

29^{ème} JOURNÉE SCIENTIFIQUE th SCIENTIFIC DAY

Résumés des communications
Presentation abstracts



Institut du Monde Arabe Paris 13 juin / 13 June 2019

Paris, le 13 juin 2019

Bonjour,

La journée scientifique d'Epicentre est une opportunité rare de se plonger au cœur de projets d'épidémiologie et de recherche en situation humanitaire. Aux côtés de MSF depuis plus de 30 ans les équipes d'Epicentre évoluent dans une grande diversité de situations. Elles doivent ainsi employer un large éventail de méthodes avec l'ambition constante de conduire des études dont les résultats doivent faire évoluer les pratiques médicales.

Présents au sein des programmes de MSF nous avons pour objectif de décrire et analyser les difficultés rencontrées par les équipes soignantes. Nous le montrerons sur une série de cas d'œdèmes chez l'enfant. La première session de la journée consacrée à l'infection à VIH abordera la question de l'efficacité thérapeutique, de la connaissance du statut VIH et de la résistance au traitement antirétroviral. Toujours sur les grandes endémies nous consacrerons une session de l'après-midi à la tuberculose, maladie toujours difficile à diagnostiquer mais sur laquelle apparaissent certaines avancées thérapeutiques.

Un autre axe fort de la politique opérationnelle de MSF est le soin aux victimes de violence. Il en sera question lors de l'analyse des projets d'Amman et de Gaza lors de la deuxième session du matin, ainsi qu'à Nairobi dans le cas particulier des victimes de violence sexuelle.

Nous contribuons également à la construction de stratégies de réponse non seulement pour MSF mais également pour les acteurs de santé publique nationaux ou internationaux. Deux séries de travaux en témoignent, sur l'hépatite C au Cambodge avec un modèle de soins basé sur les antiviraux à action directe et dans la réponse aux épidémies de fièvre jaune avec des doses fractionnées du vaccin. La réponse aux

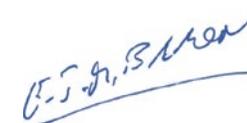
épidémies est aussi une occasion d'élargir nos connaissances sur l'épidémiologie d'une maladie. L'analyse de la dissémination d'une souche de choléra d'Afrique de l'Est au Yémen est un bon exemple.

La recherche dans les épidémies sera abordée de façon plus exhaustive grâce à une série de présentations dont celle de fièvre Ebola en cours en République Démocratique du Congo. Nous présentons avec nos collègues congolais du Ministère de la Santé et de l'Institut National de Recherche Biomédicale les tendances et les résultats les plus récents sur la situation épidémiologique de l'épidémie, la prise en charge médicale dans les centres de traitement et l'essai thérapeutique comparant des médicaments en développement.

Contribuer au développement de nouveaux médicaments fait aussi partie de notre expérience, comme l'illustrera la présentation du matin sur l'efficacité d'une nouvelle formulation d'antirétroviraux pédiatriques développée par nos amis de la DNDi. C'est d'ailleurs à son équipe que nous avons demandé d'exposer les difficultés de l'activité de recherche et développement dans le contexte humanitaire, une intervention qui clôturera notre journée scientifique.

Afin de poursuivre la conversation nous nous retrouverons en fin de journée autour d'un verre sur la terrasse de l'Institut du Monde Arabe qui nous accueille à nouveau cette année.

Je vous souhaite une très belle journée.



Emmanuel Baron
Directeur Général, Epicentre

Paris, June 13, 2019

Good Morning,

Epicentre's Scientific Day is a rare opportunity to immerse ourselves in the heart of epidemiology and research projects in humanitarian situations. Working side-by-side with MSF for over 30 years, Epicentre's teams have evolved through a wide range of situations. Thus, they employ a variety of methods, with the constant aim of conducting studies whose results have an impact on medical practice.

Working within MSF's programs, we aim to describe and analyse the difficulties encountered by healthcare teams. This will be seen in a presentation of a case series of edema in children. The first session of the day, which focuses on HIV, addresses the question of therapeutic efficacy, knowledge of HIV status and resistance to antiretroviral treatment. Continuing with the theme of widespread endemic diseases, one afternoon session is dedicated to tuberculosis, a disease that is still difficult to diagnose but for which there is some therapeutic progress.

Another main focus of MSF's operational policy is caring for victims of violence. The second morning session will address this by analyzing projects in Amman and Gaza, as well as in Nairobi in the specific case of victims of sexual violence.

We also contribute to constructing response strategies, not only for MSF but also for national or international public health stakeholders. Two presentations show this: one on hepatitis in Cambodia with a healthcare model based on direct-acting antivirals, and one on the response to yellow fever epidemics with fractional dose vaccine. Epidemic response is also an opportunity to increase our understanding of

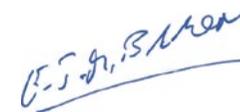
the epidemiology of a disease. The analysis of the spread of a cholera strain from East Africa to Yemen is a good example.

Research in epidemic situations will be addressed more comprehensively in a series of presentations, including one on the ongoing Ebola outbreak in the Democratic Republic of the Congo. Along with our Congolese colleagues from the Ministry of Health and Institut National de Recherche Biomédicale we present the trends and most recent analyses of the epidemiology of the epidemic, the medical care provided in treatment centers and the therapeutic trial comparing therapeutics under development.

Contributing to the development of new therapeutics is also part of our experience, as illustrated by the morning presentation on effectiveness of a new formulation of pediatric antiretrovirals developed by our friends at the DNDi. We have asked this team to talk about the difficulties of carrying out research and development activities in a humanitarian context, a presentation that will conclude our scientific day.

To continue the conversation, at the end of the day we will meet for drinks on the patio of the Institut du Monde Arabe, which is hosting us again this year.

I hope you have a wonderful day.



Emmanuel Baron
Managing Director, Epicentre

29^{ème} Journée Scientifique - 13 juin 2019

8h45 Accueil et café

9h30 Introduction générale – Emmanuel Baron

9h45 Session 1 : VIH

Modératrice : Anita Mesic, MSF Centre Opérationnel Amsterdam

- Amélioration de la suppression virale parmi les personnes infectées par le VIH dans deux zones à forte prévalence VIH. (Nolwenn Conan)
- Connaissance du statut VIH parmi les professionnelles du sexe séropositives à Nsanje, Malawi. (Damian Mauambeta)
- Résistances acquises et transmises aux antirétroviraux au Mozambique. (Valentina Carnimeo)
- Résistance aux ARV chez les patients hospitalisés à Homa Bay (Kenya) et Kinshasa (République Démocratique du Congo). (Claire Bossard)

