

Utrecht WHO Winter Meeting 2013

10 - 11 January 2013

Utrecht - WHO Collaborating Centre
for Pharmacoepidemiology and
Pharmaceutical Policy Analysis
Utrecht, The Netherlands

Venue: University Museum, Utrecht

Programme Meeting report



WHO Collaborating Centre for
Pharmacoepidemiology & Pharmaceutical Policy Analysis



Universiteit Utrecht

Utrecht – WHO Winter Meeting 2013

Thursday 10 - Friday 11 January 2013

Programme

**Utrecht - WHO Collaborating Centre for
Pharmacoepidemiology and
Pharmaceutical Policy Analysis
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Programme Meeting report



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Welcome

We are very pleased to welcome all of you to the 5th edition of the UU - WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis Winter Meeting. The meeting brings together around 60 researchers and policy makers from many different countries and professional backgrounds.

The meeting will start on Thursday with (young) researchers presenting their ongoing or planned work. We were very pleased with the number and quality of the submitted abstracts and look forward to inspiring discussions. We sincerely hope that these discussions will contribute to bringing evidence-based policy making on pharmaceuticals to a higher level.

We are proud that one of the centre's PhD students, Alexandra Cameron, will defend her thesis entitled "Understanding access to medicines in low- and middle-income countries through the use of price and availability indicators" on Thursday as well. We hope you will enjoy participating in the public ceremony that will take place in the Academic Hall of Utrecht University.

The second day of the meeting will focus on "Priority Medicines for Europe and the World 2013". A European Commission-supported WHO publication "Priority Medicines for Europe and the World" will be launched in July 2013. This report provides an update of the 2004 report, which looked at the pharmaceutical gaps that exist, and recommended ways in which pharmaceutical research and innovation could best address health needs and emerging threats in Europe and the World. During the winter meeting invited authors of different chapters will present their current work for this project. The focus will be on subchapters dealing with new approaches to promoting innovation such as private public partnerships, pricing and reimbursement policies, redesigning the regulatory system and stakeholder involvement including patients and citizens. The meeting aims to involve all participants in discussing results so far.

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We would like to thank all of you for your contributions in advance and hope that you will continue to contribute by sharing your thoughts and expertise throughout the meeting.

We wish you a joyful meeting with intensive discussions and inspiring new thoughts!

On behalf of the Organizing Committee,

Bert Leufkens, Pieter Stolk and Aukje Mantel



General Information

Venue

University Museum
Lange Nieuwstraat 106
3512 PN Utrecht
Phone: +31 30 253 8008

Date

Thursday, 10 January – Friday 11 January, 2013

For all practical matters during the meeting, please contact:

Aukje Mantel (a.k.mantel@uu.nl)
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Organizing Committee

Utrecht - WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis

- Aukje Mantel
- Pieter Stolk
- Bert Leufkens

Department of Essential Medicines and Pharmaceutical Policies, World Health Organization

- Richard Laing

Time schedule WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis

Thursday 10 January 2013

Presentations of ongoing pharmaceutical policy analyses

- 08:30-09:00 Registration, coffee
- 09:00-09:30 Welcome; introduction and overview
Bert Leufkens (UU, MEB) and Richard Laing (WHO)
- 09:30-12:30 Paper discussion - 2 parallel sessions
1a: Drug regulatory science (**Zaadhuis**)
1b: Clinical Pharmacy (**Grote Vergaderzaal**)
- 12:30-13:30 Lunch
- 13:30-15:30 Paper discussion - 2 parallel sessions
2a: Pharmaceutical policy analysis (**Zaadhuis**)
2b: Impact of policies on drug use and prices (**Grote Vergaderzaal**)
- 15:30-16:15 Tea break
- 16:15-17:30 Public thesis defence by **Alexandra Cameron, Senaatszaal, Academic Hall, Domplein 29, Utrecht**
- 17:30-18:30 Drinks after the public defence in the **Academic Hall**

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Friday 11 January 2013

Priority Medicines for Europe and the World 2013

- 09:00-09:20 Welcome and introduction to Priority Medicines 2013
Bert Leufkens (UU, MEB) and Richard Laing (WHO)
- 09:20-09:40 What has changed 2004-2013? Background and methods
Warren Kaplan (BU)
- 09:40-10:45 Demography, global burden of disease and special populations (children) + General questions and discussion
Julisca Cesar (UMCG, WHO intern) and Verica Ivanovska (UU, University of Stip)
- 10:45-11:15 Tea / Coffee
- 11:15-12:00 New approaches to promoting innovation – short presentations followed by discussions
Moderators: **Bert Leufkens (UU, MEB) and Bart Wijnberg**
Presenters: **Pieter Stolk (UU)** - Regulatory incentives for innovation
Jacoline Bouvy (EUR) and Sabine Vogler (GOEG) - Pricing and reimbursement policies: impact on innovation
Pieter Stolk (UU) - PDPs and PPPs: learning from multi-country experiences
Tjeerd van Staa (MHRA, UU) - Real-life data and learning from practice to advance innovation
Ghislaine van Thiel (UMCU) – Patient and citizen involvement in priority setting
- 12:00-13:00 Lunch
- 13:00-15:30 New approaches to promoting innovation – short presentations followed by discussions - continued
- 15:30-16:00 Wrap up and day closure
Richard Laing (WHO) and Bert Leufkens (UU, MEB)



Presentations of ongoing pharmaceutical policy analyses

Session 1a – Thursday 10 January 2013

09.30 - 12.30 - parallel session -

Drug regulatory science

Session Chairs: **Tim Reed** and **Aukje Mantel**

Nr	Author	Title
1	Tafari	Exploring and understanding critical factors driving the decision-making process for the evaluation of anticancer medicines in the EU and the US
2	Wahlster	Multi-criteria decision analysis (MCDA) to inform decision-making in the innovation process of medical technologies
3	Hernandez	Public trust in pharmaceutical companies, regulatory authorities, and doctors: “what’s the state of the nation?”
4	Lisman	New falsified medicines legislation: Prospective study on the impact of Directive 2011/62/EU on the availability and pricing of (generic) medicinal products in the Netherlands
5	Rausch	Quantifying the frequency of substandard, falsified and counterfeit drugs in low and middle countries

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Session 1b - Thursday 10 January 2013

09.30 - 12.30 - parallel session -

Clinical pharmacy

Session Chair: **Bert Leufkens**

Nr	Author	Title
6	Ankrah	Influence of adherence on switching therapy among HIV patients at the Korle-Bu teaching hospital in Ghana
7	Tetteh	Tolerability of highly active anti-retroviral therapy (HAART) in post-exposure prophylaxis program at the Korle-Bu Teaching Hospital (KBTH) in Ghana: A retrospective cohort study
8	Ebenezer	Reducing Medicine administration Errors in developing Counties: Using Patient bedside medicine lockers as against Medicine Trolleys
9	Sagwa	Antiretroviral therapy and the risk of serious aminoglycoside-induced auditory damage in patients concomitantly treated for drug-resistant tuberculosis: preliminary findings from Namibia
10	Advinha	Policies for a successful aging: need of elderly functional ability assessment to manage their own medication

Session 2a - Thursday 10 January 2013

13.30 - 15.30 - parallel session -

Pharmaceutical policy analysis

Session Chairs: **Richard Laing and Hans Hogerzeil**

Nr	Author	Title
11	Ismail	Identifying priorities for promoting good governance for medicines in the WHO Eastern Mediterranean Region
12	Nsabagasani	Improving Access to Appropriate Medicines for Children in Uganda: Analysis of Relevant Policies
13	Bazargani	Selection of oncology medicines in low and middle income countries
14	Gispen	International drug control from a human rights perspective

