfortable and requires execution by trained staff. Nasal mid-turbinate sampling is more convenient and feasible. Comparison of nasal and nasopharyngeal (NP) swabs using culture methods showed high concordance in detecting SPN carriage in youngest children with prevalent respiratory tract infections (RTI). Our goal was to determine the agreement between the NP and nasal swab to detect SPN carriage in children and adults using PCR.

Methods
In a prospective cohort study on influenza viral shedding in Canadian Hutterite communities, pairs of NP and nasal flocked swabs were obtained in participants with and without RTI. The stored samples were analysed for the presence of SPN using a real-time PCR assay targeting lytA gene. We determined sensitivity and specificity of the nasal swab with the NP swab as reference standard and applied McNemar's test for differences in proportions. We assessed the difference in means of log10 copies/ml SPN using the paired sample t-test.

Results
Of 152 individuals 53 (34.9%) tested positive for SPN. Median age (range) was 11 (0-74) years. Ninety-seven (63.8%) subjects had at least one symptom suggesting ARI with the highest proportion (91%) among children < 6 years of age. Overall sensitivity of the nasal swab was 67.4% [95% confidence interval (CI) 51.5-80.9], and specificity was 90.8% (95% CI 83.8-95.5). Sensitivity was 95.2% (95% CI 76.2- 99.9) in children < 6 years of age but was only 52.6 (95% CI 28.9-75.6) in 6-15 year olds. The difference in proportions of subjects positive in the NP swab (29.3%) compared to those with a positive nasal swab (25.7%) was not statistically significant (P=.54). The difference in mean SPN log10 copies/ml was -0.06 (SD 1.4) (P=.83).

Conclusion
PCR from nasal and NP specimen yielded similar SPN log amounts. Consistent with previous studies agreement between NP and nasal swab was high in youngest children where the less convenient NP swab could be substituted by a nasal swab. This did not hold true for older children and adults.

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P35 | Detecting antimalarials in blood from community surveys in Tanzania.

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The assessment of the impact of diagnostic or treatment strategies on antimalarial drug use often rely on histories of drug intake in community surveys. Estimating accurately the levels of circulating antimalarials in a population allow an unbiased measure of drug consumption. Here, we explored the relationship between endemicity, health facility practices and blood drug concentration in malaria-endemic communities. The study took place in three regions of Tanzania (Mwanza, Mbeya and Mtwara) in 2015. In each region, surveys were conducted in three districts. All health facilities from randomly selected wards were visited to assess treatment and diagnosis practices. Information on demographics, health seeking behavior and drug use was obtained through community surveys, while health facility based surveys collected information on diagnosis and treatment practices. Finger-prick blood samples were obtained for on-site testing as well as for collecting samples on filter paper. Antimalarial blood concentration including Lumefantrine was measured later by LC–MS/MS. Parasite prevalence was 20% (506/2463) in Mwanza, 4% (84/1985) in Mbeya and 26% (559/2152) in Mtwara. Participants with any antimalarial in the blood were 34% (844/2463), 20% (399/1985) and 26% (554/2152) respectively in Mwanza, Mbeya and Mtwara. Individual who tested positive with a RDT had a marginally higher frequency of being detected with an antimalarial (29.7% vs 26.8%). Indeed, the association of RDT positivity and presence of drug was relatively poor (OR=1.15, 95% CI:1.00-1.33). Results from health facilities showed that amongst the febrile patients, 67% (151/226) were tested for parasite. Prevalence of persons with residual antimalarials in the blood was relatively high, especially in Mbeya where endemicity was low. This indicates poor use of diagnostic testing and inappropriate prescription of antimalarials. This might result in high levels of circulating drug in a population, probably the most important driver of the development of drug resistant pathogens. Effort should therefore be made to reduce these poor practices and prevent emergence of resistance.

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P36 | Treatment seeking behavior, diagnosis and treatment practices in Tanzania: comparison between community surveys conducted soon after the implementation of The Affordable Medicines Facility – malaria and the mRDTs roll out, and three years later.

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Considerable efforts have been made to increase access to first-line antimalarials and mRDTs across Africa. In Tanzania mRDTs were rolled out in the public sector from 2009-2012, while ACTs are subsidized in the public and private sectors. We present findings from community surveys conducted in 2012 and three years later to assess the degree to which these interventions have led to sustained changes in case management. Both surveys took place in the same three regions of Tanzania (Mwanza, Mbeya and Mtwara) after the rainy season. In each region, community surveys were conducted in randomly selected wards of urban and rural districts. Health seeking behavior and drug use were inquired from individuals reporting fever in the previous two weeks. All participants were tested for malaria using mRDTs. Between 2012 and 2015, parasite prevalence increased from 16% (1428/8834) to 21% (497/2351) in Mwanza, 2% (125/5941) to 4% (82/1980) in Mbeya and 16% (837/5327) to 26% (554/2138) in Mtwara. A larger proportion of febrile cases who sought treatment were tested in 2015 (20% (210/1037)) than in 2012 (10% (169/1653)). This also translates into more antimalarials delivered. Results from both surveys show that in private as in public sectors, febrile cases were more likely to be treated than tested for malaria (14% (379/2690) tested and 35% (949/2690) received an antimalarial), especially in regions of high parasite prevalence. The majority of antimalarial therapies were obtained from the private sector (25% (669/2690) and 10% (280/2690) in the public sector), which is also the sector where the febrile cases were the least tested (10% (108/1096) of individuals seeking treatment in the private sector tested against 55% (195/354) in the public sector). Despite increasing between 2009 after roll-out of RDTs and 2012, testing still remains poorly used, especially in the private sector. Increase of drug use consumption may reflect better health seeking behavior but probably more a remaining overuse of antimalarials. These results highlight the importance of targeting the private sector for improving and encouraging the use of mRDTs in order to ensure rational and adequate use of antimalarial treatments.

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P37 | Method for the simultaneous measure of the level of nine antimalarial drugs in dried blood spot samples using LC–tandem mass spectrometry and relationship of lumefantrine concentrations in dried blood spot samples and in plasma

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Measurement of the concentration of antimalarials in the blood of the general population helps estimating the overall drug pressure and is used in efficacy studies. Storage and transportation of blood samples are common problems for studies in areas with a high prevalence of malaria. The dried blood spot (DBS) sampling technique is promising for that use, enabling easier storage and transportation requirements. We present a method for the analysis of antimalarials in DBS and show the relationship between the concentrations of lumefantrine in DBS and with the usual method of plasma sampling. We added known concentrations of amodiaquine, desethylamodiaquine, quinine, chloroquine, mefloquine, sulfadoxine, pyrimethamine, lumefantrine and desbutyl-lumefantrine in whole human blood. A 10µl aliquot of this blood was applied on a filter paper card and allowed to dry for three hours at room temperature. We took a 3 mm punch out of each dried blood spot and extracted it with 100 µl of methanol containing the stable isotopically labeled Internal Standards for all the antimalarials. We used a multiplex chromatography coupled to tandem mass spectrometry (LC-MS/MS) method for the simultaneous measure of the 9 antimalarials. We measured the concentrations of lumefantrine both in DBS and in plasma obtained at different time points in 16 healthy volunteers after they had received a single dose of artemether-lumefantrine. Lower limits of quantification were 2 ng/ml for pyrimethamine, 6 ng/ml for desthylamodiaquine, and 20 ng/ml for the other antimalarials. The inter-day variation coefficient was 2.1–15.2%. Lumefantrine concentrations measured in plasma were twice as high as those measured in DBS and were highly correlated (r=0.99) but plasma levels were twice as high as those in DBS. Our technique enables both precise and sensitive measurement of antimalarials in DBS, despite the low volume of blood sampled. The correlation between lumefantrine concentrations in DBS and in plasma is almost perfect. This relationship could thus contribute to defining the therapeutic ranges of lumefantrine concentrations measured in DBS. The ratio between the concentration in DBS and in plasma could reflect the distribution of lumefantrine in the different blood compartments. The DBS sampling method is suitable for antimalarials level measurements and could be convenient for epidemiological studies.

P38 | Staphylococcus aureus carriage at admission predicts early-onset pneumonia after burn trauma

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Background
Early-onset pneumonia (EOP) is frequent after burn increasing morbidity in the critical resuscitation phase following trauma which may preclude early aggressive management of burn wound. Currently, preemptive treatment is, however, not recommended. The aim of this study was to search for predictive factors of EOP that could be used to possibly justify for early empirical antibiotic treatment.

Material/methods
Data of all burn patients requiring mechanical ventilation for >4h between January 2001 and October 2012 were extracted from the hospital's computerized information system. We reviewed episodes of EOP (occurring within 7 days from admission) among those for whom an endotracheal aspirate (ETA) was obtained within 5 days from admission. Univariate and multivariate analyses were performed to search for independent factors associated with EOP.

Results
During the study period, 396 burn patients were admitted. Among the 291 patients mechanically ventilated >4h, an ETA was obtained within 5 days in 205 patients. 107 patients developed an EOP, including 47 due to Staphylococcus aureus, 36 to Haemophilus influenza and 23 to Streptococcus pneumoniae. Among the 62 patients with a S. aureus positive ETA, 43 (69%) developed a S. aureus EOP. Among the 143 S. aureus non-carriers, only 62 (43%) developed an EOP. S. aureus carriage independently predicted EOP (OR=84, $p<0.0001$). Using S. aureus carriage as a unique criterion to initiate early empirical treatment would result in 19 unnecessary antibiotic treatment (31%).

Conclusion
We identified S. aureus carriage as an independent and strong predictor of EOP. Since rapid point-of-care testing of S. aureus is readily available, we recommend testing all patients at admission after burn trauma and considering early preemptive treatment in all positive patients. Further studies are needed to evaluate this new strategy.

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P39 | A pseudostratified human airway epithelial model with an air-liquid interface to study pneumococcal colonisation and invasive diseases

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Background and Aims
Modelling host-pathogen-interaction of S. pneumoniae (SP) and the human airway epithelium (HAE) in-vitro might allow to identify mechanisms to reduce the burden of respiratory SP disease. We recently developed a pseudostratified HAE model with air-liquid interface (ALI) to study viral infection. This proof-of-concept study adapted the HAE model to study SP colonisation and invasive pneumococcal disease (IPD).

Method
Bronchial epithelial cells were isolated from 3 human donors and cultured for 30 days until the establishment of a confluent cell population and mucus production at the ALI apical side. SP strains, TIGR4 or ATCC 49619, were inoculated in the apical side at different multiplicity of infection (MOI). Pneumococci colonizing the apical side or invasive bacteria in the basolateral compartment were counted (cfu/ml). Transepithelial resistance (TEER), cellular components (nuclei, tight junctions, cilia and SP) as well as inflammatory host response (e.g. mRNA IL-1β) were evaluated at different time points.

Results
Differentiation and integrity of human cells was observed by confocal images showing ciliated structures and formation of a tight junction complex, and confirmed by TEER measurements. A significant drop of TEER was observed 8h post-inoculation with loss of ciliated structures and tight junctions. Colonizing bacteria were observed 6h post-infection, at a MOI=50, whereas invasive pneumococci were detected after 19h. Colonization and invasion coincided with an increased expression of IL-1β and this expression was dose-dependent and SP strain specific.

Conclusion
This differentiated HAE model simulates pneumococcal colonization of the human lower airways and IPD.

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P40 | SOF/VEL for 12 weeks results in high SVR12 rates in subjects with negative predictors of response to treatment: an integrated analysis of efficacy from the ASTRAL-1, ASTRAL-2 and ASTRAL-3 Studies

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Background
The once-daily fixed-dose combination tablet of sofosbuvir/velpatasvir (SOF/VEL) was evaluated for the treatment of genotype 1-6 HCV infection in three phase 3 studies in patients with and without compensated cirrhosis (ASTRAL-1, ASTRAL -2, ASTRAL -3). Overall SVR12 rates were > 95% across all HCV genotypes. This post-hoc analysis assesses efficacy in patients with traditional negative predictors of response.

Methods
This was a retrospective analysis of data from 1035 patients treated with SOF/VEL in the Phase 3 ASTRAL-1, ASTRAL -2, and ASTRAL -3 studies. Presence of cirrhosis was determined by histology, blood tests or transient elastography. Viral load and other clinical and laboratory assessments were determined prior to treatment with SOF/VEL. Prior treatment records were source verified and race was self-reported by the patient to the investigator.

Results
Overall, 21% of patients had cirrhosis, 74% had HCV RNA ≥ 800,000 IU/mL, 28% had prior treatment failure, 12% were ≥ 65 years old and 6% were black. Table 1 provides SVR12 rates by HCV genotype overall and for each patient subgroup. The overall SVR12 rate was 98% and was ≥96% among all subgroups. In general SVR12 rates were lower in patients with genotype 3 HCV infection compared with other HCV genotypes but were ≥90% across all subgroups.

Conclusions
The ASTRAL-1, ASTRAL -2, and ASTRAL -3 studies enrolled a diverse patient population that included a significant number of patients with historically negative predictors of response. There was little effect of these factors on the efficacy of treatment with SOF/VEL for 12 weeks in subjects with genotype 1-6 HCV infection.

Table 1 SVR in Patient Subgroups in ASTRAL1-3

SVR12	GT1	GT2	GT3	GT4	GT5	GT6	Overall
Overall	98% (323/328)	99% (237/238)	95% (264/277)	100% (116/116)	97% (34/35)	100% (41/41)	98% (1015/1035)
Cirrhosis	99% (72/73)	100% (29/29)	91% (73/80)	100% (27/27)	100% (5/5)	100% (6/6)	96% (212/220)
HCV RNA ≥ 800,000	98% (251/255)	99% (185/186)	94% (179/191)	100% (74/74)	100% (26/26)	100% (31/31)	98% (746/763)
Prior Treatment Failure	99% (109/110)	100% (44/44)	90% (64/71)	100% (52/52)	100% (11/11)	100% (3/3)	97% (283/291)

Age> 65	100% (36/36)	100% (53/53)	100% (7/7)	100% (11/11)	100% (16/16)	(0/0)	100% (123/123)
Black	96% (24/25)	95% (18/19)	100% (3/3)	100% (14/14)	(0/0)	(0/0)	97% (59/61)

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P42 | Population pharmacokinetics analysis of dolutegravir in HIV-1 infected individuals

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Objectives

Dolutegravir (DTG), the latest integrase inhibitor (INIs) approved for HIV treatment is coformulated in a single tablet regimen with abacavir and lamivudine. DTG has demonstrated potent antiviral activity and a very good tolerability and is widely prescribed in HIV-infected patients (1). DTG is primarily metabolized via UDP-glucuronosyltransferase (UGT 1A1) with a minor component of CYP3A4 (2). The aim of this observational study was to characterize DTG pharmacokinetic profile, to quantify interpatient variability and to identify potential factors that could influence drug exposure.

Methods

All dolutegravir concentrations data were collected as part of routine therapeutic drug monitoring performed in our hospital, between June 2014 and December 2015 from HIV treatment-naive and experimented patients. A population PK analysis was performed by comparing various structural models using NONMEM®. The effect of relevant demographic factors and co-medications were on dolutegravir disposition was explored.

Results

A total of 594 plasma levels were measured in 514 HIV-positive patients under steady state regimen conditions. Plasma concentrations ranged between 31 and 7971 ng/mL. A one-compartment model with first order absorption and elimination best characterized dolutegravir pharmacokinetics. Average DTG clearance was 0.93 (L/h), volume of distribution 18.9 (L), and mean absorption time 1.27 (h-1). The inter-subject variability on CL was estimated at 27%. Among the demographic covariates tested, body weight and age influenced positively and moderately DTG CL (29% and 24% respectively) as well as smoking status (17%). Coadminisation of atazanavir

P43 | Drug-Drug Interactions Studies between HCV Antivirals Sofosbuvir and Velpatasvir and HIV Antiretrovirals

E Mogalian [1], S Naik [1], C Oberle [1], J Llewellyn [1], L Stamm [1], A Osinusi [1], G Shen [1], K Sajwani [1], J McNally [1], A Mathias [1]

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Background
A once-daily fixed-dose combination tablet composed of sofosbuvir (SOF; nucleotide analog NS5B inhibitor) and velpatasvir (VEL; pangenotypic NS5A inhibitor) is under regulatory review for the treatment of chronic HCV infection. Phase 1 studies were conducted in healthy volunteers to evaluate potential drug-drug interactions (DDIs) between SOF/VEL and HIV antiretroviral regimens (ARVs) to support coadministration in HIV/HCV co-infected patients.

Methods
These were multiple-dose, randomized, cross-over DDI studies. Subjects received SOF/VEL and the following ARVs: EFV/FTC/TDF, RPV/FTC/TDF, DTG, RAL+FTC/TDF, EVG/COBI/FTC/TDF, DRV/r + FTC/TDF, ATV/r + FTC/TDF, LPV/r + FTC/TDF, or EVG/COBI/FTC/TAF alone and in combination. Steady-state plasma concentrations of SOF, its predominant circulating nucleoside metabolite GS-331007, VEL, and ARVs were analyzed. PK parameters were calculated and geometric least-squares means ratios and 90% confidence intervals (combination vs. alone) for SOF, GS-331007, VEL, and ARV AUCtau, Cmax and Ctau were estimated and compared against lack of PK alteration boundaries of 70-143% for all analytes. Safety assessments were conducted throughout the study.

Results
The majority of adverse events (AEs) were Grade 1 and there were no serious AEs. 230 of 237 enrolled subjects completed the studies; 5 subjects withdrew consent, 1 discontinued due to Grade 1 urticaria and 1 discontinued due to pregnancy. Table 1 reports the effect of coadministration on HIV ARVs and SOF/VEL. No clinically significant changes in the PK of HIV ARVs, except TDF, were observed when administered with SOF/VEL.

Conclusions
Study treatments were generally safe and well tolerated. Results from these studies as well the phase 3 study ASTRAL-5 demonstrate that SOF/VEL may be administered safely and efficaciously with RPV, RAL, DTG, EVG, COBI, DRV/r, ATV/r, and LPV/r with a backbone of FTC/TDF or FTC/TAF.