10h45 Session 2 : Présentations courtes

Modérateur : Olivier Bouchaud, Hôpital Avicenne, Bobigny

- Diffusion du choléra du Kenya au Yémen. (Francisco Luquero)
- Blessés de guerre : une décennie de prise en charge à l'hôpital d'Amman, Jordanie. (Rami Malaeb)
- Résistance antibiotique parmi les blessés de guerre pris en charge dans l'hôpital d'Amman, Jordanie. (Rasheed M. Fakhri)
- De mars à septembre 2018, 2 000 blessés traités dans les hôpitaux par MSF à Gaza, Palestine. (Alessandro Pini)
- Description des cas d'œdèmes bilatéraux chez les enfants hospitalisés au Mali et en République Démocratique du Congo. (Jihane Ben-Farhat)
- Efficacité d'une nouvelle formulation du traitement antirétroviral pédiatrique. (Juvenal Nkeramahame)

11h45 Pause café

12h15 Session 3 : Hépatite C au Cambodge

Modérateur : Yap Boum II, Epicentre Cameroun

- Enquête de prévalence de l'hépatite C et facteurs de risque dans trois districts ruraux. (Chhorvy Sun)
- Perspectives nationales. (Jean-Philippe Dousset)

13h00 Buffet sur place

15h00 Session 4 : Tuberculose

Modératrice : Maryline Bonnet, Institut de Recherche pour le Développement, Mbarara

- Utilité du test LAM dans le diagnostic de la tuberculose. (Helena Huerga)
- Innocuité des nouvelles molécules contre la tuberculose multirésistante : résultats de l'étude observationnelle endTB. (Cathy Hewison)

16h00 Session 5 : Session générale

Modérateur : Thierry Allafort-Duverger, MSF Centre Opérationnel Paris

- Doses fractionnées de vaccins contre la fièvre jaune dans la réponse aux épidémies. (Aitana Juan)
- Dépistage actif des violences sexuelles ou basées sur le genre à Nairobi, Kenya. (Augusto Llosa)
- Situation actuelle de l'épidémie d'Ebola en République Démocratique du Congo. (Rebecca Coulborn et Luigino M. Minikulu)

17h00 Recherche et Développement : pas si facile...

Nathalie Strub-Wourgaft, Drugs for Neglected Diseases initiative, Genève

17h30 Pot de clôture sur place, 9^{ème} étage Terrasse
Institut du Monde Arabe

29th Scientific Day - 13 June 2019

8h45 Welcome and coffee

9h30 Introductory remarks – Emmanuel Baron

9h45 Session 1: HIV

Moderator: Anita Mesic, MSF Operational Center Amsterdam

- Progress in viral suppression among HIV-infected people in two high HIV prevalence settings. (Nolwenn Conan)
- HIV status awareness among seropositive female sex workers in Nsanje, Malawi. (Damian Mauambeta)
- Acquired and transmitted drug resistance to antiretroviral drugs in Mozambique. (Valentina Carnimeo)
- Drug resistance among ART experienced hospitalized patients in Homa-Bay (Kenya) and Kinshasa (the Democratic Republic of Congo). (Claire Bossard)

10h45 Session 2: Short presentations

Moderator: Olivier Bouchaud, Hôpital Avicenne, Bobigny

- Geographical dissemination of cholera from Kenya to Yemen. (Francisco Luquero)
- War wounded patients: one decade of treatment in Amman hospital, Jordan. (Rami Malaeb)
- Antibiotic resistance among war wounded patients in Amman hospital, Jordan. (Rasheed M. Fakhri)
- March to September 2018, 2 000 wounded patients treated in hospitals by MSF in Gaza, Palestine. (Alessandro Pini)
- Description of bilateral oedema cases among children hospitalised in Mali and the Democratic Republic of Congo. (Jihane Ben-Farhat)
- Effectiveness of a new ART formulation for children. (Juvenal Nkeramahame)

11h45 Coffee break

12h15 Session 3 : Hepatitis C in Cambodia

Moderator: Yap Boum II, Epicentre Cameroun

- Hepatitis C prevalence and risk factors survey in three rural districts. (Chhorvy Sun)
- National perspectives. (Jean-Philippe Dousset)

13h00 Lunch on site

15h00 Session 4 : Tuberculosis

Moderator: Maryline Bonnet, Institut de Recherche pour le Développement, Mbarara

- Use of LAM test for tuberculosis diagnosis. (Helena Huerga)
- Safety of new multidrug-resistant TB drugs: results from the end TB observational study. (Cathy Hewison)

16h00 Session 5 : General session

Moderator: Thierry Allafort-Duverger, MSF Centre Opérationnel Paris

- Fractional dose yellow fever vaccines for outbreak response. (Aitana Juan)
- Active screening for sexual and gender-based violence in Nairobi, Kenya. (Augusto Llosa)
- Current Ebola outbreak in the Democratic Republic of Congo. (Rebecca Coulborn and Luigino M. Minikulu)

17h00 Research and Development: not so easy...

Nathalie Strub-Wourgaft, Drugs for Neglected Diseases initiative, Geneva

17h30 Farewell drinks on site, 9th floor Terrace Terrasse
Institut du Monde Arabe

Session 1: HIV

Moderator: Anita Mesic,
MSF Operational Center Amsterdam

Progress in viral load suppression among HIV-infected people in two high HIV prevalence settings

Nolwenn Conan, Epicentre, South Africa

Background

Studies have shown that HIV-infected individuals who receive antiretroviral therapy (ART) and maintain an undetectable viral load (VL) cannot transmit the virus to others. In 2015, the World Health Organization recommended countries adopt universal ART initiation regardless of CD4 count (“Treat all”). We evaluated changes in the HIV cascade of care coverage, and viral load suppression (VLS) (VL<1,000 copies/ml), at the community level in two different settings.

Methods

Cross-sectional population-based surveys were implemented in Eshowe-Mbongolwane sub-district (South Africa) in 2013 and 2018 and in Ndhiwa sub-county (Kenya) in 2012 and 2018. Using multistage cluster sampling, we recruited all individuals aged 15-59 years living in selected households. Consenting participants were interviewed, tested for HIV at home and assessed for viral load when HIV-positive regardless of ART-status.

Results

Overall, 5 649 and 3 278 individuals were included in the surveys conducted in 2013 and 2018 in Eshowe-Mbongolwane, and 6 076 and 6 029 individuals were included in the surveys conducted in 2012 and 2018 in Ndhiwa, respectively.

In Eshowe- Mbongolwane, HIV-positive status awareness was 76.4% (95% CI: 74.1–78.6) in 2013 vs 89.9% (95%CI: 87.7- 91.8) in 2018. ART coverage among HIV-infected was 53.5% (50.6- 56.3) in 2013 vs 84.3% (95%CI: 81.7- 86.5) in 2018.

In Ndhiwa, 59.4% (95% CI 56.8–61.9) of the HIV-infected participants knew their status in 2013 vs 93.4% (95%CI: 91.7- 94.8) in 2018, and ART coverage among HIV-infected was 39.6% (36.7-42.5) in 2012 vs 90.4 % (95%CI: 88.5- 92.2) in 2018.