Session 2b - Thursday 10 January 2013

13.30 – 15.30 - parallel session -

Impact of policies on drug use and prices

Session Chairs: **Warren Kaplan and Sabine Vogler**

Nr	Author	Title
15	Leopold	Analyses of the impact of the financial recession on medicine utilization in Europe
16	Oliveira-Martins	Off-label use of antiepileptic drugs and its costs – a drug utilization study in Portugal
17	Santa-Ana-Tellez	Analysis of antibiotic utilization in Brazil and Mexico before and after over-the-counter sales restrictions in 2010
18	Ewen	UN Relief and Works Agency for Palestine Refugees in the Near East's medicine procurement processes and prices: a comparative performance assessment

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Posters - Thursday 10 January 2013

During breaks

Nr	Author	Title
19	Gwaza	The influence of point estimates, variability, sample size and statistical power on the demonstration of bioequivalence between generics by adjusted indirect comparisons
20	Barroso	Health and crisis in Portugal
21	Alves	Patient and Consumer Organisations at the European Medicines Agency: Financial disclosure and transparency
22	Vranken	Perception of barriers in accessing opioid medicines
23	Notenboom	Ease and accuracy of subdivision of tablets by elderly people
24	Duthey	Alzheimer's Disease Opportunities to Address Pharmaceutical Gaps



List of participants UU-WHO winter meeting 10 + 11 January 2013

(as of 22 December 2012)

■ Aginus Kalis	CBG-MEB	The Netherlands
■ Ana Advinha	University of Lisbon	Portugal
■ Anke Hövels	Utrecht University	The Netherlands
■ Aryanti Radyowijati	ResultsinHealth	The Netherlands
■ Aukje Mantel	Utrecht University	The Netherlands
■ Barikpoar Ebenezer	University of Port Harcourt	Nigeria
■ Bart Wijnberg		The Netherlands
■ Beatrice Duthey	WHO	Switzerland
■ Bert Leufkens	Utrecht University / MEB	The Netherlands
■ Birte van Elk	CBG-MEB	The Netherlands
■ Chris Rausch	RijksUniversiteit Groningen	The Netherlands
■ Christine Leopold	Austrian Health Institute	Austria
■ Clara Setiawan	WHO	Switzerland
■ Clemence Sagwa	Katutura Intermediate Hospital	Namibia
■ Daniel Ankrah	Korle-Bu Teaching Hospital	Ghana
■ Evans Sagwa	Management Sciences for Health	Namibia
■ Faraz Chavoushi	Utrecht University	The Netherlands
■ Francisco Hernandez	Utrecht University	The Netherlands
■ Ghislaine van Thiel	UMCU	The Netherlands
■ Giovanni Tafuri	AIFA / Utrecht University	Italy
■ Hans Hogerzeil	UMCG	The Netherlands
■ Iga Lipska	CIRS	Poland
■ Jacoline Bouvy	Erasmus University	The Netherlands
■ Jan Raaijmakers	Utrecht University / GSK	The Netherlands
■ John Lisman	Lisman Legal Life sciences B.V.	The Netherlands
■ Julisca Cesar	University of Groningen / WHO	The Netherlands
■ Kees de Joncheere	WHO	Switzerland
■ Kim Nooteboom	RIVM	The Netherlands
■ Luqman Tariq	Utrecht University / GSK	The Netherlands
■ Luther Gwaza	Washington State University	USA
■ Maaïke Esselink	ResultsinHealth	The Netherlands
■ Marie-Hélène Schutjens	Utrecht University	The Netherlands
■ Margaret Ewen	HAI Global	The Netherlands
■ Marie Elske Gispen	Utrecht University	The Netherlands
■ Marjolein Vranken	Utrecht University	The Netherlands
■ Michelle Putzeist	Utrecht University	The Netherlands
■ Mohamed Ramzy Ismail	WHO EMRO	Egypt
■ Monica Eimunjeze	NAFDAC	Nigeria
■ Nga Tong	Boston University School of Public Health	USA
■ Pepijn Spek	RIVM	The Netherlands
■ Peter Paul Basazemajja	RijksUniversiteit Groningen	The Netherlands
■ Peter Stephens	IMS Health	United Kingdom
■ Philip Wahlster	University of Erlangen-Nuremberg	Germany
■ Pieter Stolk	Utrecht University	The Netherlands
■ Priya Bahri	European Medicines Agency	United Kingdom
■ Raymond Tetteh	Korle-Bu Teaching Hospital	Ghana
■ Richard Laing	WHO	Switzerland
■ Rutger Top	ResultsinHealth	The Netherlands
■ Sabine Vogler	Austrian Health Institute	Austria
■ Sander van den Bogert	Utrecht University	The Netherlands

■ Shuichi Suzuki	WHO	Switzerland
■ Sofia Oliveira-Martins	University of Lisbon	Portugal
■ Susanne Vijverberg	Utrecht University	The Netherlands
■ Teresa Leonardo Alves	Utrecht University / La Revue Prescrire	The Netherlands
■ Tim Reed	Health Action International	The Netherlands
■ Tjeerd van Staa	MHRA / Utrecht University	United Kingdom
■ Toine Pieters	Utrecht University	The Netherlands
■ Verica Ivanovska	University “Goce Delcev” / UU	Macedonia
■ Warren Kaplan	Boston University School of Public Health	USA
■ Xavier Nsabagasani	Makerere University / University of Copenhagen	Uganda / Denmark
■ Yared Santa Ana Tellez	Utrecht University	The Netherlands
■ Yaser Bazargani	Utrecht University	The Netherlands



Overview abstracts 10 January 2013

Exploring and understanding critical factors driving the decision-making process for the evaluation of anticancer medicines in the EU and the US

Giovanni Tafuri^{1,2}, Pieter Stolk², Francesco Trotta¹, Michelle Putzeist²,
Hubert G. M. Leufkens², Richard O. Laing³, Manuela De Allegri⁴

¹Italian Medicines Agency ²Utrecht University ³World Health Organization ⁴Heidelberg University

Rationale

Clinically relevant differences in the outcome of the EMA and FDA approval process can occur, even when the assessment is based on the same data package. Qualitative methods can provide useful insights into decision making processes.

Objective

This comparative qualitative study aims to analyse and understand which factors, related or unrelated to the data package of a drug application, drive the decision-making process of the EU and US regulators with regard to anticancer drugs.

Method

A combination of purposive and convenience sampling techniques was used. EMA and FDA regulators with extensive experience in the evaluation of anticancer medicines were invited to participate in the study as interviewees. Data collection took place between April and June 2012. Data was collected through means of in-depth semi-structured interviews conducted with EMA and FDA regulators in a face-to-face setting. The interviews were audio recorded and verbatim transcribed. The analysis was carried out manually on the transcribed text. Data was independently coded and categorized by two researchers: one relied on a deductive approach based on the themes of the interview guide, while the other relied on an inductive approach, letting codes and categories emerge as the reading proceeded. Interpretation of the findings emerged through a process of triangulation between the two.

Results

Overall seven EMA and six FDA qualified/senior regulators were interviewed.

There is an open dialogue between the FDA and EMA, with the two moving closer and exchanging information, but not opinions.

Differences in decision-making may be due to a different evaluation of endpoints (e.g. Progression Free Survival seen as a clinical benefit per se by EMA, not by FDA; FDA more open to base approval on activity data) and to different roles of public opinions/exchanges with patients, fully incorporated only at the FDA. Regulatory divergence may have cultural roots: unlike the EU, the US may have a prevailing attitude to take risks in order to guarantee quick access to new anticancer treatments.