Table 1. Effect of Coadministration on HIV ARVs and SOF/VEL

ARV with SOF/VEL	Effect on SOF/VEL AUC	Effect on ARV AUC
EFV/FTC/TDF	SOF: ↔	EFV: ↔
	GS-331007: ↔	FTC: ↔
	VEL: ↓ 53%*	TFV: ↑81%
FTC/RPV/TDF	SOF: ↔	FTC: ↔
	GS-331007: ↔	RPV: ↔
	VEL: ↔	TFV: ↑40%
DTG	SOF: ↔	DTG: ↔
	GS-331007: ↔	
	VEL: ↔	
RAL + FTC/TDF	SOF: ↔	RAL: ↔
	GS-331007: ↔	FTC: ↔
	VEL: ↔	TFV: ↑40%

DRV/r + FTC/TDF	SOF: ↓28%	DRV: □
	GS-331007: □	RTV: □
	VEL: □	FTC: □
		TFV: ↑40%
ATV/r + FTC/TDF	SOF: □	ATV: □
	GS-331007: □	RTV: □
	VEL: ↑142%	FTC: □
		TFV: □
LPV/r + FTC/TDF	SOF: ↓29%	LPV: □
	GS-331007: □	RTV: □
	VEL: □	FTC: □
		TFV: □
EVG/COBI/FTC/TDF	SOF: □	EVG: □
	GS-331007: □	COBI: □
	VEL: □	FTC: □
		TFV: □
EVG/COBI/FTC/TAF	SOF: ↑37%	EVG: □
	GS-331007: ↑48%	COBI: □
	VEL: ↑50%	FTC: □
		TAF: □
		TFV: □

P45 | Sofosbuvir/Velpatasvir Fixed Dose Combination for 12 Weeks In Patients Co-Infected With HCV And HIV-1: The Phase 3 ASTRAL-5 Study

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The once-daily fixed-dose combination (FDC) tablet of sofosbuvir/velpatasvir (SOF/VEL) has demonstrated high efficacy in genotypes 1-6 HCV-infected patients when administered for 12 weeks. We therefore performed a prospective clinical trial to evaluate the safety and efficacy of SOF/VEL in patients coinfected with HCV and HIV-1. This single arm, open label study enrolled treatment naïve and -experienced HCV/HIV co-infected patients of all HCV genotypes, with or without cirrhosis. Patients who were on stable antiretroviral (ARV) regimens with fully suppressed HIV RNA received SOF/VEL (400 mg/100 mg daily) for 12 weeks. Patients were on a wide range of ARV regimens including emtricitabine/tenofovir disoproxil fumarate or abacavir/lamivudine with a backbone of raltegravir, cobicistat/elvitegravir, rilpivirine, ritonavir boosted atazanavir, darunavir or lopinavir. Safety evaluations included adverse event (AE) and standard laboratory parameter monitoring in addition to frequent renal function monitoring, CD4 count and HIV-1 RNA levels. The primary endpoint was sustained virologic response 12 weeks after treatment (SVR12). A total of 106 patients were enrolled and treated with SOF/VEL for 12 weeks. Overall 86% were male, 45% were black, 77% had IL28B non-CC genotypes, 29% had prior treatment failure (primarily PegIFN/RBV), and 18% had compensated cirrhosis. The genotype distribution was 62% GT1a, 11% GT1b, 10% GT2, 11% GT3 and 5% GT4. The median baseline CD4 count was 598 cells/uL (range: 183-1513 cells/uL) with a median estimated glomerular filtration rate of 97 mL/min (range 57- 198 mL/min). Boosted protease inhibitor (PI) regimens were the most commonly used HIV ARV regimen. SVR12 rates by HCV genotype are presented in the table below. The most common AEs were fatigue (25%), headache (13%) and nausea (7%). 2 patients experienced a serious adverse event (toe infection and acute radial nerve palsy) which were considered unrelated to study drugs. No patient experienced confirmed HIV virologic rebound (HIV-1 RNA ≥400 copies/mL). No significant changes in lab abnormalities including renal function were observed. Complete efficacy and safety outcomes including HIV parameters and the impact of HCV resistance variants on outcome will be presented. SOF/VEL administered once daily for 12 weeks is well tolerated and results in high SVR12 rates in HCV/HIV co-infected patients with GT 1-4, regardless of past treatment experience or presence of cirrhosis.

ASTRAL-5 : SVR12 rates by HCV genotype

HCV Genotype	Total (N = 106)	GT-1a (N = 66)	GT-1b (N = 12)	GT-2 (N = 11)	GT-3 (N = 12)	GT-4 (N = 5)
SVR12* %, (n/N)	95% (99/104)	95% (62/65)	92% (11/12)	100% (11/11)	92% (11/12)	100% (4/4)

*2 patients pending SVR12 visit, both achieved SVR4

P46 | The Severity of Infection Determines the Tonotopic Localization of Damage and Extent of the Resulting Sensorineural Hearing Loss in Experimental Pneumococcal Meningitis

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Hearing loss is an important sequela of pneumococcal meningitis (PM), occurring in up to 30 % of survivors. The role of the severity of infection on hearing function and pathomorphological consequences in the cochlea secondary to PM have not been investigated to date. Using a well- established model of PM, we systematically investigated the functional hearing outcome and the long-term fate of neurosensory cells in the cochlea, i.e. hair cells (HCs) and spiral ganglion neurons (SGNs), with a focus on their tonotopic distribution. Intracisternal infection of infant rats with increasing inocula of Streptococcus pneumoniae resulted in a dose-dependent increase in cerebrospinal fluid levels of Interleukin(IL)-1β, IL-6, Tumor necrosis factor α (TNF-α), IL-10 and Interferon-γ (IFN-γ) in acute disease. The severity of long-term hearing loss at 3 weeks after infection, measured by auditory brainstem response recordings, correlated to the initial inoculum dose and to the levels of pro-inflammatory cytokines determined in the acute phase of PM. Quantitative cochlear histomorphology revealed a significant loss of SGNs and outer hair cells that strongly correlated to the level of infection, with the most severe damage occurring in the basal part of the cochlea. Inner hair cells (IHCs) were not significantly affected throughout the entire cochlea. However, surviving IHCs lost synaptic connectivity to remaining SGNs in all cochlear regions. These findings provide evidence that the inoculum concentration, i.e. severity of infection, is the major determinant of long-term morphological cell pathologies in the cochlea and functional hearing loss.

P47 | Adjuvant Dexamethasone Impairs the Neuroregenerative Capacity of the Hippocampus in Experimental Infant Rat Pneumococcal Meningitis

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Pneumococcal meningitis (PM) causes neurological sequelae in up to half of the surviving patients. Neuronal damage associated with poor outcome is largely mediated by the inflammatory host response. Dexamethasone (DXM) is used as an adjuvant therapy in adult PM, but its efficacy in the treatment of pneumococcal meningitis in children is controversially discussed. While DXM has previously shown to enhance hippocampal apoptosis in experimental PM, its impact on hippocampal cell proliferation is not known. This study investigated the impact of DXM on hippocampal proliferation in infant rat PM. Eleven days old nursing Wistar rats (n=90) were intracisternally infected with Streptococcus pneumoniae to induce experimental meningitis. Treatment with DXM or vehicle was started 18h after infection, concomitant with antibiotics (ceftriaxone 100 mg/kg ip, bid). Clinical parameters were monitored and the amount of cells with proliferating activity was assessed using in vivo incorporation of bromodeoxyuridine (BrdU) and an in vitro neurosphere culture system at 3d and 4 d post-infection. DXM significantly worsened weight loss and survival. Density of BrdU-positive cells, as an index of cell with proliferating activity was significantly lower in DXM-treated animals compared to vehicle controls ($p<0.0001$). In parallel, DXM reduced neurosphere formation as an index for stem/progenitor cell density compared to vehicle treatment ($p=0.01$). Our findings provide clear evidence that DXM exerts an anti-proliferative effect on the hippocampus in infant rat PM. We conclude that an impairment of regenerative hippocampal capacity should be taken into account when considering adjuvant DXM in the therapeutic regimen for PM in children.

P48 | High expression of macrophage migration inhibitory factor counterbalances the innate immune deficiencies of neonates

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Objective
To determine the developmental profile of MIF expression and the impact of MIF on the innate immune response of newborn monocytes.

Methods
MIF plasma levels were measured by ELISA in 200 healthy subjects, from birth to adulthood. Cord blood monocytes from healthy term newborns were transfected with MIF siRNA, or incubated with the MIF antagonist ISO-1, recombinant MIF, adenosine and prostaglandin E2 (PGE2) and then stimulated with endotoxin, bacterial lipopeptide, Escherichia coli and Group B Streptococcus (GBS). Intracellular proteins and cell-culture supernatants were collected to quantify MAPK phosphorylation by Western blot and cytokines by ELISA/Luminex. One-2 days-old newborn mice were treated with or without ISO-1 and challenged intraperitoneally or intranasally with E. coli O18:K1:H7. Bacterial burden, blood concentrations of cytokines and survival were recorded.

Results
Circulating MIF levels were higher in cord blood than adult blood (92.4±51.2 vs 7.1±3.8 ng/ml, $p<0.0001$), and gradually decreased during infancy. Newborn monocytes expressed high levels of MIF, and released MIF upon stimulation with Escherichia coli and GBS. Inhibition of MIF expression with MIF siRNA or MIF activity with ISO-1 reduced 1.5-5.7-fold microbial product-induced secretion of pro-inflammatory (TNF, IL-1β, IL-6, IL-8, IL-12p40, IL-12p70, IL-23) and anti-inflammatory (IL-10, IL-20, IL-27) cytokines and phosphorylation of p38 and ERK1/2 MAPKs. Recombinant MIF counter-regulated adenosine and PGE2-mediated inhibition of TNF production in newborn monocytes exposed to Escherichia coli. Circulating levels of MIF were markedly higher also in newborn (day 0-2) compared to postnatal (day 5-6) and adult mice. Finally, in agreement with the concept that once infection is established high levels of MIF are detrimental to the host, ISO-1 reduced systemic inflammatory response, bacterial proliferation and mortality of septic newborn mice.

Conclusion
MIF expression is developmentally regulated, with strikingly elevated levels in newborns compared to adults. These data provide a mechanistic explanation for how newborns may cope with an immunosuppressive environment to maintain a certain threshold of innate defenses. However, the same defense mechanisms may be at the expense of the host in conditions of severe infection, suggesting that MIF could represent a potential attractive target for immune modulating adjunctive therapies for newborn sepsis.

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P50 | Microbiology of early-onset and late-onset bloodstream infections in neutropenic patients after high-dose chemotherapy: A prospective multicenter cohort study of 16,378 episodes of neutropenia

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Background
Coagulase-negative staphylococci and Escherichia coli are the leading pathogens in bloodstream infections (BSI) of neutropenic patients. However, cumulative exposure to antibiotics, propagation of commensal flora via indwelling catheters in the bloodstream, and colonization with nosocomial pathogens may change spectrum of BSI over time. The current study's aim was to assess the influence of the duration of neutropenia on causative pathogens.

Material/methods
From 2002 to 2014, BSIs during neutropenia in patients that receive antineoplastic therapy for hematologic malignancy were prospectively identified by active surveillance in 20 hematologic centers in Germany, Switzerland and Austria. BSI incidence, microbiology and time to infection were analyzed in adult patients.

Results
During the study period, 16,378 patients with a first episodes of neutropenia developed 2519 BSI. BSIs occured after a median of six days (3-10 days) of neutropenia. The incidence density of BSI in the first week of neutropenia was 14.73 per 1000 neutropenic days, compared to 9.26 in the second week and 5.45 in the third. The median duration of neutropenia before onset of BSI differed significantly among pathogens. While it took four days of neutropenia before bloodstream isolation of E. coli (interquartile range 3-7 days), Klebsiella spp. (2-8 days), and S. aureus (3-6 days), enterococcal BSI developed after a median of nine days (6-14 days, $p<0.001$ vs. E. coli), candidemia after 11 days (7-17 days, $p<0.001$), and bacteremia with Stenotrophomonas maltophilia after 12 days (7-17 days, $p<0.001$). Taken together, 1600 BSIs (63.5%) occurred during the first week of neutropenia (early-onset) and 919 (36.5%) thereafter (late-onset). Patients with late-onset BSI, the relative risk for BSI Enterococcus spp. and Candida spp. was 1.74 (CI95% 1.55-1.95) and 1.98 (1.66-2.36), while it was 0.50 (0.41-0.60) for E. coli.

Conclusions
A longer duration of neutropenia is associated with pathogens resistant to broad-spectrum such as E. faecium, S. maltophilia, and Candida spp.

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P51 | A new in-vitro bioassay for the detection of Clostridium botulinum neurotoxins

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Background
Clostridium botulinum neurotoxins (BoNTs) are the most poisonous naturally occurring protein toxins known to mankind, the toxicity range in humans starting as low as 0.3 ng/kg when administered intravenously. All BoNT serotypes (A-G) consist of two subunits, a ≈ 100-kDa heavy chain (HC) and a ≈ 50-kDa light chain (LC), which are linked by a disulphide bond. Upon binding to specific membrane receptors on the neurolemma of neurons, the HC translocates the LC over the membrane where it exerts its cleaving activity against SNARE proteins, thus inhibiting neurotransmitter release. Currently, the potency of biologically active BoNT is monitored using the murine LD50-assay.

Aim
To develop an in vitro assay capable of detecting BoNT activity on neurons using electrophysiological recording techniques.

Method
Mouse embryonic stem cells (mESC) are differentiated towards neurons by embryoid body (EB) formation. After 7 days the EBs are dissociated and the cells are cultured for 3 weeks on multi-electrode arrays (MEAs) allowing the extracellular recording of spontaneous neuronal activity. The cultures are then treated with different concentrations of BoNT serotype A (BoNT/A) and spontaneous network bursts, evoked through synaptic transmission, as well as total network activity are recorded 6 hours after exposure to the toxin.

Results
48 cultures from 6 independent experiments were assessed. 23 cultures were used to quantify the effect of the toxin on synapses and treated with either 25ng/ml or 2.5ng/ml BoNT/A. 25 cultures served as control and did not receive any treatment. Exposure to BoNT/A for 6 hours resulted in a significant decrease of the burst rate for toxin concentrations of 25ng/ml (49.5 ± 27.2; $p<0.0005$; n=7) and 2.5ng/ml (66.7 ± 42.5; $p<0.005$; n=16) compared to untreated cultures (100 ± 20.3; n=25). A significant decrease in the total network activity was observed for toxin concentrations of 25ng/ml (45.5 ± 48.0; $p<0.005$; n=7) and 2.5ng/ml (78.0 ± 70.9; $p<0.05$; n=16) compared to untreated cultures (100 ± 31.9; n=25)

Conclusion
The present assay detects toxin activity of BoNT/A. Thus proof of principle has been achieved. Given sufficient robustness and a further increase in sensitivity to detect BoNT/A, this assay may replace the murine LD50-assay in e.g. the batch control of pharmaceutical products.

P52 | Differential dynamics of HIV infection in MISTRG and MITRG mice

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Humanized mice (hu-mice) are a valuable tool to study HIV pathogenesis. MI(S)TRG mice, which harbor human versions of four cytokines important for innate immune cell development with or without the human SIRPα transgene, develop a human lymphoid system supporting the development of monocytes, macrophages and NK cells as compared to previous hu-mouse models. We aim to explore the impact of the improved innate immune cell compartment on the dynamics of HIV infection. MI(S)TRG newborn mice were transplanted intra-hepatically with cord-blood-derived CD34+ cells. Human immune cell reconstitution was assessed after 9 weeks, followed by intra-peritoneal HIV infection with the R5 strain YU2. Plasma viral load (determined by RT-PCR), frequencies of cell subsets (analyzed by flow cytometry), and cytokine secretion (measured by multiplexed particle-based flow cytometry) were monitored up to 12 weeks post-infection (p.i.). HIV infection in MISTRG mice was characterized by a fulminant viremia, which rapidly declined. Human blood engraftment drastically decreased during the first 4 weeks p.i., which was associated with a disappearance of myeloid cells (CD33+, CD14+ and CD14+CD16+ cells), while T cells steadily increased over the time of infection. Plasma levels of IFN-γ and IL-12p70 peaked at around 4 weeks p.i.. In contrast, HIV infection in MITRG mice was characterized by a slow progression, an expansion of myeloid cells and the secretion of IL-6 and TNF-α.T cell frequencies were much lower throughout the infection than in MISTRG mice. In conclusion, the dynamics of HIV infection, myeloid cell frequencies and cytokine profiles were different between MISTRG and MITRG mice. Early control of viral replication in the MISTRG mice might be explained by a transient Th-1 response. Future experiments will assess the impact of each myeloid cell subset on HIV infection though cell-specific depletion protocols.

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P53 | Host depletion sample preparation increases sensitivity of metagenomics analysis of cerebrospinal fluid samples of patients suffering from central nervous system infections

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Management of patients with central nervous system (CNS) infections is a challenge since the aetiology by clinical diagnostic assays remains unknown in up to 60% of meningo-/encephalitis cases. We developed a method for host depletion before applying NGS methodology and custom bioinformatics analysis to cerebrospinal fluid (CSF) samples with the aim to identify unknown aetiologies of CNS infections. The host depletion method consists firstly of a homogenization to release eukaryotic nucleic acids (NA) while integrity of viruses and bacteria is preserved. Then, host NA is enzymatically degraded and subsequently depleted by a magnetic bead separation. Surrogate CSF samples consisting of artificial CSF, controlled amount of human cells and defined virus and bacteria concentrations were used to evaluate the method. Combined RNA and DNA sequencing of native and host depleted surrogate and patients' CSF samples was run using Ion Torrent™ and Illumina® technology. Sequencing data were analysed using a tentative bioinformatics pipeline involving a taxonomic sequence classifier to remove residual host sequences followed by identification of the remaining non host sequences. A 100.000 fold depletion of host NA with minimal loss of viral and bacterial NA was confirmed in surrogate CSF samples by qPCR. This drop of the host NA proportion after depletion is reflected in a higher match rate of pathogens' sequences after bioinformatics analysis compared to native samples of a pathogen dilution series in surrogate CSF samples. Sequencing was confirmed to be at least as sensitive as qPCR. HSV was confirmed by sequencing in a HSV positive diagnosed patient's CSF sample.

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P54 | Imported infectious diseases among newly arrived Eritrean refugees in Basel – preliminary results from the Immigration Health Study Switzerland

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Background
A quarter of refugees arriving in Switzerland in 2015 originated from Eritrea. Yet, data on health status of Eritrean immigrants in Switzerland are scarce. We report preliminary data from screening for selected infectious diseases among asymptomatic newly arrived Eritrean refugees in Switzerland.

Methods
The study started in January 2016 with recruitment still on-going. Asymptomatic Eritrean refugees aged ≥16 years who arrived in Switzerland after 1st of January 2015 are recruited via cantonal refugee registries. Screening for infectious diseases comprises 2 stool samples for protozoa and helminths, serology for HIV, hepatitis B and C, syphilis and schistosomiasis, circulating cathodic antigen (CCA) in urine and malaria PCR in blood. We anticipate having enrolled ≥150 participants by November 2016.

Results
At submission of the abstract 54 participants (45 male, 9 female), median age of 21 years (Inter Quartile Range: 19-28) were enrolled. Eighteen participants had at least one pathogenic parasite detected in stool examination (7 Schistosoma mansoni, 6 Hymenolepis nana, 5 Giardia lamblia), 21 (43%) had a positive CCA test in the urine, indicating active schistosomiasis infection. Among participants tested CCA positive 45% had level D peri-portal liver fibrosis according to World Health Organization's ultrasound classification. Despite of the relatively low rate of active scabies (28%), most participants reported history of previous disease. Out of the 37 asymptomatic participants with PCR result available at submission of the abstract, 4 (11%) had a positive PCR for Plasmodium vivax. All had negative serology for HIV, hepatitis B and C and syphilis.

Conclusion
More than one out of three asymptomatic Eritrean refugees had at least one pathogenic parasite detected in stool examinations, nearly half had evidence of active schistosomiasis - none was aware of it. And 1 out of 9 had a Plasmodium vivax infection. Routine screening for stool-parasites, schistosomiasis using CCA and malaria using PCR may be considered in refugees arriving from Eritrea to prevent long term sequelae from untreated schistosomiasis or relapsing malaria episodes.

Table 1_ Infectious Diseases

Parasites	**Screened participants**	**Detected parasites**	**N (%)**
Schistosomiasis	56	Positive CCA in urine	26 (47)
		Positive serology	24 (43)
		Egg-detection in stool microscopy	8 (14)
Other stool parasites	56	*Hymenolepis nana*	7 (13)

		Giardia lamblia	5 (8)
Malaria (PCR)	*56*	*Plasmodium vivax*	4 (7)
Scabies	58		16 (28)

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P55 | Daptomycin versus vancomycin in the treatment of infections with methicillin-resistant staphylococci or beta-lactam-resistant enterococci in neutropenic cancer patients: a pilot study

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Background
We conducted a pilot study to assess the efficacy and safety of daptomycin compared to vancomycin in neutropenic cancer patients with beta-lactam-resistant Gram-positive cocci infection.

Methods
Eligible subjects were adult hemato-oncological patients with febrile neutropenia and proven or suspected infection with methicillin-resistant staphylococci or beta-lactam-resistant enterococci. Patients were randomly assigned (2:1 ratio) to receive empirical therapy with daptomycin or vancomycin, in combination with broad-spectrum beta-lactam therapy. The study drug was discontinued if the causative organism was found to be susceptible to the concomitant beta-lactam antibiotic. The primary endpoint was the global response (clinical + microbiological) at the end of therapy (EOT) in the modified intention-to-treat (MITT) population. Secondary endpoints included global response and survival on day 7 after the end of treatment, time to defervescence and time to bacteraemia clearance. A PK/PD analysis was performed in the subset of patients receiving at least 3 days of daptomycin.

