

# Epidemiology of poor-quality medicines

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BOSTON UNIVERSITY

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JULY 10<sup>TH</sup>, 2017

**MORU**  
Tropical Health Network  
**LONWRU**



LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



**IDDO**  
INFECTIOUS DISEASES DATA OBSERVATORY



## SÃO PAULO **Epidemic of counterfeit drugs causes concern in Brazil**

The problem of counterfeit drugs in Brazil has finally received the attention it deserves. During the past few weeks, there have been reports of 200 suspected unwanted pregnancies caused by use of a dummy contraceptive pill and several deaths attributed to a false anticancer drug.

Emergency action was taken by the Ministry of Health—and even by Congress—but experts predict that the population will have to live with the risk of buying counterfeit drugs for a long time. Nevertheless, the scandal produced some good results: consumers became aware of the risk, and politicians approved a law that

theft but kept it secret for 30 days while conducting their own investigations. If Schering do Brasil had made an immediate public alert, unwanted pregnancies might have been avoided.

At almost the same time, news broke that a dummy drug for the treatment of prostate cancer (also produced by Schering do Brasil) was

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**“It is estimated that 10% of the annual Brazilian pharmaceutical production is either stolen or falsified”**

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Official and press inquiries continued, and it was disclosed that about 30 technicians working for the National Secretariat of Health Surveillance (a department of the Ministry of Health) were assistants to local pharmacists in the region of Brasilia. This prompted the resignation of the head of the department, Marta Nóbrega. A Gonzalo Vecina Neto, was appointed by the minister. The minister also announced that the health surveillance secretariat was transformed into an independent agency, similar to the US Drug Administration.



# Once again, children are the main victims of fake drugs

Maurizio Bonati

Within a fortnight in November 2008, 34 Nigerian children, aged 4 months to 3 years, died and more than 50 others were hospitalised with severe kidney damage after taking the drug “My Pikin” (“my child” in local pidgin), a teething mixture containing paracetamol.<sup>1</sup> The outbreak was due to the use of diethylene glycol (DEG)<sup>2</sup> as a solvent for the paracetamol. DEG was present because of inadvertent or deliberate substitution of propylene glycol, which is much less toxic than DEG and is widely used in the pharmaceutical industry.<sup>3</sup> DEG is a colourless and odourless liquid, commonly used in industry, and can

Acute renal failure is an unusual cause of death among children. Thus, when an outbreak occurs, there are two main possibilities: infection or poisoning. Bacterial cultures and viral tests can confirm an infection, whereas chemical analyses of both biological samples and suspected products are needed to identify the toxic substance. Unfortunately, in developing countries the availability of chemical and biological diagnostic tests is limited. Additionally, the only effective renal management of DEG poisoning is haemodialysis or peritoneal dialysis. Thus, these tragedies affect the health rights of

# The Lahore disaster

## *2011-2012*

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125 cardiology patients died in Lahore with bone marrow failure after taking 'isosorbide mononitrate 20mg'

However, it contained an excessive dose of the antimalarial pyrimethamine, resulting in fatal bone marrow suppression

Probably a gross factory error (i.e. substandard) but was it criminal negligence ?



Ref. RHT/SAV/M

2<sup>nd</sup> July 2015

**Adverse**

**tral Africa**



Centre Publications Countries Programmes Governance About WHO

**Media centre**

**Counterfeit medicines: the silent epidemic**

## Kenya: fake HIV drugs detected

Date Published: 03/10/2011 09:57

On 5th and 7th September, Médecins Sans Frontières MSF (Doctors Without Borders) missions in Kenya detected quality problems with one antiretroviral medicine (ARV) named Zidolam-N used to treat people with HIV.

MSF nurses reported irregularities on the appearance of the product such as friability and discoloration of the tablets.

### Supply lapse

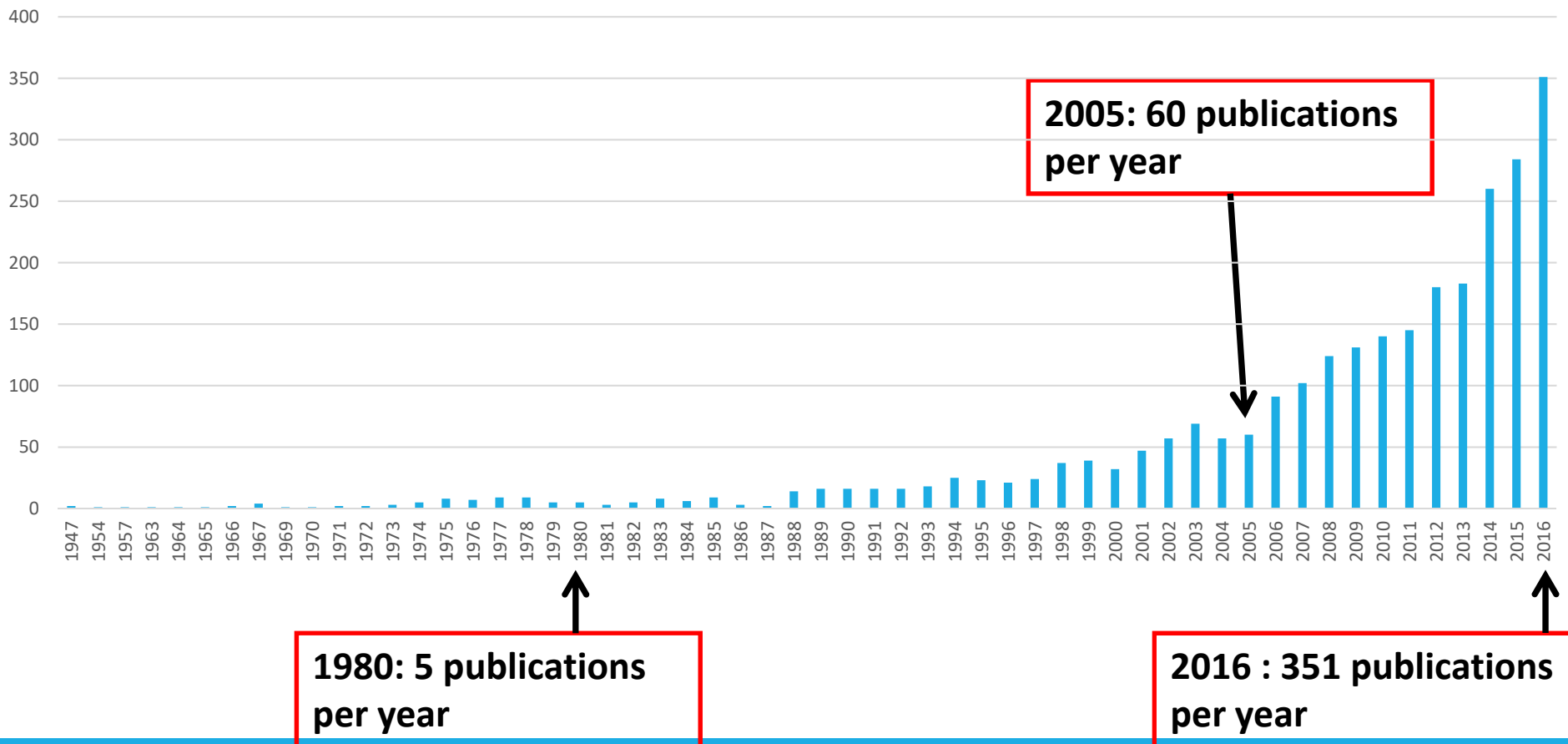
Last week, these ARVs were confirmed to be falsified versions of World Health Organization (WHO) quality-assured ('prequalified') drugs that were purchased via a distributor certified by the Kenya Pharmacy and Poisons Board.

Fake ceftazidime (containing streptomycin), flu vaccine, rabies vaccine, 'insecticide-treated' bednets, HIV tests.....

### Non-communicable diseases:

Poor quality paracetamol syrup, blood pressure medicines, anti-cholesterol medicines, condoms, oral contraceptive pills, diabetes test strips, cardiac stents, emergency pills, oral antidiabetics, anti-cancer medicines, heparins.....

