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OPERATIONAL RESEARCH DAY

29 MAY 2015, BRUSSELS

MSF Operational Centre Brussels



Cover photo:

*In Foya, Liberia, Helena talks to her son Moses
who is an Ebola confirmed patient.*

*A MSF health promoter supports this difficult moment
for the young mother.*

Meinie Nicolai

Bertrand Draguez

Rony Zachariah

Bart Janssens

Tom Ellman

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FOREWORD

Dear friends,

It is an honour and a pleasure to welcome you to the fourth OCB Operational Research Day.

Our research is mostly about analysing routine data in a retrospective manner. We have a unique position in the world, treating patients in very isolated places. MSFs response to the Ebola epidemic is historical; we have been the leading organisation by default and not only expanded our operational capacity but also our research on different elements of this massive operation. We have been involved in clinical and vaccine trials as well as testing new diagnostic tools.

We are constantly trying to give quality care but given the nature of our organisation this is often in extremely difficult conditions. We need to adapt to local circumstances, invent new ways of working, be flexible and in the meantime always try to do better. Our research is often about documenting the adaptations of tools and techniques to the realities of the field. And we want to show that impact is possible with relatively simple interventions. In addition our research is meant to help us cast a critical eye on our work. In order to convince other agencies and decision-makers that good care is possible, it is important that we have sound data, analyse our work, be self-critical, present and share these results with a wider audience.

Today we will not only listen to field experiences in dealing with Ebola, but also with questions such as surgery on head trauma and antibiotic over-prescription, measles vaccination strategies during an outbreak and the long-term effects of caesarean sections. We will also hear about ongoing challenges in our HIV work: managing children with treatment failure, viral load level in women in a PMTCT+ programme, the use of adherence clubs beyond HIV for non-communicable diseases and DR –TB in HIV infected in Mumbai. We will learn about our experiences in Ebola, the epidemic and our response, the clinical lessons learnt, the community perspective and the ethical questions related to trial design.

We should collectively learn from these experiences and I hope that this day stimulates you to document your work. We should influence future humanitarians and learn from our successes and failures.

Meinie Nicolai

President, MSF Belgium and MSF Operational centre Brussels

AGENDA

09.00 OPENING

Meinie Nicolai (MSF)

09.15 Slot 1: Glimpse into a spectrum of today's operations

Chairs: Sebastien Spencer (Saint-Jean Clinic) and Bart Janssens (MSF)

Management and outcomes of patients with head trauma in Kunduz, Afghanistan

Mahboobullah Shafiq

Hit early, hit hard: feasibility and efficiency of the "Coup de Poing" measles outbreak response in the Democratic Republic of Congo

Guido Benedetti

Antibiotic use in a district hospital in Kabul, Afghanistan: are we overprescribing?

Sahar Bajis

"They eat it like sweets": Perceptions of antibiotics and antibiotic-use by patients, prescribers and pharmacists

Doris Burtcher

The Mothers status: two years after undergoing caesarean section in a rural emergency obstetrics care centre in Burundi

Wilma van den Boogaard

11.00 COFFEE BREAK

11.30 Slot 2: Quality matters: Emerging challenges in HIV/ Tuberculosis care

Chairs: Nathan Ford (WHO) and Tom Ellman (MSF)

Viral load outcomes after ART initiation among women in a PMTCT B+ programme in Zimbabwe

Teresa Bonyo

"It's not just about giving the drugs." Medication Adherence Clubs for HIV and Non Communicable Disease patients in an informal setting in Kibera, Kenya

Jeffrey Edwards

Managing children and adolescents with HIV treatment failure: results from a pilot project in Khayelitsha, South Africa

Gilles van Cutsem

Alarming levels of drug-resistant Tuberculosis in HIV-infected patients in Metropolitan Mumbai, India

Petros Isaakidis

13.00 LUNCH

14.00 Slot 3: Ebola: the epidemic, our response and the lessons learnt

Chairs: David Heymann (London School of Hygiene and Tropical Medicine) and Hilde de Clerk (MSF)

General epidemiology

Michel van Herp

Highlights and snapshots of programmatic and clinical lessons learnt

Armand Sprecher

The human face of the epidemic – a community perspective

Emilie Venables

15.10 COFFEE BREAK

15.30 Slot 4: Panel discussion: Clinical trials in Ebola: What about ethics?

Chairs: Philippe Calain (MSF UREPH) and Annick Anthierens (MSF)

Presentation

State of affairs of the clinical trials in Ebola

Annick Anthierens

Panel Discussion

Denis Malvy (University Hospital of Bordeaux)

Steven Van Den Broucke (Institute of Tropical Medicine)

Piero Olliaro (Special Programme for Research and Training in Tropical Diseases)

Annick Anthierens (MSF)

Daouda Sissoko (INSERM)

Amanda Rojek (Oxford University)

16.50 CLOSURE

Bertrand Draguez (MSF)

17.00 RECEPTION

SLOT 1

GLIMPSE INTO A SPECTRUM OF TODAY'S OPERATIONS

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1. Management and outcomes of patients with head trauma in Kunduz, Afghanistan

Introduction

Traumatic brain injury (TBI) is a leading cause of death worldwide, with an estimated 10 million individuals affected and 1.5 million deaths on a yearly basis. Most of the burden of TBI falls on low- and middle-income countries, where populations are at increased risk and health systems are poorly equipped to deal with this type of injury. Provision of care for patients with TBI was for the first time introduced in Médecins Sans Frontières-Operational Centre Brussels in Kunduz Trauma Centre in Afghanistan. In order to assess the capacity of MSF to provide high level care for a complex condition such as TBI, we set out to describe:

- 1) the clinical and socio-demographic characteristics and treatment outcomes of such patients
- 2) the overall programme performance, using the CRASH model (an international model predicting 14-day mortality among TBI patients) as a benchmark.

Methods

A retrospective analysis was conducted on data collected in the routine TBO database in Kunduz Trauma Centre, Afghanistan, between February and October 2014. Severity of cases was assessed using the Glasgow Coma Scale (GCS). Overall programme performance was assessed by calculating the monthly number of expected deaths using the CRASH Head Injury Prognosis tool. The actual deaths were then compared with the expected number of deaths.