Overall, in Eshowe-Mbongolwane, 57.1% (54.6- 60.1) of all HIV-positive participants were virologically suppressed in 2013 compared to 83.8% (95%CI: 81.1- 86.1) in 2018. In Ndhiwa, VLS coverage was 39.7% (95% CI 37.1–42.4) in 2012 compared to 88.3% (95%CI: 86.1- 90.1) in 2018.

Conclusion

HIV status awareness, linkage to care and viral load suppression improved dramatically in each setting.

These surveys document a clear progress in the coverage of HIV status awareness, linkage to care and viral load suppression in two high prevalence countries.

HIV status awareness among seropositive female sex workers in Nsanje, Malawi

Damian Mauambeta, Médecins Sans Frontières, Malawi

Background

Globally, female sex workers (FSW) are 14 times more likely to be infected with HIV than adult women of the general population. In Nsanje, a large number of women engage in sex work near the mostly male work sites and transport routes. The MSF FSW project in Nsanje is a community-based SW peer-led intervention aiming to provide the continuum of care for this group.

Method

Between February and April 2019, a cross-sectional study was implemented in 3 sites in Nsanje district using respondent driven sampling (RDS). Eligible participants were women and girls aged 13 years or older who had lived and worked in the district in the last six months and had sexual intercourse with someone in exchange for money or goods in the last 30 days (excluding intercourse with their main partner). Consenting participants were interviewed and tested for HIV as well as for syphilis, gonorrhoea and chlamydia. Viral load (VL) and CD4 count were measured for all HIV-positive participants and RDS-adjusted proportions were calculated.

Results

In total, 363 participants were included, of whom 64.7% [95%CI: 59.6-69.5] were already receiving care from MSF. The median age was 26 [IQR: 20-33] years and the median duration of sex work was 4 years [3-7]. HIV prevalence was 52.4% [47.3-57.6], HIV status awareness was 95.2% [91.3-97.4], ART coverage (self-reported) was 95.2% [91.2-97.4] and VL suppression was 80.8% [74.7-85.8]. The prevalence of syphilis was 29.7% [25.3-34.5], gonorrhoea 9.5% [6.9-12.9] and chlamydia 12.5% [9.3-16.6]. Among HIV-positive participants, the median CD4 was 552 cells/ μ L [394-781]. Half of the participants reported having ever experienced sexual violence (47.6% [42.4-52.7]).

Conclusions

Our findings suggest a population with high exposure to sexual violence, and a relatively high prevalence of HIV and STIs. Participants demonstrated a high awareness of HIV-positive status and a high linkage to care.

Using respondent driven sampling, female sex workers were recruited to assess the HIV cascade of care in a rural area in Malawi.

Acquired and transmitted resistance to antiretroviral drugs in Mozambique

Valentina Carnimeo, Epicentre, France

Background

Since 2013, MSF has supported viral load (VL) testing scale-up in rural and urban Mozambique where programmatic data showed a high rate of HIV-1 virological failure (VF, VL \geq 1 000 HIV-1 RNA copies/ml). This study estimates the proportion of VF and acquired drug resistance (ADR) among patients receiving first-line ART for more than 6 months, as well as the level of pre-treatment drug resistance (PDR) among HIV patients initiating/re-initiating ART in both settings.

Methods

Two cross-sectional studies were conducted between October 2017 and October 2018 in MSF-supported health centres (HC) among patients aged \geq 18 years (ADR survey: 1 HC in Maputo, 2 in Tete District; PDR survey: 1 HC in Maputo, 7 in Tete). VL was quantified and drug resistance testing (DRT) performed if VL \geq 1 000. HIV-DR was defined by low, intermediate or high levels of resistance (StanfordHIVdb). PDR was reported as the proportion of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance.

Results

Among 1 113 participants on ART for at least 6 months (57.5% in Maputo, median age 42 years, 67.7% female), 11% (95CI% 9.4-13.2) had VF. Among these, 91.2% (N=114, CI95% 84.7-95.5) had any HIV-DR,

73.6% (95CI% 65.0-81.0) had any nucleoside reverse transcriptase inhibitors (NRTI) resistance and 89.6% (95CI% 82.8-94.3) had any NNRTI DR. Among 735 ART initiators/re-initiators (39% in Maputo, median age 34 years, 55% female, 12.7% ART-pre-exposed), 525 (71.4%) had VL $>$ 1 000 and DRT available. Of these patients, 25.9% (95CI% 22.2-29.9) had NNRTI resistance (vs. 55% among those pre-exposed to ART).

Conclusion

Among patients on treatment for at least 6 months, VF on first-line was low but most patients with a high VL were on a failing regimen. The level of PDR among ART initiators/re-initiators exceeded the 10% threshold, and about 1/4 of patients initiated ART with an ineffective first-line regimen.

Non-NNRTI first-line ART should be recommended for ART initiation in Mozambique, and HIV-1 drug resistance surveillance should be implemented at a national level.

Drug resistance among ART experienced hospitalized patients in Homabay (Kenya) and Kinshasa (the Democratic Republic of Congo)

Claire Bossard, Epicentre, South Africa

Background

In sub-Saharan Africa, an increasing number of patients hospitalized with advanced HIV are ART-experienced, and mortality is extremely high. In those with an elevated viral load ($VL \geq 1000$ copies/ml), WHO recommends enhanced adherence counselling and a switch to second-line ART if VL remains elevated 3 months after the initial assessment.

Method

A mixed methods study was conducted between September 2017 and April 2018 in two MSF-supported hospitals in Kinshasa, (DRC) and Homabay, Kenya. Hospitalised patients aged ≥ 15 years receiving first line ART for < 6 months and with $CD4 < 350$ cells/ μ L were eligible. $CD4$ count, VL and genotype were assessed at inclusion. Resistance was defined as having any major (intermediate/high) NRTI or NNRTI drug resistance. In-depth interviews were conducted to explore patient pathways to care. Interviews were audio-recorded, transcribed, translated and analysed thematically.