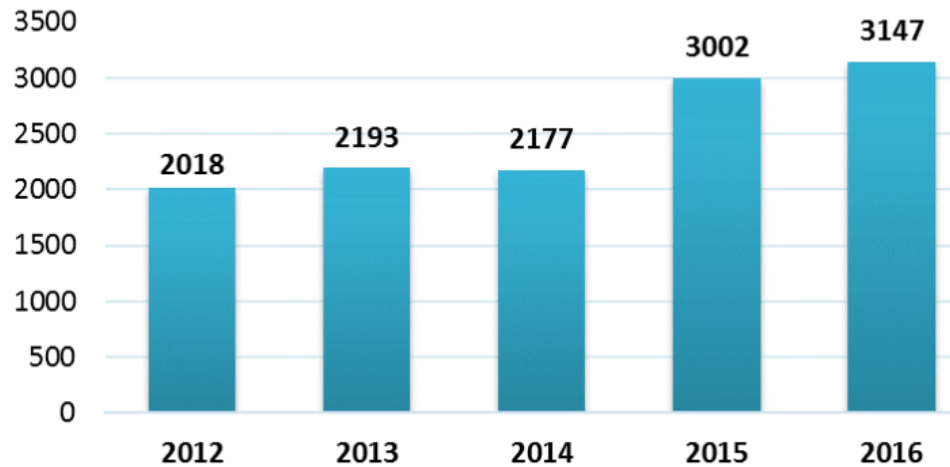
# Scientific literature



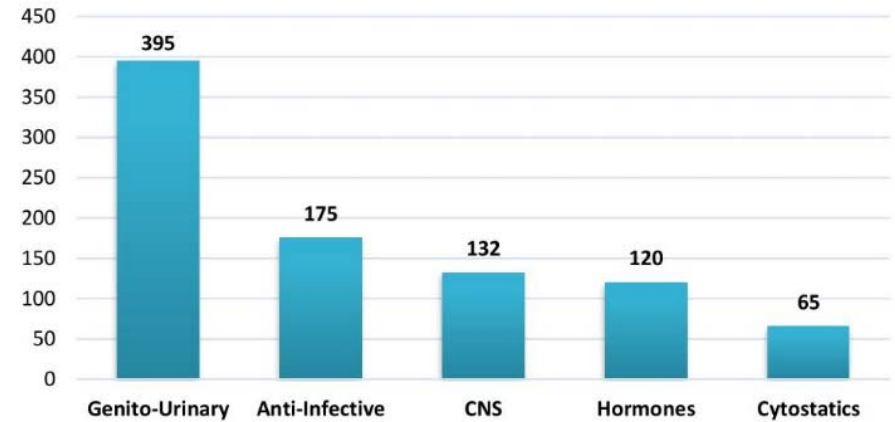


# Pharmaceutical Security Institute

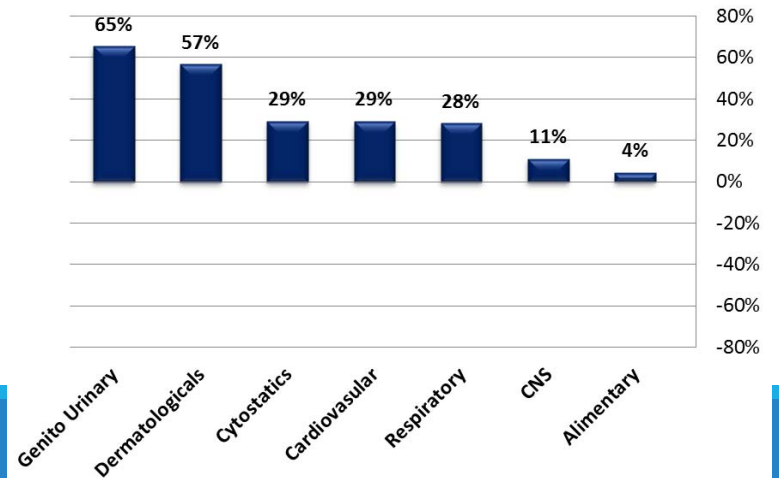
### Total Number of Incidents CY 2012 - CY 2016



### CF Incidents & Therapeutic Categories Top Five - CY 2016



### Therapeutic Categories Counterfeit Incidents Percent Change CY 2015



# Epidemiology of Poor Quality Medicines (PQM)

*Many questions...few answers*

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What are we talking about?

How common are PQM? Who is affected?

Geographical distribution?

Significance for patients and public health?

Determinants?

Impact of interventions?

.....



# Sources of information

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WHO rapid alert

WHO – reports

United States Pharmacopeia Database

Scientific literature, AJTMH press release; 2015

E-drug, E-med

Quamed

Pharmaceutical Security Institute

Securing Industry

WWARN/IDDO

Partnership For Safe Medicines – USA, India, China

EDQM – European Directorate for the Quality of Medicines

.....

# Sources of information Newspapers

## TRAFFICKING OF COUNTERFEIT VIAGRA IS EXPLODING IN SPAIN

Posted on 18 November 2015



**daily sun**

Online Today's Newspaper Magazine E-paper

National Business World Sports Entertainment Health Life Style

### FRONT PAGE

#### 128 substandard medicines on the market

Tarik Hasan Shahriar 29 October, 2015 23:49



HEALTH Syndrome: A mobile court backed by SAJ members busted a fake medicine factory at Mirpur Cantonment, Dhaka, on Thursday. Sun photo

**bdnews24.com**  
Bangladesh's First Internet Newspaper

LATEST: Jessore man shot hours after arrest in 'shootout'

Home > Bangladesh

### Doctor couple held for manufacturing spurious medicines in Chittagong

Mosstafa Yusuf, bdnews24.com  
Published: 2015-12-14 14:45:07.0 BIST | Updated: 2015-12-14 14:45:07.0 BIST



Pharmaceutical Packaging and Labeling Infographic

News / China / Society / CRIME

### Police in southern China raid labs churning out fake Viagra and antibiotics

PUBLISHED: Tuesday, 29 September, 2015, 7:58pm  
UPDATED: Tuesday, 29 September, 2015, 7:42pm



### THE PERUVIAN AUTHORITIES UNCOVERED 50 ILLEGAL PHARMACIES SELLING COUNTERFEIT MEDICINES

Posted on 18 November 2015



SOCIÉTÉ

### Saisie de 2 millions de comprimés de médicaments contrefaits

PUBLIÉ LE VENDREDI 9 OCTOBRE 2015 À 1 H 55 | Mis à jour le 9 octobre 2015 à 2 h 07



La SQ, la CRC ainsi que les policiers de Laval et de Longueuil ont démantelé un réseau de fabrication et d'exportation de médicaments contrefaits. Ils ont saisi plus de 2 millions de comprimés. PHOTO: JACQUES BISSONNET



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Pharmaceutical Food & Beverage Electronics & Industrial Cosmetics

Fake Xanax claims two more lives in California

**entorno INTELIGENTE**

CONTENIDO ORIGINAL ÚLTIMA HORA SALUD BELLEZA SUCEOS INTERNACIONAL TECNO NEGOCIOS

Inicio > SUCEOS | Publicada el Viernes, 21 de Agosto del 2015

### COLOMBIA: Cae red de traficantes de medicamentos falsificados



Vente illicite de médicaments à yeumbeul: 200kg de produits contrefaits et

# Sources of information

## Medicines Regulatory Authorities

**CENTRAL DRUGS STANDARD CONTROL ORGANIZATION**  
 DIRECTOR GENERAL OF HEALTH SERVICES,  
 MINISTRY OF HEALTH AND FAMILY WELFARE,  
 GOVERNMENT OF INDIA