Results

A total of 963 cases with head trauma were seen in the ED of Kunduz. Of these, 791 (82%) had mild, 85 (9%) had moderate and 86 (9%) had severe TBI. Most cases (496; 52%) were road traffic accidents. 294 (31%) ED cases had an indication for a CT scan, which was only provided for 116 (39%) cases. 229 cases (24%) were admitted: 103 (45%) to the inpatient department, 113 (49%) to the intensive care unit, and 13 (6%) for palliative/comfort care. An increase in median GCS scores was observed for all classes of cases, with the strongest increase observed for moderate TBI cases. Overall programme outcomes were: 711 (74%) discharged, 200 (21%) referred, 26 (3%) defaulted and 26 (3%) died. Referral reasons and final outcomes for those referred were unknown. In terms of programme performance, with the exception of one month (May 2014), the hospital outperformed typical facilities in low- and middle-income countries, and was comparable to facilities in high-income countries. Survival and functional survival rates among the most severe cases were both 53%, while rates of 30% and 8-10% respectively are reported in the literature.

Discussion

This study provides a first overview of the management of TBI patients in Kunduz Trauma Centre: a good overall performance was observed compared to other low- and middle-income countries and even high-income countries. In particular, a considerable impact of the interventions was observed for patients with moderate TBI. Areas which require further attention were:

- 1) provision of CT scans to all patients in need**
- 2) better follow-up of referred patients.**

2. Hit early, hit hard: feasibility and efficiency of the “Coup de Poing” measles outbreak response in the Democratic Republic of Congo

Introduction

Measles outbreak response vaccination in the Democratic Republic of Congo (DRC) is highly demanding in terms of logistics and financial means if high vaccination coverage is to be achieved. As a first step to developing a new, lighter model for outbreak responses, the so-called “Coup de Poing” strategy was trialled since June 2013. In this strategy, the focus is placed on the epicentre of the measles outbreak: a rapid response targets the Aires de Santé (health areas) with the highest burden in an attempt to stop early transmission, thus reducing caseloads and reducing the scope of the outbreak. Such interventions, if feasible, could form the basis of lighter, easier-to-implement strategies for measles outbreak management among the different actors in DRC and beyond. We therefore conducted a comparison between 6 classical and 4 Coup de Poing measles outbreak interventions in 2012-2013.

Methods

In this retrospective analysis, the classical interventions in the Zones de Santé of Yambuko, Yaleko, Yalimbongo, Yahuma, Yahisuli and Djolu (2012-2013) were compared with the Coup de Poing interventions in Kamonia, Tembo, Wamba and Mutena (2013), in terms of timing of the intervention, attack rate, case fatality rate, and mortality rate.

Results

Implementation of the Coup de Poing interventions was systematically more rapid than for the classical interventions, with a mean delay of 17 days between start of the intervention and first actual vaccination activities, compared to 35 days for the classical interventions. For the Coup de Poing, the intervention was initiated on average 16 days prior to the epidemiological peak and the first vaccination was concurrent with the peak, while for the classical interventions, the start of the intervention fell on average 5 days prior to the peak, and the first vaccination only 28 days after the peak. Total coverage rates post-intervention were similar between strategies (>95%), but attack rates (median 1.3% for Coup de Poing versus 2.6% for classical), case fatality rates (median 1.6% versus 3.3%) and overall mortality rates (median 0.02% versus 0.07%) were better under the Coup de Poing interventions. Detailed analysis of the Coup de Poing intervention in Wamba showed how the outbreak did not spread from the worst-hit Aires de Santé that were targeted by the intervention, while in the classical intervention in Yalimbongo, such spreading to other Aires de Santé was observed.

Discussion

Our results indicate that the Coup de Poing strategy is feasible and can achieve favourable results in the management of a measles outbreak. Data on the logistics and cost of the two models of intervention should be added in order to allow advocacy on the scalability of this model of care and its uptake by other partners. Additionally, further fine-tuning of the Coup de Poing strategy can be conducted to reduce the financial and logistical burden of the intervention, to increase the feasibility of its uptake by other partners.

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GLIMPSE INTO A SPECTRUM OF TODAY'S OPERATIONS

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3a. Antibiotic use in a district hospital in Kabul, Afghanistan: are we overprescribing?

Setting

A district hospital in Kabul, Afghanistan, supported by Médecins Sans Frontières (MSF).

Objectives

To assess antibiotic prescribing practices in the out-patient department in summer (August 2013) and winter (January 2014).

Design

Cross-sectional study, using routinely collected hospital data and using World Health Organization (WHO) defined daily dose (DDD) methodology.

Results

An analysis of 4857 prescriptions (summer) and 4821 prescriptions (winter) showed that respectively 62% and 50% of all out-patients were prescribed at least one antibiotic. They could not be assessed in the summer period, as total diagnoses were not collected in this period. The antibiotic prescription rates were highest for patients with UTI (100%), for those with a dental consultation (100%) and for diarrhoea (97%). Among patients with URTI and those without a registered diagnosis, 40% received an antibiotic. Prescriptions without a recorded diagnosis represented a sizeable proportion of all antibiotics prescribed. For upper respiratory tract infections (URTI), dental indications, urinary tract infections (UTI) and diarrhoea, good adherence to dosages recommended in the MSF standard treatment guidelines was observed when measured by DDD. However, certain drugs not indicated in the guidelines were prescribed, such as amoxicillin and metronidazole for UTI and azithromycin for URTI.

Conclusion

Rates of antibiotic prescriptions for out-patients in a district hospital in Afghanistan were high, double the WHO recommendation of 30%. While systematic non-adherence to recommended dosages was not observed, inappropriate prescriptions for specific conditions may have occurred. This study suggests that knowledge about context-specific determinants of antibiotic prescribing is a first step towards promoting rational prescribing practices in such settings.

GLIMPSE INTO A SPECTRUM OF TODAY'S OPERATIONS

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3b. “They eat it like sweets”: Perceptions of antibiotics and antibiotic-use by patients, prescribers and pharmacists in a district hospital in Kabul, Afghanistan

Introduction

Over- and misuse of antibiotics increases the spreading of antibiotic resistance. Underlying reasons for misuse include limited understanding by healthcare providers and patients, unregulated dispensing, circulation of sub-quality antibiotics and incorrect usage. Therefore, we conducted an ethnographic study to understand drivers of choice of antibiotic prescription among patients, caregivers, prescribers and providers in Ahmad Shah Baba (ASB) hospital in Kabul, where antibiotic over-prescription has been reported.