Multi-criteria decision analysis (MCDA) to inform decision-making in the innovation process of medical technologies

Philip Wahlster

Interdisciplinary Centre for Health Technology Assessment and Public Health,
University of Erlangen-Nuremberg

Introduction

Decision-making within the innovation process of medical interventions is very complex. There are different levels of diffusion from translational research to reimbursement decisions with different decision criteria and different decision-makers, which translate into different levels of uncertainty.

Methods

A methodological approach to address uncertainty within the decision processes is Multi Criteria Decision Analysis (MCDA), which separates the evaluation of criteria and evidence. A systematic review about the application of MCDA in the innovation process was conducted identifying literature from 1990 to 2012. Original research articles were included which used an MCDA methodology for medical interventions with specific focus on use of economic criteria.

Results

From 417 identified articles, 18 studies were included in the final analysis. Six studies used a Discrete Choice (DC) approach, five studies an Analytic Hierarchy Process (AHP) and seven studies used another direct MCDA approach. In terms of economic consideration, cost-effectiveness was the most important criteria used in ten studies. Six studies used the total costs of an intervention as criterion. Two studies (AHP) used costs aspects in several sub criteria. With regard to the time horizon, four studies were conducted in early development of technologies. 14 studies supported a reimbursement decision at time of market access. Different time points of the innovation processes result in different involvement of stakeholder groups.

Conclusion

Transparency is increased if stakeholders and their criteria are part of the innovation process. In terms of economic issues and effectiveness, the evidence base of criteria used in early development of a technology is mostly lacking. However, generating evidence and transparency is crucial to decrease uncertainty around policy decisions. These results can support the development of a MCDA approach within a structured forecasting in the sense of “prospective” HTA, i.e. before the launch of a technology.

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Public trust in pharmaceutical companies, regulatory authorities, and doctors: “what’s the state of the nation?”

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³GlaxoSmithKline, External Scientific Collaborations Europe, Zeist, The Netherlands

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Background

Drug safety controversies, regulatory flaws, unethical practices and the resulting media coverage have initiated and fueled an on-going debate about the lack/loss of public trust in the pharmaceutical sector (i.e., industry, regulatory agencies, and doctors). Although public opinion polls and surveys have been conducted to study public trust, we hypothesize that these studies lack analytical rigor and a predefined definition of the concept of public trust in the pharmaceutical sector.

Objectives

To compile and appraise the empirical evidence about public trust in the pharmaceutical sector.

Methods

A systematic review of the scientific literature was performed to identify articles analyzing public trust in pharmaceutical companies, regulatory authorities, and doctors. Empirical articles were searched using pre-defined keyword sets in PubMed, Scopus, and Web of Science. We included only empirical articles (e.g., questionnaires, interviews, polls, or surveys) with no time span, and that were written in English, Dutch, or Spanish. In-deep appraisal of empirical articles will include: type of study (interview, questionnaire, poll), whether or not trust was pre-defined, number of participants, response rate, region, and representativeness.

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Preliminary results

For pharmaceutical companies, we extracted in total 432 articles (n=165 PubMed, n=93 Web of Science, and n=174 Scopus), which 88 articles were duplicates, 332 articles out of context, and 12 articles were included as empirical studies. For regulatory authorities, 156 studies were extracted (n=32 PubMed, n=118 Web of Science, and n=6 Scopus), which 8 articles were duplicates, 145 articles out of context, and 3 empirical studies were included. For doctors, 488 articles were extracted in total (n=154 PubMed, n=93 Web of Science, and n=265 Scopus), which 26 articles were duplicates, 27 not found, 420 out of context, and 39 empirical studies were included. In-deep appraisal of empirical articles is currently ongoing.



New falsified medicines legislation: Prospective study on the impact of Directive 2011/62/EU on the availability and pricing of (generic) medicinal products in The Netherlands

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²Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, Utrecht, the Netherlands

Rationale

Directive 2011/62/EU aims to prevent falsified medicines entering the legal supply chain and reaching patients by introducing harmonised safety and strengthened control measures. One of the new control measures is introduced in the new article 46b of Directive 2001/83/EC (amended by Directive 2011/62/EU). Based on article 46b as of 2 July 2013 Active Pharmaceutical Ingredients (“APIs”) may only be imported into the EU from third countries if (i) the national legislation on Good Manufacturing Practice for starting materials is on the same level as in the EU; and (ii) the local authorities enforce this legislation on the same level as in the EU. The import of APIs is therefore restricted to those third countries that introduce and enforce EU GMP-legislation. Possible negative implications that we expect to result from these new requirements are: 1. decreased availability of APIs for the EU market, 2. higher costs for manufacturing medicinal products and decreased availability of medicinal products on the EU market.

Objectives

This study aims to determine whether implementation of the new falsified medicines legislation, focusing on article 46b of Directive 2001/83/EC, is associated with reduced availability and increased prices of (generic) medicines in the Netherlands.

Methods

Data on the availability and pricing of (generic) medicinal products in the Netherlands will be collected 5 years before and after the implementation of Directive 2011/62/EU in the Netherlands, using the register of the Medicines Evaluation Board as well as the Netherlands database of available medicinal products held by Z-Index. Time regression analysis will be used to study the impact of Directive 2011/62/EU on the overall availability and pricing of (generic) medicinal products. Literature searches and additional studies will be conducted to distinguish the effects of the introduction of article 46b from other (legal or regulatory) effects.

Quantifying the frequency of substandard, falsified and counterfeit drugs in low and middle countries

Chris Rausch, Peter Paul Basazemajja, Hans Hogerzeil
RijksUniversiteit Groningen, the Netherlands

Background and objective

The current studies and reports on the topic of sub-standard, falsified and counterfeit drugs do not adequately represent the presence of the afore mentioned types of drugs in low- and middle income countries. In this review, we focus on quantifying the frequency of substandard, falsified and counterfeit drugs in low and middle countries.

Methods

A search was conducted in PubMed in English using the search terms stated below with a publication date from 01-01-2006 to 01-07-2012.

- 1 “Pharmaceutical Preparations”[Mesh]
- 2 drug [TIAB] OR drugs [TIAB]
- 3 medicine [TIAB] OR medicines [TIAB]
- 4 “medical product” [TIAB] OR “medical products” [TIAB]
- 5 pharmaceutical [TIAB] OR pharmaceuticals [TIAB]
- 6 “pharmaceutical product” [TIAB] OR “pharmaceutical products” [TIAB]
- 7 substandard [TIAB] OR “sub standard” [TIAB] OR sub-standard [TIAB]
- 8 falsified [TIAB] OR fake [TIAB]
- 9 “Counterfeit Drugs”[Mesh]
- 10 counterfeit [TIAB] OR counterfeiting [TIAB]

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We obtained 449 articles, which were selected based on the main subject being counterfeit-, fake-, falsified-, or substandard drugs according to the search criteria, and had conducted a study as in collecting samples, analysing samples and depict the acquired results. Articles were then further selected based on the country of study being a high-, middle-, or low income country according to the ranking by the world bank (Gross national income per capita 2010).

Influence of adherence on switching therapy among HIV patients at the Korle-Bu teaching hospital in Ghana

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Introduction

Antiretroviral therapy (ART) is the mainstay in the management of HIV patients. ART naïve patients are normally initiated on first line treatment but this may be switched to another first line or to a second line or a combination of the two depending on treatment outcomes. Such changes may be as a result of a compromise to adherence, the emergence of drug related side effects, or other factors of interest. This study aims to find out if adherence influences switching from one treatment to another.

Methodology

Data on existing records of all adults (>=15 years) patients who were put on ART from 01/01/2004 – 31/12/2009 (at the Korle-Bu Teaching Hospital) were extracted from clinical and pharmacy records as well as from the electronic database with the use of a structured questionnaire. All cases who switched therapy during the period were identified. A case control study was carried out by selecting controls from the same source as cases. Controls were HIV patients who had never switched treatment at the time of selecting the corresponding case and the two were matched on index date. Adherence was determined using the proportion of days covered approach and measures of effects were calculated using conditional logistic regression. A level of 95% adherence was used as the cut-off.