HOME ABOUT US ACTS AND RULES EVENTS STATE DRUGS CONTROL FAQs RELATED LINKS RTI TENDERS VACANCY CONTACT

You are here: HOME | Safety Alerts

**Safety Alerts**

Sr. No	Name
1	Drugs banned in the Country
2	Medical Device and Diagnostics Alert
3	ORDER IN RESPECT OF STOP COLLECTION AND SALE OF GENETIC CELLS
4	Oxytocin Drug Alert
5	Surveillance of Drugs Manufactured in the Country by CDSCO

File No. DDC (I)/SD/Misc.-21/2015  
 Directorate General of Health Services  
 Central Drugs Standard Control Organization  
 (O/o Drugs Controller General India)

FDA Bhawan, Kotla Road  
 New Delhi-110002  
 Dated: -

To,  
 All State/U.T. Drugs Controllers

Subject: Oxytocin Drug Alert-regarding

U.S. Department of Health and Human Services

**FDA** U.S. Food and Drug Administration  
 Protecting and Promoting Your Health

Home Food Drugs Medical Devices Radiation-Emitting Products

### Drugs

Home > Drugs > Drug Safety and Availability > Drug Recalls

### Drug Recalls



FOR IMMEDIATE RELEASE

HEALTH SCIENCES AUTHORITY  
 PRESS RELEASE  
 16 JANUARY 2004

HSA DETECTS COUNTERFEIT CIALIS AND CAUTIONS  
 AGAINST BUYING FROM ILLEGAL SOURCES

NATIONAL AGENCY FOR FOOD AND DRUG  
 ADMINISTRATION AND CONTROL  
**NAFDAC**

HOME PRODUCTS GUIDELINES REGULATIONS PUBLICATIONS

LATEST NEWS AND EVENTS **RECALLS & ALERTS** REPORT A PROBLEM

5% Dextrose Injection Up In Pab Container Recall- Leakage And Particulate Matter  
 Written on Wednesday, 25 May 2016 11:28



**MINISTERIO DE SALUD**  
**DIRECCIÓN DE REGULACIÓN DE PRODUCTOS DE INTERÉS SANITARIO**  
 San José, Distrito Hospital, Calle 16, Avenidas 6 y 8, Edificio Norte 4º piso  
 Teléfonos: 2258-6765 / 2257-2090 Fax: 2257-7827 / 2257-20-90

### EMA warns of tampered, falsified Herceptin

Vials of Roche's breast cancer drug Herceptin - stolen in Italy - have been falsified and re-introduced into the EU supply chain, according to the European Medicines Agency (EMA).



ALERTA SANITARIA

FALSIFICACIÓN DE PROPOFOL

11 de setiembre del 2015

# Pharmacovigilance and PQM

Drug Saf (2015) 38:373–382  
DOI 10.1007/s40264-015-0271-2

ORIGINAL RESEARCH ARTICLE

## Using VigiBase to Identify Substandard Medicines: Detection Capacity and Key Prerequisites

Kristina Juhlin · Ghazaleh Karimi · Maria Andér · Sara Camilli · Mukesh Dheda · Tan Siew Har · Rokiah Isahak · Su-Jung Lee · Sarah Vaughan · Pia Caduff · G. Niklas Norén

Drug Saf  
DOI 10.1007/s40264-016-0499-5

SHORT COMMUNICATION

## Identification of Substandard Medicines via Disproportionality Analysis of Individual Case Safety Reports

Zahra Anita Trippe<sup>1,2</sup> · Bruno Brendani<sup>1</sup> · Christoph Meier<sup>2</sup> · David Lewis<sup>1,3</sup>

## Uppsala Monitoring Centre, WHO

- VigiBase assessment
- Retrospective study
- Limited potential of the database to detect signals to PQM

The screenshot shows the WHO website interface. At the top, there is the WHO logo and navigation links for 'Home', 'Publications', 'Countries', 'Programmes', 'Governance', and 'About WHO'. Below the navigation is a search bar. The main content area features a news article titled 'A possible boost for patient safety in South-East Asia region' with a sub-header 'Essential medicines and health products'. The article includes a large group photograph of people at a meeting and a caption: 'WHO annual meeting of national pharmacovigilance centres in New Delhi on 4-6 November'. A sidebar on the left contains a menu with links for 'Medicines and health products', 'About us', 'Access', 'Innovation', 'Regulation', 'Publications', 'News', and 'Contacts'.

Establishing close links between national pharmacovigilance centers, medicine analysis laboratories and pharmaceutical inspectorate ----> **Ensuring rapid responses to suspected PQM**

# How common are PQM?

*Estimation - 2006*

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Globally 10% of medicines = PQM

<1% in most developed countries

10-30% in many developing countries

≥ 50% of medicines purchased over Internet from sites that conceal their actual physical address



Changes through time and space



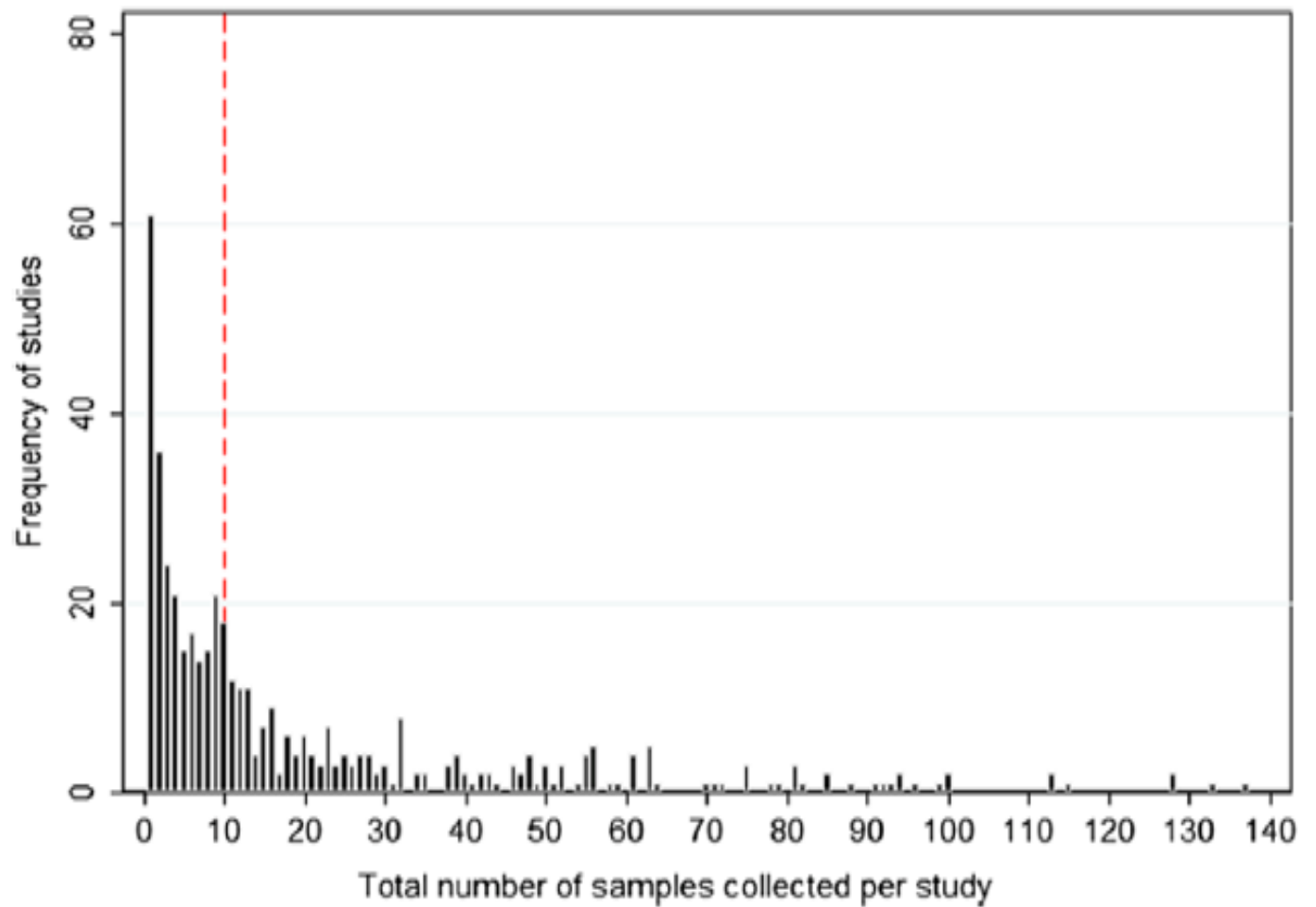
# Evaluating the scale of PQM

## *Challenges*

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- Diverse methodologies
  - Sampling strategies
  - Definitions and terminology
  - Covert vs Overt collection
- Small sample sizes