Methods

Data was collected using non-participant observation, field notes, and in-depth interviews guided by topic-led questions. Respondents were purposively selected with the help of MSF team members. Transcriptions were screened for relevant information, organised, coded, categorised and interpreted. Methodological triangulation was applied; in-depth individual interviews (33) were combined with group discussions (4), non-participant observations, document reviews and analysis of deviant cases.

Results

Poor education is a driving factor for patients' over- and misuse of antibiotics and disregard of doctors' recommendations. The high demand and perceived “need” for antibiotics results from people's rationale that they live in a polluted environment: patients, doctors and pharmacists alike consider dirty and dusty living conditions as cause of “disease” in the body, requiring antibiotics to “clean” and “strengthen” it. Antibiotics are called “dirty drying medicine”; the antibiotic is meant to clean the body of the dirt. Additionally, antibiotics are believed to “quickly” cure illnesses. In a war-affected context where people are faced with social suffering and insecurity, a “quick” medication is considered an important asset. Additionally, patients prioritize quantity over quality and expect “many drugs” to be prescribed.

Conclusions

The majority of the population attending ASB lacks knowledge of the risks of antibiotic misuse. Antibiotics are much preferred in the population, mainly to treat the consequences of the “polluted environment”. Culturally appropriate health promotion should raise awareness on the risks of antibiotic misuse among the population. Additionally, enhanced regulation of antibiotics at national level is recommended, in order to curb excessive antibiotic use.

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4. The Mothers status: two years after undergoing caesarean section in a rural emergency obstetrics care centre in Burundi

Introduction

Burundi has one of the highest Maternal Mortality Ratios (MMR) globally with 800 maternal deaths per 100,000 live-births (400 times higher than Sweden or Belgium).

Since 2008, MSF has offered emergency obstetrics and neonatal care (EmONC) through a dedicated hospital in rural Burundi. About half of all annual emergency interventions are caesarean sections. Due to the high risk of uterine rupture and maternal death in subsequent pregnancies, such women are counselled to wait at least 24 months for another pregnancy (so that the uterine scar heals well) and ensure hospital delivery.

Two years post caesarean section, we determined the a) uptake of family planning at hospital discharge b) number who became pregnant c) inter-pregnancy interval d) number with hospital delivery and e) frequency of uterine rupture and maternal death.

Methods

A structured questionnaire, instituted July-October 2014, by a trained research team, among women who underwent caesarean sections between July and September 2012.

Results

Of 156 women who underwent a caesarean section in the hospital register, 31 (20%) were not known by the village chiefs (false addresses?), 8 (5%) migrated out of the catchment area and one had died of cholera. Of the remaining 116 included in the study, median age was 24 years (Interquartile Range, IQR, 20-30) and median follow up time was 25 months (IQR:24-26). The indications for caesarean sections were: 31(27%) obstructed labor, 24 (21%) previous caesarean section, 23(20%) mal-presentation and 38 (33%) other reasons. None had suffered from post-natal complications within 42 days post-discharge.

Eighty three (72%) women accepted family planning at discharge (oral contraceptives= 45, injectable=20, implant=9, tubal ligation=9), 20 (17%) needed prior consultation with their husbands and 13 (11%) refused. Among 27 individuals who became pregnant despite accepting family planning the median inter-pregnancy-interval was 16 months (IQR:10-18). Among 13 who had not accepted family planning and became pregnant this interval was not different (15 months, IQR:9-19, $P > 0.05$).

Two women on implants had them removed and became pregnant before the desired inter-pregnancy interval. Of 23 women who had already delivered, 18 (78%) delivered in hospital, three (13%) in a health center and two (9%) at home. One woman had a uterine rupture which was managed at hospital. There were no maternal deaths among women in the catchment area. Unascertained deaths outside the catchment area could not be verified as part of this study.

Conclusions

This first community-based follow up study conducted two years after a caesarean section shows that the acceptance of family planning per-se did not influence the inter-pregnancy interval and socio-cultural factors are probably playing a more important role in child spacing. This needs specific investigation. Further research is also needed to enhance early engagement of husbands and investigate why vulnerable women still end up delivering outside hospital when they should have had access.

SLOT 2

QUALITY MATTERS: EMERGING CHALLENGES IN HIV/TUBERCULOSIS CARE

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1. Viral load outcomes after ART initiation among women in a PMTCT B+ programme in Zimbabwe

Introduction

The WHO 2013 guidelines recommend that all HIV-infected pregnant and breastfeeding women take ART to prevent mother-to-child transmission (PMTCT). A high viral load (VL) (>1000 copies/ml) during pregnancy or breast-feeding is associated with higher rates of MTCT. In Zimbabwe, routine VL testing was introduced in MSF-supported HIV programmes in 2012, with patients tested at three and twelve months after starting ART, and then annually. This analysis aimed to determine the proportion of PMTCT women with a VL >1000 copies /ml, associated risk factors, and to compare the findings to women outside the PMTCT programme.

Methods

Information was extracted from the laboratory records of women aged 15 to 45 years having routine VL testing. The analysis was stratified according to whether the women were pregnant (n=454), breastfeeding (n=1083), or neither pregnant nor breastfeeding (n=7688), at the time of testing. Binary logistic regression was used to determine factors associated with a VL >1000 copies/ml.

Results

Women in the PMTCT programme had a median age of 31 years (interquartile range [IQR]: 26 – 35) compared to 36 years (IQR: 30 – 40) among non PMTCT women and had been on ART for a median of 12 months (IQR: 3 – 35) compared to 27 months (IQR: 12 – 42) among non PMTCT women. Of those who had a viral load measured 3 months after starting ART, viral suppression to <1,000 copies/ml was 85.7% overall: 88.1% among pregnant women, 87.7% among breastfeeding women, and 84.6% among women not in the PMTCT programme. In the multivariate analysis, women in the PMTCT programme had a similar chance of suppression to women not in the programme: pregnant (RR: 1.03; 95% CI: 0.99 – 1.08; p = 0.118), breastfeeding (RR: 1.02; 95% CI: 0.99 – 1.05; p = 0.280). However the chance of suppression was related to age. Compared to those aged 35 – 45 years, suppression was less likely among those aged 15 – 25 years (RR: 0.90; 95% CI: 0.86 – 0.94; p <0.001) than those aged 25 – 35 (RR: 0.97; 95% CI: 0.94 – 0.99; p =0.002).