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Preliminary results

In all there were 298 cases with 65% (195/298) being female. Only 4.4% (13/293) and 15.7% (46/293) were smokers and consumed alcohol respectively at baseline. 79.9% switched to other first line drugs and 21.1 (60/298) switched to a second line or a combination of the two. Overall, a combination of zidovudine, lamivudine and efavirenz was the most used first line combination (25.6%) and didanosine, abacavir and lopinavir boosted ritonavir was the most consumed second line regimen (11.4% (34/298)). 51.7% of cases had body mass index (BMI) < 20 and 44.3% of controls had BMI < 20 at baseline.

Tolerability of highly active anti-retroviral therapy (HAART) in post-exposure prophylaxis program at the Korle-Bu Teaching Hospital (KBTH) in Ghana: A retrospective cohort study

Raymond A. Tetteh^{1,2}, Edmund T. Nartey³, Alexander N.O. Dodoo³, Margaret Lartey⁴, Aukje Mantel-Teeuwisse¹, Hubert G.M. Leufkens^{1,5}, Priscilla A. Norley⁶

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²Pharmacy Department, Korle-Bu Teaching Hospital, P.O. Box KB 77, Korle-Bu, Accra, Ghana.

³Centre for Tropical Clinical Pharmacology & Therapeutics, University of Ghana Medical School, P. O. Box GP 4236, Accra, Ghana.

⁴Department of Medicine, University of Ghana Medical School, P. O. Box GP 4236, Accra, Ghana.

⁵Medicines Evaluation Board, Utrecht, The Netherlands.

⁶Department of Epidemiology and Disease Control, School of Public Health, University of Ghana, P.O. Box LG 25, Legon, Accra, Ghana.

Background

Following the introduction of HIV post-exposure prophylaxis program to healthcare workers (HCWs) and healthcare students (HCSs) in Korle-Bu teaching Hospital (KBTH) in January 2005, the incidence of adverse drug reaction (ADR) and adherence in occupationally exposed HIV-negative patients on highly active anti-retroviral therapy (HAART) was documented. We evaluated the incidence, type and risk factors associated with adverse drug reactions (ADRs) and non-adherence in this PEP program at the KBTH in Ghana.

Methods

Occupationally exposed HCWs/HCSs initiated on PEP program between January 2005 and December 2010 were evaluated in a retrospective cohort analysis in KBTH. Regimens prescribed were 3TC/AZT, 3TC/AZT/EFV or 3TC/AZT/PI. Patients were followed up on day 3 of the 3-day regimen and on days 10, 20 and 28 of the 28-day regimen schedule. Adverse drug reactions were classified using both Preferred Term (PT) and System Organ Classification (SOC) of World Health Organization. Adherence was based on the completion of the 3 days or 28 days regimen. Descriptive statistics, chi-square tests and relative risk were employed to assess associations among variables.

Results

During the study period of 72 months, a total of 295 exposures were reported by HCWs/HCSs of which 289 were administered PEP regimen of 3TC/AZT (227), 3TC/AZT/EFV (9), and 3TC/AZT/PI (53). Six patients were not administered any medication due to late reporting. There were 36 patients lost to follow-up on their ADR assessment. Out of the 253 patients followed-up, a total of 159 patients reported of ADRs made up of 101 reports (3TC/AZT), 8 reports (3TC/AZT/EFV), and 50 reports (3TC/AZT/PI). The most frequent ADR reports were on the gastro-intestinal tract (126 reports) of which nausea constituted 107 reports and diarrhoea, 38 reports. A total of 143 out of 227 patients administered 3TC/AZT adhered completely whilst 8 out of 9 and 32 out of 53 patients administered 3TC/AZT/EFV and 3TC/AZT/PI respectively also adhered completely to the regimen schedule. Sixteen patients truncated their regimen schedule because the source patients of their exposure tested HIV negative. Association tests showed that patients who did not report of any ADR were more likely to completely adhere (RR, 1.54; 95% CI, 1.37-1.73; $p < 0.001$) to the regimen schedule compared with those who reported of ADR.

Conclusions

This data shows that an effective pharmaco-vigilance tool can be employed to monitor the tolerability of HAART in HIV-negative patients on PEP. In addition the advent of ADRs can raise the issue of adherence which is very critical in preventing HIV sero-conversion in patients on PEP. This requires adequate patient counselling on ADRs to minimise non-adherence of patients on PEP. Further research on the tolerability of HAART in HIV-negative patients on PEP and its effect on HIV sero-conversion in this environment is recommended.



Reducing Medicine administration Errors in developing Counties: Using Patient bedside medicine lockers as against Medicine Trolleys

Ebenezer B.¹, Chioma Ebenezer², M. Ezejiofor¹

¹University of Port Harcourt and ²School of Pharmacy University College London

Objective

To determine if the use of patient bedside medicine lockers reduces the level of Medicine administration Errors in developing countries when compared to medicine Trolleys.

Methods

A sequential mixed method approach was used in carrying out this research in 2 phases. Phase 1 involved the use of Quantitative approach while phase 2 involved the use of a Qualitative approach. In Phase I undisguised observer technique was utilised to observe the medicine administration round on four wards in two different Hospitals namely: two medical wards in Braithwaite Memorial Hospital Area Hospital (BMH) and two surgical wards at the University of Port Harcourt Teaching Hospital (UPTH). The observation was carried out both before and after the introduction of patient bedside medicine lockers. All non-intravenous medicine administrations during the morning medicines administration round were observed and timed before and after the introduction of the lockers. Medicine administration errors (MAEs), time taken were recorded and analysed. Phase 2 involved exploring stakeholders' perceptions as regards u their preferred choice and the rational/reasons for the delays noticed in phase 1 above.

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Results

The MAE rate and the time spent on the medicine administration round both decreased after the introduction of patient bedside medicine lockers. The MAE rate dropped from 15.% to 2.3% in the BMH site and from 14.3% to 2.2% in the UPTH site; the time spent per patient on medicine administration decreased from 15.80 5.44 min pre-intervention to 5.03 1.87 min post-intervention and from 12.35 4.52 min pre-intervention to 5.95 2.39 min post-intervention in AAH. Stake holders interview in both hospitals noticed that medicines were far more safer in the Bedside lockers than in the Medicine Trolleys. They preferred the Medicine trolleys because it reduces Medicine Administration Errors.

Conclusions

The introduction of patient bedside medicine lockers resulted in reduced Medicine administration errors.



Antiretroviral therapy and the risk of serious aminoglycoside-induced auditory damage in patients concomitantly treated for drug-resistant tuberculosis: preliminary findings from Namibia

Evans Sagwa, Aukje Mantel-Teeuwisse

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Introduction

A high proportion (59%) of tuberculosis patients is co-infected with the human immunodeficiency virus (HIV) in Namibia and this complicates treatment of drug-resistant TB (MoHSS, 2010). Sagwa et al. (2012) studied 59 drug-resistant (DR-TB) patients in Namibia and found that tinnitus (45%) and decreased hearing (25%) occurred frequently, mostly during the intensive phase of therapy when injectable aminoglycosides were administered. While aminoglycosides, an integral part of DR-TB treatment, are known to be ototoxic (Brummett et al., 1989; Duggal and Sarkar, 2007), studies on whether antiretroviral drugs are ototoxic have been equivocal (Marra et al., 1997; Schouten et al., 2006; Katijah, 2010; and Berke, 2011) and the question of whether antiretroviral medicines influence the cochleotoxicity of the aminoglycosides is still unanswered.