Results

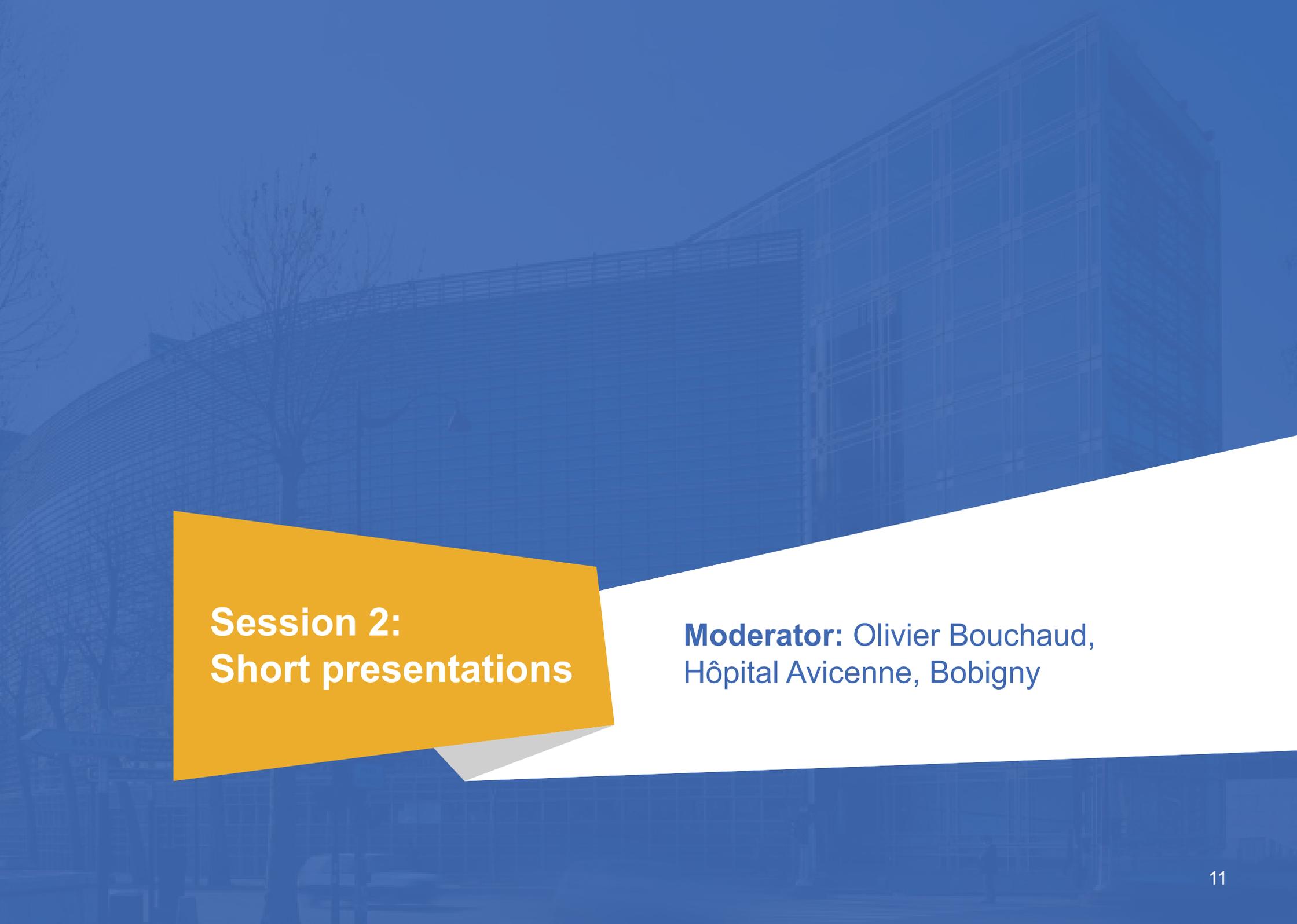
Among 317 eligible patients, 306 were included, with a median time of 5.3 years [IQR:2.5-10.3] on ART in Kinshasa and 4.0 years [IQR:1.8-8.9] in Homabay. Among them, 59% were women (68% Kinshasa, 54% Homabay) and their median age was 38 [31-48] years.

Median $CD4$ was 69 [IQR:29-134] cells/ μ L in Kinshasa and 135 [IQR:46-255] cells/ μ L in Homabay. Half had a $VL \geq 1,000$ copies/mL (71% Kinshasa, 37% Homabay). Of those with $VL \geq 1000$ copies/mL, 72% and 75% were on completely ineffective regimens in Homabay and in Kinshasa, respectively. In-depth interviews with 30 participants revealed multiple attempts to access care and experiences of hospitalisation. Patients described extreme social and financial vulnerabilities linked to illness as well as to ART adherence challenges over time.

Conclusion

A high proportion of ART-experienced patients hospitalized with advanced disease were resistant to their ARV treatment. Immediately switching to second-line ART after a single elevated VL or $CD4 < 100$ cells/ μ L should be recommended to hasten immune reconstitution. Interventions in decentralised facilities should be implemented to address missed opportunities for timely management of advanced HIV and drug resistance.

High rates of advanced HIV and mortality among hospitalized patients on ARV treatment are found in sub-Saharan Africa. Given the high level of drug resistance, treatment of these patients requires prompt action, including community-level interventions.



**Session 2:
Short presentations**

Moderator: Olivier Bouchaud,
Hôpital Avicenne, Bobigny

Geographical dissemination of cholera from Kenya to Yemen

Francisco Luquero, Epicentre, Switzerland

Introduction

Between 2013 and 2016, Kenya reported 19,192 cholera cases and 156 cholera deaths to the World Health Organization. The majority of these cases and deaths were reported in 2015, when a countrywide outbreak spread to 22 out of 47 counties. In 2016, a massive cholera outbreak started in Yemen affecting almost all districts in the country. Here we explore the epidemiological relatedness of these events.

Methods

We investigated the phylogeny of *Vibrio cholerae* isolates from Yemen and recent isolates from neighboring regions. Overall the analysis was conducted from 116 genomic sequences (42 from Yemen), which were placed within the phylogenetic context of the seventh *V. cholerae* pandemic. The sequencing and analysis were carried out in collaboration with Institute Pasteur and Sanger Institute. We also described the epidemiology of cholera in Yemen and the neighboring countries.

Results

The isolates from Yemen were collected during the two waves of the epidemic—the first between 28 September 2016 and 23 April 2017 with

25,839 suspected cases and the second beginning on 24 April 2017 with more than 1 million suspected cases—are *V. cholerae* serotype Ogawa isolates from a single sub-lineage of the seventh pandemic *V. cholerae* O1 El Tor lineage. This sub-lineage originated from South Asia and caused outbreaks in East Africa between 2013 and 2016 before appearing in Yemen.

Conclusion

The outbreaks in Kenya and Yemen are part of a larger regional outbreak, which has affected several hundreds of thousand people and caused thousands of related deaths. These findings highlight the importance of considering both the regional nature of cholera epidemics and the need to nationally control spread to protect local and neighboring populations. They also show that the systematic integration of genomic analysis in the surveillance of cholera could help to identify new lineages at the beginning of outbreaks and should help to trigger intensified control measures.

This combined epidemiological and genomic analysis shows that the ongoing cholera epidemic in Yemen is part of a larger regional outbreak that started in East Africa in 2013-2014, and reinforces the importance of detecting the emergence of new lineages earlier.

War wounded patients: one decade of treatment in Amman hospital, Jordan

Rami Malaeb, Epicentre, United Arab Emirates

Background

The Reconstructive Surgery Hospital (RSP) was established in 2006 in Amman, Jordan. It acts as a regional centre treating war victims in the Middle East. The programme offers elective surgery for those with orthopaedic sequelae, maxillofacial injuries and plastic surgery patients. The objective of this study is to describe the demographic characteristics, types of injuries, treatment and sequelae of patients seen at the RSP since its inception.