Results
Thirty-two patients were enrolled, 15 were included in the MITT population and 13 in the PK/PD analysis. Global response rates in evaluable patients were 90% in the daptomycin group vs. 100% in the vancomycin group at EOT and 75% vs. 100% at day 7. There was one case of relapsing S. epidermidis bloodstream infection among daptomycin-treated patients. Duration of fever, time to clearance of bacteraemia and overall mortality were identical in both groups. A higher incidence of skin rash was surprisingly identified in the daptomycin group (43% vs. 9%), leading to treatment interruption in two patients. All reactions were mild and reversible. Median values of daptomycin clearance and volume of distribution at steady-state were 30% and 71% higher than those reported in healthy subjects. Despite this finding, a two-log bacterial count reduction was reached in 6/7 with staphylococcal infection. The relapsing infection occurred in the only patient with suboptimal daptomycin exposure.

Conclusion
The results of this pilot study suggest that daptomycin may be an effective and safe alternative to vancomycin for the treatment of beta-lactam-resistant gram-positive organisms in neutropenic patients. Daptomycin was associated with an unusually high incidence of skin rash that deserves further evaluation.

P56 | A prospective multicentre study of healthcare provider preference in rapid HIV testing kits: determine versus INSTI

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Background
Rapid HIV testing may circumvent the practical barriers to HIV testing in several settings. User preference of the testing kits available has been relatively underexplored. We examined healthcare provider (HCP) ratings of two validated rapid testing kits in clinical practice.

Methods
We prospectively recruited HCPs with varying experience in rapid HIV testing from three outpatient clinics linked to Lausanne University Hospital, Lausanne, Switzerland. The HCPs performed rapid HIV testing using DetermineTM Combo (DETE) or INSTI™ (INSTI), according to a predefined randomization sequence, and rated practical aspects of each test using a Likert scale.

Results
Globally, the testing procedure was rated as easy or very easy by 97% of participants without test preference and HCP confidence in the testing procedure increased rapidly (after 11-13 tests). Median time to result was 23 minutes for DETE and 4 minutes for INSTI. DETE was rated easier than INSTI for blood collection ($p=0.009$) and kit storage ($p<0.001$) while INSTI was rated easier than DETE for blood application ($p=0.001$) and test interpretation ($p<0.001$). Overall, HCPs stated they would recommend INSTI over DETE based on the time to result, ease of test interpretation and overall ease of use.

Conclusion
Rapid HIV testing was easy to perform, even by inexperienced medical or nursing staff. Confidence in performing testing was gained rapidly and independently of professional background and experience. Both tests were considered easy to use but participating HPCs preferred INSTI to DETE overall due to rapid time to result and overall ease of use.

P59 | Legionnaires' disease in Switzerland: a look into the sparse literature

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Legionnaires' disease (LD) is caused by Legionella spp. and is notifiable in Switzerland. Cases reported to the Federal Office of Public Health (FOPH) have increased substantially from 69 cases in 1999 to 380 cases in 2015. Reasons for this increase could include changes in diagnostic methods, disease awareness, risk factors and climate. We searched the literature to identify knowledge gaps in the epidemiology of legionellosis in Switzerland with a focus on diagnostic procedures, identification of clusters, and LD case management. Culture-based diagnosis is considered the gold standard. However, sputum samples are difficult to obtain as LD is characterised by pneumonia with a non-productive cough. The urinary antigen test for Legionella pneumophila serogroup 1 has facilitated LD diagnosis substantially. However, the test is sensitive for one serogroup only. Hence, relying on this test leads to under-ascertainment of LD caused by other serogroups or species. Guidelines on the management of community acquired pneumonia in adults are available for Switzerland. In the outpatient setting, microbiological investigation is not recommended. Consequently, only severe cases of LD would be diagnosed. However, it is not known to what extent the guidelines are followed in clinical practice. Nevertheless, it is likely that the LD cases reported to the National Notification System for Infectious Disease (NNSID) represent a highly selective sample of rather severe and hospitalised cases. The difficulty involved in obtaining legionella cultures together with the convenience of using the urinary antigen test for diagnosis reduces the number of isolates available. Without isolates, molecular methods that can link cases to one another and sources to cases cannot be used. Understanding the (applied) diagnostic practices of Swiss physicians and difficulties in laboratory diagnosis is crucial to interpret surveillance data and to design future studies investigating risk factors and risk exposures.

P60 | Prevalence of Schistosomiasis in asylum seekers from subsaharian Africa

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Background
Although a rise of asylum seekers from the middle east has been observed in the last years, still over 30 % are persons from sub saharian africa. Prevalence of Schistosomiasis in these persons is unknown, as most of the patients are asymptomatic.

Methods
We collected urine samples in 4 asylum centres in the region Olten. Urine was analysed for schistosomiasis with Circulating Cathodic Antigen (CCA-Ag, Rapid medical diagnostics®). As this was a substudy of the investigation of multiresistant organisms in asylum seekers in Switzerland, only urine from persons of subsaharian Africa were analysed. We grouped the data in east and central/west Africa.

Results
19/71 (26.8%, CI95 17.8-38.1%) urine samples from east Africa and 1/13 (7.7% CI95 1.7-33.8%) from central/west Africa were tested positive. Most persons were asymptomatic.

Conclusion
Prevalence of Schistosomiasis is high in persons from subsaharian Africa, especially from east Africa. Even if the test is highly sensitive according to publications, the setting in Europe with possibility of eradication schistosomiasis and absence of reinfection could help.

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P61 | Depletion of FoxP3+ regulatory T cells promotes T helper 1/17 cell immunity and leads to an improved control of larval Echinococcus multilocularis infection

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Background
The growth potential of the tumor-like Echinococcus multilocularis metacestode (causing alveolar echinococcosis, AE) is directly linked to the nature/function of the periparasitic host immune-mediated processes. Previous studies showed that regulator T cells (Tregs) become gradually up-regulated in the course of both chronic human and murine AE. So far, little is known about the contribution of the respectively associated transcriptional factor FoxP3 and FoxP3-regulated long non-coding RNAs (lncRNAs) to the control of this chronic helminthic disease.

Methods/Findings
As a key parameter for infection outcome, parasite load (i.e. wet weight of parasitic metacestode tissue) was assessed in E. multilocularis-infected DEREG mice with/without diphtheria toxin (DT) application either for prevention or treatment at 1 and 4 month(s) post-infection. Flow cytometry and qRT-PCR were used to assess Treg, Th17-, Th1-, Th2-type immune responses and maturation of dendritic cells (DCs). A mouse lncRNA array was employed to obtain information on FoxP3-regulated lncRNA expression in the spleen cells at 1-month post infection. We showed that E. multilocularis-infected DEREG mice treated with DT exhibited (as compared to infected DEREG-mice without DT application) (a) a significantly lower parasite load, (b) an increased T cell proliferative response to ConA, (c) reduced Treg function, and (d) a persisting capacity of Th1-polarization and DC-maturation. Biological pathways identified through the lncRNA microarray screening were categorized into six major groups: infection and inflammation, metabolism, signaling and transcriptional regulation, cell processing, nucleosome assembly, cell adhesion and migration.

Conclusions
FoxP3+ Tregs appear as one of the key players in immune regulatory processes favoring metacestode survival by down-regulating T cell activity and DC maturation, and FoxP3 is involved in the expression of distinct lncRNAs. Prospectively, targeting Foxp3 or specific lncRNA could be an option to develop an immunotherapy against AE, and putatively also against other chronic parasitic diseases that exhibit a similar pathogenesis.

P62 | A dual PCR-based sequencing approach for the identification and discrimination of Echinococcus and Taenia

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Reliable and rapid molecular tools for the genetic identification and differentiation of Echinococcus species and/or genotypes are crucial for studying spatial and temporal transmission dynamics. Here, we describe a novel dual PCR targeting regions in the small (rrnS) and large (rrnL) subunits of mitochondrial ribosomal RNA (rRNA) genes, which enables (i) the specific identification of species and genotypes of Echinococcus (rrnS+L-PCR) and/or (ii) the identification of a range of taeniid cestodes, including different species of Echinococcus, Taenia and some others (17 species of diphyllidean helminths). This dual PCR approach was highly sensitive, with an analytical detection limit of 1 pg for genomic DNA of Echinococcus. Using concatenated sequence data derived from the two gene markers (1225 bp), we identified five unique and geographically informative single nucleotide polymorphisms (SNPs) that allowed genotypes (G1 and G3) of E. granulosus sensu stricto to be distinguished, and 25 SNPs that allowed differentiation within E. canadensis (G6/7/8/10). In conclusion, we propose that this dual PCR-based sequencing approach can be used for molecular epidemiological studies of Echinococcus and other taeniid cestodes.

P63 | Legionnaires' disease in Switzerland 1999 to 2015: strong increase of case numbers – causes unknown

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Introduction
A growing number of cases of Legionnaires' disease (LD) is observed in Switzerland and other European countries. It is important to investigate the causes to achieve better knowledge of the sources and transmission routes.

Methods
In Switzerland, legionella infections are notifiable. We analysed data of 1999 to 2015 with respect to temporal, regional and demographic factors. All cases with a positive laboratory result for Legionella spp. and the clinical picture of pneumonia, hence, with LD, were included. Reporting rates were calculated using yearly data of the permanent Swiss resident population (provided by the Swiss Federal Statistical Office).

Results
The number of cases has more than quintupled during the observation period: from 69 cases in 1999 (reporting rate of 0.9 per 100,000) to 380 cases in 2015 (reporting rate of 4.6 per 100,000). In 2001, a significant reporting increase was recorded after the introduction of the urinary antigen test. Ever since case numbers are steadily rising. Highest case numbers are observed during the warm and humid months in summer and autumn. The median age remains constant at 64 years. The reporting rate increases with age. People aged 50+ years account for 89% of all cases. Men are 2-3 times more frequently affected than women. The source of infection is unknown at least for 75% of the cases. Reporting rates vary considerably between regions: Reporting rates for LD are significantly higher in the canton of Ticino than in the rest of Switzerland.

Conclusion
Increased testing for LD contributes only in part to the additional cases observed as reporting rates continue to rise after the establishment of the urinary antigen test. Moreover, the analysis of the age-specific notification rates shows that the rising trend is only partly attributable to a demographic shift. The seasonality and the fact that especially the canton of Ticino with higher temperatures and more precipitations has the highest reporting rates underlines the likely importance of climatic conditions as determinant for legionella transmission.

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P65 | How common is acute gastroenteritis in primary care? Results from a study using the Swiss Sentinel Surveillance Network "Sentinella"

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Acute gastroenteritis (AG) is a common disease worldwide. The incidence in European countries has been estimated at 0.5-1 episodes per person-year. Even though AG is usually self-limiting, it can lead to considerable health system use, work loss and socio-economic impact. In Switzerland, information on AG incidence is basically limited to notifiable pathogens such as Campylobacter spp., Salmonella spp., Shigella spp. and enterohaemorrhagic E. coli. However, only cases consulting a physician and providing a stool sample which is tested positive for a notifiable pathogen can end up in the mandatory surveillance system. We used the Swiss Sentinel Surveillance Network "Sentinella" to assess the frequency of consultations due to AG, the diagnostic and treatment approaches of primary care physicians and the days of work lost due to the disease. During the Sentinella-year 2014, 172 primary care physicians participated in the network. They had to report all first consultations due to AG on a weekly basis and provided supplementary information for a subsample of patients. In total, 3867 cases were reported. For 2357 cases, supplementary information was available of which 2200 were included in the analysis. The estimated incidence of consultations due to AG is 7/1000 consultations. Around 20% of cases need more than one consultation. The general state of patients, as rated by the physicians, is fairly good (median of 7 on a 1-to-10 rating scale). Nevertheless, 86% of employed cases were on sick leave. Physicians requested stool samples in 12% of cases and prescribed antibiotics in 9% of cases. Almost 3% of patients were hospitalised. This study showed that AG leads to a considerable burden of disease and socio-economic impact due to absence from work. Surveillance data underestimates the burden of AG considering that in the majority of cases no stool testing is performed. This fact should be taken into account when interpreting surveillance data.

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P66 | Evaluation of Schistosomiasis Urine-CCA-Ag® in Comparison to Serology

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Background
Schistosomiasis is relatively difficult to diagnose. Serology may be positive despite adequate treatment history, and direct identification of the pathogen is elaborate and requires good experience and expertise. Schistosomiasis CCA-Ag ® (Rapid Diagnostics®) is and easy to perform urine test with a high sensitivity. However, data regarding specificity of the test are scare. We compared positive test results with serology.

Methods
In a substudy of the MRSA/ESBL Prevalence in asylum seekers investigation, we analysed the prevalence of Schistosomiasis in refugees from subsaharian Africa. Persons with positive test results were further investigated and treated according to guidelines. Schistsomiasis and Cysticerkosis–Serology was performed in all patients before treatment. In treated patients, CCA-AG test was performed one month after treatment.

Results
30 Patients with positive CCA-Ag could be identified. 6 patients were transferred elsewhere and further evaluation was not possible. Of the remaining 24 patients, 17/24 (70%; CI95 51-85%) had a positive Schistosomiaisis serology. In 4/7 patients with negative serology, control CCA-Ag without treatment was negative, in 1/7 patients, it was not done, and in 1/7 patient, CCA-AG remained positive. In 1/7 patient with negative serology, treatment was performed, but CCA-Ag remained positive. In 19/24 patients we looked for eosinophilia, with was present in 8/19 (43% CI 23-64%) patients, but only in one patients, it was above 1 G/L. All patients were asymptomatic. Cysticerkosis serology was positive in 3/24 patients, all with normal radiographic neurocranium.

Conclusion
Even if CCA-Ag might have a high sensitivity and can be performed as screening test, specificity is moderate and a positive test should be confirmed by serology. As most persons had left their country of origin more than 3 month ago, we interpret the constellation positive CCA-Ag and negative serology as false positive result.

P68 | Development of a movement-based in vitro screening for new anti-cestodal compounds

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High throughput in vitro drug screens against nematodes are often based on monitoring the movement of larvae in microwell plates. This system is well established for various species. In contrast, an in vitro-screening assay for identifying cestodices is more difficult to establish due to the fact that (i) oncospheres in the eggs (of which a high number is produced) do not represent the target of interest, (ii) the larval stages are located in intermediate hosts and normally can only be found in limited numbers and (iii) adult cestodes are not suitable for use in microwell plates due to their size. The in vitro-drug assay presented below uses protoscolices of Echinococcus multilocularis, which are well suited for use in a 384 well format. Protoscolices, which form the “head” of the adult tapeworm, can be produced in large numbers, and their movement is measured and quantified by image analysis. Active compounds can also be directly assessed in terms of morphological effects. The use of the 384 well format minimizes the amount of parasites and compounds needed and allows rapid screening of a large number of chemicals. So far, standard drugs (e.g. praziquantel and nitazoxanide as positive- and monepantel as a negative-control) have been tested. They showed the expected dose-dependent effect on the movement and on the morphology of the protoscolices. A difference in IC50 was observed for the praziquantel enantiomers. A new compound from the open access MMV (Medicines for Malaria Venture) box exhibited excellent in vitro activity. Corresponding morphological alterations were visualized by scanning electron microscopy (SEM), and showed that this compound exhibits a mode of action clearly distinct from praziquantel. The compound will, together with other drugs, be further evaluated also.

P69 | Theileria annulata interacts with adaptor proteins of its bovine host cell

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Theileria annulata is a tick-transmitted apicomplexan parasite that causes fatal leukoproliferative disease in susceptible cattle. Shortly after invasion of a leukocyte, Theileria dissolves the surrounding host-derived membrane, giving the parasite access to an ideal position in the host cell cytoplasm to interact with host cell proteins. The parasite modulates host cell signalling pathways, leading to uncontrolled proliferation, resistance to apoptosis and increased metastasis of infected host leukocytes. The schizont ensures its propagation within the cytoplasm of the continually dividing host cells by stably interacting with the host cell microtubule network. We made use of a method called BioID to identify proteins on the schizont surface. A promiscuous biotin protein ligase (BirA*) is fused to a protein of interest that guides the fusion protein to its normal cellular location. Biotin is activated by BirA* and binds covalently to any primary amine in close proximity to the fusion protein. Biotinylated proteins can subsequently be isolated and identified by mass spectrometry. With this method we identified two host cell adaptor proteins, CD2AP and CIN85, which associate with the schizont surface. Adaptor proteins are molecules possessing two or more protein-binding domains that function to allow the formation of large signalling complexes. CD2AP contains several SH3 domains and a proline-rich domain and has been implicated in both signal transmission and cytokinesis - cellular processes that are used by the parasite to transform its host cell and to ensure its distribution to both daughter cells. In a second BioID screen we also identified the previously uncharacterized Theileria protein TA20980, which is secreted into the host cell and interacts with CD2AP. Currently I am investigating the interaction network of the adaptor proteins and TA20980 on the schizont surface using microscopy, proximity ligase assays and co-immunoprecipitation. The function and the potential contribution of these proteins in modulating host cell signal transduction pathways will be tested in Theileria infected macrophages depleted for the adaptor proteins. Because the schizont cannot be genetically manipulated, the function of TA20980 will be tested by over-expression of the protein in non-infected macrophages. By studying the way in which CD2AP interacts with Theileria, we hope to learn more about the strategies this fascinating parasite employs to survive within its host.

P70 | Drugs against alveolar echinococcosis: the hunt goes on

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Echinococcosis is a neglected disease affecting humans and animals all across the globe. Echinococcus multilocularis (fox tapeworm) is the etiological agent of human alveolar echinococcosis (AE), a disease with fatal consequences. Current chemotherapeutic treatment consists of the benzimidazole derivatives albendazole and mebendazole. However, while these compounds inhibit further parasite growth, they fail to kill it. Moreover, they are ineffective in some cases, and they can lead to adverse side effects which demand treatment discontinuation. Thus, new chemotherapeutic agents are urgently needed. AE has not yet attracted the attention of pharmaceutical companies. Thus, the repurposing of already described drugs is a promising strategy to find new agents against AE. We assessed two compounds for their efficacy against the metacestode (disease-causing) stage of E. multilocularis: Buparvaquone and MMV665807. Buparvaquone is already in use for the treatment of theileriosis in cattle, whereas MMV665807 is an experimental compound related to niclosamide and derived from the Medicines for Malaria Venture (MMV) malaria box. Both compounds exhibited high parasiticidal activity against in vitro cultured metacestodes and in germinal layer cell-based in vitro assays, but only relatively low toxicity against human fibroblasts and rat hepatoma cells, thus opening a potential therapeutic window. Additional electron microscopy revealed specific ultrastructural changes induced by both drugs. However, experimental treatment in E. multilocularis infected mice failed to significantly reduce the parasite burden, probably due to poor bioavailability. In order to characterize the mode of action of these drugs, affinity chromatography and subsequent mass spectrometry with E. multilocularis cell extracts was performed. Whereas no buparvaquone-binding protein could be identified, MMV665807 was found to be a major interaction partner of the Calmodulin orthologue Em-Cmd1. Additional enzymatic assays could verify the functional inhibition of calmodulin by MMV665807. Taken together, the two compounds buparvaquone and MMV665807 exhibit promising activities against E. multilocularis in vitro, but failed to do so in vivo. This demonstrates that further studies also need to focus on the pharmacokinetics of these compounds and how their bioavailability could be improved in vivo. Thus, the search for new drugs against AE continues.

P71 | Ran as a potential effector for host cell transformation in Theileria annulata infected macrophages

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Theileria annulata is an apicomplexan, strictly intracellular parasite that causes a severe leukoproliferative disease, Tropical Theileriosis, in susceptible cattle. Theileria possesses the outstanding ability to transform and immortalise its host cell, causing uncontrolled proliferation and resistance to apoptosis. By closely interacting with host microtubules and central spindles during mitosis the parasite ensures its distribution to both daughter cells, which is important to keep the transformed state of the host cell. The mechanisms leading to the unique transforming ability of Theileria are still not clarified. We recently discovered that RanGTPase activating Protein 1 (RanGAP1) binds to the parasite surface, where we hypothesise that it contributes to host cell transformation. RanGAP1 is one of the regulators of the Ran GTP/GDP cycle and participates in nuclear-cytoplasmic transport, mitotic spindle assembly and cell cycle regulation. The excessive activation of Ran has been associated with cellular transformation and cancer formation in several studies. Therefore we investigated the expression and localisation of Ran in Theileria infected cells. Useing live cell imaging we showed that Ran associates with the parasite surface in a cell cycle dependent manner, and demonstrated the localisation of endogenous Ran on the schizont surface by using a proximity ligase assay (DuoLink). We are using RanBP1 coated agarose beads to pull down GTP-bound Ran in order to compare Ran activation in Theileria infected and non-infected cells. Now we plan to make use of shRNAs and specific Ran mutants to investigate the functional contribution of Ran expression and activation to Theileria-dependent transformation.

