Utrecht WHO Winter Meeting 2012

5 - 6 January 2012

Utrecht - WHO Collaborating Centre

for Pharmacoepidemiology and

Pharmaceutical Policy Analysis

Utrecht, The Netherlands

Location: Faculty Club Helios, Utrecht

Programme Meeting report

World Health Organization

Universiteit Utrecht

Foto cover: Michael Kooren

Programme Meeting report

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Programme

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

World Health Organization

Universiteit Utrecht

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Welcome

We are very pleased to welcome all of you in Utrecht to the fourth edition of the Utrecht - WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis Winter Meeting. The meeting brings together around 50 researchers and policy makers from many different countries.

The meeting will start on Thursday with young researchers from different professional backgrounds who will discuss their ongoing or planned work. We sincerely hope that these discussions will contribute to bringing evidence-based policy making on pharmaceuticals to a higher level.

We have chosen "Bridging the worlds of medicines and medical devices" as central theme for the second day. This day will build on the outcomes of the Priority Medical Devices project produced under the direction of Josée Hansen. This project was initiated in 2007 by WHO in collaboration with the Dutch Ministry of Health, Welfare and Sports to determine whether medical devices currently on the market were meeting the needs of health care providers and end-users throughout the world and if not, to propose research to identify—and action to remedy—inadequacies or shortcomings. Invited speakers including those involved in the Priority Medical Devices project will discuss differences and similarities between medicines and medical devices and opportunities for joint learning.The meeting aims to involve all participants in summarising key lessons learned and identifying research subjects in the field of medical devices and medicines.

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 fruitful meeting with exciting discussions and inspiring new thoughts!

On behalf of the Organizing Committee,

Bert Leufkens and Aukje Mantel

General Information

Location

Faculty Club
Achter de Dom 7
3512 JN Utrecht
Phone: +31 (0)30 253 99 11

Date

Thursday, 5 January – Friday, 6 January, 2011

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
- Josee Hansen
- Bart Wijnberg
- Bert Leufkens

Department of Essential Medicines and Pharmaceutical Policies, World Health Organization

- Richard Laing

Time schedule

Thursday 5 January 2012

Presentations of ongoing pharmaceutical policy analyses

12:00-13:00	Registration, lunch	
13:00-13:15	Welcome	**Bert Leufkens (UU, MEB) + Richard Laing (WHO)**
13:15-14:45	Paper discussion - 2 parallel sessions 1a: Regulatory issues and challenges (room: Belle van Zuylen) 1b: Access to medicines (room: Kanunniken)	
14:45-15:30	Coffee break with poster session	
15:30-17:00	Paper discussion - 2 parallel sessions 2a: The added value of responsible use of medicines (room: Belle van Zuylen) 2b: Issues and challenges in rational use of medicines (room: Kanunniken)	
17:00-18:00	Drinks	
18:30-	Dinner (by invitation only)	

Friday 6 January 2012

'Everything you wanted to know about ..... but were afraid to ask' – Bridging the worlds of medicines and medical devices

From 8:30	Coffee	
09:00-09:15	Welcome	**Bert Leufkens (UU, MEB) + Richard Laing (WHO)**
09:15-09:45	Commonalities and differences between medicines and medical devices. How to get the best of both worlds?	**Josée Hansen (Dutch Health Care Inspectorate, former project leader WHO Priority Medical Devices Project)**
09:45-11:00	From research and development to market launch/authorisation – research choices from a public health perspective	Medicines: **Bert Leufkens (MEB)** Medical devices: **Gert Bos (BSI Group)**
11:00-11:20	Tea / Coffee	
11:20-12:30	Selection and health technology management and assessment – clinical choices in regions, countries and health care facilities	Medicines: **Richard Laing (WHO)** Medical devices: **Geoffrey Graham (WHO)**
12:30-13:15	Lunch	
13:15-13:30	Medicines and medical devices: two worlds not so much apart anymore	**Erik Vollebregt (Axon Lawyers)**
13:30-13:45	Bridging the academic worlds	**Speaker Technical University (tbc)**
13:45-14:30	Break out session in small groups – to discuss ways forward and research questions (clinical research, regulatory science, HTA and policy analysis)	
14:30-14:50	Tea / Coffee	
14:50-15:30	Group reporting and final discussions	
15:30-15:40	Wrap up and future (research) outlooks	**Josée Hansen + Bert Leufkens**
15:40-15:45	Day closure	**Richard Laing + Bert Leufkens**

Presentations of ongoing pharmaceutical policy analyses

Session 1a – Thursday 5 January 2012

13.15 - 14.45 - parallel session -

Regulatory issues and challenges
Session Chairs: (tbc)

Nr	Author	Title
1	**Ebbers**	A comparison of post-authorisation adverse events of biopharmaceuticals and small molecules
2	**De Vries**	Reliability of a patient-reported adverse drug event questionnaire
3	**Tafuri**	The level of transparency amongst regulatory agencies: the case of withdrawn and refused applications
4	**Putzeist**	Reasons for failure of new active substances in the EU: was it the drug or was it the development plan?

Session 1b - Thursday 5 January 2012

13.15 - 14.45 - parallel session -

Access to medicines
Session Chairs: (tbc)

Nr	Author	Title
5	**Onwuka**	Pharmaceutical Quality and Access in Nigeria: Evaluation of the Mobile Authentication Technology and stakeholder perceptions on quality and access
6	**Hessels**	The reasons behind a regulatory change around Tumour Necrosis Factor alpha inhibitors in Portugal and the impact on utilisation
7	**Jünger**	Legal and policy barriers to opioid availability in 12 European countries: results from a WHO self-assessment checklist for national situation analysis
8	**Vranken**	Legal and regulatory barriers in accessing opioid medicines in twelve European countries

Session 2a - Thursday 5 January 2012

15.30 - 17.00 - parallel session -

The added value of responsible use of medicines
Session Chairs: Veronika Wirtz (INSP) and Anke Hövels (UU)

Nr	Author	Title
9	**Wahlster**	Access to high cost medicines: a systematic review of the literature
10	**Stephens**	Variation in the use of NICE approved cancer drugs
11	**Tariq**	Disease trajectory economic evaluations: moving towards better practice
12	**Oliveira-Martins**	General practitioners' views and attitudes on generic medicines in Portugal

Session 2b - Thursday 5 January 2012

15.30 – 17.00 - parallel session -

Issues and challenges in rational use of medicines
Session Chairs: (tbc)

Nr	Author	Title
13	**Hernandez**	Long-term evidence on the effects of the regulatory warnings and increased media coverage on paroxetine use and other SSRIs
14	**Bijlsma**	The influence of guideline changes on user prevalence of benzodiazepine: age, period and cohort effects
15	**Ebenezer**	Pen-injecte2d insulin therapy: experiences and views of diabetic patients in Nigeria
16	**Ivanovska**	Measuring medicines use in children under 5: methodological issues and analysis of progress 1990-2009