**Figure 5** Number of samples collected per survey. The red line represents ten samples per study.


# Evaluating the scale of PQM

## *Challenges*

---

- Diverse methodologies
  - Sampling strategies
  - Definitions and terminology
  - Covert vs Overt collection
- Small sample sizes
- MEDQUARG rarely followed

Different thresholds to determine quality

- Techniques and assays
  - Pharmacopeia followed
- 

# Understanding the epidemiology of PQM

*Poor quality antimalarials*

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- Systematic review of reports publicly available in English, French, Spanish
- Between 1946 and 2013

Tabernerero *et al. Malaria Journal* 2014, **13**:139  
<http://www.malariajournal.com/content/13/1/139>



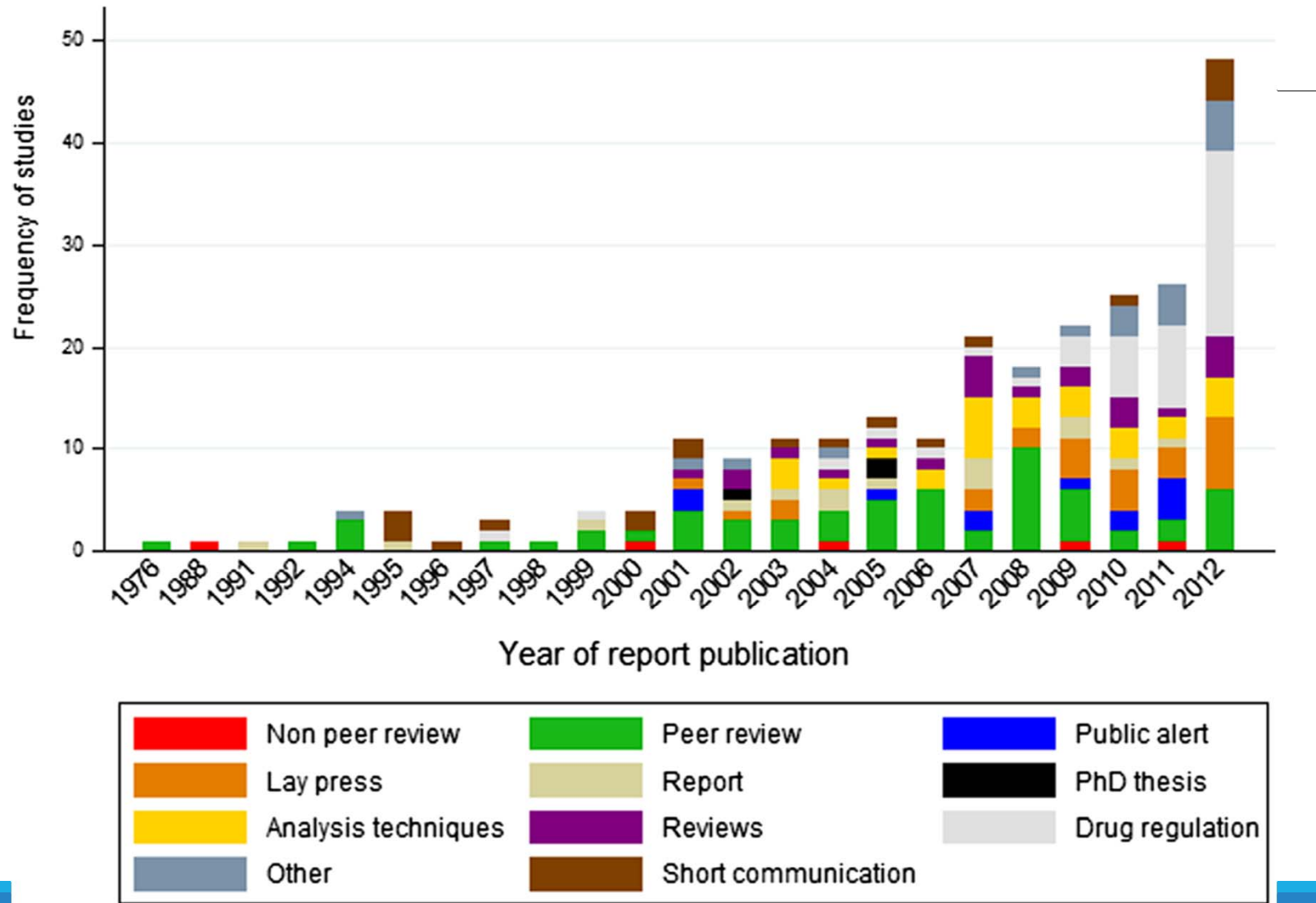
**RESEARCH**

**Open Access**

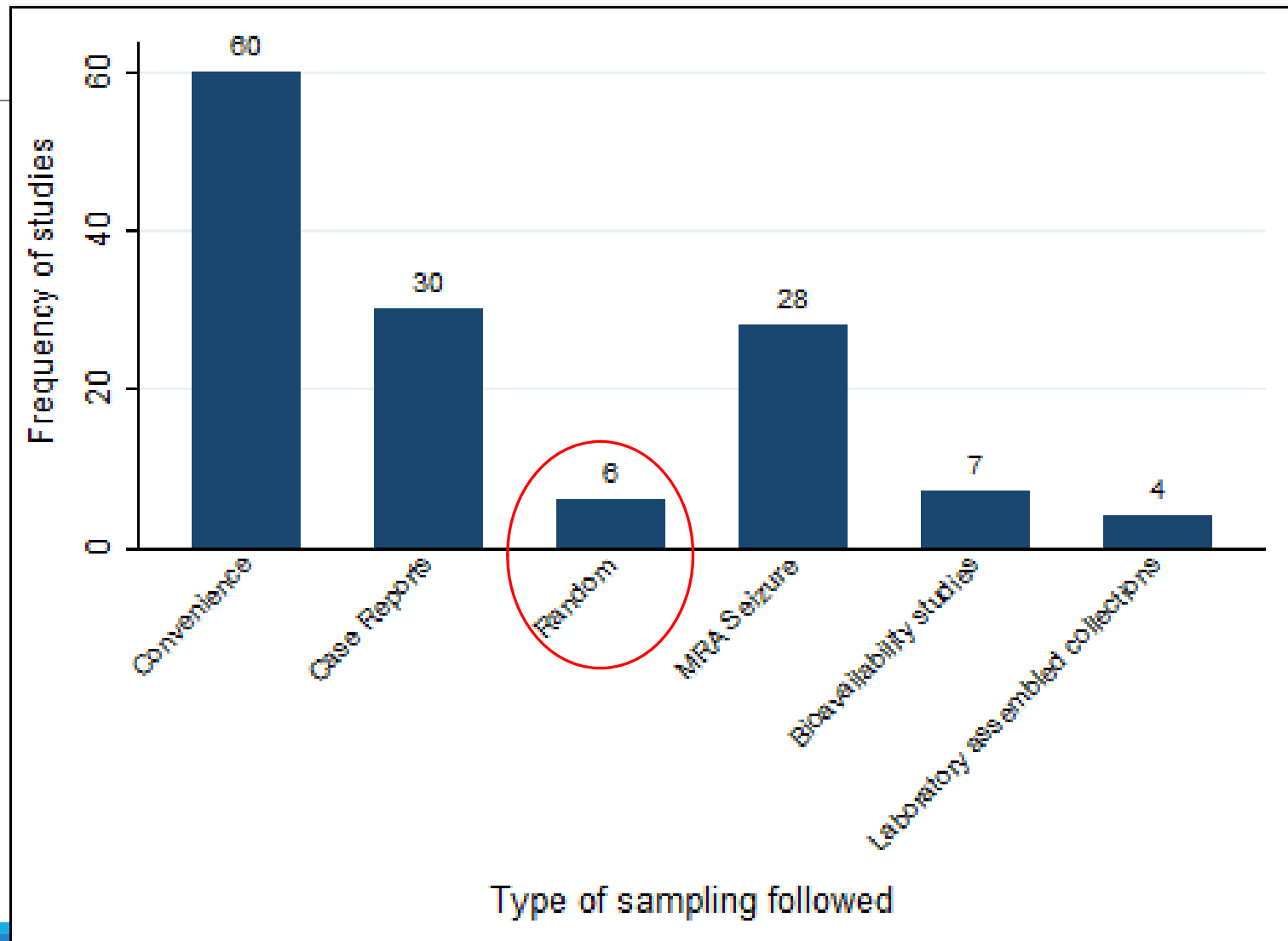
Mind the gaps - the epidemiology of poor-quality anti-malarials in the malarious world - analysis of the WorldWide Antimalarial Resistance Network database