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P73 | Evaluation of a commercial PCR based kit for the detection of parasitic protozoa in stools

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Background
Our objectives were to test the performance of a commercial diagnostic kit for the molecular detection of intestinal protozoa in fresh stool specimens, to assess the performance of our actual routine procedures and to evaluate the interest of introducing PCR based diagnostic tools in our daily routine.

Methods
Three hundred and one fresh stool specimens for which a parasitological examination was requested were tested with a commercial real-time PCR diagnostic test: RIDA®GENE Parasitic Stool Panel II (R-Biopharm) after an easyMAG (BioMérieux) nucleic acid extraction. This kit is intended for the detection of three intestinal protozoa: Giardia lamblia, Entamoeba histolytica and Cryptosporidium parvum. All specimens were also examined with our routine procedures (direct examination, SAF enrichment procedure) and with a commercial ELISA based test for the detection of Cryptosporidium parvum (RIDASCREEN® Cryptosporidium, R-Biopharm). A selection of 26 positive samples were further analysed for confirmation with the rapid multiplex PCR device: Biofire FilmArray®Gastrointestinal (GI) panel test (BioMérieux) which is designed to detect 22 intestinal pathogens including the same protozoa.

Results
We obtained both PCR and routine results for 294 samples, 7 samples could not be extracted properly or showed a PCR inhibition. Overall 29 samples tested positive, only two exhibited a mixed infection. Giardia lamblia was most frequently detected. Among those 8 Giardia were detected by PCR only. Five Cryptosporidium were found, two of which only by PCR. Only 1 true Entamoeba histolytica was diagnosed. Both commercial PCR yielded comparable results except for two Giardia which were detected only by the Biofire GI assay, one of which was microscopy positive.

Conclusions
The two diagnostics kits proved to be more sensitive than microscopic examination or ELISA testing particularly for Giardia lamblia. This parasite may be easily missed if present as trophozoite in the specimens or after antibiotic treatment. These tests are easy to perform, deliver rapid, same day results. The RIDA®GENE test can be batch processed thus could be used as screening test. However it would require careful selection of stools suspected to contain other protozoa or helminths according to clinical and anamnestic indications, in order to perform additional enrichments and microscopic examinations. The Biofire GI test is more useful as an emergency syndromic approach test.

P74 | New quantitative real-time PCR detecting Entamoeba moshkovskii in fresh stool samples

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Cysts of Entamoeba moshkovskii are indistinguishable by light microscopy (LM) from those of E. histolytica and E. dispar. Although infection with E. moshkovskii, a primarily free-living amoeba, has not yet been reported to cause severe disease, the relevance of diagnosing E. moshkovskii in stool samples has increased in the last decades. Endemicity and prevalence were found to mirror that of E histolytica and E. dispar in serveral countries of Asia. However routine molecular diagnostics are usually not detecting E. moshkovskii and are limited to E. histolytica/E.dispar differentiation. As a consequence false-negative by qPCR compared to positive results by light microscopy are occasionally observed. To verify the origin of the discrepancies between LM and molecular diagnostics, a quantitative real-time PCR (qPCR) was developed to specifically detect E. moshkovskii in DNA of fresh stool samples. This qPCR on E. moshkovskii complements therefore the existing qPCR differentiating E. histolytica/E.dispar and improved the accuracy of species determination in routine molecular diagnostics.

P75 | Immunization with Neospora caninum antigens fused to a TLR2 ligand increases pup survival in a nesporosis pregnant mouse model

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The development of effective subunit vaccines against parasitic diseases is a highly desirable but not yet accomplished goal. Protozoal pathogens prone to be vertically transmitted to the offspring and/or to induce abortion, such as the apicomplexans Toxoplasma gondii, Neospora caninum and Plasmodium falciparum, pose an additional level of complexity for the development of successful subunit vaccines due to the immunomodulation associated with pregnancy. In this work we used a pregnant mouse model of neosporosis to address how different adjuvants targeting innate immune receptors impact on the modulation of the immune response against antigens inoculated before and boosted after initiation of pregnancy. We also studied the outcome of infection in dams challenged during pregnancy, and how this affected the survival of the respective pups. For that, we fused three N. caninum antigens (PDI, ROP2 and ROP40) with the OprI lipoprotein, a TLR2 ligand, and immunized mice with or without additional TLR3 and TLR7 ligands (Poly I:C and R848, respectively). Humoral response profiles (IgG1 and IgG2a) and cytokine responses were evaluated before and after pregnancy and the parasite burden was evaluated by real time PCR in non-pregnant females, dams and pups. Different immune profiles were observed in the different groups. A significant reduction of clinical signs in dams and an improvement of pup survival were observed in the group immunized with OprI-fused antigens without additional TLR ligands. Correlations between immune response, infection status, clinical signs, and vertical transmission will be presented.

P76 | Differential manipulation of the host cell Golgi and endosomal system by Toxoplasma gondii and a related apicomplexan, Besnoitia besnoiti

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Besnoitia besnoiti and Toxoplasma gondii are two protozoan parasites and represent the etiological agents of besnoitiosis and toxoplasmosis, respectively. Both parasites are of veterinary importance, and T. gondii is also of high medical relevance, especially during pregnancy and in immunocompromised individuals. As intracellular parasites, they recruit the host cell Golgi complex, the organelle mediating protein and lipid transport, to the parasitophorous vacuole (PV). However, T. gondii induces fragmentation of the Golgi, while B. besnoiti compacts the organelle, a feature not seen before among intracellular pathogens. Using specific antibodies, we confirmed Golgi ribbon compaction in B. besnoiti, and dispersion in T. gondii, determining also that in either case the Golgi stacks of infected cells contain both cis (GM130) and trans (TGN46) Golgi proteins. In addition, we analyzed the localization of components of the secretory trafficking pathways in cells transfected with CFP-Rab constructs (Rab5C; Rab9 and Rab11A, localizing at early, late and recycling endosomes, respectively) and infected with T. gondii and B. besnoiti. At 36h post-infection, all three Rab proteins were recruited to the vicinity of the PVs in both parasites, suggesting a subversion of distinct endosomal/secretory pathways. Thus, despite exhibiting differential effects on Golgi morphology, both parasites interact with host vesicles of the related endosomal system, and hijack important regulators such as Rabs, probably to efficiently acquire nutrients and to proliferate inside the host cell.

P78 | Molecular characterization and phylogeography of Fasciola flukes in Chad and Côte d'Ivoire

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Fascioliasis is a common animal infection, caused by two liver fluke species, *Fasciola hepatica* and *F. gigantica*, and by hybrids of the two. Traditional morphological methods to distinguish the species are unreliable, particularly in the presence of hybrids. In this study, *cox1*, *nad1* and ITS1 and ITS2 loci of 46 *Fasciola* flukes from Chad and Côte d'Ivoire were sequenced to determine the flukes' species and phylogeography. Forty-five flukes were unambiguously identified as *F. gigantica*. One Chadian specimen exhibited the exact pattern of heterozygosity at 8/9 variable sites of the ITS1 and ITS2 locus previously published for hybrids, suggesting that it is a *F. gigantica x hepatica* hybrid. Overall, *cox1* and *nad1* were more variable than ITS1 and ITS2. Chadian and Ivorian *F. gigantica* populations were genetically clearly differentiated. Chadian flukes were more variable than Ivorian flukes at the *cox1* and *nad1* loci but less variable at the ITS1 and ITS2 locus. *Cox1* and *nad1* are variable enough for intraspecific phylogeographic and population genetic analyses, while ITS1 and ITS2 are valuable for species distinction. Our preliminary analysis of *Fasciola* flukes in Chad and Côte d'Ivoire suggests that *F. gigantica* is the main species present, but hybrids appear to occur at least in Chad, which has significant implications for *Fasciola* epidemiology and control approaches.

P79 | High prevalence of sub-microscopic malaria infections: relevance for control and elimination

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Prevalence of malaria infection is a key metric for determining levels of transmission and assessing the effects of interventions. To precisely determine prevalence of Plasmodium species parasites, molecular tools for ultrasensitive parasite quantification were developed and their performance was compared with microscopy, rapid diagnostic test and standard PCR cross sectional and longitudinal studies in Tanzania and Papua New Guinea. Age patterns of microscopic and sub-microscopic parasitaemia were investigated in areas of different malaria endemicity. Sub-microscopic infections constitute >50% of all infections and 40% of these carry gametocytes. Thus these low densitiy infections likely contribute to the infectious reservoir for onwards transmission. High heterogeneity was observed even on small scale geographical scale, such as between neighbouring villages. The use of precise prevalence data use useful for informing intervention strategies, but this relies on development of point-of-care molecular diagnostics and its implementation in remote areas.

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P80 | Visceral leishmaniasis (kala-azar) in Eastern Sudan: treatment of 3500 patients with Médecins Sans Frontières' support

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Visceral leishmaniasis (VL), or "kala-azar", is a deadly neglected tropical disease (NTD) transmitted by phlebotomine sandflies, causing persistent fever with malnutrition, splenomegaly, lymph nodes, severe anemia, severe white cell and platelet deficiency, resulting in death from opportunistic infections or sudden hemorrhage. VL is always deadly without treatment, but current drugs are toxic, expensive, and/or inaccessible in remote rural regions. Sudan is one of the most endemic countries worldwide. We describe here the treatment modalities and outcome of VL patients treated at the Ministry of Health (MOH) Tabarakallah hospital, Gedaref province, with the support of Médecins sans Frontières (MSF), during a 5-year period. This is a retrospective analysis of the programme database used by MSF as a monitoring tool.
From January 2010 to April 2016, 3697 patients were admitted for VL treatment with either primary VL (n=3228; 87.3%), relapses (n=253; 6.9%), or post-kala-azar dermal leishmaniasis (PKDL, n=216; 5.8%). The rK39 rapid diagnostic test (RDT) was used as first-line test for primary VL, but due to its limited sensitivity in East Africa, patients with negative rK39 RDT also underwent a Direct Agglutination Test (DAT); lymph node aspirate was the standard to diagnose borderline DAT results, and relapses.
Three types of injectable treatments were used: 30-day SSG (sodium stibogluconate) monotherapy (n=1427, 38.8%), 17-day SSG-paromomycin (PM) combination, which was introduced in July 2011 (n= 1414, 36.6%), or 10-day liposomal amphotericin B for relapses, pregnant women, ages < 2 or >45 years, HIV co-infected and other severe cases (n=840, 22.8%), or a sequence of the above for slow/non-responders.
The immediate outcomes at discharge were: 97.5% "initial cure rate" (n=3479/3570); 0.16% defaulters (n=6), 2.3% deaths (n=83, including referrals), and 0.6% slow/non-responders (n=22). 1310 (36.7%) patients presented at the 6-month follow-up visit, of whom 1270 showed a "definitive cure" (96.9%). 1 died after initial cure (0.03%), 49 relapsed (1.4%) and only 5 presented PKDL (0.1%). Multivariate regression shows decreased survival ($p<0.05$) among HIV co-infected, malnourished adults, and in patients treated with SSG monotherapy (vs. SSG-PM combination). Good treatment outcomes were obtained in a hospital located in remote eastern Sudan with optimal medical support and free access to treatment, thanks to MOH and MSF long lasting collaboration.

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P81 | Diagnostic guidance for patients presenting with persistent fever in neglected tropical diseases endemic areas of Cambodia, Nepal and Sudan

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Patients with neglected tropical diseases (NTD) such as visceral leishmaniasis (VL) and enteric fever often present with persistent (1week) fever. Existing diagnostic algorithms usually focus on a single disease (e.g. VL). We established the differential diagnosis in patients with persistent fever in several NTD endemic countries, with a focus on potentially severe and treatable diseases. We then developed guidance for diagnostic management by integrating specific clinical features with the results of rapid diagnostic tests. This study (acronym: NIDIAG) is funded by the EU (FP7).

Patients 5 years (18 years in Cambodia) presenting with 1 week fever were recruited after informed consent at three hospitals in Cambodia (Phnom Penh), Nepal (Dharan, Eastern Region) and Sudan (Tabarakallah, Gedaref Province). Data from in depth history taking and physical examination were reported on a case-report form. Blood and urine reference diagnostic tests were performed on site and in referral laboratories for malaria, VL (Nepal and Sudan), HIV, brucellosis, rickettsiosis, leptospirosis, relapsing and enteric fevers. Other investigations (e.g. chest X-ray, abdominal ultrasound, sputum or CSF examination) were done if requested by the physician. All patients were followed-up at 1 month post hospital discharge to assess clinical outcome. Final case-ascertainment was done by an experienced physician based on pre-specified definitions.

In Sudan, out of 667 patients, the most prominent diagnosis were UTI, (n=71; 10.6%), VL (n=65; 9.4%), malaria (n=55; 8.2%), RTI (n=55; 8.2%), PID (n=33; 4.9%) and brucellosis (n=28; 4.2%). In Cambodia, out of 378 patients, pneumonia (n=102; 27%), tuberculosis (n=75; 19.8%), UTI (n=36; 9.5%), skin/soft tissue infection (n=23; 6.1%), liver abscess (n=21; 5.6%), melioidosis (n=16; 4.2%) and leptospirosis (n=15; 4%) were the most frequent diagnosis. In Nepal, out of 425 patients, the differential diagnosis was led by VL (n=54; 12.7%), RTI (n=37; 8.7%), UTI (n=31; 7.3%), tuberculosis (n=23; 5.4%) and rickettsiosis (n=17; 4%). Mixed infections were frequent and the etiological cause remained undefined in 14-48%. Considering the wide differential diagnosis, we developed diagnostic guidance tools based on a panoramic approach.

Persistent (1 week) fever is a frequent reason for seeking health care in the tropics, with a broad differential diagnosis. There is an urgent need to support frontline clinicians with appropriate diagnostic guidance that goes beyond single disease algorithms and includes accessible diagnostic tools.

P82 | Mining Sudanese medicinal plants for natural compounds against neglected tropical diseases.

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It is important to emphasize the significance of the discovery of chemotherapeutic agents for the treatment of neglected tropical diseases (NTDs) as considerable populations are affected.
NTDs are a group of chronic disabling infections affecting more than a billion people world-wild, mainly in Africa and mostly those living in remote rural areas, urban slums or conflict zones. The burden of these diseases is very costly in terms of human suffering as well as contributing to poverty and under-development. The lack of effective, safe and affordable medicines against these diseases, coupled with unavailability of vaccines for any of them, represent a huge challenge.
Most of the currently available drugs have a number of shortcomings and drawbacks, for example, development of resistance, toxicity and non-affordability. On the other hand, there is a severe shortage of novel leads against NTDs that meet the desired target product profiles for these diseases. Therefore, drug discovery of new antiprotozoal compounds against NTDs is urgently needed to reduce themorbidity and mortality associated with them.
Natural products remain the successful source of inspiration for the discovery of new drugs. About two thirds of the drugs launched over the last twenty years derive directly or indirectly from natural resources. Natural products cover a much wider and larger chemical space than combinatorial and synthetic compounds due to the diversity of natural products in terms of chiral centers and richness in functional groups which render them viable for a wider ligand affinity and better specificity to biological targets.
Sudan biodiversity of medicinal plants coupled with deeply rooted ethno-botanical heritage remains a promising untapped reservoir for the discovery of diverse chemical entities.
The aim of this study is to select plant species indigenous in Sudan with known ethno-botanical use against Trypanosomiasis, Leishmaniasis and malaria, validate their respective antiprotozoal activities, and pursue bioactivity-directed fractionation to identify compound(s) as potential hits for lead optimization and further development of new antiparasitic drugs. More than 270 plant extracts and their respective fractions were screened. Plant extracts were tested against the selected strains of protozoa and their activity compared to reference drugs.
HPLC-based activity profiling will be followed to isolate the bioactive agents and finally the structures of the purified compounds emerging from these experiments will be determined.

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P84 | Retrospective study on the utility of pulse oximetry for the identification of young children with severe illnesses and severe pneumonia in a rural outpatient clinic of Papua New Guinea

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Introduction
Identification of children with potential severe illness remains difficult in rural clinics of developing countries. Diagnoses are often based on clinical presentation alone, with no special investigations, with limited predictive value in cases of pneumonia or severe pneumonia. This study investigates the usefulness of pulse oximetry in outpatient clinics of Papua New Guinea (PNG).

Method
Making use of a passive case detection system established for the Intermittent Preventive Treatment for malaria in infants trial (IPTi) in outpatient's clinics of PNG, the usefulness of pulse oximetry in identifying children aged 3 to 27 months with severe illnesses, severe respiratory infections and hospitalization was investigated. Inclusion criteria were: children taking part to the IPTi study visiting one of the clinics during an episode of illness with no previous clinic attendance within 14 days and full medical records available, including pulse oximetry measurements. Severe illnesses were defined as an episode of illness with at least one danger sign according to the IMCI algorithm.

Results
Out of 1921 illness episodes among 669 children, 1663 fulfilled the inclusion criteria. A total of 139 severe illnesses were identified, of which 93 were severe pneumonia. Among 1526 cases of non-severe illness, 727 were classified as non-severe pneumonia. The ROCs curves for pulse oximetry showed an AUC of 0.63, 0.68, and 0.65 for prediction of severe illnesses, severe pneumonia and hospitalization respectively. Pulse oximetry showed better performance in children ≤ 12 months old for all outcomes: sever illnesses (AUC 0.68 versus 0.56; p = 0.01), severe pneumonia (AUC 0.73 versus 0.60; p = 0.02) and hospitalization (AUC 0.7 versus 0.56; p = 0.019). For a threshold of Sp02 ≤ 94%, odds ratios (OR) were 6.1 (95%CI 3.9-9.8), 8.5 (95%CI: 4.9-14.6) and 5.9 (95%CI: 3.4-10.3) for severe illnesses, severe pneumonia and hospitalization respectively.

Conclusion
Pulse oximetry was helpful in identifying children with severe illnesses and severe pneumonia in outpatient facilities of rural PNG, performing slightly better than the reported performance of conventional clinical signs and symptoms alone. Considering its affordability and ease of use, it can be a valuable additional tool for the timely identification of children at risk of poor clinical outcome.

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P85 | Unpredictable checks of yellow fever vaccination certificates upon arrival in Tanzania

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Background
Yellow fever (YF) is a mosquito-borne disease, which can be prevented by vaccination. While YF vaccination (YFV) is not generally recommended for travellers to Tanzania, proof of YFV may be required upon arrival. In April 2013, the World Health Organization concluded that one dose of YFV confers lifelong protection and countries have started to adapt their entry requirements. The traveller's consultant has to balance the risk of YFV and the risk of encountering problems when entering a country without a valid YFV, especially because countries are slowly implementing the requirements.

Methods
We performed a survey among 421 travellers to Tanzania with a pre-travel consultation at the Travel Clinic of the University of Zurich about their experiences with YFV certificate inspections upon arrival in Tanzania between January and November 2015.

Results
There were three main findings: (i) most vaccine card checks were done while crossing the land border of Tanzania. Inspections were frequently conducted at Arusha airport, less often in Dar es Salaam and Zanzibar. In the latter a significantly larger percentage of individuals arriving by ferry/boat were checked than those arriving by plane. (ii) Checks appeared to be non-systematic. They were also performed in travellers who did not enter Tanzania from a YF-endemic country. No seasonal or daytime pattern could be identified; the thoroughness of checks varied widely. (iii) In the case of travel without valid YFV, an exemption certificate was always accepted. In travellers with neither a valid YFV nor an exemption certificate, travellers reported forced YF vaccination and fines before entry was granted.

Conclusions
We recommend YFV or a YF exemption certificate for all travellers to Tanzania until further notice. The decision of whether to vaccinate against YF or to issue an exemption should be based on exposure risk to YF infection in other countries during travel.