Posters - Thursday 5 January 2012

14.45 - 15.30

Nr	Author	Title
17	**Ankrah**	Influence of adherence on switching from first to second line treatment among HIV patients in Ghana: a matched case-control study
18	**Gefenaite**	Effectiveness of the influenza A (H1N1)pdm09 vaccine in a community-based sample
19	**Hoebert**	Identification of priority policy research issues on access to medicines in low and middle income countries
20	**Philbert**	The 2009 H1N1 influenza A virus outbreak: adherence to national prescription guidelines for oseltamivir
21	**Sagwa**	The risk of ototoxicity in patients concomitantly treated for drug resistant-TB and HIV-1 infection
22	**Tetteh**	Outcomes of a post-exposure prophylaxis program at the Korle-Bu Teaching Hospital (KBTH) in Ghana

List of participants UU-WHO winter meeting 5 + 6 January 2012

(as of 22 December 2012)

Amr Makady	Utrecht University, the Netherlands
Anke Hövels	Utrecht University, the Netherlands
Anne Gosselin	Access to Medicines Foundationthe, the Netherlands
Arjan van Drongelen	RIVM, the Netherlands
Artur Moura	University of Lisbon, Portugal
Aukje Mantel	Utrecht University, the Netherlands
Barbara Kashi Carasso	Carashi Consult, the Netherlands
Barikpoar Ebenezer	Birmingham City University, United Kingdom
Bart Wijnberg	The Netherlands
Benard Miregwa	Ministry of Medical Services, Kenya
Bert Leufkens	Utrecht University, the Netherlands
Chioma Joy Onwuka	University of London, United Kingdom
Christine Häfele-Abah	German Medical Aid Organization action medeor e.V., Germany
Daniel Ankrah	Korle-Bu Teaching Hospital, Ghana
Daphne Philbert	Utrecht University, the Netherlands
Erik Vollebregt	Axon Lawyers, the Netherlands
Evans Sagwa	Management Sciences for Health, Namibia
Francisco Hernandez	Utrecht University, the Netherlands
Geoffrey Graham	WHO, Switzerland
Gert Bos	BSI Group, the Netherlands
Giovanni Tafuri	AIFA / Utrecht University, Italy
Hans Ebbers	Utrecht University, the Netherlands
Joëlle Hoebert	Utrecht University, the Netherlands
Jolanda de Bie	SIR Institute for Pharmacy, Practice and Policy, the Netherlands
Josee Hansen	Dutch Health Inspectorate, the Netherlands
Katrina Perehudoff	HAI Europe / Ghent University, the Netherlands / Belgium
Kim Notenboom	RIVM / CBG-MEB, the Netherlands
Kirti Narsai	PIASA, South-Africa
Luqman Tariq	GSK / Utrecht University, the Netherlands
Maarten Bijlsma	University of Groningen, the Netherlands
Marjolein Vranken	Utrecht University, the Netherlands
Michelle Putzeist	Utrecht University, the Netherlands
Niamh Herlihy	Access to Medicines Foundation, the Netherlands
Nina Winters	Utrecht University, the Netherlands
Peter Stephens	IMS Health, United Kingdom
Philip Wahlster	Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany
Priya Bahri	European medicines Agency, United Kingdom
Raymond Tetteh	Korle-Bu Teaching Hospital, Ghana
Richard Laing	WHO, Switzerland
Rose Higgins	HAI Europe, the Netherlands
Saskia Jünger	University Hospital Bonn, Germany
Sieta de Vries	University Medical Center Groningen, the Netherlands
Sofia Oliveira-Martins	University of Lisbon, Portugal
Sofie Hessels	Utrecht University, the Netherlands
Truus Janse-de Hoog	CBG-MEB, the Netherlands
Verica Ivanovska	University of Stip, Macedonia
Veronika Wirtz	National Institute of Public Health, Mexico
Waldo Weijers	CBG-MEB, the Netherlands
Wim Weber	BMJ, United Kingdom
Yaser Bazargani	Utrecht University, the Netherlands

Overview abstracts 5 January 2012

1

A Comparison of Post-Authorization Adverse events of Biopharmaceuticals and Small Molecules

Hans C. Ebbers[1], Esraa Al-Temimi[1], Ellen H.M. Moors[2], Aukje K. Mantel-Teeuwisse[1], Hubert G.M. Leufkens[1], Huub Schellekens[2,3]

1. Utrecht Institute for Pharmaceutical Sciences (UIPS), Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht University, Utrecht, the Netherlands
2. Copernicus Institute/Department of Innovation and Environmental Studies, Utrecht University, Utrecht, the Netherlands
3. Department of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht, The Netherlands

Background

The nature of adverse events (AEs) associated with biopharmaceuticals differs from chemically synthesized, small molecules, which may require a tailored pharmacovigilance approach for these products. However, there are substantial differences between approved indications for small molecules and biopharmaceuticals. The question remains how much of the differences in observed post approval adverse events (AEs) can be attributed to differences in approved indications for these two groups.

Objectives

To investigate if the nature of AEs identified post-authorization for biopharmaceuticals differ from the AEs of small molecules within the same therapeutic class.

Methods

All safety related changes to the Summary of Product Characteristics during 2004-2011 were analyzed. All products (small molecule and biopharmaceuticals) classified in the Anatomic Therapeutic Classification System as “antineoplastic and immunomodulating agents” (‘L’) were included. Individual AEs were identified and classified according to MedDRA. Group differences were tested using 2-sided Fisher’s exact tests.

Results

A total of 843 AEs were identified for 69 products. Of these, 440 belonged to biopharmaceuticals vs. 403 to small molecules. For biopharmaceuticals, 191(43.4%) of the AEs were reported for immunostimulants, 184 (41.8%) forimmunosuppressants and 65 (14.8%) for antineoplastic agents. The majority of the AEs of small molecules were reported for antineoplastic agents, which included 296 (73.4%) of AEs, 98 (24.3%) of the AEs were reported for immunosuppressants and 9 (2.2%) for endocrine therapies. AEs reported for products within the therapeutic subgroup of immunosuppressants were compared. AEs of biopharmaceuticals were more often classified as ‘neoplasms’, 19% vs. 3% ($p<0.01$) and ‘Infections and infestations’ 20% vs. 9% ($p=0.02$). AEs for small molecules were more often’ Renal & urinary disorders’ ($p= 0.02$) and ‘Blood & lymphatic system disorders’ 9% vs. 3% ($P=0.04$).

Conclusion

The distribution of AEs identified post authorization differs for biopharmaceuticals and small molecules, even in products from the same therapeutic subgroup.

2

Reliability of a patient-reported adverse drug event questionnaire

ST de Vries[1], FM Haaijer-Ruskamp[1], D de Zeeuw[1], P Denig[1]

1. Dept. Clinical Pharmacology, University Medical Center Groningen, The Netherlands

Background

Regulatory authorities advise the use of patient-reported outcome (PRO) instruments in the measurement of concepts which are best known by patients, like symptomatic adverse drug events (ADEs). Recently, we developed a generic PRO questionnaire to assess ADEs and their nature regarding frequency, duration, timeline, burden, severity and causality. This checklist-based questionnaire contains a wide range of ADEs described in lay terms and categorized by body system.