Conclusions

A significant number of pregnant and breastfeeding women failed to suppress their VL within 3 months of starting ART, putting their infants at ongoing risk of HIV infection. Increased support is needed for counselling at ART initiation and during the first months on ART, particularly among younger women. In addition, guidance is urgently needed on the optimal timing of VL testing among women in PMTCT programmes.

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2. “It’s not just about giving the drugs”: Medication Adherence Clubs for HIV and Non-Communicable Disease patients in an informal setting in Kibera, Kenya

Introduction

Increasing numbers of patients require care for chronic conditions such as hypertension (HT), diabetes mellitus (DM) and HIV infection. In 2013, MSF and the Kenyan Ministry of Health introduced Medication Adherence Clubs (MACs) as an alternative to standard care for stable HT, DM and HIV patients in Kibera, Nairobi. MACs enable groups of up to 30 HIV/non-communicable disease (NCD) patients to collect medication refills every 3 months. This is the first integrated approach to chronic disease medication in MSF programmes. A mixed-methods analysis was conducted to explore the feasibility and acceptability of MACs. Ethics approval was received from Kenyan AMREF (African Medical and Research Foundation) and the MSF Ethics Review Board.

Methods

Routine data from a primary health-care clinic in Kibera were analysed to determine the characteristics of MAC patients and the number of MAC meetings held from August 2013–August 2014. In 2015, 19 in-depth interviews and 10 focus group discussions were conducted with health-care workers and patients to assess MAC acceptability and views around combining HIV, DM and HT patients. MAC and non-MAC patients were randomly selected from MAC groups and clinical records and a purposive sample of health-care workers recruited to represent a range of professions and variety of experience with MACs. Qualitative data collection ended when saturation was reached. Qualitative data were transcribed and a coding framework developed before analysis using NVivo (version 10, 2012).

Results

Of 5028 HIV/NCD patients, 44% were eligible and 1432 (64%) then enrolled in MACs. 43 (2%) were referred back to clinical care. 109 MAC meetings were held, representing 2208 individual refills. Most (64%) MAC members were female; 71% were HIV-positive. MACs were perceived as acceptable, time-saving, and a source of disease information and peer-support by HIV-positive and NCD patients. Implementation challenges included recruitment, patients’ understanding of MACs, and the timing of sessions. A small number of non-NCD, HIV-positive patients felt mixed groups affected disclosure but this was not considered a problem for NCD patients.

Conclusions

MACs combining HIV and NCD patients can enable the provision of medication and peer-support to large numbers of stable, chronic patients by applying lessons learned from large-scale HIV drug rollout. As HIV and NCD care are further scaled up, innovative refill strategies such as MACs should be considered in other contexts.

3. Managing children and adolescents with HIV treatment failure: results from a pilot project in Khayelitsha, South Africa

Introduction

As HIV treatment programmes mature in Southern Africa, increasing attention has been given to adults failing antiretroviral treatment (ART). In contrast, despite reported high paediatric treatment failure rates, high viral loads (VL) in children are often not addressed. A pilot programme was introduced to identify and care for children failing ART at two Department of Health primary-care clinics in Khayelitsha. The programme consists of support groups, individual consultations, home visits, and genotyping to guide regimen switches when viraemia persists despite 3 months of adherence support. We conducted a retrospective analysis of programme data with the aim of determining the effect of the programme on re-suppression rates and risk factors for treatment failure.

Methods

Patients aged 0-19 years enrolled between July 2013 and November 2014 with last VL>1000 copies/µl or last two VL>400 were included. Routine data on ART regimens and VLs was used. VLs were performed every 3 months. Re-suppression was defined as VL<400. Ethics approval was obtained from the University of Cape Town; the study met the MSF Ethics Review Board criteria for exemption from ethics review.

Results

Of 131 patients, median age at enrolment was 10 years (IQR 4.2-13.8); 60 (46%) were girls. Median time on ART was 4.0 years (IQR 2.6-7.6). VL suppression at first, second, and third follow-up VL was 55% (58/105), 72% (55/76), and 84% (38/45) respectively. Patients >12 years were less likely to re-suppress than those <12 (67% [10/15] vs. 93% [28/30], p=0.02). 77% (36/47) on protease inhibitor (PI)-based regimens re-suppressed at their second VL without switching, compared with 28% (7/25) on non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based regimens. Of those switched from NNRTI to PI regimens, 40% (10/25) re-suppressed. Of 34 genotypes, 43% (6/14) and 100% (20/20) were resistant to PI and NNRTI regimens, respectively.

Conclusions

Children failing ART should be identified and supported in HIV programmes with simple interventions that can lead to high rates of re-suppression. Most children failing NNRTI regimens showed resistance and required switching to PI regimens. Conversely, most children on PI regimens re-suppressed with adherence support, indicating the regimens' robustness and the potential benefit of adopting WHO recommendations for first line PI-based regimens for children. Adolescents in the programme required innovative strategies to attain re-suppression. Patients resistant to PIs await third-line ART availability.

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QUALITY MATTERS: EMERGING CHALLENGES IN HIV/TUBERCULOSIS CARE

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4. Alarming levels of drug-resistant tuberculosis in HIV-infected patients in Metropolitan Mumbai, India

Background

Drug-resistant tuberculosis (DR-TB) is a looming threat to tuberculosis control in India. However, no countrywide prevalence data are available. The burden of DR-TB in HIV-co-infected patients is likewise unknown. Undiagnosed and untreated DR-TB among HIV-infected patients is a major cause of mortality and morbidity. We aimed to assess the prevalence of DR-TB (defined as resistance to any anti-TB drug) in patients attending public antiretroviral treatment (ART) centers in greater metropolitan Mumbai, India.

Methods

A cross-sectional survey was conducted among adults and children ART-center attendees. Smear microscopy, culture and drug-susceptibility-testing (DST) against all first and second-line TB-drugs using phenotypic liquid culture (MGIT) were conducted on all presumptive tuberculosis patients. Analyses were performed to determine DR-TB prevalence and resistance patterns separately for new and previously treated, culture-positive TB-cases.