Patricia Tabernerero<sup>1,2,3\*</sup>, Facundo M Fernández<sup>4</sup>, Michael Green<sup>5</sup>, Philippe J Guerin<sup>1,2</sup> and Paul N Newton<sup>1,2,3,6\*</sup>

# Reports by type and year



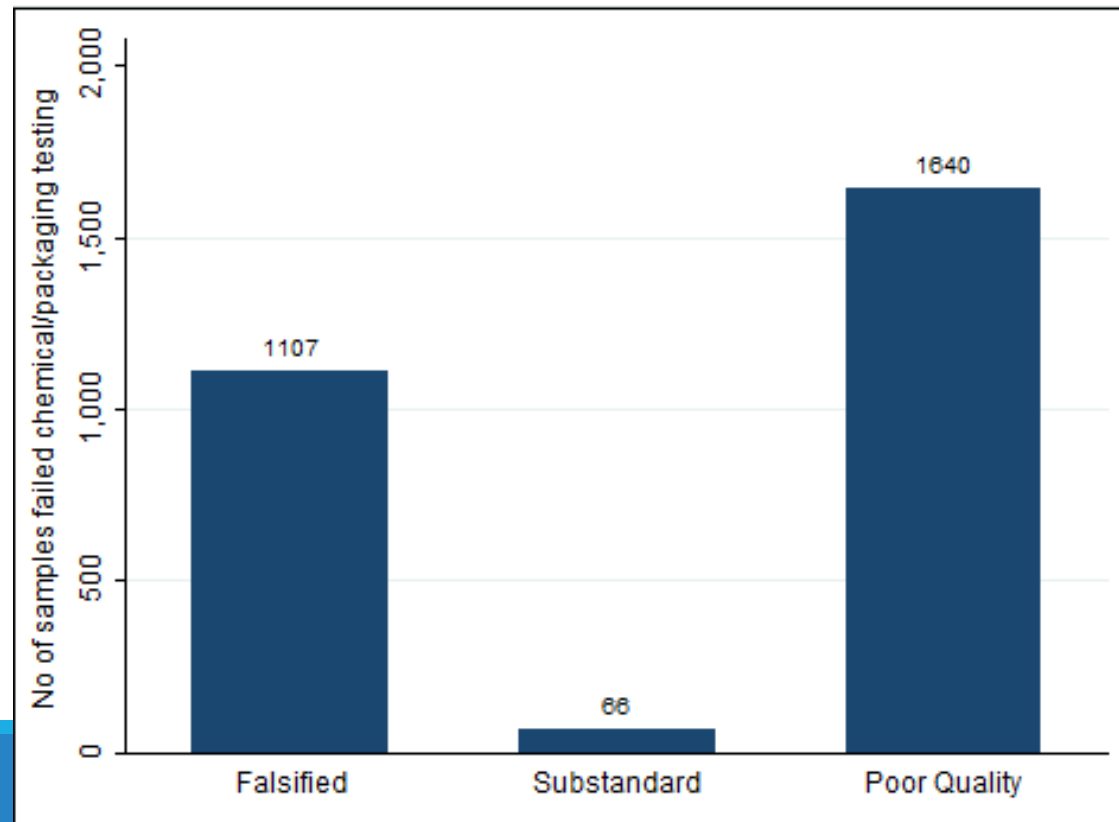
# Reports by sampling type



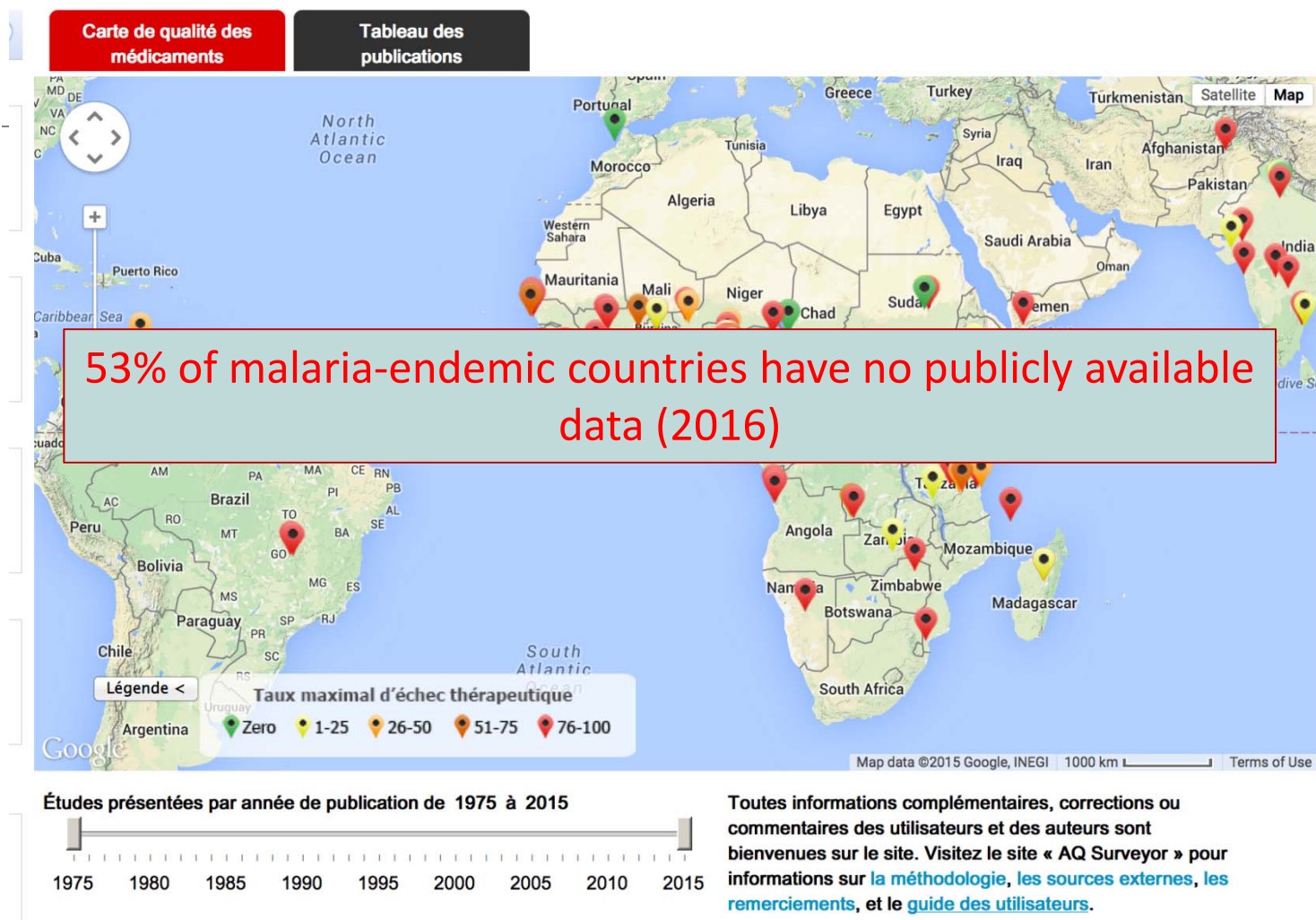
# Antimalarial quality

N=9,348

- 30.1 % of medicines failed at least one chemical/packaging quality tests
  - Oral artesunate ++