Objective

The objective of this study is to test the reliability and feasibility of the developed questionnaire. Specifically, the test-retest reliability, the impact of the ADE- categorization, and the reliability of various recall periods will be assessed.

Methods

The study consists of two parts both having a serial cross sectional design.

Part 1. Test-retest reliability and reliability of ADE-classification:
150 Patients with type 2 diabetes will be randomly divided in three groups. They will have to complete the questionnaire twice, partly using different versions of the questionnaire. One group will receive the questionnaire with ADEs categorized in body systems at To while receiving the questionnaire without the categorization at T1. The reverse is the case for the second group. The third group receives the same questionnaire twice to assess the test-retest reliability.

Part 2. Reliability of various recall periods:
200 Patients with type 2 diabetes are asked to keep a diary for recording possible ADEs during a period of 3 months, followed by the completion of the questionnaire. Patients are divided in groups and each group will receive a different recall period of the questionnaire.

The main outcome is the agreement in reported ADEs at body system level. The intraclass correlation coefficient will be used for assessing reliability. Differences between recall periods will be assessed using t-tests. Time needed to complete the questionnaire, and the percentage of missing items will be measured regarding the feasibility.

3

The level of transparency amongst regulatory agencies: the case of withdrawn and refused applications

Giovanni Tafuri[1,2], Francesco Trotta[1], Hubert G.M. Leufkens[2,3]

1. Italian Medicines Agency (AIFA), Rome, Italy
2. Utrecht Institute for Pharmaceutical Sciences, Utrecht University, The Netherlands
3. Medicines Evaluation Board (MEB), The Hague, The Netherlands

Background

A call for a greater transparency at the EMA and the FDA has been launched in the scientific community. Special attention has been posed in the US on the lack of disclosure of information related to drug applications withdrawn prior to the conclusion of the evaluation procedure or receiving negative opinion by the FDA. On the contrary, at the EU level this information is made publicly available by the EMA through the European Public Assessment Reports published on the Agency's website.

Objective

This analysis has two main objectives: i) to evaluate the availability of published information on drug applications withdrawn prior to the conclusion of the evaluation procedure, or receiving negative opinion at the end of it, among different regulatory authorities; ii) to identify the reasons leading to withdrawals and refusals of medicinal products at the EMA during the regulatory review process.

Methods

A written query has been sent to relevant regulatory authorities for which a contact detail was available.
Reports on withdrawals of applications related to all therapeutic categories as well as negative opinions were retrieved from the EMA website. Cut-off date for data retrieval was 31 December 2010. Post-approval withdrawals, which are usually related to pharmacovigilance issues, were excluded.

Results

The information on withdrawals is made publicly available just in the EU by the EMA and in Australia by the Therapeutic Goods Administration. With regard to the analysis on withdrawn/refused applications at the EMA, the majority of the active compounds were represented by four main categories: i) oncology/immunology drugs (34%), ii) CNS drugs (17%), iii) drugs for cardiovascular/metabolic diseases (16%), and iv) infectious diseases (14%).

The reasons leading to a withdrawal of a drug application or refusal can be related both to quality, safety and efficacy issues, sometimes a combination of the three: 106 objections were due to efficacy deficiencies, while 27 to safety and 23 to quality.
Within the efficacy objections, five main categories were identified, as follows: a) lack of clinical significance (44 out of 106), b) methodological issues (23 out of 106), c) PK issues including bioequivalence/non-inferiority (20 out of 106), d) lack of statistical significance (13 cases), e) five cases related to GCP issues.

Conclusions

Although there are still avenues for improvement of transparency in the regulatory authorities, the publication of the assessment reports of withdrawn and refused medicinal products seems a good starting point from a public health perspective.

[1] Drug regulatory authorities of Argentina, Australia, Brazil, Canada, Chile, China, Cuba, European Union, India, Japan, Mexico, Morocco, Namibia, New Zealand, Russia, Saudi Arabia, South Africa, Switzerland and the United States of America.

4

Failed drugs study: Reasons for failure of new active substances in the EU: Was it the drug or was it the development plan?

M. Putzeist[1,2], A.K. Mantel-Teeuwisse[1], C.C. Gispen-De Wied[2], A.W. Hoes[2,3], H.G. Eichler[4], H.G. Leufkens[1,2]

1 Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, the Netherlands
2 Medicines Evaluation Board, The Hague, the Netherlands
3 Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, the Netherlands
4 European Medicines Agency, London, United Kingdom

Rationale

The high failure rate of new active substances in the European marketing authorisation procedure is a serious concern that threatens current and future innovative drug development and access to innovative medicines. [1]. In this study we assess the association of the drug development plan and the benefit-risk assessment with marketing failure.

Methods

All marketing applications for new medicinal products with a first outcome in the centralized European marketing authorisation procedure between January 2009 and December 2010 were included. The development plan was divided in a learning phase and a confirmatory phase, each defined by five subvariables. An appropriate development plan was defined as having no major objection on any of these subvariables at day 120 of the marketing authorisation procedure. Determinants that described the benefit-risk assessment were clinical outcome (consisting of statistical significant effect on primary endpoint and serious safety issues) and clinical relevance. The study outcome was the opinion of the Committee for Medicinal Products of Human Use (CHMP) about marketing authorisation. Univariate relative risks and 95% confidence intervals (CI) were calculated for each determinant. A multivariate logistic regression analysis was conducted to assess to which extent the drug development plan or the benefit-risk assessment (clinical outcome or clinical relevance) were associated with marketing failure.

Results

In total 68 applications for new active substances entered the marketing authorization procedure, of which 23 (34%) failed and 45 (66%) were approved to the market. Of these 68 drugs, 50 (73%) had deficits in the development plan: in the learning phase only (N=9 (13%)), confirmatory phase only (N=19 (28%)) or both (N=22 (32%)). Aggregated analyses demonstrate that having both an inappropriate learning and confirmatory phase is significantly associated with marketing failure (RR 5.3 (1.2-23.6). The multivariate analysis shows that deficits in the clinical development plan (OR 10.4 CI95% 1.7-63.3), clinical outcome (lack of a statistical significant effect on primary endpoint or serious safety issues) (OR 9.7 CI95% 2.1-46.2) and lack of clinical relevance (OR 7.5 CI95% 2.0-58.5) are all associated with marketing failure.

Conclusions

An appropriate development plan, positive results on clinical outcomes and a validation of clinical relevance by regulators are very likely to lead to marketing authorisation, whereas deficits on any of these elements lead to intense discussions about marketing authorisation in which deficits of the development plan and clinical outcome, but in particular clinical relevance, are associated with marketing failure.