Results

Between March 2013 and January 2014, ART-center attendees were screened during 14135 visits, of whom 1724 had presumptive TB. Of 1724 attendees, 72 (4%) were smear-positive and 202(12%) had a positive culture for Mycobacterium tuberculosis. Overall DR-TB was diagnosed in 68 (34%, 95%CI:27%-40%) TB patients. The proportions of DR-TB were 25% (29/114) and 44% (39/88) among new and previously treated cases respectively. The patterns of DR-TB were: 21% mono-resistant, 12% poly-resistant, 38% multidrug-resistant (MDR-TB), 21% pre-extensively-drug-resistant (MDR-TB plus resistance to either a fluoroquinolone or second-line injectable), 6% extensively drug-resistant (XDR-TB) and 2% extremely drug-resistant TB (XDR-TB plus resistance to any group-IV/V drug). Only previous history of TB was significantly associated with the diagnosis of DR-TB in multivariate models.

Conclusion

The burden of DR-TB among HIV-infected patients attending public ART-centers in Mumbai was alarmingly high, likely representing ongoing transmission in the community and health facilities. These data highlight the need to promptly diagnose drug-resistance among all HIV-infected patients by systematically offering access to first and second-line DST to all patients with “presumptive TB” rather than “presumptive DR-TB” and tailor the treatment regimen based on the resistance patterns.

SLOT 3

EBOLA: THE EPIDEMIC, OUR RESPONSE AND THE LESSONS LEARNT

1. Transmission in the community

- Baize S, Pannetier D, Oestereich L, et al. **Emergence of Zaire Ebola Virus Disease in Guinea.** *N Engl J Med* 2014, **371**, 1418-25
- Hermans V, Saffa G, Decroo T, et al. **Lost in Transmission: Surveillance and chains of transmission in the Ebola outbreak in Bo, Sierra Leone, 2014.** *In preparation*

We documented the transmission chains of the start of the outbreak in Guéckédou, Guinea, and in Bo district, Sierra Leone. Analysis of the Guinean setting showed how the outbreak was introduced for the first time in the region, and identified a likely first case of the West Africa outbreak. In Bo district, Sierra Leone, preparedness was started before the first case arrived in the district, but the control over the situation was quickly lost due to the magnitude of the outbreak and the shortage of human resources in the field. Unsafe funerals, hospital transmission, and household contacts were identified as the main drivers of the outbreak early on, but documentation of transmission became sparse as control over the outbreak was lost. Both studies show how the spread of the epidemic was characterized by large jumps along the main road system, from town to town, sometimes infecting isolated villages on the way. These isolated clusters were only picked up by the authorities when several people had died and fled the village, spreading EVD to a larger town again. Such studies allow optimization of control strategies and better preparation for future outbreaks.

2. Triage at the Ebola Treatment Centre

- Vogt F, Fitzpatrick G, Patten G, et al. **Is there added value in separating admitted Ebola patients into suspect and highly suspect wards pending laboratory confirmation?** *Submitted; poster presentation at the MSF Scientific Day 2015, 7-8 May 2015, London*
- Kuehne A, Gergonne B, De Clerck H, et al. **Differentiating high and low suspect Ebola cases based on clinical presentation and history of contact.** *In preparation*

Triaging suspect Ebola cases in high and low risk categories may prevent nosocomial transmission while waiting for test results in the suspect area of a treatment centre. Studies were done in Kailahun (Sierra Leone) and ELWA 3 (Liberia) on the performance of the triage system and the value of symptoms at admission and contact history for differentiating patients. Poor correlation was found between symptoms/contact history and test positivity: identification of Ebola cases using the case definition remains poorly sensitive/specific. Accommodation of patients in single compartments instead of wards until they receive their test result, or grouping patients by their risk of transmission (such as grouping of patients with vomiting or diarrhoea as symptoms), may be the best strategy to reduce the risk of nosocomial infection.

3. Hospitalization

3a. General patient cohort

- Chertow DS, Kleine C, Edwards JK, et al. **Ebola virus disease in West Africa – clinical manifestations and management.** *N Engl J Med* 2014, **371**, 2054-7
- Dallatomasina S, Crestani R, Squire J, et al. **Ebola outbreak in rural West Africa: epidemiology, clinical features and outcomes.** *Trop Med Int Health* 2015, **20**, 448-54
- Fitzpatrick G, Vogt F, Gbabai O, et al. **The contribution of Ebola viral load at admission and other patient characteristics to mortality in a Médecins Sans Frontières (MSF) Ebola Case Management Centre (CMC), Kailahun, Sierra Leone, June – October, 2014.** In press; poster presentation at the MSF Scientific Day 2015, 7-8 May 2015, London
- MSF Ebola Task Force. **Patient characteristics and risk of mortality in the Médecins Sans Frontières Ebola Management Centres (EMCs) during the West African Ebola outbreak – Preliminary Analysis.** In preparation; oral presentation at the MSF Scientific Day 2015, 7-8 May 2015, London

We explored the characteristics of patients across the different MSF centres to better understand who the patients are, where they are coming from, and what determines their risk of dying. Patients come from all strata of society and of all age groups; the only risk factors for death that could be identified were age (the young and the elderly) and a high viral load. In Kailahun, most of the patients presented late, on average five days after symptom onset, which was likely a major driver of the epidemic in the district. On average, half of our patients did not survive Ebola. There was, however, a substantial variation of mortality over time and across treatment centres, likely linked to the variation in presenting viral load, requiring further investigation.

3b. Pregnant women

- Caluwaerts S, Lagrou D, Weber P, et al. **Blood, birthing and body fluids: Delivering and staying alive in an Ebola Management Centre.** In preparation; oral presentation at the MSF Scientific Day 2015, 7-8 May 2015, London
- Baggi F, Taybi A, Kurth A, et al. **Management of pregnant women infected with Ebola virus in a treatment centre in Guinea, June 2014.** *Euro Surveill* 2014, **19**, 20983
- Moreau M, Spencer C, Gozalbes J, et al. **Lactating mothers infected with Ebola virus: EBOV RT-PCR of blood only may be insufficient.** *Euro Surveill* 2015, **20**, 21017
- Akerlund E, Prescott J, Tampellini L, et al. **Asymptomatic Shedding of Ebola Virus from a Pregnant Woman.** In preparation

Pregnant women are a patient subgroup that deserves close attention in an Ebola treatment centre, and cases were described, along with their outcomes, in the three Ebola-affected countries in West Africa. In contrast with previous outbreaks, where almost all Ebola-infected pregnant women died, survival of more than 30 pregnant women was documented. However, most pregnancies ended with stillbirths, and no neonates born to women cured from Ebola survived longer than two days.