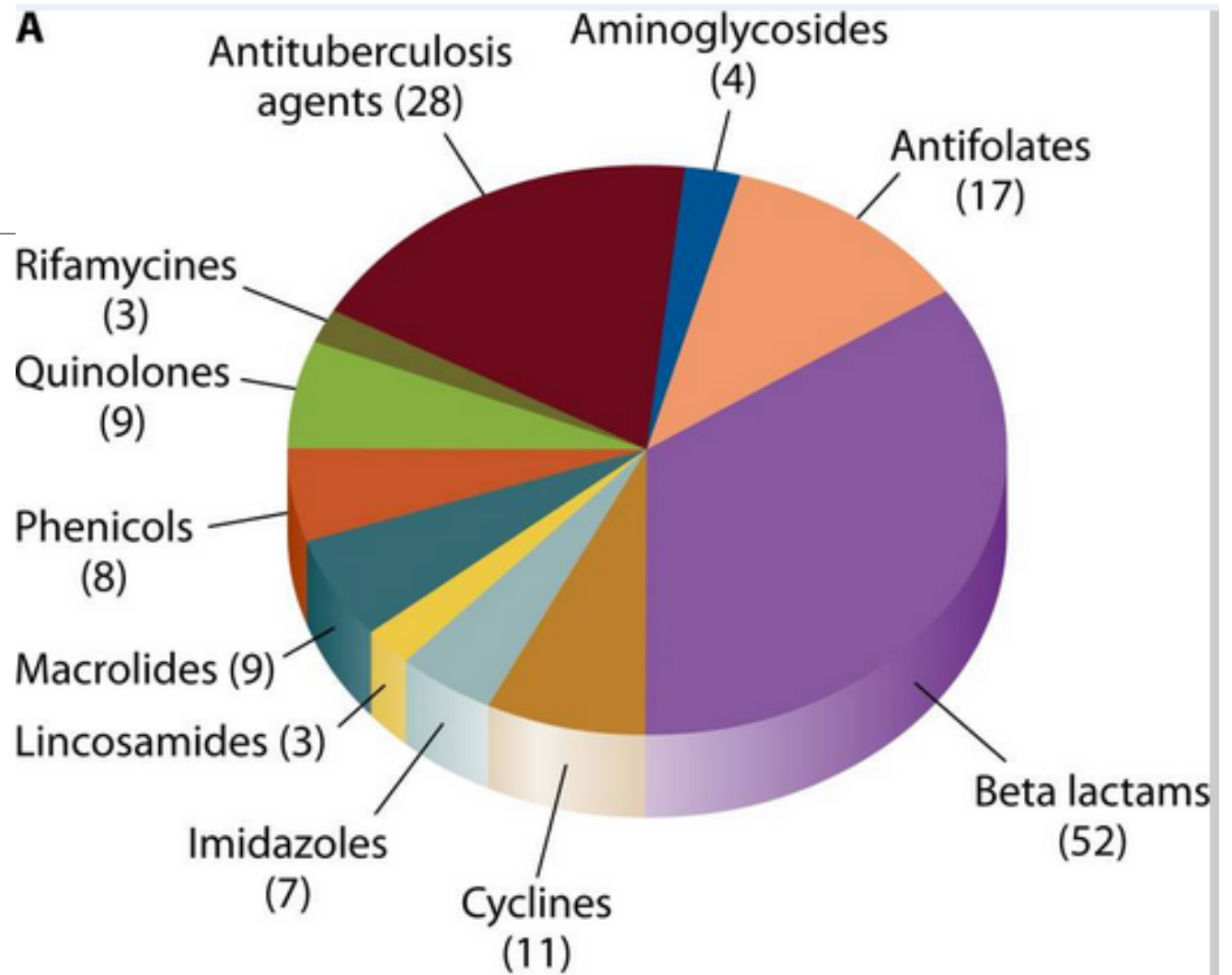


# Geography of AM quality



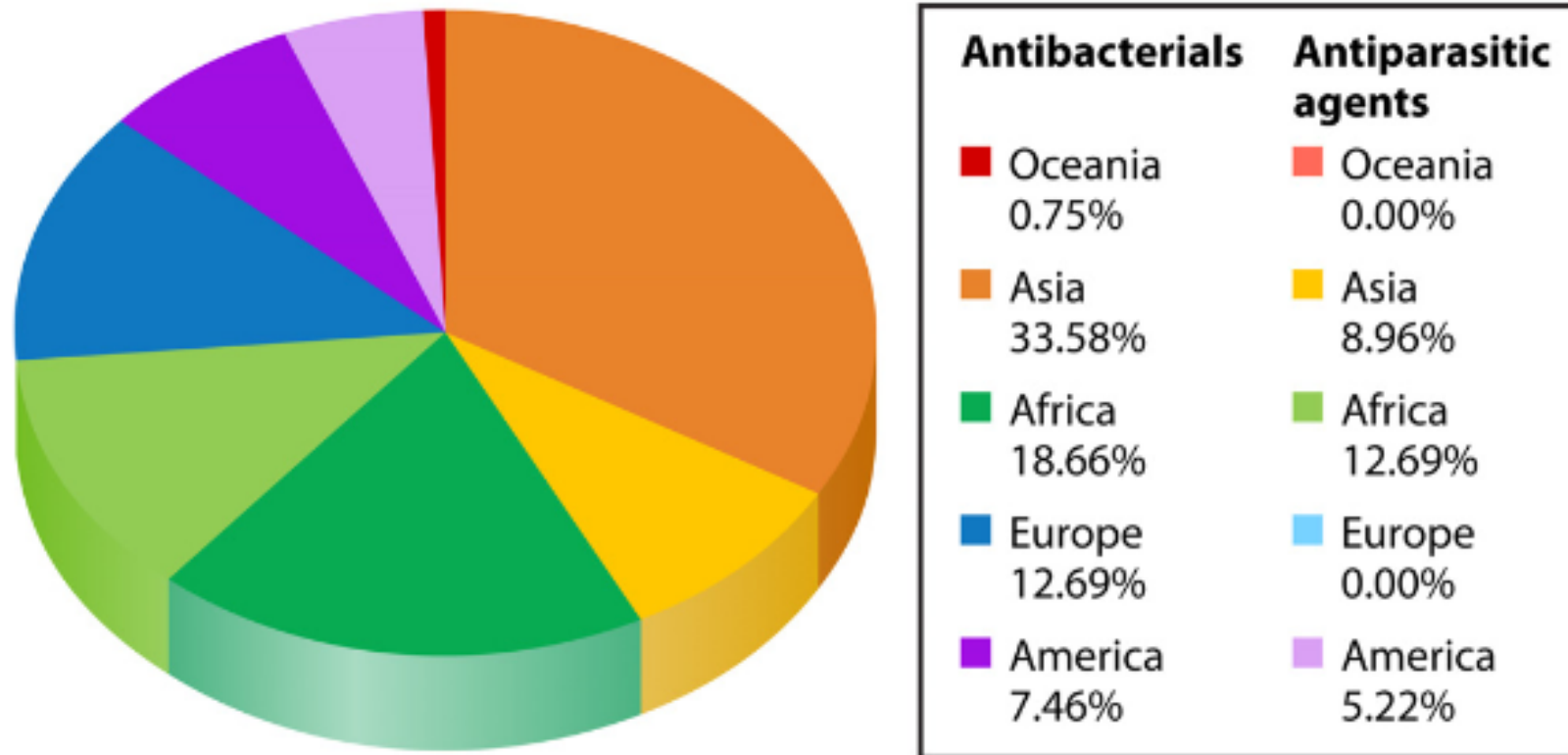
<http://www.wwarn.org/aqsurveyor/#0>

Kelesidis, Falagas  
*Clin Microb Rev* 2015





# Geographical distribution



**FIG 2** Relative geographic distribution of substandard/counterfeit antimicrobials. Darker colors indicate substandard/counterfeit antibiotics. Lighter colors indicate substandard/counterfeit antiparasitic agents.