Methods

A retrospective descriptive analysis examining data from 2006 to 2016, prior to the implementation of electronic medical records.

Results

The analysis was performed on 4,196 admissions. On average, the RSP treated 409 patients per year. The majority of patients were from Iraq (52.1%), Syria (30.6%) and Yemen (11.6%). Patients were predominantly above the age of 15 years (86%) and were admitted mostly at the orthopaedic department (57%). Males represented 81.5%. The main cause of injury was blast (52%). Thirty-seven percent (n=1,115) were admitted for subsequent stages. Forty-six different diagnosis were recorded primarily for non-union of fracture (27%) followed by 19% for burn contracture of skin and 10.5% for mechanical complication of internal fixation device.

Seventy-five percent out of 1,054 orthopaedic patients, who were tested for infection, were positive. The median length of stay was 96 days from arrival to home discharge with significant differences between specialities. As a result of the last follow up consultation recorded in the database, 1,279 (30.5%) exited the program with maximum benefit achieved, while the majority of others needed further stages to complete their treatment.

Conclusions

The study highlights the high needs for reconstructive surgery care in the Middle East where MSF is playing a crucial role to treat such patients who are left behind. The type of injuries treated at the hospital reflects the complexity of treatment and the high level of medical care required.

The Amman RSP provides MSF with an opportunity to enrich its understanding of tertiary surgery care in the Middle East.

Antibiotic resistance among war-wounded patients in Amman hospital, Jordan

Rasheed M. Fakhri, Médecins Sans Frontières, Jordan

Background

War-wounded civilians in Middle East countries are at risk of post-traumatic osteomyelitis (PTO). We describe the bacterial etiology and proportion of first-line antibiotic resistant bacteria (FLAR) among PTO cases in civilians from Syria, Iraq and Yemen admitted to the reconstructive surgical program of Médecins Sans Frontières (MSF) in Amman, Jordan.

Methods

We analyzed the laboratory database of the MSF program. Inclusion criteria were: patients from Iraq, Yemen or Syria, admitted to the Amman MSF program between 2006 and 2016, with at least one bone biopsy sample culture result. Only bone samples taken during the first orthopedic surgery were included in the analysis.

Results

Of the 727 patients included, 558 (76.7%) had ≥ 1 positive culture results. Of these, 318 were from Iraq, 140 from Syria and 100 from Yemen. Median time since injury was 19 months. Among the 732 different bacterial isolates, we identified 228 *Enterobacteriaceae* (31.5%),

193 *Staphylococcus aureus* (26.3%), 99 *Pseudomonas aeruginosa* (13.5%), and 21 *Acinetobacter baumannii* (2.8%). Three hundred and sixty-four isolates were FLAR: 86.2% of *Enterobacteriaceae*, 53.4% of *Pseudomonas aeruginosa*, 60.5% of *S. aureus* and 45% of *Acinetobacter baumannii*. There was no difference in bacterial etiology or proportion of FLAR according to the country of origin.

Conclusions

Enterobacteriaceae were frequent in PTO in war wounded civilians from Iraq, Yemen and Syria between 2006 and 2016. Proportion of FLAR was high, particularly among *Enterobacteriaceae*, regardless of country of origin.

Enterobacteriaceae were frequent in PTO in war wounded civilians from Iraq, Yemen and Syria between 2006 and 2016. Adequate management requires a high-quality laboratory, a skilled surgical team, robust antibiotic stewardship and effective infection prevention and control practices.

March to September 2018, 2 000 wounded patients treated in hospitals by MSF in Gaza, Palestine

Alessandro Pini, Epicentre, France

Introduction

Since March 2018, weekly demonstrations and Israeli army reaction in Gaza have led to thousands of casualties. MSF-OCP adapted its programmes in the strip to provide care to gunshot-wounded. Here we describe the medical and surgical needs of trauma patients.

Methods

This retrospective analysis includes all gunshot or explosion related trauma patients admitted into MSF-OCP clinics of Gaza between 1st April and 30th September 2018. We included all patients enrolled into MSF-OCP clinics because of a gunshot/explosion trauma, starting 30th March or later. We extracted data from patients' files and registers. We calculated mean and standard deviation (SD) for numeric variables and proportions for categorical variables.

Results

Of the 1 957 patients included, 70 were admitted more than once, totalling 2 027 enrolments. Of these, 1 923 (98%) were male with a mean age of 25 years (SD 6); 1 932 (99%) were the result of gunshots. Of 1 048 (54%) patients with a bone fracture, 956 (91%) were in the lower limbs and 620 (59%) had an internal or an external fixation.

We counted 235 (12%) and 181 (9%) patients with vascular and nerve injuries, respectively. Overall, 24 236 dressings, 13 133 physiotherapy sessions and 649 surgical interventions were performed. At the end of September, 807 (40%) patients were still on follow-up, and 647 (54%) had been discharged with maximum benefit achieved. Of the 478 (39%) defaulters, 174 (36%) dropped out within 7 days.

Conclusions

This analysis shows an extremely high number of young patients affected by complex gunshot wounds, at high risk for complications and sequelae, and who received high intensity care in one the MSF-OCP clinics. It argues for the need for advanced orthopedic and reconstructive care. The high proportion of dropouts suggests the need to investigate further and to adapt the project accordingly to patients.

Since March 2018, MSF clinics in Gaza have treated thousands of patients affected by complex gunshot wounds at risk of complications, requiring advanced orthopedic surgery.

Description of bilateral oedema cases among children hospitalized in Mali and the Democratic Republic of Congo

Jihane Ben-Farhat, Epicentre, France

Introduction

In Sub-Saharan Africa bilateral oedema is usually associated with Kwashiorkor, a form of severe acute malnutrition (SAM), but the sign can also be indicative of other pathologies. We aimed to describe the children presenting with bilateral oedema, to better understand their evolution and the underlying cause.

Methods

A prospective study conducted in Rutshuru, Democratic Republic of Congo (DRC) and Koutiala, Mali from October 2016 to December 2017 included children aged 6-59 months admitted with bilateral oedema. Clinical, anthropometric, biological, nutritional, and therapeutic characteristics and outcomes were collected. Description was done according to oedema severity and presence or absence of additional signs of SAM (MUAC<115 mm and/or W/H<-3Z-score).

Results

A total of 1611 (488 - DRC; 1123 - Mali) children participated. Overall 98% were ≥12 months of age, 57% had additional signs of SAM while 16% and 49% presented 3+ oedema in DRC and Mali respectively. About half of the children tested were malaria-positive and 57% anaemic. Children with additional signs of SAM were significantly more anaemic ($p<0.05$) in DRC and more likely to be hypotensive in both sites ($p<0.01$). Proteinuria was detected in 45% and 8% in DRC and Mali respectively.