EBOLA: THE EPIDEMIC, OUR RESPONSE AND THE LESSONS LEARNT

Foetuses, amniotic fluid and the placenta were highly positive for Ebola virus, even one month after the mother is cured. Breastmilk was also found to be positive, and a case of probable transmission through breastmilk was identified. Furthermore, one case of a full-term pregnant woman testing positive for Ebola virus prior to symptom onset was described. These observations carried important implications for infection control: pregnancy tests should be offered to all female Ebola patients of childbearing age, termination of pregnancy should be offered, all pregnant women surviving Ebola should deliver in an Ebola treatment centre with strict infection control measures, breastfeeding among survivors should be discouraged, and the general message of “no infectiousness prior to symptoms” should be treated with caution, in particular among pregnant women.

4. Survivors

- Fitzpatrick G, Vogt F, Moi Gbabai O, et al. **Describing readmissions to an Ebola case management centre (CMC), Sierra Leone, 2014.** *Euro Surveill* 2014, **19**, 20924
- Hugo M, De Clerck H, Fitzpatrick G, et al. **Post-traumatic stress reactions in Ebola patient survivors in Sierra Leone.** Submitted; poster presentation at the MSF Scientific Day 2015, 7-8 May 2015, London
- Venables E, Pellicchia U, Al-Kourdi Y. **What Does It Mean To Be A Survivor? The Identity and Stigmatisation of Ebola Survivors in Monrovia, Liberia.** Poster presentation at the MSF Scientific Day 2015, 7-8 May 2015, London and the MSF Southern Africa Scientific Day, 14th May 2015, Harare, Zimbabwe
- Christie A, Davies-Wayne G, Cordier-Lasalle T. **Possible Sexual Transmission of Ebola Virus – Liberia, 2015.** *MMWR Morb Mortal Wkly Rep* 2015, **64**, 479-81

Approximately one third of the Ebola suspects admitted to a treatment centre are tested negative and return home after admission; some of these subsequently return and test positive. A study was conducted in Kailahun, Sierra Leone, to assess whether such readmissions could be due to exposure in the treatment centre. All readmitted patients had at least one high-risk exposure event during their incubation period other than their first admission, suggesting that the suspect area of the treatment centre was probably not the main source of infection for these patients.

Studies were also performed among Ebola survivors: the mental health burden among survivors from the MSF treatment centres in Kailahun and ELWA 3 were assessed. Stigma in the community was frequently described, and considerable psychological sequelae existed. The pattern of post-traumatic stress reactions resembled that found in survivors of war or natural disasters. Qualitative research in Monrovia showed how survivors found themselves caught between two identities: presented as the “heroes” and “success stories” of the epidemic by humanitarian agencies, and at the same time facing stigma, loss and fear in their communities. Male survivors in particular became the targets of anger and discrimination out of fears that they could still transmit the Ebola virus through sexual intercourse, and individual male survivors were seen as a threat to the wellbeing of whole communities. Limited evidence supported this notion, with one case described in Monrovia suggestive of infection through sexual intercourse with a survivor five months post-discharge. This case carried multiple implications for public health recommendations, while underscoring the need for clear communication around Ebola survivors (beyond authority figures and community leaders), and for ongoing assistance to survivors, their families and communities through outreach activities and/or support to survivors’ organisations.

5. Community perceptions

- Pellecchia U. **The Breakdown – Report on Communities Perceptions and Practices to Ebola Epidemic in Monrovia, Liberia.** [Internal Report](#)
- Venables E. **Community perceptions of clinical trials For Ebola in Monrovia, Liberia.** [Internal Report](#)
- Venables E. **Perceptions of ELWA 3 and survivor Stigma in Monrovia, Liberia.** [Internal Report](#)
- Pellecchia U. **Social logics and communities perception on quarantine.** [Internal Report](#)
- Pellecchia U. **State-enforced Ebola containment measures in Liberia: a view from the communities.** [In preparation; oral presentation at the MSF Scientific Day 2015, 7-8 May 2015, London](#)

Community perceptions of the MSF interventions and different responses are crucial to the success of the interventions. Extensive anthropological research in Liberia showed the total disruption of social networks, family ties and solidarities. The top-down decision on mandatory cremation for all Ebola-related deaths in Liberia fed the mistrust and sense of abandonment within the communities. Similarly, enforced quarantine of households and individuals, combined with mismanagement of the supporting measures (food provision, health monitoring, etc.) led to a widening divide between aid agencies and the population, and in general the enforced nature of such measures undermined their efficacy, with unsafe burials occurring illegally, and evasion or escape from the quarantine observed frequently. It is crucial for the Ebola intervention to restore transparency, trust and mutual help in the communities.

The perceptions of the ELWA 3 Ebola management centre in Monrovia changed over time. Community members initially showed resistance and fear due to transmission risks, but over time saw a perceived benefit of having a centre nearby providing treatment and support. They also saw the centre as a resource, and felt entitled to benefit from it as a community. Ongoing engagement with the local community and transparency of treatment centres is essential to build trust and gain acceptance.

Finally, perceptions of the therapeutic treatment trials in which MSF was involved were assessed. There was a high general acceptability of trials and new drugs amongst the community, and people expressed their desperation for a way of treating Ebola. An early, clear and straight-forward communication policy was seen as essential to engage the general population. Health-care workers should be actively engaged in this process, since they function as important informal sources of information for their communities. Transparency is essential to empower and inform local populations, which is necessary to minimize rumours that could have a detrimental effect on research acceptance or health seeking behaviour in the community.