Design and Methods

A retrospective cohort study was conducted. Patients initiating aminoglycoside-based DR-TB therapy between January 2007 and December 2011 were audiologically assessed using pure tone audiometry at baseline and every 3 months until completion of aminoglycoside treatment. Some of the DR-TB patients were co-infected with HIV. Descriptive statistics, univariate and multivariate logistic regression analysis (to adjust for confounding) were applied using Epi Info version 3.5.3. (US Centers for Disease Control, Atlanta). A p-value of less than 0.05 was chosen as indicating statistical significance.

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Results

Overall, 105 patient records were obtained, of which 102 satisfied eligibility criteria. The mean patient age and baseline weight was 34.4 ± 9.9 years and 52.3 ± 11.8 kilograms respectively; 60% were males. 47% (48/102) patients suffered serious auditory damage, requiring either fitting a hearing aid or rehabilitation. 46% of the 102 patients were treated with amikacin-based regimens, 47% with kanamycin-based regimens and 3% with capreomycin-based regimens. 43% (44/102) of the DR-TB patients were HIV co-infected and 33 were on Highly Active Antiretroviral Therapy (HAART). 13 of 33 HAART patients were on AZT (zidovudine)-based regimens. In univariate analysis, the Odds Ratio (OR) of serious auditory damage in patients treated with amikacin-based DR-TB treatment regimens versus regimens containing either kanamycin or capreomycin was 9.6 (95% CI 3.6 -25.4, $p=0.000$). The OR for patients treated with AZT-based regimens as compared to either non-AZT based HAART or no HAART was 2.8 (95% CI 0.8 -9.8, $p=0.117$). In a multivariable model that included amikacin, AZT, capreomycin and kanamycin; treatment with amikacin- and AZT-containing regimens were independently associated with a significant risk of serious auditory damage (OR=14.5; 95% CI 1.1-187.4, $p=0.041$) and (OR=4.5; 95% CI 1.01-20.2, $p=0.048$) respectively.

Conclusion

Concomitant therapy of drug-resistant tuberculosis and HIV co-infection using amikacin- and AZT-based regimens is associated with an increased risk of serious auditory damage. These two pharmacologic agents appear to independently cause ototoxicity and also to interact with each other. Clinicians should be cognizant of this potential pharmacologic interaction when treating DR-TB patients who are co-infected with HIV. Further studies are required to elucidate the mechanism of this interaction and identify which patients are particularly vulnerable to the ototoxic effects of both medications.



Policies for a successful aging: need of elderly functional ability assessment to manage their own medication

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Background

The correct medication use by community dwelling elders is essential for the preservation of their health and quality of life. In Portugal, there are validated tools to assess the activities of daily living abilities. However, there is none specifically built to assess the medication management ability. A tool's validation allowing the assessment of the Portuguese elder's functional ability to manage their own medication represents an essential step, in order to devise effective policies aiming the promotion of independence, health and autonomy for the longest possible period, through the implementation of support measures in this field (1-3).

The high inability rates revealed as age advances reflects a high risk for the elders health. According to WHO data (2004), about 46% of the individuals with 60 years and over, presents some degree of inability, being the more frequently causes of this inability vision and hearing loss, dementia and osteoarthritis. All can be related with a decreasing ability to manage their own medication (non-intentional process) (4-6).

The evaluation of the elder's functional ability to manage their own medication through the application of a validated tool can be an important way to identify potential disabilities and needs of the elders in primary healthcare centers and plan policy strategies to increase their performance, self-care skills and successful aging.

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Objective

The aim of this project is to assess the functional ability of the Portuguese elderly population to manage their own medication through the application of a specific and validated tool.

Methodology

The work plan is divided into three phases:

- Phase 1 – A descriptive and systematic literature review, the first, about the available tools for assess the functional ability in medication management, and the second, about the assessment of elders functional ability to manage medication;
- Phase 2 – Linguistic and cultural adaptation and validation a selected tool (according to the results obtained in phase 1);
- Phase 3 – Application of the validated tool in a representative sample of elders' users of Portuguese healthcare centers. The validated tool will be part of a questionnaire including also the elders' medication profile, regimen complexity, adherence self-report, cognitive status, self-care abilities, supports, needs and existing health policies in the field of medication management.

Previous Results

The descriptive literature review obtained a total of fifty tools for assessment of the elders' functional ability to manage their medication. Each tool was characterized about the assessed abilities: type of medication, application time and score. The differences between the tools were essentially related with the assessed abilities and the used medication regimen (real or simulated). Of the identified tools, the ones that demonstrated the higher applicability in late studies (more available studies), were the DRUGS (with real regimen) and the MMAA (with simulated regimen). The systematic literature review was performed using a structured question through the acronym P (population) I (instruments) C (context) O (outcome). The selection process resulted in a total of eighteen papers corresponding to seventeen studies. In the majority of the studies, the functional ability of the elders to manage their medication was assessed with specific tools. Generally, all tools refer the importance of inability previous detection, as an important

way to preserve the elders' independence and health. The cognitive impairment and the age growing appear as determinant factors for functional ability loss in the medication management task.

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Identifying priorities for promoting good governance for medicines in the WHO Eastern Mediterranean Region

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Background and goal

This paper builds on work conducted in the World Health Organization (WHO) Eastern Mediterranean Region (EMR) under the WHO Good Governance for Medicines (GGM) program. The program started in the EMR in 2007 and has since been introduced to 15 Member States of the Region. The research is based on the analysis of findings from 10 national assessments of 6 functions of the respective pharmaceutical systems, namely medicines registration, inspection of pharmaceutical establishments, promotion, selection, procurement and distribution. The countries covered are Jordan, Lebanon, Morocco, Pakistan, Syria, Egypt, Kuwait, Oman, Sudan, and Yemen.

This study aims at identifying priority areas for promoting good governance in the pharmaceutical sector where the systems in target countries have been found least transparent and most vulnerable to corruption.

Methodology

The WHO instrument¹ collects qualitative information on structural indicators and perceptions by interviewing key informants using a set of questionnaires. The methodology entails a theoretical basis for assigning scores which assumes a reverse relationship between transparency and vulnerability to corruption.

The results of this paper were obtained through the secondary analysis of primary data collected through assessments in the 10 mentioned countries.

As a first step, functions were ranked for each country according to the overall score for each of the 6 functions common across all countries. The functions were assigned numbers 1 through 6, where 1 is most vulnerable and 6 is least. For each function, the assigned numbers were added to give a total rank across the 10 countries.

As a second level of analysis, the main gaps within the function identified as the highest cross-cutting priority were determined by examining individual scores for the related quantitative indicators in the assessment. Scores for each quantitative indicator were compared and the average used to identify which indicators scored lowest -collectively- in the target countries.

Preliminary results

Analysis is ongoing but preliminary results show that control of medicines promotion may be the highest cross-cutting priority.

¹ Measuring transparency in the public pharmaceutical sector

Improving Access to Appropriate Medicines for Children in Uganda: Analysis of Relevant Policies

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Background

In 2007, WHO and UNICEF launched the ‘*child size*’ campaign to improve children’s access to medicines that suit the child’s age, physiological condition and body size. The call for child size medicines at the global level leaves a lot unknown especially how this initiative works within the context of low income countries such as Uganda. A PhD study is being conducted and focusses on 4 components: (1) mapping of relevant policies for child size medicine (2) the stakeholders’ perspectives on child size medicine (3) availability of child size medicines in the health facilities (4) the realities of the child size medicines in the context of Integrated Management of Childhood Illnesses approach. This paper focuses on the methodology being used for the first component of the PhD study.