Fifty-six percent of Congolese and 91% of Malian children were discharged with no oedema within a median of 2 days [IQR:1-3] and 3 days [2-5] respectively. Seven percent of the children died while hospitalized, with 69% (DRC) and 61% (Mali) of deaths occurring in those with proteinuria and/or anaemia, and 78% and 69%, respectively, in the group with additional signs of SAM. Proteinuria at admission was associated with at least a threefold elevated mortality risk in DRC (aOR 3.0, 95% CI 1.2-7.6; $p=0.02$) and in Mali (aOR 4.4, 95% CI 1.6-12.2; $p=0.01$).

Conclusion

This study shows differences in clinical and biological characteristics of children presenting with bilateral oedema, some of which are associated with mortality. Differences observed in the resolution of oedema would deserve additional investigations to identify underlying illnesses that could explain them.

Beyond Kwashiorkor: bilateral oedema among under 5 children hospitalized in DRC and Mali showed high variability in presentation and outcome.

Effectiveness of a new ART formulation for children

Juvenal Nkeramahame, Epicentre, Uganda

Background

Lopinavir/ritonavir (LPV/r) pellets are a palatable, heat-stable and easy-to-administer, formulation for infants and young children who are unable to swallow tablets and whose families may not be able to afford the heat-labile syrup. However, there is a paucity of clinical data on effectiveness and safety in routine care. The LIVING study, sponsored by DnDi, aims to evaluate the effectiveness, safety, pharmacokinetics and acceptability of LPV/r pellets + ABC/3TC (or AZT/3TC) dispersible tablets, in HIV+ children unable to swallow tablets in Kenya, Uganda and Tanzania.

Methods

The study is an open-label, single-arm, prospective, multi-center, phase-3b study. Included children are ARV naive, on LPV/r-based or failing NNRTI-based ART; with weight ≥ 3 and < 25 kg. ART dosing is based on WHO weight bands. Children are assessed at baseline, 1 month, and then every 3-months. We evaluated viral load evolution in 4 baseline age categories.

Results

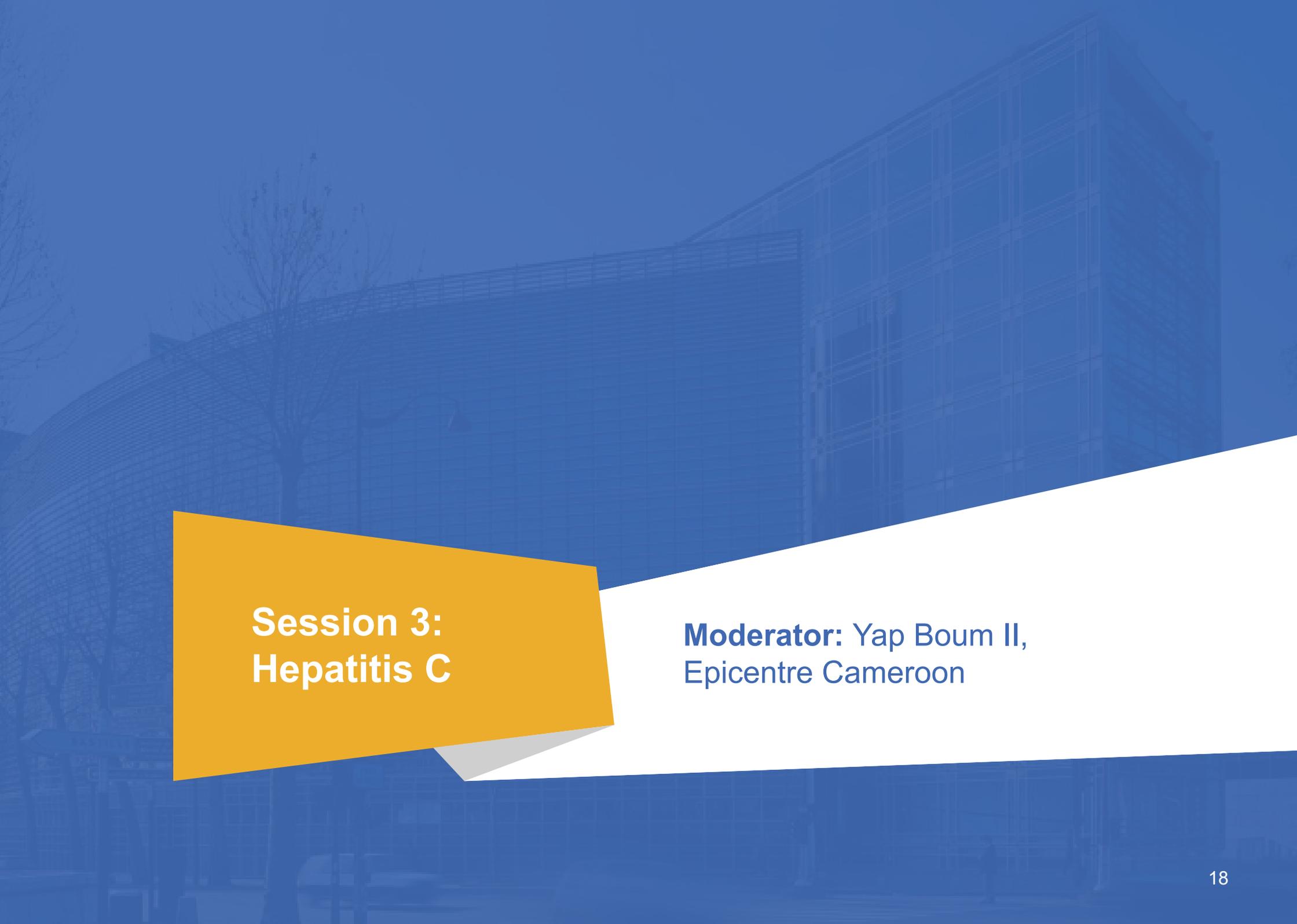
As of April 2018, 947 patients were enrolled with 100 from Epicentre in Mbarara. Baseline and week 48 viral load (VL) and CD4 were available for 354 children. The median age was 42 months, 32 (9.0%) were ART naive, 297 (83.9%) on LPV/r syrup, and 25 (7.1%) on NNRTI at baseline.

There was improvement in viral load suppression across the age categories. 25 children had 34 serious AEs, 2 leading to treatment stoppage. The pellets were acceptable among caregivers and children.

Conclusions

LPV/r pellets were associated with significant HIV viral suppression, with an acceptable safety profile and good acceptability.

The LIVING study combines the four drugs needed for the treatment of paediatric HIV into an easy-to-use combination, which is heat-stable, taste-masked, solid, and does not contain alcohol or inappropriate solvents. Results to date show that LPV/r pellets-based ART in children is associated with significant HIV viral suppression and are well accepted.



**Session 3:
Hepatitis C**

Moderator: Yap Boum II,
Epicentre Cameroon

Hepatitis C prevalence and risk factors survey in three rural districts

Chhorvy Sun, Médecins Sans Frontières, Cambodia

Background

Despite a dramatic reduction of HCV drug costs and proven, simplified models of care, many countries lack accurate prevalence estimates to scale up HCV services.