[1]. Eichler HG et al. New drug approval success rate in Europe in 2009; Nature Reviews Drug Discovery 2010: 9(355-356)

5

Pharmaceutical Quality and Access in Nigeria: Evaluation of the Mobile Authentication Technology and stakeholder perceptions on quality and access

Chioma Joy Onwuka[1], Barikpoar Ebenezer[2,3], Obinna Ekwunife[4]

1 The School of Pharmacy, University of London
2 Faculty of Pharmaceutical Sciences, University of Port Harcourt, Nigeria
3 Birmingham City University, United Kingdom
4 Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka

Rationale

There are very few studies involving qualitative field work to find out how different stakeholders perceive the problem of poor quality medicines and how it can be effectively tackled. Also there is very limited research determining the impact in practice of initiatives against medicines counterfeiting. This information is vital as it will guide development of interventions against medicines counterfeiting.

Objectives

The aims of this research are to evaluate the Mobile Authentication Technology and to identify wider issues related to accessibility of good quality medicines, from the perspective of Nigerian stakeholders

Design

Cross-country volume-weighted price analysis of a basket with 20 products in 15 countries in 2007 and 2008. Multivariable analysis was performed to account for differences on the gross domestic product, total pharmaceutical expenditure and the national employment in the pharmaceutical industry.

Methods

The study will be conducted in two phases. The first phase will involve quantitatively analysing metformin tablets (tagged Glucophage® and the cheapest available generic versions) randomly sampled from retail outlets in Lagos, Nigeria via Packaging analysis and visual inspection, Near Infra Red spectroscopy and High Performance Liquid Chromatography. Text messages will be sent as directed to authenticate the tagged Glucophage® tablets. The responses will be compared with results of the chemical analysis. The quality of the tagged Glucophage® samples will also be compared with the generic versions without the authentication tags.

The second phase will involve the use of semi-structured interview schedules for different groups of stakeholders; consumers, medicine sellers (community pharmacists, Patent Medicine Vendors, traders) and Policy makers. Purposive sampling would be used to sample the consumers and medicine sellers while snowball sampling will be employed to recruit the policy makers. Variables to be explored will be adapted from the socio-technical framework.
All quantitative data arising from the study will be analysed using the SPSS while Framework analysis will be used to analyse qualitative data.

Conclusion

This study will help to validate the Mobile Authentication Technology and explore issues related to accessibility of good quality medicines and the use of the Mobile Authentication technology from an independent stand point. This will aid formulation of recommendations for its implementation and future expansion.

6

The reasons behind a regulatory change around Tumour Necrosis Factor alpha inhibitors in Portugal and the impact on utilisation.

Sofie Hessels[1], Joëlle Hoebert[1], Aukje Mantel-Teeuwisse[1], José António Pereira da Silva[2], Francisco Batel Marques[3]

1. UIPS, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht, The Netherlands
2. Department of Rheumatology, University of Coimbra, Portugal
3. Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal

Purpose

To assess the reasons behind a policy measure around Tumor Necrosis Factor alpha (TNFalpha) inhibitors in Portugal and to study whether the policy measure led to a change in the amount of TNFalpha inhibitor used in the treatment of rheumatoid arthritis in the Coimbra region. Furthermore, to compare the effect of this policy measure with the effects of a policy measure around TNFalpha inhibitors in Norway.

Method

A literature research was conducted and interviews were held (n=3) with people involved in the prescription and/or regulatory aspects around TNFalpha inhibitors. In addition monthly volume data (in packs and DDDs) from three TNFalpha inhibitors (adalimumab, etanercept and infliximab) were derived from the University Hospital of Coimbra (HUC Hospital) (Portugal) and from the Norwegian Institute of Public Health. For both countries the data covered the period January 2003 - December 2010. Data on gender and age were available from the University Hospital of Coimbra.

Results

The policy measure in Portugal was taken to facilitate prescription of TNFalpha inhibitors by extending the prescription to the outpatient setting. However, in the HUC hospital a decrease in volume of TNFalpha inhibitors between January 2003 and December 2010 was found: formula of the trendline in defined daily doses (DDDs) before the policy measure: $y = 63{,}218x + 1993{,}8$ ($R^2 = 0{,}6199$) and after the policy measure: $y = 12{,}573x + 5808{,}6$ ($R^2 = 0{,}0295$). In Norway a decrease in volume of TNFalpha inhibitors was also found but this was the intended purpose of the policy measure ($y = 0{,}0283x + 0{,}4485$ ($R^2 = 0{,}9118$) versus $y = 0{,}0156x + 1{,}6967$ ($R^2 = 0{,}8366$)). The average age of patients using TNFalpha inhibitors increased a little in time after 2005 till 2010 from 45 till 51. The average age found for female patients was higher than male patients, except for adalimumab in 2004-2006. The Portuguese patient association (ANDAR) was pleased with the policy measure because it should lead to an easier access to treatment with TNFalpha inhibitors. This was in contrast with rheumatologists, which were not pleased by the fact that internist may also prescribe TNFalpha inhibitors and by the lack of control in private prescribing.

Conclusion

Policy measures do not always seem to work out as expected as shown by this example. Therefore when designing a policy measure, it is important to involve all concerned parties to discuss how and if the policy measure can reach its main goal.

7

Legal and policy barriers to opioid availability in 12 European countries: results from a WHO self-assessment checklist for national situation analysis

Saskia Jünger[1], Marjolein Vranken[2], Tom Lynch[3], Sheila Payne[3], Kees de Joncheere[4], Willem Scholten[5], Lukas Radbruch[1,6]

1. Department of Palliative Medicine, University of Bonn
2. Utrecht Institute for Pharmaceutical Sciences, Division Pharmacoepidemiology & Clinical Pharmacology, Utrecht University
3. International Observatory on End of Life Care, Division of Health Research, Lancaster University
4. WHO Country Office Ukraine, Kiev, Ukraine
5. Access to Controlled Medicines, World Health Organization
6. Centre for Palliative Medicine, Malteser Hospital Bonn/Rhein-Sieg

Aims

A sound analysis of legal and policy barriers to opioid availability is a prerequisite for improving access to opioids on a national level. The WHO Guidelines "Ensuring balance in national policies on controlled substances" include a country assessment checklist for analysing potential barriers to opioid availability. Within the ATOME project it was aimed at having country teams from the 12 target countries complete the checklist as a basis for their national action plans on improving access to opioids.

Methods

The teams were invited to complete the checklist and hereby explore to what extent the WHO Guidelines are met in their country. Each item of the checklist can be answered with yes/no/unknown, to be specified with explanations and a note as to whether action is required for that specific topic.

Results

To date, checklists from 8 countries are available for analysis. The results show that practical barriers do not always coincide with the formal / legal positive provisions for access to opioids. For example, 1 country stated that despite having a provision in their law that controlled medicines are absolutely necessary for medical and pharmaceutical care, health care professionals could not be free from fear of investigation, prosecution or disproportionate punishment when prescribing or administering opioids. Likewise, 2 countries reported an absence of training courses on rational use of controlled medicines for physicians, pharmacists and nurses whilst having a government policy that urges medical, pharmaceutical and nursing schools to provide education on this issue.