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P86 | Stop measles in Switzerland – The importance of travel medicine

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Aims of the study
In line with the worldwide strive to combat measles, the Swiss Federal Office of Public Heath (FOPH) launched a National Strategy for measles elimination 2011-2015. In this study, we highlight the importance of travel medicine consultations to complement measles vaccinations based on data from the Travel Clinic of the University of Zurich.

Methods
We analysed measles vaccination data from the Zurich Travel Clinic between July 2010 and February 2016 and focused on three vaccination groups: (i) all clients who received the measles vaccination, (ii) all clients above the age of two years who received the measles vaccination ("catch-up vaccination"), and (iii) all clients above the age of two years and born after 1963 ("FOPH recommended catch-up vaccination").

Results
107,669 consultations were performed at the Zurich Travel Clinic from 2010 to 2016. In 12,470 (11.6%) of these, a measles vaccination was administered; 90.9% measles vaccinations were given during a pre-travel consultation, and 99.4% were administered to individuals above the age of two years ("catch-up vaccinations"). An "FOPH recommended catch-up vaccination" was received by 13.6% of all Zurich Travel Clinic clients aged > 2 years and born after 1963.

Conclusions
In this study, we highlight the importance of travel medicine consultations to enhance the measles vaccination coverage in the adult Swiss population.

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P87 | Telemedicine for health problems while abroad: are travelers interested and willing to pay prior to departure?

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Background
Online telemedicine is emerging as a useful tool to provide expert medical advice to individuals facing health issues while traveling in remote areas. We are currently developing a telemedicine service enabling contact with our medical team within 24-36 hours. However, the needs and expectations of travelers are largely unknown. We conducted therefore a survey to evaluate opinions about the relative importance of various travel criteria that may pertain to our service.

Objectives
1) to assess if such service is deemed necessary by travelers; 2) to investigate which telecommunication link is preferred; 3) to determine which subgroup of travelers would be most interested in this service; 4) to estimate the amount of money travelers would be willing to pay for such telemedicine service.

Method
Travelers coming to our clinic for pre-travel advice were given a questionnaire to be filled in before the consultation. The questionnaire focused on demographics, travel details, health status and willingness to pay for a telemedicine service.

Results
A total of 306 questionnaires were returned. Of all, 164/276 (59%) travelers were interested and 162/164 (99%) willing to pay for a telemedicine service. Of these individuals, email was the preferred communication link in 102/164 (62%), mobile phone in 74/164 (45%), and video calls in 48/164 (29%) (cumulative answer). Travelers above 60 years were twice more likely to be interested in telemedicine than younger ones. No association was found between interest in telemedicine and destination, length of stay, purpose of travel, type of accommodation, risky activities, urbanization of visited area, estimated time to reach a medical center, previous stay in tropical country, chronic disease or immunosuppression. Median duration of travel was 3 weeks and price travelers would be willing to pay was 50 CHF. There was no correlation between travel duration and amount to be paid.

Conclusion
Among individuals consulting for pre-travel advice at a specialized clinic, there is considerable interest in telemedicine, particularly among older travelers. Based on these data, a pilot study using email communication to help travelers confronted with health issues while abroad is about to open at our travel clinic.

P88 | Enteropathogenic Escherichia coli (EPEC) infection detected by rapid multiplex panel detection after a yearlong course of persisting symptoms and unsuccessful investigations

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Background
Chronic digestive problems are a frequent problem in travelers returning from tropical countries.

Methods
Case report

Results
In March 2016 a 52-year-old woman was referred to our travel clinic because of chronic diarrhea and progressive weight loss of 12 kg dating back to May 2015. Diarrhea started on the day she returned from a trip to Morocco. After an exacerbation of symptoms in September 2015, blood tests showed no evidence of an inflammatory process and no eosinophilia. Serum creatinine, electrolyte levels, and liver function tests were within normal limits. Stool culture and microscopic examination searching for parasites including Cryptosporidium were negative. In the following months, abdominal ultrasound, abdominal computed tomography, colonoscopy and gastroscopy were unremarkable. In December 2015, the patient was started on oral metronidazole as an empiric treatment for Giardia lamblia with no improvement of symptoms. At this time, thyroid function and adrenal function tests were within the normal range. An HIV-test, the dosage of calprotectin, anti-transglutaminase antibodies, the search for Tropheryma whipplei in saliva, blood and stool, and a lactose intolerance test were all negative. In April 2016, a rapid multiplex panel of 22 agents of enteric infections revealed an infection with Enteropathogenic Escherichia coli (EPEC). The patient was started on intravenous ertapenem for 10 days with relief of diarrhea and return of normal bowel habits within 4 days. Parenteral ertapenem was chosen because of severity of infection and multi-resistance to antibiotics described in the literature. She was discharged from hospital on the 10th day after her latest admission. Three weeks later a rapid multiplex panel showed no evidence for EPEC anymore.

Conclusion
Enteropathogenic Escherichia coli (EPEC) infection should be considered as the cause of chronic diarrhea in travellers. EPEC infection can indeed produce chronic mucous diarrhea, which may remit and relapse. Rapid multiplex panel detection of the most common agents of bacterial, viral and parasitic infections from a stool specimen is a sensitive and specific tool to detect this pathogen. It should be considered as the next diagnostic test when conventional evaluation of stool for bacteria and parasites is negative.

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P89 | Application of whole genome sequencing to investigate a two year's Pseudomonas aeruginosa outbreak

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Background
From 2010 to 2012, an increase in P. aeruginosa incidence was observed in the ICUs at the University Hospital of Lausanne. A total of 689 isolates from 254 patients were typed using Double Locus Sequence Typing (DLST), and subsequently grouped into 46 DLST clusters. Cluster DLST 1-18 affected the highest number of patients (24 out of 254), mostly hospitalized due to burn injuries. Isolates of the same DLST type were found in the environment of the burn unit's hydrotherapy room, suggesting this location was the source of the outbreak. To investigate the suspected transmission events, and to infer the outbreak isolates' phylogeny, we decided to complement this investigation with the high discriminatory power of whole genome sequencing (WGS).

Methods
P. aeruginosa DLST cluster 1-18 incorporates 106 isolates, including clinical specimens of 24 patients, as well as environmental isolates. In this preliminary study, we performed WGS on ten clinical isolates randomly selected between March 2010 and October 2012. The isolates' sequence type (ST) was assigned from the short reads data. Core genome alignment of all ten isolates was acquired with Snippy. This alignment was subsequently used as an input for maximum likelihood tree construction with Gubbins, excluding regions of high SNP density suggestive of recombination.

Results
All ten sequenced isolates belonged to P. aeruginosa ST 1076. Phylogenetic analysis demonstrated the occurrence of a major ICU clade, clearly separated from one isolate retrieved from a patient possibly infected before its admission to the ICU. The ICU clade was further divided into subclade A, including six isolates from patients hospitalized in ICU 3 (burn unit), and subclade B, which comprises three isolates from other ICUs (ICU 2, 4, and 6). WGS results confirmed the occurrence of two suspected epidemiological links in the burn unit (hospitalized at the same time), while determined the close relatedness of two isolates retrieved two years apart, suggesting an environmental source.

Conclusion
Preliminary results showed a clear differentiation between P. aeruginosa DLST 1-18 isolates present in the burn unit, and isolates retrieved in other ICUs or hospital units. This suggests that different routes of transmission may have occurred during this outbreak. These results prompt us to further investigate this outbreak by sequencing isolates from other patients and from the environment in order to have a broader representation of transmission events and probable outbreak sources.

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P90 | Hyperdrymist® micro-nebulized hydrogen peroxide: effectiveness in reducing clostridium difficile infections in a tertiary hospital after introduction as routine and preventive

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Background
Infections caused by Clostridium difficile (CDI) are an major problem for healthcare facilities. CD spores can to persist on inanimate surfaces for long periods. Preventive disinfection cycles (1 ml/m3 micronebulized solution) applied in all known contaminated environments and delivered via the use of HyperDRYMist® (HDM) Technology were tested, in order to lower the overall incidence of CDI in a tertiary hospital. The same technology was successfully deployed in quelling a CDI outbreak one year earlier in two wards of the same hospital (Poster e-P265 ECCMID 2014).

Methods
CDI incidence was monitored for two 10-month periods in 2012 and 2015 spanning from Jan 1st to Oct 31st. CDI was diagnosed in patients affected by new diarrhoea started 48h after admission and positive stool for CD toxins. Deep cleaning of surfaces with a detergent/chlorine agent at 5'000 ppm concentration was executed both in 2012 and 2015. In 2015, HDM was added as a sole adjunct measure after dismissal of all CDI patients. The HDM no-touch high-level environmental disinfection technology is based on the micro-nebulization of a proprietary hydrogen peroxide based solution, which is evenly and pervasively deposited on air-exposed surfaces during the disinfection process.

Results
In 2012, out of 20'112 admittances, the CDI incidence was 1.21% for the entire hospital complex. In 2015, after HDM introduction, CDI cases decreased to 0.39% of a total admittances of 19'921 (OR 0.32, CI 0.24-0.41). Drop in CDI incidence was 67.77%. Admittance capacity remained unchanged with 627 beds.

Conclusions
The routine and extensive integration of the HDM technology at hospital-wide levels evinced a significant impact on the reduction of CDI incidence, and further substantiated the clinical benefits of adding HDM to ordinary cleaning procedures. The removal of CD spores is known to be difficult via traditional cleaning methods and the effectiveness of HDM disinfection can be ascribed as a highly plausible cause for the massive drop in CDI incidence considering that no other infection control measure was implemented in 2015. In a previous study, we showed that a CDI outbreak was interrupted though integration of the HDM technology. With this study, we demonstrated that embedding HDM technology into routine disinfection procedures and extending its regular use by implementing preventive schemes can generate a wider and systemic reduction of CDI incidence in healthcare facilities.

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P91 | Added value of a transplant infectious diseases (TID) consultation for the diagnosis and prevention of infection in solid-organ transplant candidates

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We reviewed all pre-transplant consultations between 01/2012 and 09/2015. In 2011 we established a TID consultation which included epidemiological exposition, past vaccinations review, and serological tests (including tropical serology in case of travel/exposure history). TID consultation was mandatory for all liver, lung, and heart transplant candidates, while it was optional in kidney transplant candidates. Pre-vaccination data for hepatitis A virus (HAV), hepatitis B virus (HBV, non-protected=<10 IU/ml, partially-protected=10-100 IU/ml), varicella-zoster virus (VZV) and measles-mumps-rubella (MMR), diphtheria-tetanus-pertussis (dTPa) were included. Vaccination with the pneumococcal conjugate vaccine (PCV13) was recommended from January 2014. We also analyzed results of treponemic tests, TB-spot and serology for tropical infections. Protection rates against HBV were additionally assessed at the time of transplant to patients that were transplanted at our center (heart, lung and kidney). We analyzed 210 patients, including 79 (38%) lung, 68 (32%) liver, 55 (26%) heart, 5 (2%) kidney and 3 combined transplant candidates. Vaccination against HBV was proposed to 163/210 (77%) of patients. According to the type of organ, an indication for HBV vaccination was retained in 52/68 (76%) of liver, 60/79 (76%) of lung, 45/55 (81%) of heart, and 5/5 (100%) of kidney transplant recipients. 191/210 (91%), 105/210 (50%), 11/209 (5%), and 3/207 (1.4%) of patients received dTPa, HAV, MMR, and VZV vaccination, respectively. From January 2014, 92/98 (94%) required pneumococcal vaccination; 88/92 (96%) received the PCV13 and 4/92 (4%) the polysaccharide pneumococcal vaccine. 2/209 (1%) cases of latent syphilis and 26/210 (12%) case of latent tuberculosis were detected and treated. Additional serologic tests due to a history of travel and/or exposure were performed in 72 patients. Nine cases of latent parasitic infections were detected, including four cases of Strongyloides stercoralis infection, two of leishmaniasis, one each of Chagas disease, toxocariasis and echinococcosis. Overall, 36/210 patients (17%) were diagnosed with active/latent infections that required specific therapy in the pre-transplant period. Overall, 50 patients were transplanted until 9/2015 and anti-HBs were available for 49 patients. Seroprotection against HBV was 18/49 (37%) during the TID consultation and 23/49 (47%) at the time of transplant.

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P92 | Surveillance des infections urinaires à entérobactéries productrices de beta lactamase à spectre élargi en EMS

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Introduction
Les infections urinaires dues à des bactéries gram-négatif résistantes aux antibiotiques ne cessent d'augmenter de manière générale y compris en collectivité. Les entérobactéries productrices de béta-lactamase à spectre élargi (BLSE), en particulier les Escherichia coli (E. coli), peuvent également se retrouver chez la personne âgée institutionnalisée ce qui complique leur traitement présomptif. L'instauration d'une antibiothérapie ciblée, lors d'une infection urinaire, est primordiale pour limiter le développement et la diffusion de germes multirésistants. La surveillance des infections urinaires en établissement de soins chronique (EMS) nous permettra d'évaluer le taux de portage E. coli producteurs de BLSE dans ces institutions. Pour estimer la situation dans les EMS vaudois, l'UHPCI a initié une surveillance des infections urinaires en EMS.

Objectif
Evaluer le taux de portage d'E. coli porteurs de BLSE dans les EMS vaudois.

Methode
De janvier à décembre 2015, l'Unité HPCI a instauré une surveillance des infections urinaires dans les EMS du canton en collaboration avec les laboratoires. La participation des EMS est volontaire. A chaque résultat d'analyse d'urine positive en bactériologie, une copie nous est adressée. Tous les résultats sont centralisés dans une base de données. Une description des microorganismes retrouvés est effectuée.

Resultats
86% (126/146) des EMS vaudois ont participé à la surveillance. 12 laboratoires ont transmis 1172 résultats. L'analyse des résultats a mis en évidence des entérobactéries dans 89% (1042/1172) des prélèvements dont 74% (770/1042) d'E. coli 8,3% (86/1042) des E. coli et 1.3% (14/1042) des entérobactéries sont producteurs de BLSE.

Conclusion
Ce premier état des lieux effectué dans les EMS vaudois montre une présence non négligeable d'entérobactéries porteuses de BLSE, en particulier d'E. coli, dans ces établissements. Le taux de 8.2 % d'E coli producteurs de BLSE est comparable à ceux de la surveillance européenne et nationale. Une corrélation des résultats de cette surveillance avec les résultats de consommation des antibiotiques en EMS initiée en 2015 sera une plus value pour la mise en place d'une stratégie ciblée.

P93 | Staphylococcus aureus soft tissue infection may increase the risk of subsequent orthopaedic infections

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Background
Nasal colonization with Staphylococcus aureus is an established risk factor for developing staphylococcal surgical site infections in the short term. It is not known, however, if patients with (community-acquired) S. aureus soft tissue infections have a higher risk for future "orthopaedic" infections in the long term.

Methods
We conducted an epidemiological survey of adult patients hospitalized for combined surgical and medical treatment of skin and soft tissue due to S. aureus in the only public hospital in Geneva. By reviewing nursing and medical files from the emergency department and hospital wards of our tertiary center, we assessed any other infections they developed (excluding recurrences) after the index one and last passage to, infections at the same localisation and paediatric cases.

Results
Among 802 index episodes of skin and soft tissue infections, 553 (69%) were caused by S. aureus, of which 23 were due to healthcare-associated and 15 due to community-acquired methicillin-resistant S. aureus. The patients' median age was 50 years and 204 (25%) were immune-compromised. The time span between the patient's first and last consultation (for any reason) in our center was 21.2 years (interquartile range, 10-29 years). After the initial infection and at distance of ongoing antibiotic selection, 63 patients developed other nosocomial or community-acquired infections. Future infection was more common in those who had had a skin or soft tissue infection due to S. aureus compared to a non-staphylococcal infection. Of these, patients with a S. aureus (compared to non-S. aureus) soft tissue infection had a higher rate of future orthopaedic infections: 55 (55/63; 87%) were again due to S. aureus (55/553 vs. 8/249; Pearson-χ2-test; $p<0.01$). This association was not present for the 372 cases of bursitis: 10/10 vs. 301/362; ($p=0.16$) of which 84% were due to S. aureus.

Conclusions
Adult patients previously hospitalised for moderate to severe skin and soft tissue infections (except for septic bursitis) due to S. aureus, compared to non-staphylococcal infections, may be at higher risk of other "orthopaedic" infections, in particular infections due to S. aureus.

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P94 | Low additive effect of inguinal swabs in MRSA and urine test in ESBL screening

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Background
Identification of Patients with MRSA and/or ESBL colonisation is important for building up adequate isolation precautions and choosing empirical treatment, if required. However, more tests increase costs, so finding an optimal strategy is helpful in lowering microbiological expenditures.

Methods
In the MRSA/ESBL prevalence in asylum seekers investigation, we screened 261 asylum seekers in four Swiss refugee centres. For MRSA, one swab for throat and both nostrils, and one moistened swab for both groins was used. For ESBL, a moistened rectal swab and urine was taken from each person. The swabs/urine were analysed according to published protocols. We calculated the additive effect of groin swabs in MRSA and urine test in ESBL screening.

Results
MRSA Screening was performed in 261 persons. 10 declined groin swabs. Throat/Nostril swab alone was positive in 21/261 persons, both throat/nostrils and groin in 19/261 patients and isolated groin swabs in 3/261 persons. 20 persons declined rectal swab and were excluded for calculation of ESBL prevalence. Rectal swab was positive in 55/241 persons, both rectal swab and urine were positive in 7/241 persons, but none was positive in urine without rectal colonisation.

Conclusion
The additive effect of groin swabs is moderate. Only 3/43; 6% of positive and 1.15% (CI95 0.4-3.3%) of all persons would have been missed with throat/nostrils swab only. Urine testing had no additive benefit in ESBL screening.

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P95 | Delayed isolation precautions for varicella-zoster virus have minimal impact on health care workers: management and outcomes in a high-prevalence area

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Background
Delayed airborne isolation of hospital patients with varicella-zoster virus (VZV) infection usually triggers an investigation of potential transmission to exposed healthcare workers (HCW). Our aim was to describe these investigations at Bern University Hospital, Switzerland, from 2004-2014.

Methods
Index patients and corresponding HCW contacts were identified via records of the infection prevention program and the occupational health service. For the contacts, history of prior VZV disease or vaccination, results of current and previous VZV IgG tests, and measures taken by the occupational health service (vaccination and/or work restriction) were determined.

Results
During the 11-year study period there were a total of 81 index cases and 2106 HCW contacts, for 972 (46.2%) of which a VZV IgG result was available (see Figure 1). Of these 972, 965 (99.3%) were VZV IgG-seropositive and most of them, 851 (87.5%) had been known before. In multivariable linear regression, increasing study years correlated positively with the proportion of HCW with previously documented VZV IgG ($R=0.11$, $p<0.001$) but not with the annual number of contact tracings ($R=0.01$, $p=0.12$). Among the seven (0.7%) HCW contacts with negative VZV IgG, four (57%) were known from previous testing. Five of these seven contacts received active VZV vaccination within a median of 10 days (range, 1-30) but 2/5 (40%) became symptomatic despite vaccination (see Table 1).

Conclusion
A very small number of VZV IgG-seronegative HCW were identified in this 11-year contact tracing and clinical consequences were even fewer. Efficacy of active VZV vaccination in this "real-life" setting was poor. Although the proportion of contacts with documented VZV IgG prior to exposure increased over the study period, the overall number of evaluated contacts remained high. Based on this analysis we suggest, that in countries with a high childhood VZV prevalence HCW should be offered screening/vaccination upon employment, however, contact tracing of HCW following VZV exposition can be omitted.