Methods

We conducted a cross-sectional, multi-stage cluster design survey of HCV sero-prevalence in adults ≥ 18 years old, with an oversampling of the population ≥ 45 years. 147 clusters of 25 households were randomly selected in two sets (set 1=24 clusters, ≥ 18 -year-old respondents; set 2=123 clusters, exclusively ≥ 45 -year-old respondents). A multivariate analysis assessed risk factors for sero-positivity among participants aged ≥ 45 . The study was conducted in rural Moug Ruessei Health Operational District, Battambang Province, in Western Cambodia.

Results

A total of 5 103 individuals and 3 616 households participated in the survey. The overall seroprevalence for the entire adult population aged ≥ 18 years was 2.61% (CI_{95%} 2.25-2.96), with 5.10% (CI_{95%} 4.55-5.65) for adults aged ≥ 45 , and 0.58% (CI_{95%} 0.27-0.89) for adults 18-44. Viraemic prevalence for these same populations was 1.87% (CI_{95%} 1.62-2.14), 3.62% (CI_{95%} 3.22-4.01), and 0.47% (CI_{95%} 0.17 - 0.76), respectively.

Men were more likely to be positive both serologically and by viral load; considering the population aged ≥ 18 , the serological prevalence for men was 3.03 (CI_{95%} 2.54 - 3.52), and 2.27 (CI_{95%} 1.87 - 2.66) for women.

Risk factors identified for the population ≥ 45 years included: more advanced age, lower education level, membership in an ID poor card program, injection for medical use or surgery before 1990, blood donation or transfusion before 1980 and having ever had dental or gum treatment.

Conclusions

This study provides the first large-scale prevalence data on HCV infection in the general adult population of three rural districts of Cambodia and clarifies several important infection trends: for adults ≥ 45 years, sero-positivity was more likely with increased age, poverty, a low level of education, and past routine medical interventions (especially prior to 1990 and 1980).

This study of HCV prevalence in adults in Cambodia shows higher sero-positivity with older age, poverty, lower education levels, and past routine medical interventions.

National perspectives

Jean-Philippe Dousset, Médecins Sans Frontières, Cambodia

Approximately 1.1% of the world population, and 1.6 % of the population (257 000 people) in Cambodia, are estimated to be chronically infected with Hepatitis C virus (HCV), with the rate in Cambodia being the second highest in the Western Pacific Region. In 2016, MSF and the Cambodian Ministry of Health launched an HCV project at Preah Kossamak Hospital in Phnom Penh.

As part of this project, MSF implemented a simplified model of care (MoC) for HCV, with Gene-Xpert for point of care viral load testing and Sofosbuvir/Daclatasvir as the pan-genotype treatment regimen. This simplified MoC resulted in a 97% success rate (n = 10 000). With no reduction in the treatment safety or effectiveness, the MoC reduced the number of patient visits, the time between diagnosis and initiation of direct-acting antivirals (DAA). This increase in efficiency resulted in more patients initiating DAA and an overall reduction in staffing and cost requirements.

The simplified MoC was then adapted to a rural setting, where sero-diagnosis and follow up care were conducted by nursing staff at health centers, while viral load testing and DAA initiation were managed by physicians at a referral hospital.

In 2018, Epicentre/MSF conducted an HCV prevalence survey of the adult population in Moug Russei district, identifying very low population awareness of HCV and an overall adult seroprevalence of 2.6%, with seroprevalence twice higher (5.1%) among adults aged ≥ 45 years. These results allowed MSF to incorporate active case finding among older adults and to better understand the limitations of passive screening.

Supported by the findings of the MSF HCV-project, the Cambodian Ministry of Health will develop a national strategic plan for HCV for 2019. Together with the simplified MoC – capable of decentralization and complemented by targeted screening strategies – this is a promising next step to accelerate HCV elimination in Cambodia.

The screening strategies and simplified model of care implemented by the MSF HCV-project in Phnom Penh and in a rural district bring critical evidence tools for designing national programs in affected countries.

Session 4: Tuberculosis

Moderator: Maryline Bonnet,
Institut de Recherche pour le
Développement, Mbarara

Use of LAM test for tuberculosis diagnosis

Helena Huerga, Epicentre, Belgium

Background

Tuberculosis (TB) is the major killer in HIV-positive patients, but remains difficult to diagnose. The lipoarabinomannan assay (LAM) is a urine-based point-of-care test that has shown utility in immunosuppressed HIV-positive patients. Current international guidelines recommend LAM in ambulatory or hospitalized patients with TB symptoms and, CD4<100 cells/ μ L or seriously ill. We aimed to assess the diagnostic value of LAM in a broader group of patients.

Methods

A prospective observational study conducted in 6 health facilities in Malawi and Mozambique included 4 groups of HIV-positive patients. All patients had a clinical exam and LAM, chest X-ray, sputum microscopy, and Xpert MTB/RIF assay (Xpert) requested. Culture in sputum was done for a subset of patients. The diagnostic yield was defined as the proportion of patients with a positive assay result among those with laboratory-confirmed TB.

Results

Among 456 ambulatory patients with TB symptoms and CD4<200 cells/ μ L (group 1), LAM results were available in 99.6%, compared to 77.0% with Xpert results. LAM could diagnose 82.4% of the patients with laboratory-confirmed TB (Table). Among 485 ambulatory patients with TB symptoms irrespective of their CD4 (group 2), LAM could diagnose 77.9% of the patients with TB. Of the 360 HIV-positive ambulatory patients with CD4<100 cells/ μ L irrespective of their symptoms (group 3), 11.9% (43/360) were LAM-positive overall, and 6.6% (13/198) among those with no TB symptoms. Among 387 hospitalized patients irrespective of their symptoms and CD4 count (group 4), 25.8% (100/387) were LAM-positive overall, and 19.4% (26/134) among those categorized as “no TB suspects”.

Conclusion

Expanded use of LAM would be useful in HIV-positive ambulatory patients with TB symptoms and CD4<200 cells/ μ L, in hospitalized patients regardless of symptoms and, possibly in symptomatic patients with no CD4 result. In ambulatory patients with very low CD4 count coming for initial or regular HIV-consultation, systematic LAM along with symptom screening may also have value for identifying TB.