SLOT 4

**PANEL DISCUSSION: CLINICAL TRIALS
IN EBOLA: WHAT ABOUT ETHICS?**

Presentation

State of affairs of the clinical trials in Ebola – Annick Anthierens

Discussion

Denis Malvy, Steven Van Den Broucke, Piero Olliaro, Annick Anthierens, Daouda Sissoko, Amanda Rojek

CHAIRS AND SPEAKERS

Annick Antierens graduated as a medical doctor specialized in anaesthesia, intensive care and emergency medicine from the Catholic University of Leuven. She also obtained her license in public health at the University of Nancy. Her first humanitarian missions were as anaesthesiologist in Bosnia for MSF and in Rwanda for the Belgian Red Cross. From 1999 to 2007 she occupies different positions for different MSF sections; field coordinator in Kenya, general and medical coordinator in Mauritania, Sudan and Ethiopia. Between missions, she is working in different French and Belgian hospitals as anaesthesiologist and emergency doctor. In 2009 she is appointed hospital director the MSF run hospital in Amman, Jordan. From 2010 to mid-2014 she becomes deputy medical director at the MSF Operational centre Geneva. And since September 2014 she is the manager of the Ebola Investigational Platform at MSF.

Sahar Bajis is a clinical pharmacist with experience in both community and hospital pharmacy. She received her Master of International Public Health from The University of Sydney in 2014. She started with MSF in 2011 as Pharmacist Coordinator in Yemen, and has since worked in South Sudan and Afghanistan. Currently she's working on MSF pharmacy practice guidelines for OCB, and is pursuing a PhD to start in July 2015.

Guido Benedetti was born in Florence, Italy. After graduating as a dentist, he got a PhD in Preventive Dentistry in 2011 and is currently attending a Master of Public health programme at the Liverpool University, UK. Before joining MSF, he has been working for different organizations and agencies, while reorienting his field of interest towards public health. From May 2014 to May 2015 he served as the epidemiologist of the MSF-OCB Emergency pool for DRC.

Teresa Bonyo is a medical doctor with experience in HIV/AIDS clinical care, management of community clinical programs and HIV prevention research. She obtained a Master of Public health from University of Liverpool, UK in 2012 and joined MSF in 2013. She is currently working as a project doctor in one of the HIV/AIDS/TB projects in Zimbabwe. Her research interests include HIV/AIDS and TB, reproductive health as well as policy and its effects on public health.

Wilma van den Boogaard worked 10 years as a nurse in Holland before leaving for humanitarian aid in Indonesia and deciding to join with MSF, more than 20 years ago. After joining several emergencies in Liberia and South Sudan, she worked as a health promoter, field coordinator followed by medical coordination mainly in longer term projects, where deciding on change of strategies and national health policies were of high importance. She has experience of OR in Luxembourg in 2010/2011 after doing her Master in Public Health, but returned to the field as epidemiologist and medical coordinator in 2012/2013. She returned to the OR unit in Luxembourg to support and coach the field in performing OR in order to improve the performance of their project which allows having greater quality access to care to those in need.

Doris Burtscher holds a PhD in medical anthropologist and works at the Vienna Evaluation Unit. Since 2001 she has worked as a medical anthropologist for MSF, and has undertaken fieldwork for MSF and other NGOs in Mauritania, Kenya, Sierra Leone, Zimbabwe, Liberia, Niger, Swaziland, Lebanon, India, Chad, Iraq, Kyrgyzstan, Afghanistan, Senegal, and Albania. Her main fields of interest are how people deal with health and illness in different contexts (HIV/AIDS, MDR TB, malnutrition...) and health seeking behaviour.

Philippe Calain is a medical doctor specialized in infectious diseases and tropical medicine. After several years of clinical activities in Belgium and Switzerland, he joined the Department of Microbiology at the University of Geneva. He received a doctorate in biology in 1995, and was appointed as a virologist at the USCDC from 1995 until 1997. He later worked in Rwanda, Laos, and Afghanistan. In 2006 he joined the headquarters of MSF Switzerland, where he is currently a senior researcher at the Research Unit on Humanitarian Stakes and Practices (UREPH). He served as an external member of the WHO Research Ethics Review Committee in 2010-2013. His current areas of interest include humanitarian ethics, public health ethics, the governance of global health, and extractive industries.

Gilles Van Cutsem is the Medical Coordinator for MSF in South Africa and Lesotho and an Honorary Research Associate at the Centre for Infectious Disease Epidemiology and Research at the University of Cape Town. A medical doctor and epidemiologist, he has been working with MSF since 1998, in South Sudan, Angola, Mozambique, and since 2003 in South Africa, mostly in the Khayelitsha project. His interests include implementation and operational research, particularly of pragmatic strategies to reduce TB and HIV related mortality and morbidity and maternal and child mortality, as well as advocacy to reduce health inequities.

Bertrand Draguez graduated as a medical doctor from Louvain Catholic University. He started working with MSF as a practitioner in East Timor, and continued gaining experience as a doctor and then a Field Coordinator in Angola, South Sudan and Afghanistan. From 2002 until 2004, he was Medical Coordinator for projects in RDC and then in Ivory Coast. He became Medical Polyvalent for missions in Rwanda, Burundi, DRC and CAR. Since 2008, he is the Medical Director of the Operational Centre Brussels.

Jeffrey Edwards worked as a physician in rural primary/emergency care for over 15 years in the US before completing a Master of Public Health at Johns Hopkins University and joining MSF in 2013. Since then he has worked in Kenya and Liberia. He is now Mobile Implementation Officer for non-communicable diseases, an operational research fellow with LuxOR and continues to work with Johns Hopkins as an International Health Fellow.

Nathan Ford works for the Dept. of HIV/AIDS and Viral Hepatitis at World Health Organization, Geneva. Prior to that, he worked with Médecins Sans Frontières (MSF) from 1998-2012. He holds a degree in Microbiology and Virology (Warwick) a Master in Public Health and Epidemiology (Cape Town) and a PhD in Clinical and Public Health and epidemiology (Vancouver). He serves on various editorial boards, including the Journal of the International AIDS Society, Tropical Medicine and International Health, and Conflict and Health. Areas of concern include evidence based humanitarian action, and simplification and adaptation of HIV/AIDS care in resource limited settings.

David Heymann is currently professor of Infectious Disease Epidemiology at the London School of Hygiene and Tropical Medicine; Head of the Centre on Global Health Security at Chatham House and Chairman of Public Health England. Previously he worked with WHO in various leadership positions from which he headed the global response to the SARS outbreak, led the global polio eradication initiative and the field response to a major Ebola outbreak in Kikwit, and established the programme on Emerging Infectious Diseases. Before joining WHO, he worked for 13 years as a medical epidemiologist in sub-Saharan Africa with the US Center for Disease Control and Prevention (CDC), where he participated in the investigation of the first and second Ebola outbreaks; and conducted field research on

prevention and control of diseases ranging from haemorrhagic fevers and yaws to malaria and childhood vaccine preventable diseases. He is an elected fellow of the US Institute of Medicine of the National Academies, and the UK Academy of Medical Sciences.

