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Outcome of the first Medicines Utilization Research in Africa group meeting to promote sustainable and rational medicine use in Africa

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The first Medicines Utilization Research in Africa group workshop and symposium brought researchers together from across Africa to improve their knowledge on drug utilization methodologies as well as exchange ideas. As a result, progress was made on drug utilization research and formulating future strategies to enhance the rational use of medicines in Africa. Anti-infectives were the principal theme for the 1-day symposium following the workshops. This included presentations on the inappropriate use of antibiotics as well as ways to address this. Concerns with adverse drug reactions and adherence to anti-retroviral medicines were also discussed, with poor adherence remaining a challenge. There were also concerns with the underutilization of generics. These discussions resulted in a number of agreed activities before the next conference in 2016.

Medicines Utilization Research in Africa (MURIA) is a multidisciplinary research group striving to promote sustainable, rational medicine use in Africa [1]. Activities include the first MURIA workshop and symposium held at the University of Botswana from 27th to 29th July 2015 [1]. This was opened by the Deputy Vice Chancellor of Academic Affairs (Prof Totolo) and the Minister of Health, Hon Dorcas Makgato. Hon Dorcas Makgato emphasized the importance of addressing the potential misuse of antibiotics as well as critically looking at antiretroviral (ARV) medicines, non-communicable diseases and generic medicines. Anti-infectives and non-communicable diseases are also of particular importance globally. She stressed that we can only act on data, facilitated by cross-national studies.

Delegates subsequently attended either introductory or advanced workshops. Ilse Truter opened the Introductory Group workshop by giving an outline of key issues for drug utilization (DU) research including

guidelines, types of research, data sources and classification systems [2,3] as well as giving examples. Margaret Oluka expanded on this by discussing the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) classification in more detail including DDDs/1000 inhabitants/day (DIDs) to assess DU across countries. Olayinka Ogunleye discussed developing standardized indicators, which included together with pertinent goals: average number of medicines prescribed/patient encounter (<2); percentage of medicines prescribed by generic name (close to 100%); percentage of encounters prescribed an antibiotic (<30%); percentage of encounters with an injection prescribed (<10%); percentage of medicines prescribed from an essential medicines list or formulary (close to 100%).

Brian Godman closed the morning session by discussing ways to influence the rational use of medicines, broken down into the 4Es – education, economics, engineering and enforcement [4]. Multiple measures have enhanced the

prescribing of generic versus patented statins, angiotensin converting enzyme inhibitors (ACEIs) versus patented angiotensin receptor blockers and generic versus patented angiotensin receptor blockers [5,6] as well as reduced antibiotic utilization [7]. Day one for the Introductory Group ended with Marike Cockeran discussing basic statistics applied to DU research.

Andy Gray opened the Advanced Group workshop by discussing key issues concerning antibiotic DU research, with potential alternatives including DDDs/100 bed days/unit of time and DDDs/100 patient encounters/unit of time [8]. Potential data sources vary by country, and include both private and public sectors as well as data from surveys [9]. Matthias Adorka subsequently discussed novel approaches to DU research, including developing new methodologies to assess appropriate antibiotic prescribing [10]. Brent Knoesen then discussed key principles involved with undertaking qualitative research, including when it should be undertaken and potential applications in DU research.

Challenges for cross-national studies include using standard utilization methods, the same protocol, robust datasets, working with health authorities to accurately document country measures and ensuring a good mix of countries and interventions to enhance future learnings [5,6,11]. Johanita Burger discussed pharmacoconomics including the four basic study approaches alongside examples. Finally, Theunis Kotze ended the first day by discussing advanced statistical methods.

Day two for the Introductory Group started with Rianda Joubert discussing applications of DU research including quantitative and qualitative studies, for example questionnaires among physicians in Namibia ascertained first-line treatment of patients with upper respiratory tract infections was typically amoxicillin with clavulanic acid and ciprofloxacin for urinary tract infections, against recommended Namibian guidelines [12]. Household surveys are also an important source of DU data in Africa, especially where there is appreciable self-purchasing of medicines [13]. Finally Andy Gray discussed the basic principles of medical and research ethics, including the need for ethics in research, basic biomedical research principles, informed consent, the need for transparency as well as the challenges involved in retrospective and epidemiological research.

Lars Gustafsson started the second morning for the Advanced Group by exploring drug safety and the use of databases in DU research, especially with limited knowledge about adverse drug reactions (ADRs) in a number of countries [14]. Examples include early warning indicators for HIV drug resistance [15], the use of open source clinical trials software systems [16] and the comprehensive longitudinal database regarding HIV therapy and the outcomes in patients in Botswana during the past decade [17]. Interdisciplinary groups working together analyzing, communicating their findings and following up DU in practice are all important considerations for changing prescribing behavior. This is seen in Stockholm, Sweden, with high adherence rates to the 'Wise List' through a comprehensive approach and physician trust in those developing the formulary of just over 200 medicines in ambulatory

care [18]. The advanced workshop ended with Joseph Fadare leading discussions regarding ethics, especially key issues and challenges. This was illustrated with examples [19].