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Figure 1 Overview of health care workers with varicella-zoster virus exposure

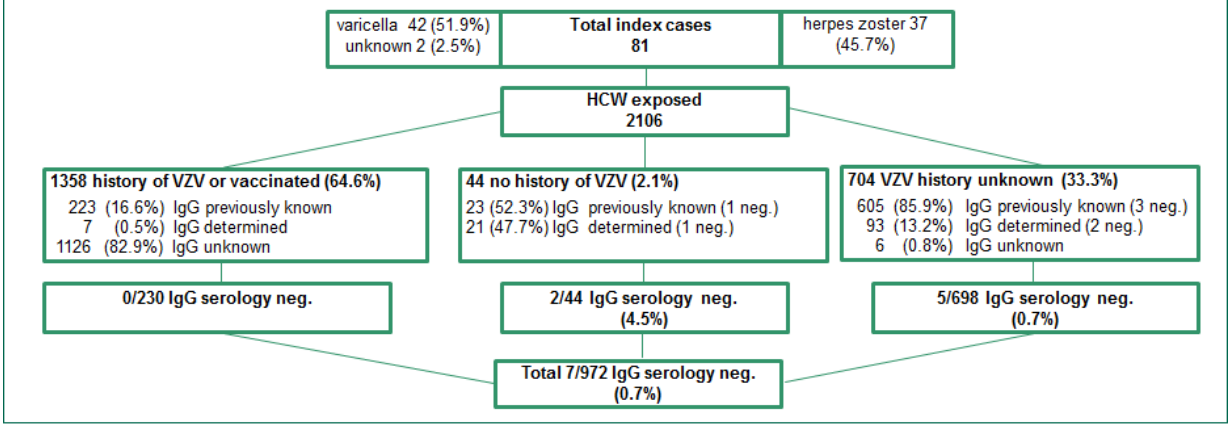

Table 1 VZV IgG – seronegative HCW (n=7)

Serostatus previously known	Received active VZV vaccination	Days from first contact with index patient to vaccination	Developed active VZV	Days from first contact with index patient to disease	Work restriction
No	Yes	30	No	na	Yes
No	Yes	1	Yes	10	No
No	Unknown	na	Unknown	Unknown	Yes
Yes	Yes	≥ 4	Unknown	Unknown	Unknown
Yes	Yes	15	Yes	15	Yes
Yes	No	na	No	na	No
Yes	Yes	3	Unknown	Unknown	Unknown

Abbrevations: VZV: Varicella-zoster
HCW: Health care
na: not available

P96 | Zwei Jahre Influenza-Surveillance: Erfahrungen am Kantonsspital St. Gallen

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Einführung
Mit dem Ziel, Patienten vor Influenza zu schützen, wurde das „Healthcare-associated Influenza Prevention" Projekt (HaIP) gestartet. Dieses gliedert sich in die drei Phasen (i)Entwicklung eines Surveillance-Konzeptes zur Monitorisierung von Patienten mit (nosokomialer) Influenza und des Präventionsverhaltens von medizinischem Personal,(ii) Entwicklung einer komplexen Intervention zur verbesserten Prävention in Spitälern und (iii)Prüfung der Wirksamkeit der Intervention über mehrere Spitäler. Im Folgenden wird über die Erfahrungen beim Aufbau einer Influenza-Surveillance berichtet.

Methodik
Am Kantonsspital St. Gallen (KSSG), einem Tertiärspital mit 700 Betten, wurden die Kliniken aufgefordert, während der Grippesaison bei Patienten mit klinischen Symptomen einer Influenza eine Diagnostik durchzuführen.

Resultate
2014/15 und 2015/16 fanden sich bei 25% resp. 11% aller hospitalisierten Patienten mit Influenza eine nosokomiale Infektion (Details zur Methodik der Diagnostik Resultate siehe Tabelle). Die Unterschiede des Anteils nosokomialer Infekte der beiden Perioden sind wahrscheinlich nicht nur durch Virulenzfaktoren des Virus, sondern auch durch Änderungen der Prädiagnostik bedingt: - 2014/15 erfolgte die Diagnostik hauptsächlich auf internistischen Abteilungen mittels Nasopharyngealabstrich (nur durch Ärzte). Bei vermutetem eingeschränkten Bewusstsein für Influenza bei chirurgisch tätigen Ärzten erfolgte 2015/16 die Diagnostik mittels Nasenabstrich durch die Pflege. Es zeigte sich jedoch, dass nicht im Bereich der Schleimhäute, sondern im Bereich der äusseren Nasenöffnung abgestrichen wurde. Dass damit die Sensitivität des Tests reduziert wurde, ist zu vermuten. - Insbesondere während des Beginns der Saison 2015/16 zeigte sich ein überproportional grosser Anteil negativer Nasenabstriche. Die Überprüfung der Krankengeschichten zeigte, dass ein grosser Anteil dieser Patienten die klinischen Kriterien einer Influenza nicht erfüllte.

Konklusion
Generell sind Vergleiche zwischen Influenzasaisons schwierig. Unsere Erfahrungen zeigen, dass trotz gleichbleibender Diagnosekriterien und gleichem mikrobiologischen Test die Resultate einer Surveillance durch Änderungen in der Prädiagnostik beeinflusst werden, diese aber schwierig quantitativ nachweisbar sind. Geplant ist die Bestimmung von „Influenza-Verantwortlichen" an den Kliniken, und praktische Übungen zur korrekten Durchführung der Probenentnahmen.

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Tabelle: Methodik und Resultate der Influenzasurveillance am KSSG für die Grippesaisons 2014/15 und 2015/16

	Influenzasaison 2014/15	**Influenzasaison 2015/16**
Kriterien Influenzadiagnostik	Temperatur > 37.7° oder Fiebergefühl und akute respiratorische Symptome oder Myalgien/ Kopfschmerzen	
Definition (nosokomiale) Influenza	Kriterien Influenzadiagnostik + positiver Influenzatest (nosokomial: positiver Test >72 h nach Eintritt)	
Influenzatest	Isothermaler Nukleinsäureamplifikationstest (Alere™ i Influenza A & B) (Bei negativem Test und weiterhin Vd zusätzliche Realtime-PCR)	
Lokalisation Diagnostik	Nasenrachenabstrich durch Ärzte	Nasenabstrich durch Pflege
Anteil stationäre Pat mit positivem Abstrich (Anzahl pos. Patienten/alle abgestrichenen Patienten)	29% (86/298)	25% (104/421)
Anteil Pat mit nosokomialer Infektionen (Anzahl Pat mit nosokomialer Infektion/alle hospitalisierten Pat mit Influenza)	26% (22/86)	11% (11/104)
Interventionen	Keine	Keine
Durchimpfung medizinisches Personal	Niedrig	Niedrig

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P97 | Universal screening and decolonization for control of MRSA in nursing homes: follow-up to a cluster randomized controlled trial

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Background
MRSA frequently has a high burden in nursing homes (NHs), directly linked to resident comorbidities and the frequent use of antibiotics. In 2010-2011, we conducted a randomized controlled trial (RCT) in NHs of Canton Vaud that showed no significant benefit of MRSA screening and decolonization over standard precautions only, in terms of prevalence of MRSA carriage (Bellini et al. ICHE 2015). However, this prevalence significantly declined in both the intervention and the control groups over the study period.

Objective
To evaluate the evolution of MRSA carriage in NHs who participated to the RCT by planning a follow-up survey.

Methods
Of the 157 NHs in Canton Vaud, 53 were randomized in the intervention group and 51 in the control group in 2010. Primary outcome was the evolution of the prevalence of MRSA carriage in 2015 in NHs previously allocated to intervention or control groups in the 2010-2011 RCT. Secondary outcomes included the determinants of this evolution at the NH level. MRSA prevalence in the 2 randomization groups was then compared to a new group that did not participate in the 2010-2011 RCT.

Results
92/157 NHs participated to the 2010-2011 RCT and to the 2015 follow-up survey. Moreover, 33 NHs participated in 2015 only (new group). Overall, 88% of the NHs population was screened. In 2010, 47 NHs were randomized in the intervention group and 45 in the control group. MRSA prevalence was significantly different between the 2 groups in 2015, 4% in the intervention group and 8.1% in the control group (p=0.01), whereas it was not in 2011 (p=0.296). In 2015, MRSA prevalence in the new group was 4.7%. In an adjusted model including the group as a predictor, MRSA prevalence in the new group was comparable to the intervention group (OR=1.48, p=0.183) and lower to control group, but not significantly (OR=0.61, p=0.075).

Summary
The prevalence became eventually significantly lower in NHs that applied a one-year strategy of decolonization of carriers five years earlier. However MRSA prevalence in 2015 was not significantly different from 2011, within randomization groups. Moreover, the average MRSA prevalence in 2015 in a new group was similar to the prevalence of the intervention group. A long-term effect would be difficult to interpret at resident level given that nursing homes residents are not the same that participated in the RCT.

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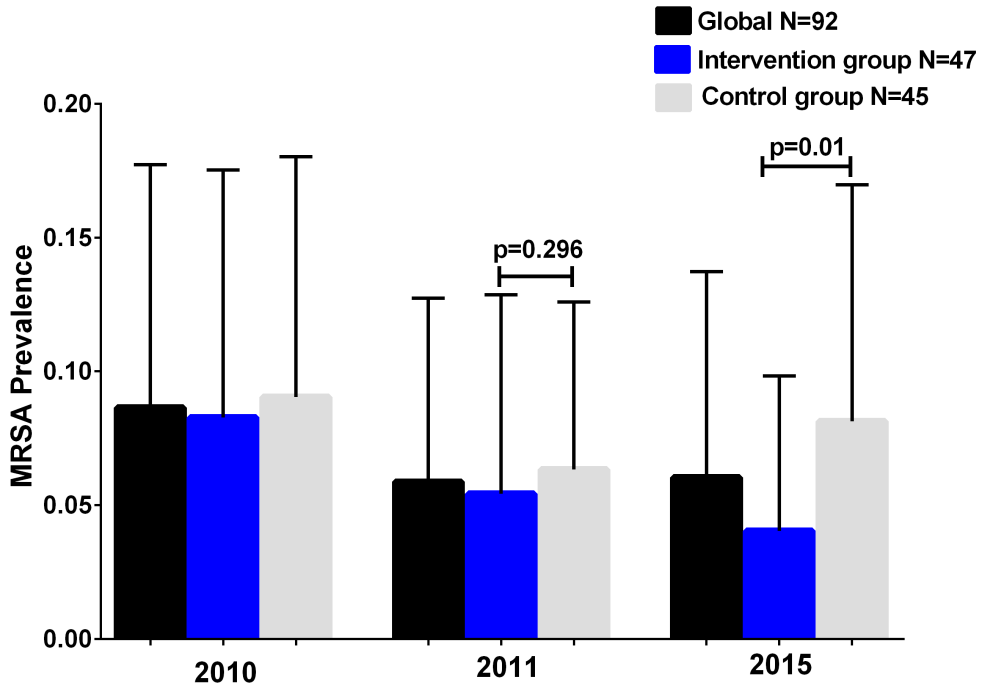

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P99 | Routine testing and isolation for influenza based on a clinical case definition – staff compliance rather than epidemiologic background matters for success.

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Background
Hospital transmission of influenza is of special concern. Universal testing and isolation of all patients with suspected influenza based on a clinical case definition proofed very effective in our hospital in 2014. We assessed the validity of our case definition in the 2015/16 epidemic with a lower case burden.

Method
Routine testing and droplet isolation of all suspect cases using RT-PCR from nasopharyngeal swabs is performed during the yearly epidemics based on the following case definition: temperature >38° C plus ≥2 symptoms of: rhinitis, pharyngitis, cough, dyspnea, head or body aches and diarrhea.

Results
In 2015/16, 101/254 swabs of inpatients with suspected influenza were positive, including 77/105 (70%) positive tests in adults and 24/149 (16%) in children. Six (6%) patients needed ICU-treatment and one patient died. In adults, 66/92 swabs taken on admission were positive (72%), as were 11/13 (85%) swabs taken after admission on the wards including 5 (6%) cases of nosocomial influenza. Among the 77 suspect influenza patients with subsequently confirmed diagnosis, 55 (60%) were correctly isolated on admission, while isolation was missed in 22 (40%). Among the 28 suspect influenza patients with subsequently negative swabs, 9 (32%) were isolated despite very short turnaround time awaiting results, resulting in 11/373 (3%) excess isolation days. Compared to the 2014/15 epidemic, the number of inpatients with influenza dropped in 2015/16 from 204 to 54 causing 892 vs. 362 isolation days with 11% vs. 3% excess isolation days. However, the proportion of missed isolations increased from 7% to 40%, as did the rate of nosocomial cases (1.5% vs. 6%). Positivity rates of screening remained high in adults (70% each).

Discussion
Universal testing and isolation of suspected influenza cases based on a clinical case definition proofed very effective during the epidemic of 2014/15 with high influenza case load. In 2015/16, despite the predominance of the influenza B vic strain covered only by the quadrivalent vaccine much lower numbers of influenza cases were noted. Remarkably, the clinical case definition kept its accuracy. However, the testing and isolation compliance was lower. In epidemiological settings with a low influenza burden, instruction must be intensified to preserve staff awareness. Only consequent testing and isolation – together with staff vaccination - can ascertain low nosocomial transmission rates.

P100 | Spitalhygienische Aspekte beim Bau einer Milchküche

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Ausgangslage
Im Universitätsspital Bern wurde der Neubau einer Milchküche in einem bestehenden Gebäudeteil geplant. Das Bauprojekt wurde von der Spitalhygiene begleitet, welche folgende Ziele formulierte: 1. Die infrastrukturellen Voraussetzungen beim Milchküchenneubau zu definieren 2. Zu entscheiden, ob sich die zur Verfügung gestellten Räumlichkeiten für eine Milchküche eignen 3. Die Begleitung des Bauprojektes von Seiten der Spitalhygiene festzulegen

Methode
Es wurde eine systematische Literaturrecherche durchgeführt. Die vorhandene Infrastruktur der gegenwärtigen Milchküche wurde unter Berücksichtigung von hygienischen Aspekten analysiert. Um Anhaltspunkte für eine optimale Infrastruktur zu gewinnen, wurden sechs Milchküchen in Spitälern der Deutschschweiz besucht und die Infrastruktur anhand eines Standardprotokolls bewertet. Die vorgeschlagene neue Lokalität wurde besichtigt und bezüglich Standort, Grundriss und vorhandener Infrastruktur analysiert.

Resultate
Die wissenschaftliche Evidenz zum Thema Milchküche und Infektionsprävention ist begrenzt. Es sind keine qualitativ hochwertigen Studien verfügbar. Die gegenwärtige Milchküche weist mehrere Schwachpunkte auf, wie beispielsweise Materialdefekte an der Infrastruktur sowie suboptimale räumliche Trennung von Nahrungsweg und schmutzigem Material. Die Flächen der besuchten Milchküchen waren unterschiedlich und standen in Abhängigkeit von Personalbedarf, benötigten Räumen und Lagerfläche. Glatte und fugenlose Materialien wurden deutlich bevorzugt. Anhand der Resultate der Besuche in den externen Kliniken, der Ergebnisse der Literaturrecherche, der kritischen Analyse der Räumlichkeiten der gegenwärtigen Milchküche sowie des vorgeschlagenen Standortes wurde eine Checkliste erstellt, welche die notwendige Infrastruktur definiert.

Schlussfolgerungen
Aus spitalhygienischer Sicht konnte dem Bau am vorgeschlagenen Standort zugestimmt werden. Die Massnahmen zur Infektionsprävention während der Bautätigkeit im Klinikbetrieb sowie die Begleitung durch das Spitalhygienefachteam wurden definiert. Trotz fehlender wissenschaftlicher Evidenz konnte eine Checkliste mit spitalhygienischen Anforderungen erstellt werden, die auf Expertenmeinungen und Quervergleich mit anderen Milchküchen beruht. Diese Checkliste kann im Rahmen von Neu- und Umbauprojekten von Milchküchen in anderen Spitälern verwendet werden und ermöglicht eine Erhöhung des Qualitätsstandards.

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P101 | CleanHands – successful implementation of a new module by Swissnoso

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Background
Since the beginning of 2015 Swissnoso provides the new module CleanHands for hand hygiene surveillance according to the five moments (WHO) for all interested hospitals, developed by the cantonal hospital of St. Gallen. Data entry using a mobile device and direct data transfer to a web-based database provide immediate automated analysis of results for direct feedback and anonymised benchmark among participating institutions.

Aims
We evaluated expansion and utilisation of the module CleanHands after the introduction and primary data of the observations.

Methods
Data extraction from the online database of CleanHands beginning with the date of first utilisation, i.e. 14 April 2015 followed by preliminary analysis was performed.

Results
After one year 85 institutions all over Switzerland are participating, whereof 67 are actively using CleanHands. Data from acute hospitals of various sizes, rehabilitation, psychiatric clinics and nursing homes comprise around 24'000 opportunities. Overall adherence to hand disinfection is 72% (95%-CI: 71.9-73.0%) on average. Highest rates have been observed in inpatient care settings and outpatient care compared with operating theatres 76% (95%-CI: 75.4-76.7%) vs. 75% (95%-CI: 73.8-77.0%) vs. 54% (95%-CI: 52.8-56.0%) respectively. Differences among professional groups and indications in inpatient care are as follows: Physicians show lower adherence rates to hand disinfection than nursing personnel of 72% (95%-CI: 70.7-73.6%) vs. 78% (95%-CI: 76.7-78.2%) respectively. Moments like "before patient contact" and "before invasive procedure" show lower adherence rates of 68% (95%-CI: 66.5-69.1%) and 71% (95%-CI: 68.6-72.5%) respectively compared to other indications 81% (95%-CI: 80.4-81.9%). Further analysis shows differences in public vs. private hospitals 77% (95%-CI 76.5-77.9%) vs. 72% (95%-CI 70.0-73.0%), long-term care facilities vs. acute care hospitals 85% (95%-CI: 82.8-86.3%) vs. 75% (95%-CI: 74.4-75.8%) and small institutions with <200 vs. ≥200 beds 78% (95%-CI: 77.4-79.0%) vs. 72% (95%-CI: 70.8-73.1%) in inpatient care settings.

Conclusions
CleanHands has been successfully established as a nationwide monitoring system for continuous hand hygiene surveillance. Comparing the data with the Swiss handhygiene campaign during 2006/07 (overall adherence of 68%), adherence remained improvable during the last years. Using CleanHands as a training instrument will hopefully improve adherence with hand hygiene.

Table: Adherence (inpatient care) with the 5 moments (14.04.15-13.04.16)

	Adherence in % (all opportunities (n); 95%-CI)			
	Physicians	**Nurses**	**Others**	**Overall**
Before patient	64.9 (1432; 62.4 - 67.4)	69.5 (3193; 67.9 – 71.1)	60.6 (193; 53.7 – 67.5)	67.8 (4818; 66.5 - 69.1)
Before invasive proced.	42.0 (143; 33.9 – 50.1)	72.9 (1871; 70.8 – 74.9)	62.1 (29; 44.4 – 79.7)	70.5 (2043; 68.6 - 72.5)

After body fluid	60.7 (117; 51.8 – 69.5)	84.4 (1839; 82.7 – 86.1)	75.3 (81; 65.9 – 84.7)	82.7 (2037; 81.0 - 84.3)
After patient	83.5 (1671; 81.8 – 85.3)	82.4 (3859; 81.2 – 83.6)	75.7 (267; 70.5 – 80.8)	82.4 (5797; 81.5 - 83.4)
After patient surrounding	56.7 (187; 49.6 – 63.8)	78.6 (1711; 76.6 – 80.5)	74.4 (270; 69.2 – 79.7)	76.2 (2168; 74.4 - 78.0)
Overall	72.2 (3550; 70.7 - 73.6)	77.5 (12473; 76.7 - 78.2)	71.3 (840; 68.3 - 74.4)	76.0 (16863; 75.4 - 76.7)

*Data for hand hygiene were collected from 85 hospitals participating at CleanHands within the framework of Swissnoso. Members of Swissnoso are Carlo Balmelli, MD, Lugano; Marie Christine Eisenring, RN, ICP, CNS, Sitten; Stephan Harbarth, MD, MS, Geneva; Stefan P. Kuster, MD, MSc, Zürich; Jonas Marschall, MD, MSc, Bern; Virginie Masserey Spicher, MD, Bern; Didier Pittet, MD, MS, Genf; Christian Ruef, MD, Zürich; Hugo Sax, MD, Zürich; Matthias Schlegel, MD, St. Gallen; Alexander Schweiger, MD, Basel; Nicolas Troillet, MD, MSc, Sitten; Andreas F. Widmer, MD, MSc, Basel; Giorgio Zanetti, MD, MSc, Lausanne.