Conclusion

The results confirm findings from previous research that there may be discrepancies between the legal provisions regarding rational use of opioids and the actual barriers in medical practice. The findings highlight the need for a combined approach on the levels of legislation, policy, health care and education for an effective improvement of access to opioids for medical use.

8

Legal and regulatory barriers in accessing opioid medicines in twelve European countries

Marjolein Vranken[1], Saskia Jünger[2], Tom Lynch[3], Aukje Mantel-Teeuwisse[1], Marie-Hélène Schutjens[1]

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2. Department of Palliative Medicine, University of Bonn, Bonn, Germany
3. International Observatory on End of Life Care, Division of Health Research, Lancaster University, Lancaster, United Kingdom

Aims

Aims

Methods

A method to identify legal and regulatory barriers to opioid medication was developed focusing on six different categories of barriers (importation/exportation, prescribing, dispensing, manufacture, registration and miscellaneous) in twelve European countries (Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Serbia, Slovakia, Slovenia and Turkey). Legislation was obtained from key experts who were selected based on their expertise in the field of pharmaceutical law and health policy. The legislation was analyzed ('quick scanned') using WHO criteria. Overly restrictive provisions were identified, as well as provisions that contain stigmatizing language and incorrect use of definitions. The selected provisions were independently scored by two reviewers into two categories: 1) a probable barrier and 2) a potential barrier. A barrier was recorded if both reviewers concurred witch each other.

Results

Legislation was obtained from eleven European countries. All eleven countries showed legal and regulatory barriers in the areas of prescribing (most frequently observed barrier). Several (but not all) countries showed barriers in other categories, but no barriers concerning the manufacture of opioid medicines were identified. Ten countries showed stigmatizing language and incorrect use of definitions in their legislation. In total five countries showed more than twenty-four barriers in their legislation. The number of identified barriers was the lowest for Cyprus (‹15).

Conclusion and discussion

This study shows that legal and regulatory barriers can be identified using a quick scan method. Commonalities in the selected countries include the areas of prescribing and the use of stigmatizing language and incorrect use of definitions. Additional research is needed to assess the extent of the barriers and their impact on access to opioid medicines.

9

Access to high cost medicines: a systematic review of the literature

Philip Wahlster[1]

1. Interdisciplinary Centre for Public Health and Health Technology Assessment (IZPH) at the University of Erlangen-Nuremberg (FAU)

Problem Statement

Healthcare systems in western countries face increased rationing of drugs due to the incresaing costs related to medicines. There is an ongoing debate regarding the availability and funding of newer expensive medicines, often termed as “high cost medicines”.

Objective

Aim of this project is to provide a critical review of the literature pertaining to high cost drugs. The specific objectives were to identify the viewpoints and perceptions of different stakeholders regarding “access to high cost drugs” and to identifying barriers which influence the access and usage of high cost drugs. This knowledge would help us to formulate policy questions which inturn could be neficial to improve access for patients.

Stakeholders involved

Politicians, decision-makers, physicians, patients, public.

Methodology

Retrospective review of the literature published between 1999 to 2010: Different databases were searched for papers about high costs drugs. We found 374 papers and selected 39 for the final analysis and synthesis of the systematic review.

Results

Many stakeholders are concerned about the challenges regarding high cost drugs. They worry that physicians might not consider certain medicines if they cause high out-of-pocket drug costs for patients. Patients want to be informed about all treatment options, however, even if they cannot afford them. Viewpoints of the stakeholders and barriers to access were identified on several levels.

Conclusion

This review concludes that stakeholders agree that access could be promoted through transparency and involvement of all stakeholders, especially patients and public in the decision making process. The relationship of physicians and patients are affected by high cost drugs. Moral issues and the rule of rescue could have a big influence on the decisions regarding increasing inequalities, especially empowered by the media. Barriers normally lead to inequality. There is a complex interdependence of access limitations, opportunity costs and the fourth hurdle.

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Variation in the use of NICE approved cancer drugs

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Introduction

An alternative to comparison of total volumes across countries may be to apportion volume by indication using sample data. This paper examines use in advanced Non Small Cell Carcinoma (aNSCLC), metastatic Colorectal Cancer (mCRC) and advanced Renal Cell Carcinoma (aRCC).

Objectives

To describe:

i. use according to NICE guidelines across countries
ii. the influence of treatment size, age and relative adherence to NICE guidelines
iii. the clinical impact of variation

Settings

(A) Physicians in France, Germany, Italy, Spain and UK contributing pseudonymised records to IMS' sample database, Oncology Analyzer between April 2010-March 2011 (aNSCLC=2651 records; 1st line mCRC=2156; 1st line aRCC=724; 7 drugs assessed and approved for the 3 conditions, 7969 records).
(B) Pharmacies releasing data to IMS on total volume dispensed

Outcome measures – use within NICE guideline by country

(1) Total kilograms divided by number of people dying from lung, colorectal and kidney cancer as appropriate (Globocan, 2008)
(2) % eligible patients treated
(3) Planned treatment size
(4) Proportion treated aged >70
(4) Impact of variation on costs, survival, Quality Adjusted Life Years

Results – use within NICE guideline

(1) Total kilograms used for mCRC and aRCC similar across countries.
Total kilograms for aNSCLC in UK significantly lower.
(2) % eligible population treated within NICE guidelines significantly higher in the UK
(3) Significant differences in planned treatment size in aNSCLC but insufficient to explain volume variation
(4) No consistent evidence of bias against elderly
(4) Limited or no efficacy data or models for majority of non-recommended regimens. Where assumptions deemed to be reasonable, results suggest NICE guidance impact on survival greater for mCRC but QALY impact greater for aRCC.

Discussion

aNSCLC results suggest differences in diagnosis, referral or attitudes to treatment/toxicity. Impact analysis thwarted by the absence of data.

Contributions

PS devised the concept and method, the summary of the NICE guidelines and cost-effectiveness data and for all data analysis. VC, JW and CA extracted data and advised on interpretation of data elements.

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Disease Trajectory Economic Evaluations: Moving Towards Better Practice

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Abstract

In the Netherlands, economic evaluations are used by health policy decision makers to take policy and reimbursement decisions about the introduction of new health technology. Currently, health policy decisions are taken based on cost-effectiveness ratios resulting from economic evaluations of single interventions. Also, economic evaluations of different alternatives from different health care domains (prevention, cure, care) are compared to each other while taking health policy decisions on health care spending. In addition, methodology applied in economic evaluations vary greatly in terms of model inputs, model assumptions, costs and effects identification, measurement and valuation.