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Methodology

Documents reviewed included 3 policy strategies, 3 policy statements, 4 treatment guidelines and 2 essential medicine lists. Some of the documents were retrieved from ministry of health officials, development partners and others were highlighted in the Ministry of Health website as core policy documents. An operational checklist focusing on aspects of medicines for children in the documents was developed and used for extraction of the data. A rating index for *child size* medicines was developed by the principal investigators based on the characteristics defined by WHO and was later reviewed by the pediatricians to verify the relevancy of these characteristics for the local context. Medicines used as first line treatment for: malaria, pneumonia, asthma and bilharzia among under-five children were subjected to the index to determine whether they are child size.

Acknowledgements

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² See WHO annex 5: Development of pediatric medicines: points to consider in formulation.



Selection of oncology medicines in low and middle income countries

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Background

Restrictions in health care resources and high rate of mortality due to cancer in low and middle income countries (LMICs) has raised major concerns regarding access to oncology medicines. Essential medicines are those which satisfy the primary health care needs of the societies and thus provide a basis for prioritization of medicines for public procurement or reimbursement decisions in LMICs. In this study we explore selection of oncology medicines in LMICS through investigating national essential medicines lists (NEML) for cancer treatments.

Methods

Recently updated NEMLs were retrieved from WHO website for 76 countries. Oncology medicines were classified based on therapeutic categories and subcategories. Countries were later clustered based on geographic regions, income levels and burden of cancer (in terms of mortality and morbidity). Indicators of frequency (number of medicines), diversity (number of therapeutic categories and subcategories) and more importantly absence were measured and compared using parametric and non-parametric tests and regression analysis.

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Findings

The overall median number of oncology medicines on a NEML was 16 (IQR=23) chosen predominantly from the category of “antineoplastic agents” (median of 15, IQR=20). 68.4% of the studied countries did not have any “Hormones and related agents” in their NEML. Median number of the medicines ranged from 30 (IQR=21) to 3.5 (17) among different geographic regions and 11 (IQR=13) to 26 (IQR=34) in different income levels. Approximately 3 out of 4 of the countries have chosen medicines from all five different subcategory of antineoplastic agents, whereas 5 countries did not select any oncology medicine. The cluster of countries suffered most from burden of cancer employed more essential oncology medicines and diversified further. Newer technologies like targeted therapies were not incorporated into the vast majority of the NEMLs.

Interpretation

The observed deficiencies in selection of oncology essential medicines can reflect insufficiencies and inequalities in access to cancer treatments at least in the public sector of LMICs. Further resources needs to be allocated from governments and international organizations to tackle the problem of access to oncology drugs.

International drug control from a human rights perspective

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Poor access to controlled essential medicines is a serious global public health deficit. It is estimated that 83% of the world's population lacks sufficient access to pain relief services because opioid analgesics are widely unavailable.¹ Another 90% of all epilepsy patients in Sub-Saharan Africa have no access to anti-epileptic drugs² and on an annual basis an estimated 70.000 mothers could be prevented from dying during childbirth if medicines were available.³ In addition, only 2% of all injection drug abusers receive opioid substitute treatment.⁴

One out of the many reasons underlying the poor access to controlled essential medicines is the present international drug control system. The system is based on the 1961, 1971, and 1988 Conventions.⁵ State parties should give effect to the twofold obligation to allow medicinal access and to control illicit use. To monitor this obligation, states should comply with an annual estimate and quarterly statistical return procedure. The demands are highly burdensome on states, in particular for developing countries.⁶ As a result many patients remain, or even die, under inhuman and undignified conditions, resulting in many human rights violations.

Under human rights law states are bound to protect individuals against inhuman and degrading treatment and to facilitate access to essential medicines⁷ as one of the core obligations under the right to health. Against the backdrop of the poor access to controlled essential medicines, taking into account the obligations of states under the international drug control and human rights treaties, this presentation is a first exploration in assessing the double obligation of access and control from a human rights perspective. The broader research is based on comparative legal methods including a normative and qualitative case study research to inform a human rights approach to drug control from both a top-down and bottom-up perspective.

- 1 M.J. Seya *et al.*, 'A First Comparison Between the Consumption of and the Need for Opioid Analgesics at Country, Regional and Global Levels' (2011) 25 *Journal of Pain and Palliative Care Pharmacotherapy* pp. 6-18, at pp. 14-15.
- 2 See World Health Organization, *Medicines: Access to Controlled Medicines (Narcotic and Psychotropic)* (Factsheet No. 336, June 2010). Available at: <http://www.who.int/mediacentre/factsheets/fs336/en/index.html> [accessed 10 December 2012].
- 3 Post partum bleeding could easily be treated with oxytocin or ergometrine. See World Health Organization, *Medicines: Access to Controlled Medicines (Narcotic and Psychotropic)* (Factsheet No. 336, June 2010). Available at: <http://www.who.int/mediacentre/factsheets/fs336/en/index.html> [accessed 10 December 2012].
- 4 See World Health Organization, *Medicines: Access to Controlled Medicines (Narcotic and Psychotropic)* (Factsheet No. 336, June 2010). Available at: <http://www.who.int/mediacentre/factsheets/fs336/en/index.html> [accessed 10 December 2012].
- 5 Respectively: Single Convention on Narcotic Drugs, 1961; Convention on Psychotropic Substances, 1971; United Nations Convention Against the Illicit Traffic in Narcotic and Psychotropic Substances, 1988.
- 6 See A.L. Taylor, 'Addressing the Global Tragedy of Needless Pain: Rethinking the United Nations Single Convention on Narcotic Drugs' (2007) 35 (4) *Journal of Law, Medicines and Ethics* pp. 556-570, at p. 562. Notably, the deficit of poor access to controlled essential medicines is particularly traced to these countries.
- 7 As defined by the World Health Organization's essential drugs programme.

Analyses of the impact of the financial recession on medicine utilization in Europe

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Objectives

To analyze the impact of the financial crisis by understanding the pharmaceutical pricing and reimbursement policy environment with its effects on pharmaceutical sales by volume and value in eight European countries. In specific, we look at the development of three variables: indicators for economic wealth, national pharmaceutical policies and pharmaceutical sales.

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Methodology

We used descriptive analysis of the economic indicator gross domestic product (GDP) and unemployment rate and the pharmaceutical policy context including policies changes between 2008 and 2011 as well as statistical analysis of quarterly pharmaceutical sales in IMS standard units and constant dollar by using looking at the difference of actual and projected values.

Results

Austria and Finland were among the economically stable countries prior and past the financial recession. Estonia, Greece, Portugal, Slovak Republic and Spain were categorized as unstable as unemployment rates rose and GDP decreased after the recession in the first quarter of 2009.

Conclusions

Economically less stable countries implemented a bundle of policy measures, whereas stable countries implemented only a few well planned policies. We could show that countries which implemented well in advanced systems changes - as it was the case in Finland with the implementation of the reference price system – lead to a reduction in sales and a moderate reduction on utilization. Whereas quickly implemented measures such as price cuts, lead to immediate reductions in sales but did not lead to stable utilization.



Off-label use of antiepileptic drugs and its costs – a drug utilization study in Portugal

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Background

According to the Portuguese Medicines Authority (INFARMED) the use of antiepileptic drugs (AEDs) has grown in the last few years eventually as a result of an off-label use.

An off-label use can be harmful for the patients as no clinical trials were performed in indications outside the SPC. It also increases costs for the National Health System (NHS) as these drugs are reimbursed in Portugal at the maximum level (95%).

Objectives

This study aimed to analyse the pattern of prescription and use of antiepileptic drugs (AEDs), being its main focuses the characterization of off-label use and its costs.