Table: Tuberculosis diagnostic tests availability and diagnostic yield in HIV-positive patients

	Ambulatory patients with symptoms and CD4<200 cells/ μ L		Ambulatory patients with symptoms irrespective of CD4		Hospitalized patients irrespective of symptoms and CD4	
	Result available N=456 n (%)	Diagnostic yield N=205 n (%)	Result available N=485 n (%)	Diagnostic yield N=104 n (%)	Result available N=387 n (%)	Diagnostic yield N=120 n (%)
LAM	454 (99.6)	169 (82.4)	480 (99.0)	81 (77.9)	384 (99.0)	101 (84.2)
Microscopy	383 (84.0)	69 (33.7)	425 (87.6)	45 (43.3)	243 (62.8)	32 (26.7)
Xpert	351 (77.0)	84 (41.0)	312 (64.3)	44 (42.3)	235 (60.7)	33 (27.5)

LAM would be useful in a broader population than in the one currently recommended, and can be expanded for use in HIV-positive ambulatory symptomatic patients less severely immunocompromised and in HIV-positive hospitalized patients irrespective of their symptoms.

Safety of new multidrug-resistant TB drugs: results from the end TB observational study

Cathy Hewison, Médecins Sans Frontières, France

Background

Multidrug-resistant tuberculosis (MDR-TB) requires long treatment using a combination of drugs known to cause adverse events. Injectable drugs may cause hearing loss, renal failure and electrolyte depletion; linezolid may cause peripheral neuropathy and myelosuppression. Bedaquiline and delamanid, the first new TB drugs registered in 40 years, as well as other commonly used drugs, may cause QT interval prolongation, a risk factor for sudden death. We aimed to assess the safety of MDR-TB regimens containing bedaquiline or delamanid.

Methods

This is a multi-centre prospective observational study of patients who received bedaquiline or delamanid as part of a MDR-TB regimen from April 2015 until June 2017 in 15 countries. Safety data collection included reporting of a predefined set of nine adverse events (AE) of special interest irrespective of severity. Clinically relevant adverse events were defined as an AE of special interest reported at a severity grade considered to be clinically relevant, either because it should lead to a change in TB regimen, or because it required supplementation.

Results

In total, 1244 patients were included. The most common clinically relevant AEs of special interest were electrolyte depletion (26%), peripheral neuropathy (24%) and hearing loss (17%). The least common were myelosuppression (4%), acute renal failure (4%), QT interval

prolongation (3%) and optic neuritis (2 %). Overall, AEs commonly associated with injectables or linezolid were frequent: 35.6% of 643 patients who received an injectable from the start experienced at least one of hearing loss, acute renal failure, or electrolyte depletion, 11.0% of 1020 patients who received linezolid from the start, experienced at least one peripheral neuropathy, optic neuritis or myelosuppression. In contrast, QT interval prolongation was experienced by 2.7% of patients who received bedaquiline (848) or delamanid (354) or both (42) from the start.

Conclusions

Bedaquiline and delamanid are safe and QT interval prolongation is infrequent. However, AEs frequently associated with the other drugs in MDRTB regimens are common. Close monitoring and management of AEs in patients treated for MDR-TB is required.

Bedaquiline and delamanid are safe but adverse events associated to other drugs in MDRTB regimens are common. Close monitoring and management of adverse events in patients treated for MDR-TB is important.



**Session 5:
General**

Moderator: Thierry Allafort-Duverger,
MSF Operational Center Paris

Fractional dose yellow fever vaccines for outbreak response

Aitana Juan, Epicentre, France

Background

Yellow fever (YF) vaccine supply for outbreak response is limited. In 2016, large urban YF outbreaks occurring concurrently in different parts of Africa and the risk of further spread led WHO to develop recommendations for use of fractional dose vaccination as a dose-sparing strategy. We are conducting a trial in Mbarara, Uganda and Kilifi, Kenya, to assess the applicability of fractional dose of all four WHO-prequalified YF vaccines and the performance of fractional dose in young children and populations with HIV.

Methods

This is a double blinded, randomized, non-inferiority trial. Fractional dose was defined as 1/5th of a standard dose. Unvaccinated adults were randomly assigned to vaccine manufacturer and dosage (standard or 1/5th) and seen 10 days, 28 days and 1 year post-vaccination for immunogenicity and safety assessment. The primary objective is non-inferiority in seroconversion, with a 10% margin, of a fractional dose compared to standard dose for each pre-qualified vaccine at 28 days post-vaccination, measured by PRNT50. Sub-studies on children and HIV+ adults are ongoing with one vaccine.

Results

A total of 1029 adult participants were screened and 960 vaccinated (240 per manufacturer and 120 per dose). Overall, 55.1% of participants were female and mean age at enrollment was 35.7 years.

At baseline, 5.1% participants were positive for yellow fever by PRNT50. Baseline characteristics were not significantly different between standard and fractional dose groups for each manufacturer. At 28 days post-vaccination 99.4% participants seroconverted. The maximum difference between fractional and standard dose group was -6.1%.

Conclusions

Fractional dose of YF vaccine meets non-inferiority criteria for all pre-qualified manufacturers 28 days after vaccination. There were no safety concerns of the reduced dose. Results are pending to evaluate the rapidity of protection (10 days follow-up) and the persistence of antibodies at 1 year post-vaccination.

The stockpile of yellow fever vaccines has been shown to be insufficient to respond to large outbreaks. Fractional doses could be used in emergency situations when there are insufficient standard doses to protect the population at risk.

Active screening for sexual and gender-based violence in Nairobi, Kenya

Augusto Llosa, Epicentre, France

Background

Despite the high physical and psychological burden of sexual and gender-based violence (SGBV), survivors often do not disclose to service providers. SGBV active screening is being piloted in two MSF-supported Ministry of Health facilities in Nairobi to increase service uptake. We aimed to evaluate its feasibility, acceptability and resulting service uptake.

Methods

A mixed methods study assessed SGBV active screening and related service use at Mama Lucy Kibaki Hospital and Makadara Health Center between November 2018 and March 2019. Data on screening and service use was collected alongside structured questionnaires with patients screened positive and linked to services. In-depth interviews explored the perspectives of 26 screened patients and health workers. Interviews were transcribed, translated and analysed thematically.

Results

Among 6033 people screened, 421 (7%) had experienced SGBV in the previous year, 168 (40%) agreed to a referral to services; 100 (60%) accessed SGBV services and 89 (89%) enrolled in the study. Of the 89 participants, 81 (91%) were adult women and three quarters had experienced intimate partner violence. Screening was viewed as acceptable by 84/89 (94%) participants.

Survivors reported persistent barriers to seeking help including community norms condoning violence, fear of retribution or economic consequences from their partner, concerns about confidentiality of services, and lack of social support for care-seeking. Many survivors were unaware that IPV services existed suggesting that screening also raised awareness. Whilst one-off counselling sessions and other support services were valued by participants, various patient needs especially around IPV remained inadequately addressed.

Conclusions

Clinic level active screening for SGBV was feasible and acceptable in this high prevalence setting, and increased related-service utilization. However, most participants were survivors of intimate partner violence and faced specific challenges in accessing services, some of which were not adapted to their needs.

SGBV active screening was acceptable, and increased identification of survivors and uptake of services. Challenges in accessing services remain.

**Research and
Development:
not so easy...**

Nathalie Strub-Wourgaft,
Drugs for Neglected Diseases initiative,
Geneva



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