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P102 | Follow up results from the intervention study: change management with empowerment of nursing staff to reduce urinary catheter use

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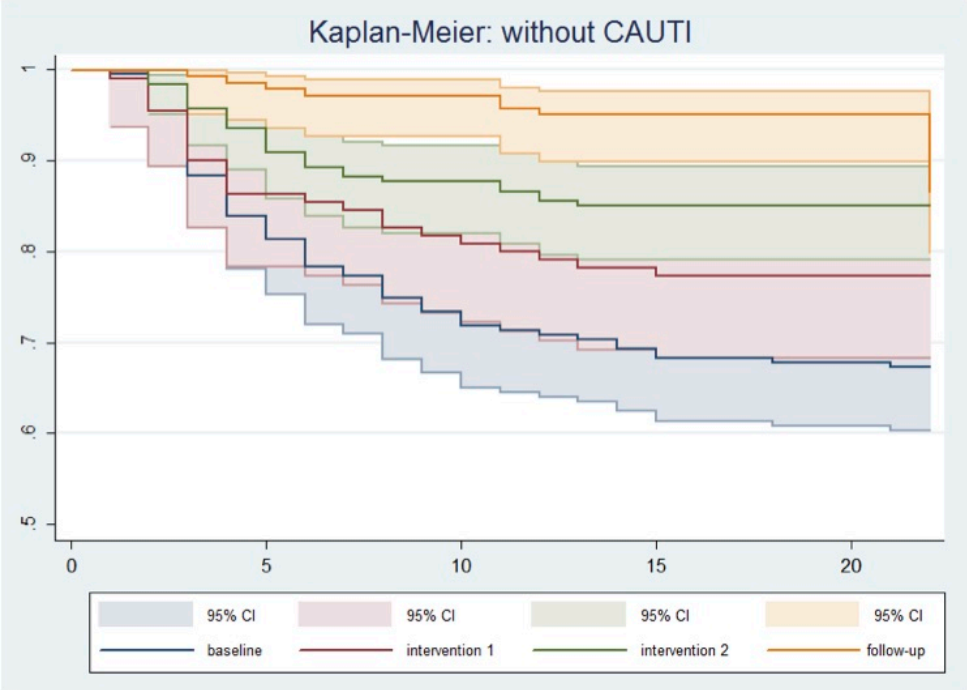
Objective
Catheter-associated urinary tract infections (CAUTI) are the most common, and a widely preventable healthcare-associated infection. In our study between July 2013 and August 2014, we used a multimodal interdisciplinary intervention to reduce CAUTI with three key elements: stringent indications for urinary catheter (UC) insertion, shifting the task to decide on UC removal from physicians to nurses and an automatic electronic alert for catheter removal. After one year we performed a follow-up to document the sustainability of the intervention.

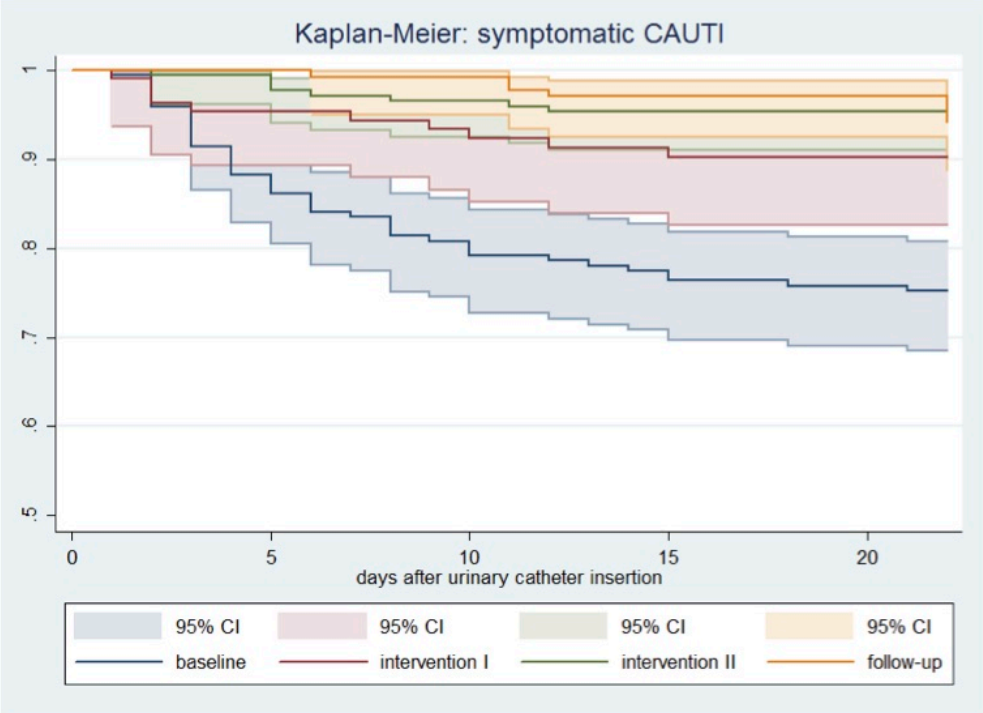
Design
Four months follow-up cohort study between June and September 2015 starting ten months after completion of the primary study.

Patients and methods
As well as for the primary study, we included patients who received an UC in the emergency department on admission or any time during hospitalization on a medical ward. Primary endpoint was the number of catheter days per 1`000 hospital days. Secondary endpoints were the number of UC per 1`000 hospital admissions and per 1`000 hospital days, the duration of catheterization per UC and the number of CAUTI per 1`000 hospital admissions as well as per 1`000 hospital and catheter days. Results were compared with the outcomes of the primary study.

Results
Overall, 142 patients were included during follow-up. Patient characteristics were similar to the primary study. With 31.9 and 30.5 (p= 0.90) catheter days/1`000 hospital days the rate remained stable between the intervention period II (after the implementation of all interventions) and follow-up, and was lower than at baseline 88.5 (p= <0.001). The mean and median duration of catheterization remained unchanged with 3.8 vs. 3.8 days and 3.8 vs. 3.0 days, respectively (p= 0.85), which was two days shorter compared to baseline. Compared to the intervention period II, a further reduction of CAUTI/1`000 hospital admissions was observed from 8.5 to 5.6 (p= 0.45), as well as a reduction of CAUTI/1`000 catheter days from 41.1 to 35.1 (p= 0.49).

Conclusions
With a further reduction of UC catheter days and CAUTI during follow-up compared to the end of the main study not only the effectiveness, but also the sustainability of our multimodal intervention could be documented. While stringent UC indications reduce catheter insertion, the empowerment of nursing staff together with the automatic electronic alert has a strong impact on the UC indwelling time. Therefore, all three interventions are now introduced in the entir





Number at risk					
Baseline	214	120	49	25	13
Intervention I	110	47	16	4	0
Intervention II	189	45	8	5	2
Follow up	142	41	10	2	0

P103 | Fokusgruppeninterviews zu Ventilator-assoziierten Pneumonie und deren Prävention

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Hintergrund
Im Jahre 2011 wurde im UniversitätsSpital Zürich ein Präventions-Bundle mit neun Elementen für die Ventilator-assoziierte Pneumonie (VAP) von einer interdisziplinären Arbeitsgruppe ausgearbeitet und 2013 implementiert. Eine Adhärenz-Messung im Jahr 2015 zeigte Verbesserungspotenzial in der Umsetzung.

Ziel
Erfassung von persönlichen Haltungen und Gedanken der Mitarbeitenden zu Nutzen, Stand der Umsetzung und Verbesserungspotential des VAP-Bundles sowie zu VAP im Allgemeinen.

Methode
Auf allen sechs Intensivstationen wurde ein Fokusgruppeninterview durchgeführt, insgesamt 41 Fachexperten/-innen Intensivpflege und 4 Ärzte/-innen nahmen teil. Zur Anwendung kam ein semi-strukturierter Fragebogen. Die Interviews wurden wortwörtlich transkribiert. Die Datenanalyse erfolgte induktiv - einem "Grounded theory"-Ansatz folgend - Kategorien wurden anhand des Textmaterials entwickelt.

Resultate
Die VAP wird als relevantes Problem wahrgenommen, das Risiko einer VAP für den einzelnen Patienten wird auf 50-80% geschätzt. Die Interviewten schätzten, dass bis die Hälfte der VAP durch Präventionsmassnahmen verhindert werden kann. Die Präventionsmassnahmen mit den besten Effekten wurden die Händehygiene, die subglottische Absaugung und eine gute Mundhygiene genannt. Als Risikofaktoren für eine VAP wurden die Beatmungsdauer, die Mikroaspiration und die Schwere der Grunderkrankung gesehen. Es bestand die Meinung, dass die einzelnen Bundle-Elemente grösstenteils gut umgesetzt werden, Verbesserungspotential wurde aber in der Durchführung der Oberkörperhochlagerung (OKH) und des täglichen Sedationsstopps gesehen. Als Hindernisse für die Umsetzung der Bundle-Elemente wurden medizinische Gründe beim Patienten, die Arbeitsbelastung des Personals, ungeeignetes Material und fehlendes Problem-Bewusstsein erwähnt. Verschiedene Verbesserungsvorschläge wurden genannt, unter anderem die Verwendung eines Winkelmessers für die Durchführung der OKH und die engere Zusammenarbeit mit der Physiotherapie und der Logopädie. Als fehlendes Element im Bundle wurde mehrfach die Früh-Mobilisation und Lagerungen genannt.

Schlussfolgerung
Die Bereitschaft, nosokomiale Infektionen wie die VAP zu verhindern und das Wissen über die Risikofaktoren ist vorhanden, ebenso Ideen für die Verbesserung des Bundles und Umsetzung der Bundle-Elemente. Mit einem Themenmonat soll eine Sensibilisierung des Problems erreicht werden, damit die konsequente Umsetzung der Präventionsmassnahmen besser gelingt.

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P104 | Growth of Mycobacterium chimaera in heater-cooler units is not completely suppressed by an intensified cleaning and disinfection procedure

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Background
Mycobacterium chimaera is an emerging pathogen associated with devastating infections of heart valve prostheses, vascular grafts, and disseminated infections after open heart surgery. Evidence indicates airborne transmission after aerosolization of M. chimaera from contaminated heater-cooler units (HCU) used in cardiopulmonary bypass. We studied the colonization dynamics of M. chimaera in factory-new Sorin 3T HCU initially testing negative.

Methods
Due to repeated detection of M. chimaera and other nontuberculous mycobacteria (NTM) in HCU samples our center replaced a total of 5 HCU in 2014 (2 in 01/14, 1 in 04/14, 2 in 09/14). HCU were serviced according to manufacturer's recommendations until April 2014, when cleaning and disinfection was intensified. The protocol consisted of daily water changes with use of all-bacteria filtered (Pall-Aquasafe AQ14F1S; 0.2µm) tap water and addition of hydrogen peroxide (100ml of 3%) combined with disinfection performed every 2 weeks. Surveillance cultures composed of HCU water samples and exhaust air samples were obtained ~ every 4 weeks.

Results
Overall, 134 water samples were taken from the study HCU, 127 after implementation of the intensified protocol. Of all samples, 90 (67.2%) remained sterile for nontuberculous mycobacteria (NTM), 6 (4.5%) were contaminated by bacterial overgrowth, and 38 (28.4%) yielded NTM: M. chimaera (22; 57.9% of all NTM), M. gordonae (12; 31.6%), M. chelonae (1; 2.6%), M. paragordonae (1; 2.6%) and a combination of M. chimaera and M. gordonae (2; 5.3%). NTM were found in both HCU water circuits (Table 1). Out of 91 air samples, 90 remained without mycobacterial growth. One (1.1%) grew M. chelonae, but no mycobacteria were detected simultaneously in the corresponding HCU water. NTM growth was recorded after a median of 174 days (range, 158–358) in HCU water samples. Regarding M. chimaera, one out of five HCU remained permanently negative, whereas four HCU became positive at a median of 250 days (range, 158–358).

Conclusions
HCU provide favorable environmental conditions for M. chimaera and NTM growth. Intensified cleaning and disinfection does not suppress growth completely, but may attenuate density and aerosolization. It remains unresolved when HCU were contaminated, most probably during production. Our findings emphasize the need for a change in technology for temperature management during heart surgery to guarantee patient safety.

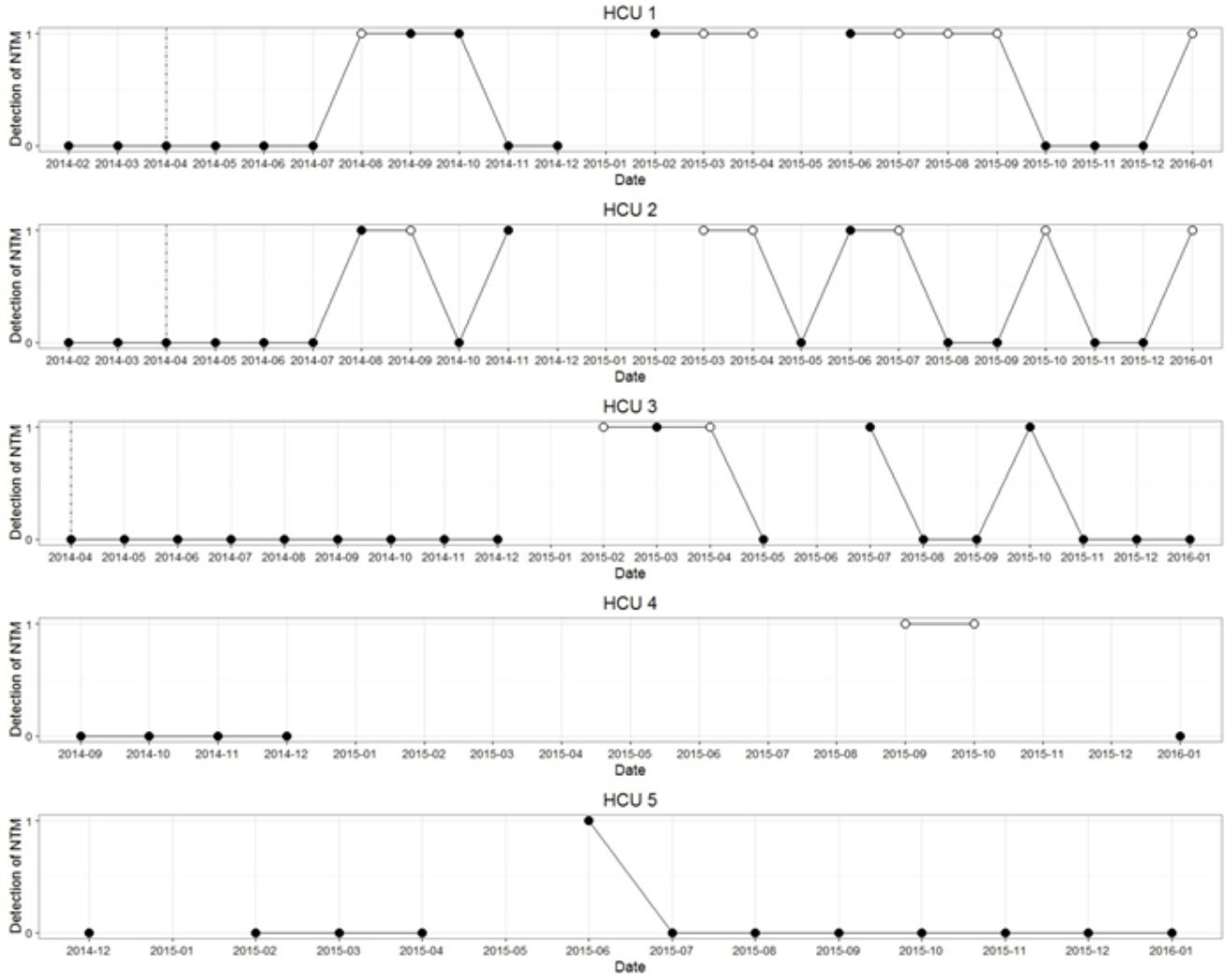

Figure 1. Results of heater-cooler unit water surveillance cultures

Legend: The y-axis displays results of mycobacterial cultures: 0, negative culture for NTM; 1, positive culture for NTM, circles indicating *M. chimaera* and dots indicating NTM other than *M. chimaera*. Dashed line shows the implementation of the intensified protocol. HCU 4 was for repair at the manufacturer from December 2014 to September 2015.

Table 1. Microbiology results of heater-cooler unit water samples

Circuit	Microbiology results			
	N (samples)	No growth	*Mycobacterium chimaera*	NTM other than *M. chimaera*

Cardioplegia solution-cooling circuit	48	34 (70.8%)	10 (20.8%)*	5 (10.4%)*
Patient blood-warming circuit	49	30 (61.2%)	12 (24.5%)*	8 (16.3%)*
Circuit not specified	37	26 (70.3%)	2 (5.4%)	3 (8.2%)#

* One culture with growth of both, *M. chimaera* and *M. gordonae*
# Six (16.2%) samples with bacterial overgrowth

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P106 | An MRSA outbreak with a rare spa type in a maternity ward in a low-prevalence setting: look beyond your neighbourhood

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Aim

Here we report an MRSA outbreak investigation with an unusual spa type in a single obstetrics and gynecological ward in Eastern Switzerland.

Methods

Within 3 weeks in October and November 2015, 3 patients were identified with clinical MRSA infection (2 mastitis, 1 surgical site infection (SSI) after caesarean section). The patient with the SSI was a resident of a local asylum centre. All 3 patients had shared the same maternity ward during the day of delivery, which was 10-31 days prior to onset of clinical infections. We subsequently screened all available patients (n=9) who had been hospitalized at the same time as the 3 index patients, all neonates (n=4) of mothers with MRSA colonization or infection, all midwives (n=10), and those nurses and gynaecologists with eczema or who requested screening (n=5).

Results

Overall, we identified 3 women with clinical infections and 4 asymptomatically colonized patients (1 woman, 3 neonates) through screening during this outbreak. No healthcare worker was MRSA positive. Of the 4 women with MRSA detection, 2 (1 infected, 1 colonized) were refugees from Eritrea and resided in the same asylum centre. All MRSA isolates had the same antibiotic resistance pattern. They showed an identical previously unknown pulse-field gel electrophoresis (PFGE) type. The MRSA belonged to a very rare spa type (t5100, only accounting for 0.01% of spa types), which had been detected only in Northern Europe but not previously in Switzerland. Surprisingly, through retrospective searches in our database, the same PFGE pattern had already been detected in 2 patients with MRSA skin infections who were hospitalized in the same hospital but different wards in 2010 and 2014. The presumed index case in 2010 regular travels to Sri Lanka. No further transmission from these cases was detected by clinical surveillance only.

Conclusions

Based on currently available typing information, we suspect that this unusual, probably travel-related MRSA outbreak strain has circulated in this hospital since 2010. The simultaneous detection of this MRSA type in asylum seekers is more likely due to importation from the hospital and subsequent transmission to the asylum center than this being the source of this outbreak.

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P107 | Results of an admission-screening for multidrug-resistant Gram-negative bacteria in St.Gallen, Switzerland

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Aim

As recommended by health authorities (ECDC, CDC) we conducted an admission-screening for multiresistant Gram-negative bacteria (MRGN)in patients with epidemiological links/risk factors. Our aim was to determine the utility of a MRGN admission-screening.

Methods

All patients who had been hospitalised abroad within the last 6 months were screened with rectal swabs within 5 days after admission to our hospital. If open wounds or invasive devices were present, additional samples were obtained from wounds, urine or tracheal secretions. Samples were incubated in an enrichment broth and subsequently inoculated on screening plates for ESBL and Oxa-48. We used the BD PhoenixTM 100 system for susceptibility testing. Suspected ESBL or carbapenem resistance was investigated with phenotypic methods. PCR was applied for suspected carbapenemase production. Since local guidelines do not ask for putting patients colonised with ESBL-E.coli under contact precautions, samples with suspected ESBL-E.coli were not further investigated.