*Kelesidis, Falagas Clin Microb Rev 2015*

# Epidemiology of Poor Quality Medicines (PQM)

*Many questions...few answers*

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What are we talking about?

How common are PQM? Who is affected?

Geographical distribution?

Significance for patients and public health?

Determinants?

Impact of interventions?

.....



# Estimated number of deaths associated with PQ antimalarials

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Renschler *et al.* , ASTMH, 2015

Estimation of the number of <5 deaths in 39 Sub-Saharan African countries:

*N° private sectors AM consumed \* % PQ antimalarials in private sector  
\*case fatality rate of <5 malaria+ children who consumed PQ AM*

Median number of <5 deaths in 39 countries = **122,350**



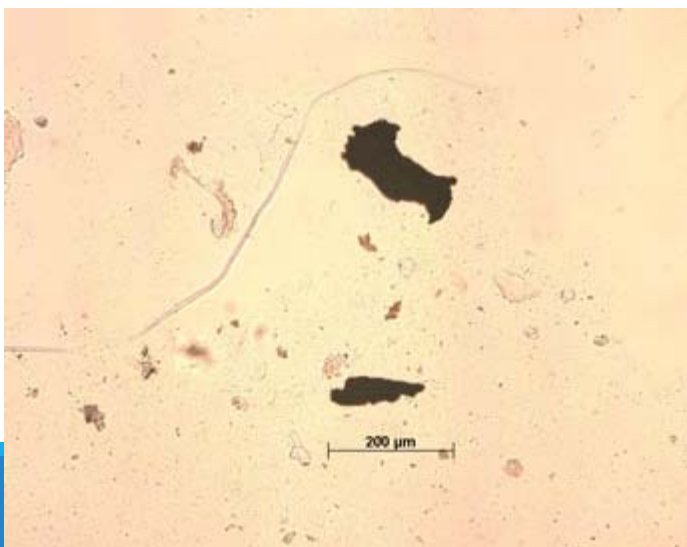


# Where do PQM come from?

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WHO teamed with Interpol, CDC, Georgia Tech, GNS Science, USP, TGA (Australia) & University of Oxford to try to find evidence as to where the fakes were coming from.....