Anti-infectives were the principal theme of the oral and poster sessions for the symposium. A qualitative study among households in Kampala revealed the common cold was the most prevalent acute respiratory infection. There was high use of antibiotics in 43% of cases, mainly amoxicillin and cotrimoxazole, before seeking medical care, with a strong correlation between antibiotic use, presence of pneumonia symptoms, level of education of the caregiver and the source of medicines. Johanita Burger presented findings from a study conducted by Agyakwa *et al.*, who found high prescribing of fluoroquinolones by physicians in the private healthcare sector in South Africa, representing 28% of all antibiotic prescriptions [20]. Qualitative research undertaken by Thatoyaone Kenaope *et al.* found among pharmacists in South Africa, the socio-economic status of patients, patient satisfaction, their knowledge of antibiotic indications and the professional relationship between healthcare professionals influenced physician prescribing behavior. Consequently, there is a need to target all stakeholder groups to improve antibiotic use.

The irrational use of antibiotics was also seen among government facilities in Swaziland, with respiratory tract infections as the most common diagnosis. This led to suggestions that the government should strengthen hospital drugs and therapeutic committees as well as antibiotic management programs. A retrospective study carried out by Bene Paramadhas and Tennyson Mgutshini among HIV-infected patients at a tertiary care facility in Botswana revealed a high degree of empiric prescribing with culture and sensitivity tests rarely ordered. There was a high degree of IV antibiotics prescribed in 52% of prescriptions, with only a limited number of patients switched to oral medicines. Positively, all antibiotics prescribed were on the Botswana essential medicines list, and 86% of all antibiotics were prescribed by their generic name. Further studies and interventions are planned to address concerns. There are also plans in Botswana to undertake DU studies among private physicians treating patients for upper respiratory tract infections following the publication of national guidelines in 2012. This will form the basis of future measures.

Mwangana Mubita *et al.* found the implementation of a multifaceted antimicrobial care approach around 'Start smart, then focus' among six Internal Medicine wards at a University Teaching Hospital in Zambia led to improvements in the quality of antimicrobial prescribing in terms of compliance with the outlined care elements of an antimicrobial prescribing care bundle. Multifaceted approaches have also worked in other countries [7].

There are also concerns regarding ADRs and adherence to ARVs. Francis Kameera *et al.* using Namibia's Adverse Reporting database—VigiFlow[®]—ascertained that a nevirapine safety signal was detected after shifting the initiation of nevirapine to patients with higher CD4-counts than previously recommended. This resulted in the Ministry of Health in

Namibia halting this move, demonstrating that locally derived ADR data can protect patients. This is important as the characteristics of patients with HIV in Africa are different from those in Europe and the US.

Razia Gaida discussed a systematic review of efavirenz and its side effects that she *and colleagues* had undertaken [21]. They found a total of 13 articles between 2001 and 2014 and concluded that as efavirenz does not commonly induce severe side effects that warrant discontinuation, it can be considered for use in psychiatric patients.

Poor adherence remains a major challenge in patients, especially those on highly active antiretroviral therapy. Contributing factors include ADRs with highly active antiretroviral therapy, high tablet count (typically >4) and lower earnings as discussed by Norah Katende-Kyenda [22]. Current adherence rates to ARVs are also being followed up in Botswana following national guidelines changing ARV eligibility to better plan for the future.

There were also presentations on other disease areas. Paulina van Zyl undertook a study to examine the prevalence and comorbidity of irritable bowel syndrome, depression and anxiety among retirement village residents in South Africa using a variety of questionnaires. Overall, there was a lower than expected rate of irritable bowel syndrome. However, the majority of participants using antidepressants, anxiolytics and PPIs were taking these for 1 year or longer, with participants taking PPIs or antidepressants more likely to experience irritable bowel syndrome symptoms [23].

Adedunni Olusanya assessed the effects of co-administration of other drugs on compliance, ADRs and seizure control in patients taking carbamazepine monotherapy for epilepsy. She found that compliance was significantly lower in patients co-administered with other medicines; however, there was no significant difference in seizure control or reports of ADRs. Studies showed there are concerns with generic medicines in a number of African countries. Joseph Fadare *et al.* in Nigeria identified a number of gaps in physician perception of generics and their prescribing and dispensing. Margaret Oluka found

prescribing of generics was sub-optimal at only 52% of prescriptions in an outpatient department of a national referral hospital in Kenya. Both need to be addressed before key stakeholders benefit from low cost generics.

Finally, there are ongoing initiatives to progress collaboration between centers in Africa through simplifying processes, thereby strengthening both capacity for drug development and improving the rational use of medicines (RUM) in Africa [24].

The feedback from the meeting was very positive, with attendees typically finding workshop presenters knowledgeable in their areas (4.3 out of a maximum of 5) with the content relevant to their needs. In addition, the information could be applied to their workplace to help achieve their professional goals (4.6 out of 5) and enhance their professional expertise (90% stated substantially). The main criticism was not enough time to debate key issues and their implications.

A number of activities are planned for 2015/2016, and we look forward to the second MURIA Group meeting in Botswana in July 2016.

All abstracts, workshop presentations including planned projects in 2015/2016 and the speech by the Minister of Health can be found on [25]. MURIA membership forms can be found on [26].

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