Results

From June 2013 until April 2016 217 patients were available for analysis. 37 (17%) patients were colonised with MRGN, but only 21 (9.7%) required contact precautions according to our guidelines. 3 (1.4%) patients were colonised with >1 species. Most identified species were Escherichia coli (18, 8.3%) and Klebsiella pneumoniae (14, 6.5%). Most resistance mechanisms were ESBL (33,15%), only 7 (3.7%) bacteria harboured a carbapenemase. Only two (0.9%) patients had positive screening results from urine without positive rectal screenings. 10 (4.6%) patients had >1 positive screening sites. In univariate analysis, we identified 6 risk factors for MRGN colonisation requiring contact precautions (see table). 20/21 of those patients had ≥1 risk factor. In multivariable analysis, only urinary and central venous catheter remained significant. The number of risk factors was significantly correlated with risk of colonisation ($p<0.001$). Colonisation with MRGN resulted in longer length of stay (25 vs 14 days,$p=0.001$).

Conclusion

MRGN colonisation, mainly ESBL Enterobacteriaceae, was present in 17% of patients recently hospitalised abroad. Rectal screening was efficient compared to other sites. Risk factors were consistent with previously published data. If only patients with ≥1 risk factor were screened, 95% of colonized patients would be detected and screening would be reduced by 30%. In our setting, risk-based admission screening may be effective.

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Risk factor	Colonised (n=21)	Non-colonised (n=196)	Relative risk (95%-CI)	p-value univariate analysis	p-value multivariable analysis
Urinary catheter	16 (24.6%)	49 (75.4%)	7.5 (2.9-19.6)	<0.005	<0.005
Central venous catheter	6 (60%)	4 (40%)	8.3 (4.1-16.7)	<0.005	0.03
Invasive ventilation	5 (38.5%)	8 (61.5%)	4.9 (2.2-11.3)	0.004	0.40
Open wound	7 (20%)	28 (80%)	2.6 (1.2-6.0)	0.042	0.09
Antibiotics before screening	15 (14%)	92 (86%)	2.6 (1.1-6.4)	0.04	0.38
Risk region (Africa, Asia, Eastern or Southern Europe)	19 (12.6%)	132 (87.4%)	4.2 (1.0-17.3)	0.03	0.07

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P108 | Extended-spectrum beta-lactamase producing Enterobacteriaceae among healthy pregnant women: preliminary results of an ongoing cross-sectional study

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Introduction

Colonization rates of extended-spectrum beta-lactamase producing enterobacteriaceae (ESBL-E) in pregnant women vary from 3-15%. ESBL-E positive mothers have been identified as most important risk factor for subsequent colonization of their preterm infants. Outcomes of ESBL-E infected neonates are often worse and outbreaks in neonatal intensive care units have been reported. No guideline exists for ESBL-E screening in pregnancy. We aim to determine the prevalence of ESBL-E in pregnant women, to identify potential risk factors for ESBL-E colonization and to compare the ESBL-E detection rate of a vaginal-perineal swab to the standard rectal swab.

Methods

At the outpatient obstetrics clinic of the University Hospital Basel, we are recruiting women attending their routine follow-up visit at 36-38 weeks of gestational age. Women at risk for preterm delivery and those on antibiotic treatment are excluded. A paired rectal and vaginal-perineal swab are obtained and analysed for the presence of ESBL-E. On a case basis neonates of ESBL-E positive mothers undergo screening for ESBL-E. We used Fisher's exact test and t-test to compare differences in proportions and means and determined the sensitivity and specificity of the vaginal-perineal swab compared to the rectal swab.

Results

Since November 2014, 6 (3.2%) of the first 190 recruited women of mainly European nationality have been tested positive for ESBL E. coli. In the univariable analysis only quinolone use but none of the other potential risk factors showed a statistically significant association with ESBL-E carriage (P=.03) (Table). Sensitivity and specificity (95% confidence interval) of the vaginal-perineal swab was 0.33 (0.06 –0.76) and 1.00 (0.97-1.00), respectively, compared to the rectal swab. One healthy neonate had ESBL E. coli confirmed in stool culture.

Discussion

The low ESBL-E carriage rate among pregnant women likely reflects the prevalence in the general population but use of quinolones may increase the risk of colonization. The low sensitivity of the vaginal-perineal swab suggests that this site is inappropriate for screening pregnant women. However, confidence in the estimates is weak due to the low number of ESBL-E positive women and the results need to be confirmed after completion of the study. The impact of routine screening for ESBL-E in a low prevalence setting remains to be determined and may rather be limited to mothers of preterm infants during delivery.

Table. Univariable analysis of potential risk factors for ESBL-E carriage in pregnancy.

	ESBL negative (n=184)	**ESBL positive (n=6)**	**p-value**
Age (in years), mean (SD)	32.6 (5.0)	34.3 (2.7)	0.39
Non-European, n/total (%)	22/160 (13.8)	2/5 (40.0)	0.15
History of recurrent UTI, n/total (%)	12/173 (6.9)	0/5 (0.0)	1.00

Diarrheal illness during travelling, n/total (%)	18/142 (12.9)	0/5 (0.0)	1.00
Hospital stay in foreign country, n/total (%)	8/147 (5.4)	1/5 (20.0)	0.30
≥ 1 antibiotic course during pregnancy, n/total (%)	5/171(2.9)	0/5 (0.0)	1.00
Fluorquinolone treatment during pregnancy	0/173 (0.0)	1/5 (20.0)	0.03*
Amoxicillin/Clavulanic acid treatment during pregnancy	14/173 (8.1)	0/5 (0.0)	1.00

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P110 | Rapid MALDI-TOF mass-spectrometry-based detection of nosocomial Rhizobium radiobacter bloodstream infections from a common source

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Background
Rhizobium radiobacter, an environmental Gram-negative bacterium, can occasionally cause infection in humans. Between November 29 and December 7, 2015, our hospital's microbiology laboratory reported two cases of R. radiobacter bacteremia admitted to the cardiology department, which triggered an outbreak investigation.

Methods
We generated a line list to identify possible common sources for the bacteremia that both patients were exposed to, followed by on-site audits and environmental swabs. Blood culture isolates were identified by MALDI-TOF mass-spectrometry (MS) and 16S-rDNA analyses. Relatedness of the two outbreak isolates (A, B) and two independent control R. radiobacter isolates (B, C) was determined by MALDI-TOF MS based typing via visual examination of the peak profiles and principal components analysis (PCA). We used pulsed-field gel electrophoresis (PFGE) to confirm the relatedness of the isolates.

Results
Case 1 was a 72 year-old male admitted for an elective transcatheter aortic valve implantation. Case 2 was an 83 year-old female admitted because of congestive heart failure. Based on the line list the patients shared two locations: the cardiac catheterization laboratory A and the radiology room 1. The timeline is shown in Figure 1. Audits revealed no breaches of infection prevention precautions by the involved healthcare personnel. We suspected the contrast injector pump mechanism used in laboratory A (a semi-open system) to pose an infection risk, however, the pump was not found to be contaminated. Ongoing construction works in the adjacent room may have been the source of transient contamination. MALDI-TOF MS recorded differences in 58 peaks (m/z range of 2 – 10 kDa) of the four strains. The mass spectra of isolates A and B showed no difference. The PCA dendrogram indicated close relatedness of the two isolates, which was confirmed by PFGE (Figure 2).

Conclusion
We report a self-limited outbreak with two cases of R. radiobacter bloodstream infections likely to originate from a common source. Partly open systems destined to be sterile - such as the contrast injector pump - represent an infection risk. Here, we highlight the successful use of MALDI-TOF MS as a potential tool for outbreak analysis.

Figure 1: Timeline of clinical, microbiological, environmental, and therapeutic features of the two cases

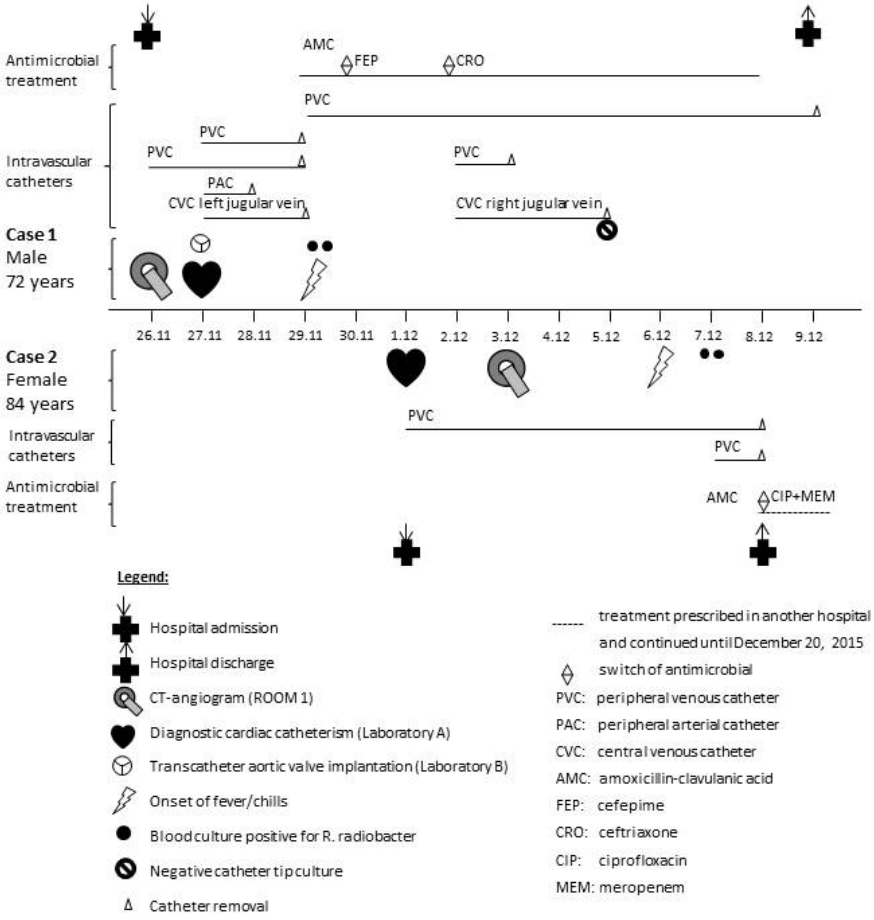
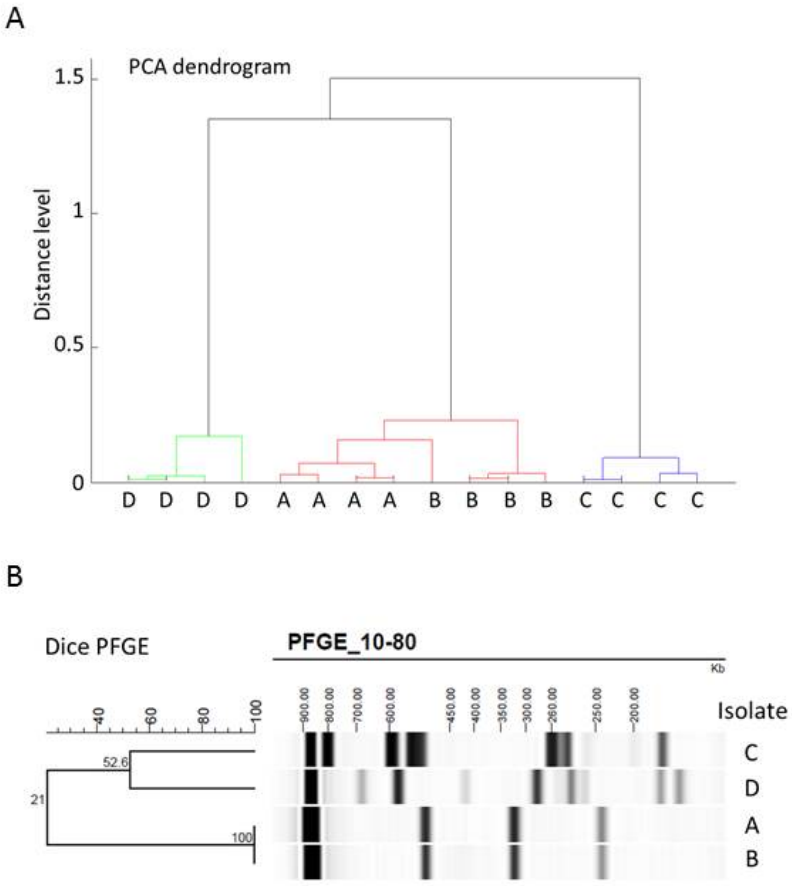


Figure 2 (A) PCA dendrogram based on MALDI-TOF MS. Four spectra were recorded for each isolate A-D. Isolate A was recovered from patient 1, isolate B from patient 2, isolates C and D are epidemiologically unrelated control strains. (B) PFGE based typing of the same isolates. Chromosomal DNA was digested with *PmeI*.



P111 | Verwendung von Urinkathetern: Retrospektive Datenanalyse

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Ziel der Studie
Dauerkatheter (DK)-assoziierte Harnwegsinfekte (CAUTI) stellen die dritthäufigste nosokomiale Infektion dar. Ziel dieser Studie war die Bestimmung der Häufigkeit von DK, deren Indikationen und Liegedauer sowie der Häufigkeit von CAUTI.

Material und Methoden
Retrospektive Datenanalyse aller erwachsenen Patienten, die im Mai und Juni 2015 am Kantonsspital St. Gallen Standort Rorschach (ca. 80 Betten) hospitalisiert waren. Erfasst wurden Einlage, Indikation und Liegedauer eines DK und Häufigkeit von CAUTI.

Resultate
87 (17.6%) der 494 hospitalisierten Patienten erhielten während der Hospitalisation einen DK mit 19.7 Kathetertagen/100 Hospitalisationstagen. 41 (15%) Männer und 46 (20%) Frauen erhielten einen DK (p=0.06). Auf der Orthopädie hospitalisierte Patienten (27.8%) erhielten signifikant häufiger (p=0.04) einen DK als Patienten auf der Medizin (16.0%) oder Chirurgie (15.5%), die entsprechende mittlere (±SD) DK-Liegedauer war 6.1 (±3.7), 5.9 (±4.5) und 2.4 (±1.3) Tage. Gründe für DK-Einlage waren Operationen (15.1%), Harnverhalt (18.7%), pflegerische Gründe (12.5%), Monitoring bei kritisch Kranken (10.7%), Diagnostik (2.7%), Komfort bei Palliativpatienten (5.3%) und prolongierte Immobilisation (12.4%). Bei 4 DK-Trägern (3.5%) wurde eine DK-assoziierte asymptomatische Bakteriurie nachgewiesen, bei 1 Patienten erfolgte eine Antibiotikatherapie. Bei keinem der 87 Patienten mit DK-Neueinlage trat während der Hospitalisation ein Infekt auf. 10 Patienten traten mit einem bereits liegenden DK ein. Bei 3 dieser Patienten (33%) wurde bei Eintritt ein CAUTI diagnostiziert. Diese 3 Patienten waren Langzeit-DK Träger bei Tetraplegie, Rollstuhlmobilität mit Inkontinenz und terminalem Tumorleiden (jeweils n=1). Die Hospitalisationsdauer der Patienten mit DK war signifikant länger als bei Patienten ohne DK (9.3 versus 6.0. Tage, p<0.001).

Schlussfolgerung
Die Häufigkeit der DK-Einlage entspricht mit 17.6% dem europäischen Durchschnitt bei allerdings langer Liegedauer. Dies weist auf vermutlich verpasste Indikationen für eine frühere DK-Entfernung hin, wobei dies aufgrund des retrospektiven Studiendesigns schwierig zu beurteilen war. Der fehlende Nachweis von CAUTI bei neu-eingelegten DKs kann unter anderem die geringe Fallzahl bedingt sein. Eine prospektive Surveillance mit Überprüfung der Indikation bei der Einlage bzw. der Entfernung hat Potential, die Anzahl Katheter und die DK-Liegedauer zu verkürzen.

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P112 | "We are not irresponsible": Nurses perception of strategies to improve nosocomial influenza prevention

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Background
Seasonal influenza can be a serious health problem for hospitalized, vulnerable patients. Hand hygiene, face masks and vaccination by health care workers are considered important preventive strategies. Limited evidence shows insufficient implementation of these strategies by health care workers. However there are differences in implementation at the level of strategy, profession and discipline. The aim of this investigation was to describe what factors enable implementation of preventive strategies by nurses in hospital settings.

Methods
This qualitative investigation is part of the HaiP study (Health care associated Influenza Prevention) aiming at reducing nosocomial infection by developing complex interventions for hospital settings. Contextual knowledge is considered important for intervention development. As a part of this knowledge generation, we conducted open-ended interviews with nurses, the largest group of health care workers. We conducted 22 single and 3 focus group interviews. Data were analyzed using of thematic analysis as described by Braun & Clarke (2006).

Results
The central theme emphasized by participants was "Taking responsibility for patient protection". Participants described a range of strategies used to keep patients and themselves as healthy as possible. Whereas the implementation of some strategies such as hand hygiene was perceived as a collective responsibility: others, for example vaccination, were not. Within four subthemes the process of taking responsibility is described: 1) "understanding what works", 2) "discussing what can be done", 3) "weighing individual and collective interests" and 4) "learning from experiences". An underlying theme that influenced the process of taking responsibility was "dealing with collective blaming". Participants experienced moralizing pressure on the profession of nursing that focused on vaccination or mask wearing. This led to active resistance or a collective understanding of resistance by nurses. In this situation leadership for influenza prevention seemed to work better by persons who demonstrated high influenza expertise combined respectful communication.

Conclusion
A non-blaming culture seems to be an important premise for nurses to play an active part in nosocomial influenza prevention. Multi component interventions that include content on leadership within the profession of nursing and decision support to weigh individual and collective interests are needed.

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P113 | Whole-genome sequencing in real-time investigation of a vancomycin-resistant Enterococcus faecium outbreak at a tertiary care hospital

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Background
Between January and March 2015, an outbreak of vancomycin-resistant Enterococcus faecium (VREfm) occurred at the University Hospital of Lausanne. We performed whole-genome sequencing (WGS) to determine characteristic genetic signatures in the outbreak isolates for developing a specific multiplex PCR that could be implemented in the outbreak control measures. Furthermore, we investigated the relatedness, molecular features and the transmission events of the outbreak isolates.

Materials and Methods
In total, 39 VREfm isolates were retrieved from clinical samples and rectal swabs of 30 patients during the outbreak. WGS of 15 VREfm isolates was performed at the beginning of the outbreak (end of January 2015), while the remaining 24 isolates were sequenced retrospectively (July 2015). All isolates were sequenced using the Illumina MiSeq platform. Genome sequences were subjected to in-silico multi-locus sequence typing (MLST) and the identification of genetic determinants of antibiotic resistance. Comparative genome analysis of the assembled ordered draft genomes was performed using Mauve software. To infer the isolates' phylogeny, all paired-end reads were mapped to the most related reference genome and, subsequently, a maximum likelihood tree was constructed using single nucleotide polymorphisms (SNPs) from a core genome alignment. Estimations of the transmission tree, dates of infections, and imported cases were performed using the R-package outbreaker.

Results
The in-silico MLST analysis of the initial run revealed that fourteen of the sequenced isolates represented multilocus sequence type (ST) 17, while the remained isolate belonged to ST80. Using the comparative genomic approach, we have identified genetic loci responsible for polysaccharide biosynthesis that were specific to all ST17 outbreak isolates. These loci were used to develop a multiplex PCR to differentiate between outbreak and non-outbreak isolates, which preceded and followed the outbreak period. This specific PCR revealed that 15 further patients were part of the outbreak, and we were able to exclude ten patients from the outbreak. The phylogenetic analysis demonstrated that outbreak isolates were very closely related with only 0-4 SNPs differences. The transmission tree revealed that three main clusters of cases that are likely linked (patient-to-patient transmission) and patient 01 (from November 2014) is likely to be the index case.

Conclusion
WGS analysis provided comprehensive evidence of a clonal outbreak of VREfm, and was able to precisely distinguished outbreak from non-outbreak isolates. Furthermore, it suggests that there were further undiscovered cases prior to the index case; and that VREfm was introduced from a point source with secondary transmissions. WGS demonstrates the prospect to substitute currently used phenotypic and molecular typing approaches in focused outbreak investigation.