Methodology

Cross sectional survey, carried out from Sept. 2009 to Feb. 2010 in 20 pharmacies of Lisbon Region. *Inclusion criteria:* pharmacy users with a prescription including at least 1 AED (all medicines listed under the Anatomical, Therapeutic Chemical code N03-Antiepileptics having epilepsy in the SPC as main indication). Information was collected by interview, conducted by trained pharmacy students based on self-reported data. Prescription expenditures was obtained by crossing the official price of each medicine single unit at the time of the study, with data on posology reported by each patient. Aggregate annual expenditures were calculated based on that information.

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Results

Data from 543 patients was analyzed (61.3% females), age range 2-91 years (mean: 50.9). The main consumed AEDs were valproic acid (18.0%), pregabalin (16.2%), topiramate (15.7%) and carbamazepine (14.7%). The first prescriber was in 36.1% of the cases a neurologist and in 31.9% a psychiatrist. Epilepsy was the indication in 29.5% of the patients. Off-label use was found in 33.1% of the sample. Among the off-label sample, topiramate (28.2%), clonazepam (17.2%), valproic acid (16.7%) and gabapentine (10.9%) were the anticonvulsants most widely used off-label. Clonazepam (85.7%) and topiramate (59.0%) had most of their uses in off-label indications. Psychiatrists (59.2%) were the prescribers in the majority of the off-label cases. The main off-label indications were depression (31.4%) and mood stabilization (19.4%). Total costs with AEDs were 210,851.57€ in which 48,424.04€ (23.0%) represents off-label use costs.

Conclusions

Approximately 1/3 of the sample used AED's in off-label indications. Extrapolating to national data, it is estimated that more than €14 billion were paid for AEDs in off-label use (more than €13 billion paid by the NHS)

Analysis of antibiotic utilization in Brazil and Mexico before and after over-the-counter sales restrictions in 2010

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Background

In Latin American countries there are some common problems related to the use of antibiotics (AB) such as over-the-counter (OTC) sales. In 2010, Mexico and Brazil both implemented policies to enforce existing laws of restricting the OTC sales of AB to those who present a prescription.

Objective

To examine the trends and characteristics in antibiotic utilization in Brazil and Mexico before and after the OTC sales restrictions in 2010.

Methods

We analyzed retail quarterly sales data from IMS Health of oral and injectable AB between 2007 and 2012 for Brazil and Mexico. Consumption was calculated for all AB and for each therapeutic group including penicillins, macrolides and quinolones. The unit of analysis used was the defined daily dose per 1,000 inhabitants per day (DDD/TID) according to the WHO ATC classification system. We calculated the change in percentage of consumption between 2007 and 2012.

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Results

Between 2007 and 2012 total AB utilization increased in Brazil (from 5.66 to 8.45 DDD/TID, +49.3%) and decreased in Mexico (10.54 to 7.47, -29.2%). In both countries, penicillins had the largest percentage of consumption 33.8% out of the total in Brazil with an increase in consumption of 53% (from 1.91 in 2007 to 2.91 DDD/TID), whereas in Mexico this group occupied 38.6% out of the total consumption of ABs with a decrease in consumption of 34% during the time lapse studied (4.07 to 2.69 DDD/TID). The quinolones was the second largest group of consumption 14.5% out of the total with a change of consumption of 78% (0.82 to 1.46 DDD/TID) for Brazil; and 10.8% out of the total consumption in Mexico without changes between 2007 and 2012. The third largest group was the macrolides with 13.7% out of the total in Brazil with an increase of 60% (0.77 to 1.24 DDD/TID) while in Mexico the consumption decreased by 12% (1.13 to 0.99 DDD/TID).

Conclusions

Mexico and Brazil had different changes in consumption by subgroups between 2007 and 2012 after the policy implementation. The total consumption of AB decreased in Mexico while in Brazil the total consumption increased.



UN Relief and Works Agency for Palestine Refugees in the Near East's medicine procurement processes and prices: a comparative performance assessment

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Background

UN Relief and Works Agency for Palestine Refugees in the Near East (UNRWA), which is the main primary health-care provider for 4.9 million Palestinian refugees, including 2 million from the Gaza Strip and West Bank, occupied Palestinian territory, spent US\$18.3 million on essential medicines dispensed free of charge through clinics in five areas of operation (fields) – Gaza Strip, Jordan, Lebanon, Syria, and West Bank in 2010. Because of budget constraints and increasing demand for medicines to treat chronic illnesses, we assessed UNRWA's medicine procurement processes and prices of medicines.

Methods

In July 2011, we undertook 11 in-depth interviews with staff at UNRWA headquarters and selected facilities, and gathered data for procurement prices and amounts. WHO's operational principles for good pharmaceutical procurement were used as our framework for the assessment of processes. The prices of the top 80 medicines accounting for 93% of UNRWA expenditure on medicines were analysed and compared with international, regional, and national references. Headquarter and field prices were compared for the few medicines procured centrally and locally.

Findings

Analysis of the data indicated that UNRWA's procurement responsibilities are well defined, procedures are followed, and central procurement adheres strictly to UNRWA's formulary. However, only 101 suppliers were quality assured (prequalified) with UNRWA, of which 66 (65%) were from Europe or Jordan and only two (2%) were from East Asia. Criteria and processes for prequalifying suppliers were not clearly defined and there were few requirements for testing product quality. Despite open tenders, awarded prices were not reported or shared with bidders. Quantification of needs was according to previous allocations, and budgets were set at a field level without the possibility of interfield transfer. The lack of integrated information-technology systems hindered inventory management and information sharing. Prices obtained through central procurement did not differ from reference prices: median ratios of UNRWA's prices to the Management Sciences for Health, Jordan's Joint Procurement Department, and the Gulf Cooperation Council reference prices were 0.99 (IQR 0.66-1.49), 1.00 (0.73-1.47), and 0.98 (0.59-1.39) respectively. Antidiabetic medicines and antibiotics accounted for 30% and 14% of medicine expenditures, respectively. Application of the lowest comparator prices for the five products (one insulin, one oral antidiabetic and three β lactams) that accounted for about 20% of the total expenditure on medicines would save \$1.4 million. Local procurement was generally less cost effective than was central procurement, with notable differences across fields and products.

Interpretation

Our results indicate that UNRWA's procurement of medicines is competitive. However, to improve the process, the following are needed: establishment of regulatory standards for supplier prequalification and product quality assurance to obtain better prices by prequalifying more suppliers while focusing on product quality; reporting of prices of awarded tenders to increase competition and transparency; building of an integrated information-technology system to improve information sharing, quantification of needs, and monitoring of procurement; recentralization of medicine budgets to increase equitable allocation of resources.

The findings also show the burden of antibiotics and antidiabetic medicines on UNRWA's expenditures and the need for public health policies to target antibiotic overuse and preventable risk factors for diabetes.

Acknowledgements

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The influence of point estimates, variability, sample size and statistical power on the demonstration of bioequivalence between generics by adjusted indirect comparisons

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Rationale

Given that several generic products can be available and conducting bioequivalence studies between generics for regulatory purposes is impossible, indirect comparison between generics products is a useful approach to determine the bioavailability and interchangeability between them.

Objective

The objective of this study is to investigate the influence of point estimate and variability of bioequivalence studies on the success of demonstrating equivalence between generics by adjusted indirect comparisons.

Method

Simulations of point estimate differences and variability will be used to explore the maximum differences between point estimates in indirect comparisons. Based on previous work, the adjusted indirect comparisons assuming homogeneity of variances between studies will be used for the analysis. Microsoft Excel (MS) based data analysis tool will be used for the simulations and statistical calculations will be done using STATA software package.