In this paper, we provide the rationale for performing disease trajectory economic evaluations which can help base health policy decision making on cost-effective ratios from a whole disease trajectory. A disease trajectory economic evaluation would provide an overview of the cost-effectiveness of the whole disease trajectory, from preventive measures till the required care at home, resulting in a disease trajectory cost-effectiveness ratio (DTCER). This ratio would not be a sum of individual ICERs of interventions, but would be calculated based on a disease-trajectory chain model, one unique core set of assumptions, and a consistent way of identification, measurement and valuation of costs and effects of interventions which are part of the disease trajectory. Performing disease trajectory economic evaluations requires (i) Markov chain-models in order to provide an overview of the cost-effectiveness of the disease trajectory, (ii) consistency in the methodology applied in economic evaluations in order to make the study results comparable, and (iii) a different societal threshold value for costs per Quality Adjusted Life Year (QALY) gained. Disease trajectory economic evaluations can be of added value to health policy decision makers to maximize health gains while spending the health care budget, meanwhile leading to comparable study results based on consistent methodology applied in economic evaluations.

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General practitioners' views and attitudes on generic medicines in Portugal

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Background

Over the past decades, drug expenditure has risen rapidly in most of the countries and a trend to control these increases is to encourage the use of generic drugs (GD).
Portuguese market share of GD is low as compared with European countries. The proportion of GD available on prescription has increased substantially in recent years, but market share of GD by volume only amounted to 17.5% in May 2010.
Physicians are at the centerpiece of medication use process and it is recognized that prescription is the main decision-making process regarding the consumption of a drug. Thus it is important to examine the prescriber's perceptions about GD.

Objective

To characterize beliefs and attitudes of prescribers in relation to GD.

Methodology

Cross sectional study (April-September 2009). Information was gathered from a panel of 140 general practitioners' working in health centers from the 5 Health Regions by interview (structured questionnaire). Data regarding prescribed therapy to patients was based on medical records (15 patients per doctor).

Results

Response rate was 86.4%.
Most respondents (over 3/4) considered that GD have effectiveness and safety at least equivalent to those of branded drugs, but admitted that economic power of their patients was a decisive factor in the option of prescribing a GD (>85%).
Nearly half of physicians (45%) considered there is no guarantee of bioequivalence of the GD relatively to the original product and that replacement of an original drug by the corresponding GD would compromise the patient's adherence to therapeutic regimens (35%).
Almost 3/4 of the respondents considered that their patients had a similar degree of confidence in GD relatively to branded drugs.
The surveyed physicians prescribed a total of 5342 medicines (1765 patients), from which 48.7% were generics. The higher percentage of generic prescriptions occurred for Digestive (64.3%), Endocrine/metabolic/nutritional (55.3%) and Psychological (51.2%) conditions.

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Long-term evidence on the effects of the regulatory warnings and increased media coverage on paroxetine use and other SSRIs

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Background

The SSRIs and suicidality controversy has played an important role in triggering public debates on the integrity of the pharmaceutical system. We used this controversy to assess if there is an association between the regulatory warnings and increased scientific and Dutch and British newspapers coverage on SSRI use in the Netherlands (NL) and in the United Kingdom (UK) from January 2000 to December 2009.

Methods

Monthly SSRIs sales data for the NL and the UK (IMS Health) was calculated into DDD/1000 inhabitants/day. The GIP-database provided yearly SSRI insurance/claims data stratified by age group (only NL). Use trends were analyzed with time series analyses to estimate associations between SSRIs use and the intervention (warnings and newspaper coverage).

Results

From 2000 to 2009, SSRI use increased 2-fold in the UK and 1.7-fold in NL. UK used 1.5-fold (SD:0.14) more SSRIs than NL. Paroxetine irrecoverable dropped in UK after May 2002 (pre-warnings), whereas citalopram use escalated from 2000 to 2009. This growth on citalopram use was also perceivable in the NL. The use of paroxetine moderately decreased in the NL after January 2006. Paroxetine was the most used SSRI in the NL, whereas in the UK was fluoxetine. SSRIs use within Dutch age groups showed 13-fold drop of paroxetine after 2000 in pediatrics, 5.7-fold after 2002 in adolescents, 4-fold after 2001 in young adolescents, 1.2-fold increment until 2004, followed by 1.4-fold drop in adults, and 1.2-fold growth in elderly until 2009.

Conclusion

Neither the warnings, nor increased media attention were associated with less SSRI's use in both countries. On the contrary, SSRI's use doubled during the study period. However, stratified analyses per individual SSRI and age groups showed a significant drop of paroxetine (most directly associated SSRI with suicidality). Thus, warnings and negative media attention about this controversy did not affect overall SSRI prescription behavior by Dutch and British doctors.

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The influence of guideline changes on user prevalence of benzodiazepine: age, period and cohort effects

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Rationale

Benzodiazepine has a large number of users in Western countries, a large proportion of which is a chronic user. Chronic use is, among others, caused by dependency. In order to curb benzodiazepine use, general practitioners were advised to prescribe sparsely to new users in 2002.

Objectives

To examine the effect of guideline changes on the user prevalence of benzodiazepine by looking at birth cohort trends in addition to age and period trends.

Methods

We used drug dispensing data from community pharmacies covering 500,000 individuals (IADB.nl). Our study population consists of individuals aged 18 to 85 in the Netherlands in the period 1994-2008. First, we compared age specific prevalences plotted by period (age-period plots) with age specific prevalences plotted by birth cohort (age-cohort plots). Secondly, we specified an age-period-cohort model.

Results

User prevalence, the number of individuals with a minimum of one benzodiazepine prescription per 1000 population, decreases with time. Older birth cohorts have higher user prevalence than younger birth cohorts. User prevalence of benzodiazepine remains stable within birth cohorts, possibly because of addictive effects. As older birth cohorts leave the population, overall benzodiazepine user prevalence declines. The guideline change appears to have affected the youngest birth cohorts especially.

Conclusions

The combined examination of age, period and birth cohort patterns provides additional insight for benzodiazepine and can aid the description, explanation and prediction of trends in drug use.

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Pen-injected Insulin Therapy: Experiences and Views of Diabetic Patients in Nigeria

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Rationale

There are very limited studies conducted in Nigeria to describe patients' experiences of their transition from syringe-injected insulin therapy to pen-injected insulin therapy and the impact on their diabetic management and social lives.

Objectives

The objectives of this research are to document the experiences of patients in their transition to the use of pen-injected insulin therapy in the context of their glycemic control, safety and economic implications, describe the advantages and disadvantages of syringe-injected and pen-injected insulin therapy from patients' perspectives, assess the satisfaction of patients on pen-injected insulin therapy compared to syringe-injected insulin therapy and make recommendation on the use of insulin administration devices from the perspectives of patients.

Method

A descriptive cross sectional study will be conducted. Diabetic patients meeting the inclusion criteria will be recruited from community pharmacies in Port Harcourt Nigeria. Data will be obtained using Semi structured interviews with the selected participants and from patients' medical record of their HbA1C and blood glucose levels. Interviews will be transcribed verbatim and analysed using the constant comparative analysis approach while all quantitative data will be analysed using the SPSS statistical software.