Petros Isaakidis is a medical doctor with a doctoral degree in epidemiology. He joined MSF in 1997 and has worked in Kenya, Gaza and West Bank, Greece (migrants), Cambodia and India in different positions, from field doctor to medical coordinator to regional epidemiologist. He has also worked as clinician in the public and private sectors and as epidemiologist in disease surveillance, outbreak investigations and planning for mass gatherings. Since 2012 he has been facilitating Operational Research courses as part of the MSF/ UNION/ WHO SORT-IT initiative. He's currently based in Mumbai, India.

Denis Malvy has gained his MD degree in 1988 with the graduation of internal medicine and PhD degree in 1994 at the University of Paris7. He has been Associate Professor in epidemiology in 1998 and is Professor in infectious diseases since 2005. His main institutional position is Head of the department of Infectious and tropical diseases at the University Hospital Center of Bordeaux, France and chair of tropical medicine and clinical international health at the University of Bordeaux. His field of research is translational research in global health with emphasis on non malaria febrile illnesses. He is coordinator of field studies in Western Africa and South east Asia and investigator of clinical trials on Ebola experimental therapies in Guinea.

Meinie Nicolai first worked with MSF in 1992, as a supervising nurse in Liberia. She has since gained a decade of field experience in Angola, the Democratic Republic of the Congo, Ethiopia, Rwanda, Somalia and South Sudan. Meinie returned to the Netherlands to

coordinate the national network on sexual and reproductive health and AIDS between 2002 and 2003, but her involvement with MSF continued as she became a board member of the Belgian association. In 2004, Meinie became director of operations in the Brussels office until she was elected president of MSF Belgium and of MSF's operational directorate in Brussels in October 2010.

Piero Olliaro is the head of intervention and implementation research at TDR - The Special Programme for Research and Training in Tropical Diseases. He has been with TDR since 1993, covering different functions in research and capacity building. Before joining TDR he had worked as general practitioner, hospital consultant, and as researcher in academia and the pharmaceutical private sector. He contributed to establish of the Drug for Neglected Diseases initiative (DNDi) and the Europe and Developing Countries Clinical Trial Partnership (EDCTP). He received his MD, PhD, and post-graduation in infectious diseases at the University of Pavia in Italy, and his HDR (Habilitation à diriger les recherches) at the University Joseph Fourier, Grenoble in France.

Mahboobullah Shafiq graduated from Kabul Medical University in 2005. He has been working with MSF in Afghanistan since 2011 and has been working as an Intensive Care Unit supervisor since 2013.

Emilie Venables is an anthropologist who has been working for MSF since 2012. She is currently working as a Qualitative Research MIO with LuxOR and SAMU, and is based in Johannesburg, South Africa. Emilie has worked in sub-Saharan Africa for over a decade, and has conducted research in countries including South Africa, Liberia, Kenya and Senegal. Her research interests include HIV/AIDS, sex-work, Ebola and migration and she is particularly interested in the use of qualitative methodologies in health research.

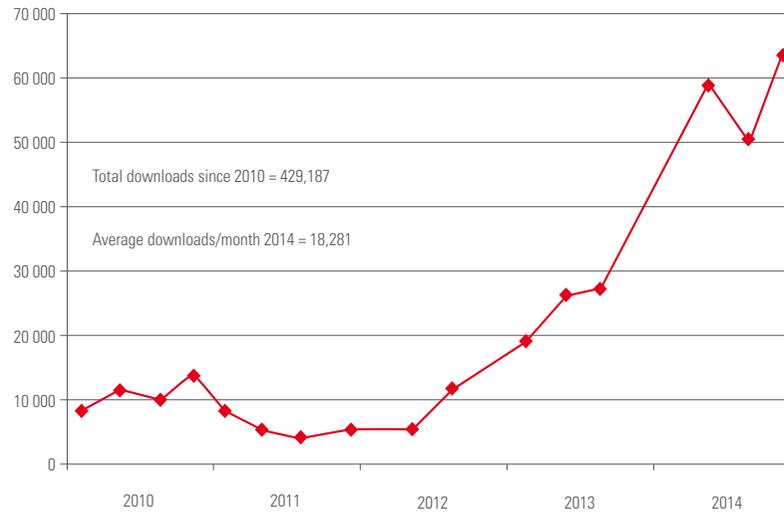
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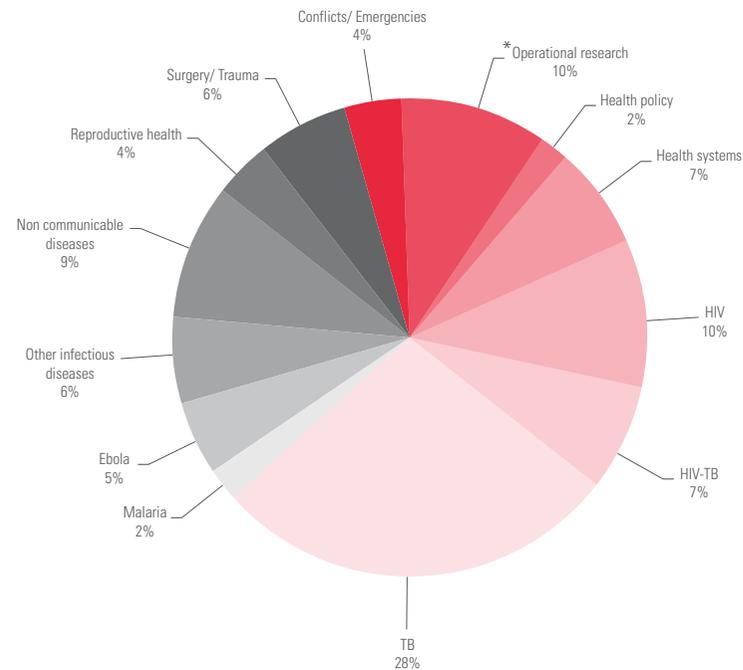
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