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Health and crisis in Portugal

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Background and objective

In Portugal, the effects and consequences of the economic crisis since 2008 on the public health are still uncertain. This study aims at summarizing the current knowledge and relating it with the Portuguese reality.

Methodology

Online search in databases for scientific articles was conducted. Reports from public and private entities, news from the media and statistics were also used.

Results

The data suggests a degradation of mental health by economic stress and unemployment. Transmittable and chronic diseases may also rise through the increase of the susceptible population and the risk factors associated with the diseases. The pharmacy network is also at risk due to the politics at work; the supply of medicine in hospitals and community pharmacies may be at risk.

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Conclusion

The financial crisis places the entire public health at risk, and if no action is taken the deterioration of health indicators will be a reality. A paradigm shift is needed; public health should be faced as an investment for the rise in economic production and not as an expenditure.



Patient and Consumer Organisations at the European Medicines Agency: Financial disclosure and transparency

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Background

The transparency criteria adopted by the European Medicines Agency require eligible patient and consumer organisations to disclose the names and contributions of their public and private revenue sources. Despite various transparency initiatives, the exact funding sources of, and amounts received by, eligible organisations remain unclear. This research examines how many patient and consumer organisations eligible to work with the Agency (n=23 in 2010; n=34 in 2012) have received corporate sponsorship between 2006 and 2011 and how much. This article also studies the trends over time, both in terms of public disclosure of financial sponsorship, as well as in the amounts received.

Methods

Financial data were retrieved during two specific periods:

- from organisations' and pharmaceutical companies' websites, in January and February 2010, as well as through direct requests for the information placed in March 2010;
- from organisations' and pharmaceutical companies' websites, as well as from the European Commission's register of Interest representatives in July, August and October 2012.

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Results

Fewer than half of the 23 organisations met EMA's financial reporting guidelines in 2010. By 2012, more than 20 eligible organisations did not publish detailed corporate sponsorship they received, although data was retrievable from other sources for 14 of these groups.

The annual average corporate contribution per sponsored organisation rose from €185,500 in 2006, to €282,090 in 2007, to €321,230 in 2008. These amounts correspond to 47%, 51% and 57% of organisational average annual revenue, respectively. (Analysis for 2009 to 2011 is underway).

Conclusions

This study indicates low compliance with financial disclosure and transparency of the organisations working with the European Medicines Agency. Levels of corporate sponsorship differ greatly between those organisations that receive no financial support and others who rely upon it heavily. The lack of a uniform and detailed reporting system hinders complete public disclosure of the nature, and extent of, corporate sponsorship of these organisations.

This study focuses on the issue of corporate sponsorship of patient and consumer organisations active at the EMA. Further research is called for on financial transparency, and the nature of corporate sponsorship and conflicts of interests of civil society representatives in European health policy making.

Eligible organisations	2010 N=23	2012 N=34
Receiving financial sponsorship from corporate sources	15	23
Receiving funding entirely from other sources	7	5
Providing no financial data or revenue sources (not directly reported and unable to be retrieved)	1	6

Table 1: Characteristics of eligible organisations in 2010 and 2012

Perception of barriers in accessing opioid medicines

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Rationale

The Access To Opioid Medication in Europe (ATOME) project aims at improving access to opioid medication in twelve European countries by, among others, identifying barriers to access and making recommendations for improvement. Discussions with national representatives of the twelve European countries indicate that health-care professionals and decision makers may have a different perception of nature and scope of barriers to opioid use. A complete understanding of the (differences in) perception of barriers of both groups is crucial to develop widely supported strategies to lift these barriers and improve access to opioid medicines.

Objectives

To study the differences in perception of barriers concerning opioid medicines used in the field of pain management, palliative care and harm reduction, comparing health-care professionals and decision makers.

Methods

Data will be collected using a questionnaire partially constructed from already existing surveys. Questions from previous surveys were adjusted in order to address health-care professionals' and policy makers' perception of barriers and to avoid the use of stigmatising language. The questionnaire contains three sections: (1) knowledge and attitudes regarding medical use of opioids; (2) perception of barriers; and (3) respondents' personal and professional details.

A "true", "false" and "don't know/uncertain"-option will be used to evaluate response of the knowledge and attitudes section. The barriers- and feasibility section will be evaluated using a 5 point Likert scale with an additional "don't know/uncertain"-option. Participants of the ATOME national conferences will be invited to complete the questionnaire, which will be distributed by email after the conferences. Data will be analysed using SPSS® and comparison between groups will be conducted using χ^2 -tests (dichotomous variables such as knowledge questions) and non-parametric rank-sum tests (Likert scales). The questionnaire was reviewed for content validity by 4 experts in pain management, palliative care, harm reduction and policy and will be pilot-tested in Cyprus and Greece by an additional feasibility section.

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Ease and accuracy of subdivision of tablets by elderly people

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Introduction

Tablets often contain a score-line to facilitate breaking into equal portions. This may be needed in case no appropriate strength is available or as a cost-saving measure. The accuracy of breaking is of great importance for appropriate dosing. Furthermore, the ease of breaking is important. Especially for elderly people as not only they more often need to administer halved or quartered tablets, they often suffer from decreased hand strength. Several studies have shown that older people encounter problems with subdividing their tablets.

Objectives

This study aims to investigate the influence of the breakability method on the ease and accuracy of breaking tablets.

Methods

Twelve scored tablets (4 products, each of 3 different brands) are broken by 4 breakability methods: in between fingers with and without using nails, and pushing down with one finger with score-line faced up and faced down. The ease and accuracy of breaking are measured using test panels of elderly (≥ 65 yr) and younger people (20-30yrs). The ease of breaking is measured by the outcomes for experienced pain and difficulty of breaking. The accuracy of breaking is acceptable when the weight of both tablets halves is within 85%-115% of the theoretical halved tablet weight.

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Discussion on preliminary data

Not all tablets can be broken easily and elderly people experience more difficulty with breaking tablets than younger people. The preliminary data indicate that the accuracy and ease of breaking is influenced by the breakability methodology. Some tablets are broken easily by more than one method, the accuracy is often acceptable for only one. Further, the best method of breaking differs between the investigated tablets, even between medicines from different brands. This may lead to confusion by patients when the brand of their medicines is changed.



Alzheimer's Disease Opportunities to Address Pharmaceutical Gaps

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Alzheimer's disease is the most frequently diagnosed form of dementia. There are no available treatments that stop or reverse the progression of the disease, which *worsens as it progresses*, and eventually leads to *death*. Alzheimer's disease mostly affects people over the age of 65 years, although the less-prevalent *early-onset Alzheimer's* can occur much earlier with a progressive decline in memory, thinking, language, behavior and management of daily life.

As the world's population ages, Alzheimer's disease has become a health priority. In 2010, 36 million people were estimated to live in dementia worldwide, this number is expected to increase dramatically and reach a level of an estimated 65.7 million in 2030, and 115.4 million in 2050. By 2050, people aged 60 and over will account for 22% of the world's population with four-fifths living in Asia, Latin America or Africa. The financial costs of managing Alzheimer's disease in terms of both public and private resources are high and our healthcare and financial systems are not prepared to face the magnitude of the situation.

Little progress in terms of novel treatment or towards cure has been made since 2004. Nevertheless, there are advances in the area of biomarkers for diagnosis and monitoring disease progression. Screenings of patients still remain very expensive and new research is necessary to develop less expensive and more reliable tests. Several EU funded projects have been launched since 2004 that aimed at developing a standardised and objective solution to enable earlier diagnosis of Alzheimer's disease, improve monitoring of treatment efficacy, identify new targets for therapy and enhance cost-effectiveness of diagnostic protocols. Consortiums of top-level European research and industrial partners will need to act in this direction and contribute to strengthen the EU's leadership on the Alzheimer's disease research.

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