Outcome

The study will inform future health policy and provision to diabetic patients based on the information obtained from patients' perspectives on the experiences of using different insulin administration devices.

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Measuring Medicine Use in Children Under 5: Methodological issues and analysis of progress 1990-2009

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Background

Many low- and middle-income countries (LMIC) have tried to improve treatment of child acute illnesses, but scant evidence exists about progress.

Objectives

To undertake a systematic review of studies in order to provide an overview of medicine use in children under 5 years in LMIC and identify effective interventions.

Search strategy and mathods

Quantitative data was systematically extracted from published and unpublished studies from 1990 to 2009 on medicine use in children under 5 years in primary health care in LMIC. Pertinent data was entered in WHO database providing details on study setting, methodology, interventions, and outcomes based on standard indicators of medicines use.

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To estimate trends over time, the average of each indicator was calculated (limited to baseline data for interventions) by study year, region, facility ownership and prescriber type. To estimate intervention impacts, summary effect sizes was calculated for studies meeting accepted design criteria. The indicator with the greatest effect size (GES) and the median effect size (MES) over all indicators were examined.

Results

Data was extracted for 394 studies conducted in 78 countries; 75% reported data from the public sector and 25% from the private-for-profit sector. From 1992 to 2009, we observed no improvements in percentage of pneumonia cases treated appropriately with antibiotics and non-pneumonia cases receiving inappropriate antibiotics. Treatment of childhood diarrhoea remains poor in regards to diarrhea cases treated with ORS and diarrhea cases treated inappropriately with antibiotics, and only use of antidiarrheals shows improvement. Public sector practices tended to be better than private sector.

Interventions were reported in 57% of studies, but of those only 20% used adequate study design. Multi-component interventions tended to have larger effects than single-component ones.

Conclusions

Treatment of child illness remains suboptimal in LMIC. Although many well-designed interventions reported positive effects, there has been no observable improvement in practice.

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Influence of adherence on switching from first to second line treatment among HIV patients in Ghana: A matched case control study

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Background

As we embark on a lifelong activity of antiretroviral therapy (ART), adherence to selected treatment regimen stands out as one of the most important areas to tackle if we should make any gains. Non-adherence to treatment will certainly jeopardize treatment benefits as a result of treatment failure. This will lead to substitution of therapy which in most instances is more expensive, even though benefits may not differ significantly. In HIV/AIDS treatment where effective adherence threshold has been estimated to be around 95%, a concerted effort is needed from both health workers and patients alike so as to meet set targets. This research examines the effect of adherence to ART on treatment switching among HIV/AIDS patients in Ghana.

Objectives

The main objective will be to determine the effect of adherence on switching from first to second line treatment among HIV/AIDS patients on antiretroviral therapy.

Methods

Adherence will be measured using the proportion of days covered (PDC) approach. The study period will be from 1st January, 2004 to 31st December, 2009. All those on first line treatment who were switched to second line treatment during the study period will be classified as cases. Controls will be chosen randomly from among the rest of the moving cohort who did not experience any therapy switch. Controls will be individually matched to cases on index date on a one control per case basis. To account for matching at the design stage conditional logistic regression will be used for the analysis.

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Effectiveness of the influenza A (H1N1)pdm09 vaccine in a community-based sample

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Background

Evidence about influenza A(H1N1)pdm09 vaccine effectiveness comes mostly from case-control studies. As case-control studies are susceptible for selection and confounding bias, we performed a population-based cohort study to assess the pandemic vaccine effectiveness (VE).

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Methods

We conducted a retrospective population-based cohort database study during the pandemic influenza season 2009-2010 among 66709 18 years and older adults. The primary outcome was medically attended influenza when medication was prescribed (MAIm). The vaccination status was recorded if at least one dose of the influenza A(H1N1) pdm09 vaccine was administered. Analyses were stratified by age (18-59 and 60 years and older) and adjusted for confounding by using the propensity score (PS) as a continuous covariate in the logistic regression. PS included comorbidities, MAIm and visits to the general practice during one year preceding A(H1N1)pdm09 pandemic season.. To adjust for unmeasured confounding we performed the analyses during a reference period when no effect of the vaccine was anticipated (odds ratio of one (OR=1)) and divided the OR during the period of anticipated vaccine effectiveness by the OR during the reference period.

Results

The cohort consisted of 47707 (71.5%) 18-59 years old and 19002 (28.5%) 60 years and older subjects. During the pandemic season the vaccine reduced MAIm, notably in subjects 60 years and older (adjusted OR .18 [95% confidence interval (95% CI) .04-.94]). The VE analysis during the reference period has shown some remaining bias (adjusted OR .74, 95%CI .14 – 3.92), after additional adjustment for unmeasured confounding the vaccine effectiveness slightly decreased (OR=.24).

Conclusions

The vaccine showed to be effective in preventing MAIm in subjects 60 years and older, but it did not seem to have a large effect in younger subjects. Adjusting for unmeasured confounding led to slightly lower vaccine effectiveness.

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Identification of Priority Policy Research Issues on Access to Medicines in Low and Middle Income Countries

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Background

The Alliance for Health Policy and Systems Research (AHPSR) at WHO has recently conducted a priority setting exercise in 15 Low and Middle Income Countries (LMIC) to identify country level policy issues and relevant health policy and systems research questions in the field of Access to Medicines (ATM). These issues and research questions have been documented in 12 country reports and 4 regional reports. This specific study aimed to generate consensus about a core set of research issues, identified from these reports, that urgently require attention in order to facilitate policy development in the field of Access to Medicines.

Methods / Results

There were three key inputs into this specific priority setting process: a) the development of a framework for research and analysis, b) the analysis of relevant country reports to identify cross-cutting priority issues, and c) key informant interviews with a group of internationally recognized experts (n=23) to validate the identified policy issues.

The framework that was developed brought together the areas Rational Selection and Use, Affordable Prices, Sustainable Financing, Reliable Health and Supply systems as developed by WHO in 2004 and the levels at which constraints operate as identified by Hanson et al. in 2003. These levels are Individual, Household and Community, Health Service Delivery, Health Sector, National Context – public policies cutting across sectors, and International and Regional level. The priority policy concerns were extracted by 2 independent reviewers by means of cross-checking and validation of discrepancies by returning to the original report and re-analysing content. The global level key informant interviews were held with people working at WHO, academia or NGOs or in international organizations such as World Bank or Global Fund.

The overview of country reports was instructive in showing which policy issues had been identified as important. The outcomes of the key informant interviews showed consistency with the issues identified in the reports although some additional issues were identified, such as the issue of substandard drugs.
Based on these outcomes, a priority agenda for health policy and system research questions on access to medicines will be established in March 2012.

2 Countries included: Cambodia, Laos, Viet Nam, Thailand, Colombia, Suriname, Dominican Republic, El Salvador, Lebanon, Iran, Pakistan, India, Cameroon, Chad, Gabon, Congo

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The 2009 H1N1 influenza A virus outbreak: adherence to national prescription guidelines for oseltamivir

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Background

The national guideline for prescribing oseltamivir during the 2009 H1N1 influenza A pandemic was adapted throughout the year. After August 7th, prescribers were advised to restrict prescriptions to patients with influenza symptoms as well as at least one additional risk factor. In this study we assessed whether oseltamivir was prescribed according to the national guideline, and investigated how patients used oseltamivir.

Methods

Pharmacists in 19 pharmacies belonging to the Utrecht Pharmacy Practice network for Education and Research (UPPER) selected all patients with a prescription for oseltamivir between August 7 2009 and February 8 2010, to be able to assess adherence to the most current guidelines. These patients were contacted for a structured telephone questionnaire.

Results

A structured questionnaire was completed for 300 patients. Of all responders, 111 (37%) received a prescription 'off-guideline' (not having both flu symptoms and at least one risk factor). Responders aged over 18 with a higher education level were two times more likely to receive an oseltamivir prescription off-guideline than responders with a low education level. Nearly all responders who received oseltamivir in accordance with guideline criteria started treatment (184 out of 189 responders, 97.4%), while only half of the off-guideline responders started treatment (62 out of 111 responders, 55.9%).

Conclusion

One in three patients who received an oseltamivir prescription during the H1N1 pandemic did not meet the guideline criteria for a prescription. In addition, nearly half of the patients who did not meet guideline criteria also did not start the oseltamivir course. It is important to make sure prescribers are properly informed about current guidelines, to reduce overprescribing due to lack of information. Furthermore, improving communication between prescribers and patients might help relieve patients' concerns and increase awareness about the limited benefits of oseltamivir treatment in healthy individuals.

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The risk of ototoxicity in patients concomitantly treated for Drug resistant-TB and HIV-1 infection

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Introduction

In Namibia, there is a high proportion (59%) of TB patients co-infected with HIV, which complicates treatment of drug-resistant TB. Aminoglycosides, which are used in second-line DR-TB regimens, are known to be ototoxic. Are antiretrovirals ototoxic too? The data available is contradictory, limited, and inconclusive (Berke, 2010; Katijah, 2011). Hearing loss was common (29%) in patients on ART and being aged ≥ 35 years was a risk factor (Marra et al., 1997). Prospective studies are needed to determine the incidence of tinnitus and hearing loss among DR-TB/ HIV-1 co-infected patients and the influence of the use of NRTIs on the risk of ototoxicity (Shouten et al., 2006). Drug-drug interactions, concomitant use of other ototoxic drugs (NRTIs?) and noise exposure may have an influence on the ototoxicity of aminoglycosides.

Research Question

Does the combined use of second-line anti-TB medicines and NRTIs increase the risk of ototoxicity in patients concomitantly treated for DR-TB and HIV-1 infection, as compared to those treated with second-line anti-TB medicines alone?

Design and Methods

Prospective cohort, with 2 groups, followed up for 9 months: (1) DR-TB only (aminoglycoside-containing anti-TB regimens) and (2) DR-TB and NRTIs (aminoglycoside-containing anti-TB regimens + NRTIs + HIV).

Sample size calculation

Related to structure a specific central distribution facility where prescriptions were prepared for delivery was organized. RECASA could count on a specific budget, information system and human resources. Not all procedures were adequately standardized and communicated to professional involved. Consistency problems between information entered in the computerized system and medical records. Most of patients (91.6%) declared to be satisfied with RECASA but only 1% were found to be totally adherent according to MBG scale.

Cohort	Expected prevalence of ototoxicity	Sample size
DR-TB therapy only (aminoglycoside-containing anti-TB regimens)	45%	108
DR-TB + HAART		
(aminoglycoside-containing anti-TB regimens + NRTIs)	70% (about RR =1.5)	108

Sampling

Consecutive sampling of patients initiating DR-TB treatment and DR-TB treatment + HAART, all ages, both genders, excluding those with prior hearing problems, prior exposure to occupational noise, other aminoglycoside treatment (e.g. streptomycin).

Data Analysis

Descriptive statistics; bivariate analysis-relative risk (RR), chi-square; and multivariate Cox PH analysis.

Results

This will be available after execution of the study.

Conclusion and Recommendations

The findings may have implications for the improved audiological monitoring of patients on both DR-TB treatment and NRTI-based HAART.

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Outcome of a post-exposure prophylaxis program at the Korle-Bu Teaching Hospital (KBTH) in Ghana

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Background

The risk for occupational exposure to HIV is a serious public health problem and has been well characterized in the developed world. However, limited information is available about this transmission risk in a resource-constrained setting facing the largest burden of HIV infection. In addition, the feasibility and utilization of post-exposure prophylaxis (PEP) programs in these settings are unclear. Ghana has developed guidelines on the use of post exposure prophylaxis since the implementation of free antiretroviral in December 2003. Therefore, we examined the rate and characteristics of occupational exposure to HIV and the utilization of PEP among health care workers (HCW) and health care students (HCS) in the Korle-Bu Teaching Hospital (KBTH), the largest, urban government teaching hospital in Ghana.

Methods

Demographic and clinical data on occupational exposures and their management were retrospectively collected from December 2005–December 2010. Data reviewed included drugs administered and adverse events reported. US Centers for Diseases Control guidelines were utilized to define risk exposures, for which PEP was recommended. Descriptive statistics and chi-square test was employed to assess association among variables. Incidence rates of reported exposures and trends in PEP utilization were examined using logistic regression. P-value less than 0.05 was considered statistically significant.

Results

Of 1930 HCW and 1400 HCS, a total of 260 and 35 exposures were reported by HCW and HCS respectively. The incidence rate was 13.5 and 2.5 exposures per 100 person-years (PY) respectively for HCW and HCS. Ward attendants reported the greatest number of exposures with an annual incidence of 38.8 per 100 PY. The incidence of high-risk exposures was 2.0/100 PY (n = 65); 60.0% occurred during a procedure of disposing of a needle and 24.6% during a canula insertion. A total of 98.5% (64) patients of high-risk cases began an extended PEP regimen of which only 54.7% completed it with 37.5% who stopped due to adverse drug reactions (ADR). The most experienced ADR was nausea which was reported by a total of 69.8% of those given 3TC/AZT/PI, 29.5% of those given 3TC/AZT and 33.3% of those administered 3TC/AZT/EFV. There was no HIV seroconversion identified.

Conclusions

The PEP service in the Korle Bu Teaching Hospital has revealed interesting outcomes which should be used to improve on the policy adopted for the service. With implementation of a hospital-wide PEP program, there was an encouraging decrease of high-risk exposures over time and appropriate use of PEP. More sensitization sessions should be held for the staffs especially ward attendants as they continue to report late for PEP despite the fact they are relatively more prone to having a needle stick injury.


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