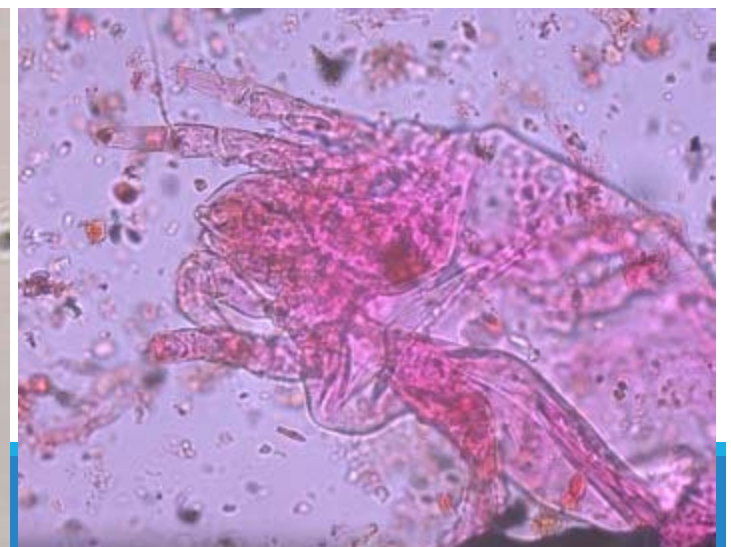
Charcoal

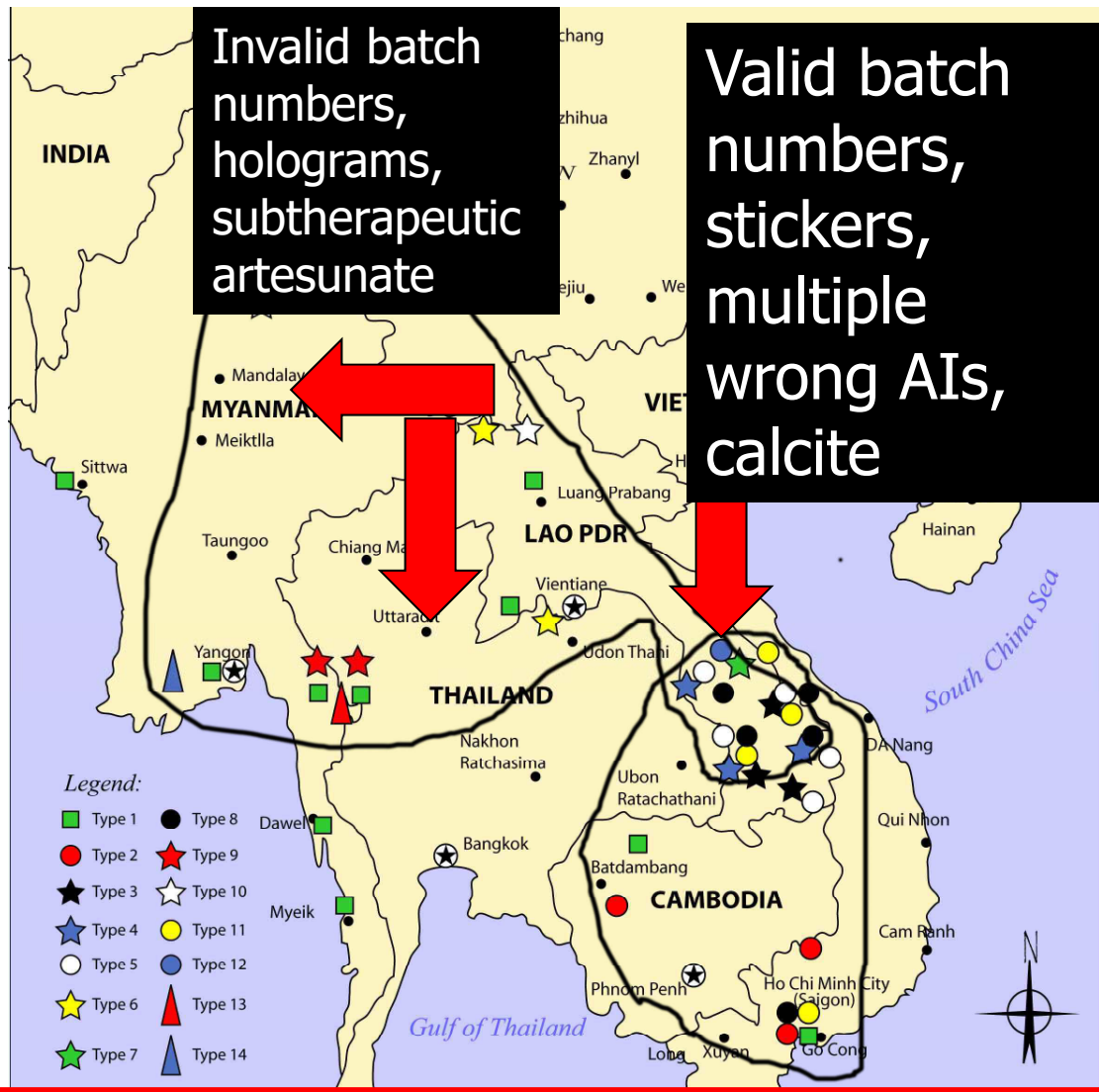


*Juglans* pollen



House dust mite






**Seized 24,000 of 240,000 blisterpacks traded by those arrested**

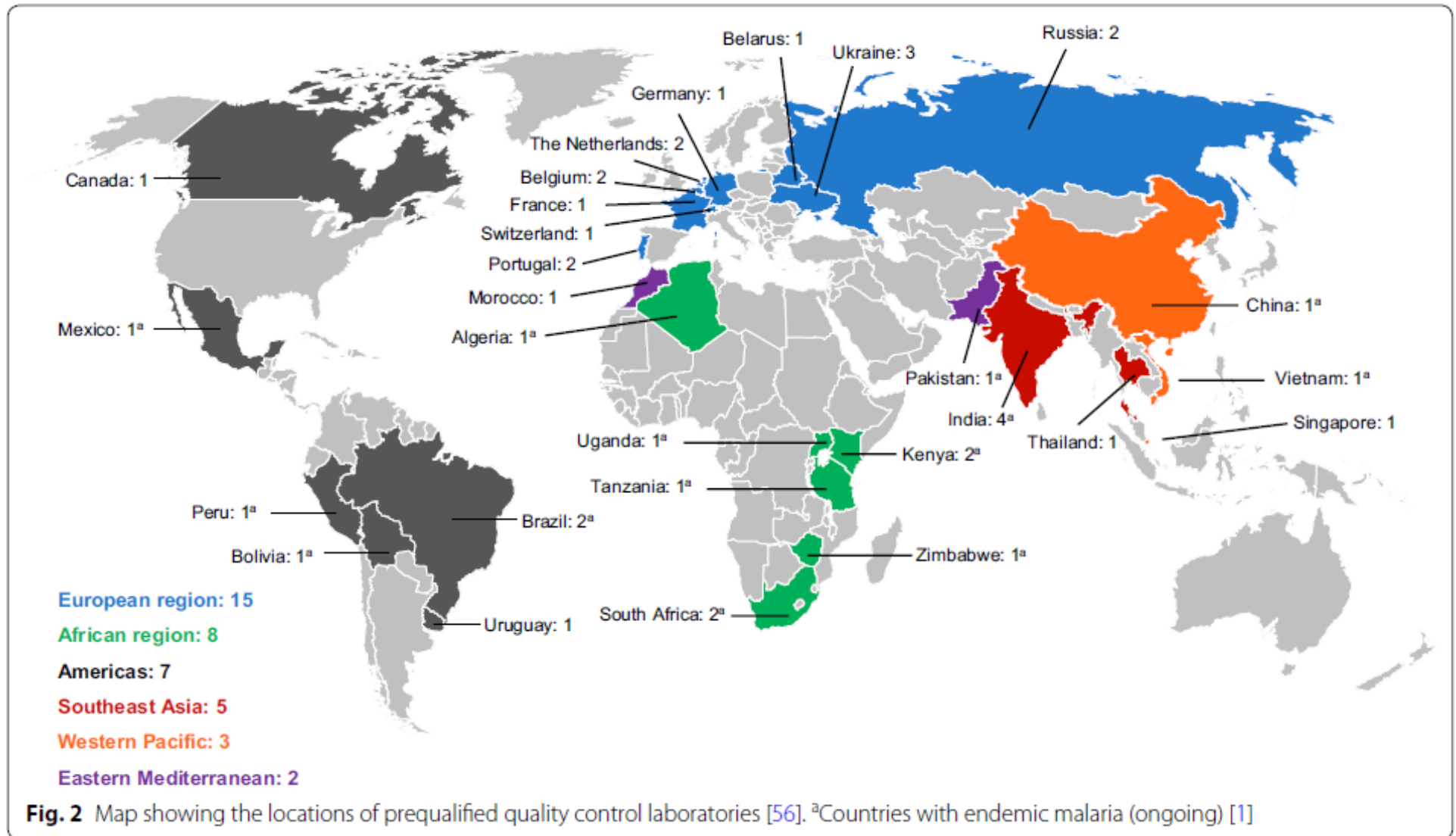
**Chinese police acted quickly when Secretary General of INTERPOL notified Chinese Government. Three traders arrested in China and 3 in Burma**

# Factors encouraging PQM

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- High prices of medicines
  - Demand exceeding supply
  - Lack of appropriate drug legislation – weak enforcement and penal sanctions
  - Complexity of supply chain
  - Cost and time of testing medicine quality
  - Limited regulation of international trading
  - Political will – Corruption/conflict of interest
  - Lack of awareness by the population
  - Inefficient cooperation between stakeholders
- 

# Pre-qualified quality control laboratories



*Bassat et al. Mal J 2016*

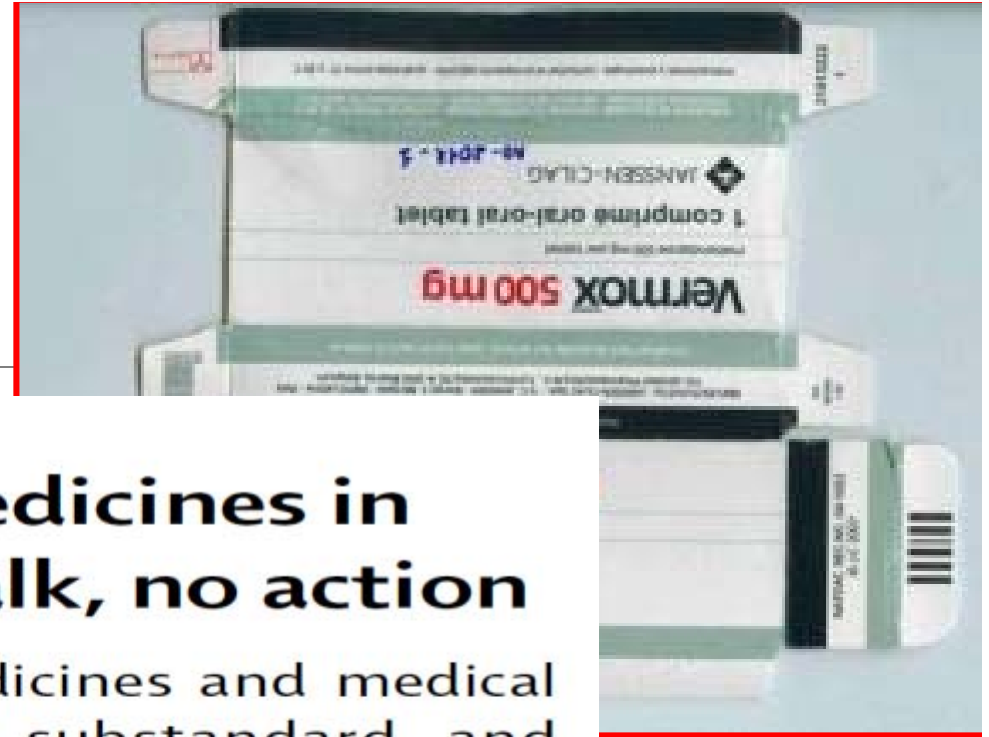
# Factors encouraging PQM *Internet*



Prescire



## Lack of communication



## Falsified medicines in Africa: all talk, no action

Poor-quality medicines and medical products, both substandard and falsified, cause avoidable morbidity, mortality, drug resistance, and loss of faith in health systems, especially in low-income and middle-income countries.<sup>1-3</sup> We report the analysis of two falsified medicines from Angola and discuss what lessons such a discovery could hold.

2012

# Investigating changes in quality of medicines

*Case-study: Lao PDR, antimalarials*

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- Repeated survey 2003 and 2012
- Random surveys, covert
- No evidence for falsification in 2012 vs 88% in 2003
- **Substandard still common**
  - 25.4% outside the 90-110% pharmacopeial limits

# Medicine quality sampling

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METHODOLOGICAL CONSIDERATIONS



# Guidelines to conduct MQ surveys



- USP, 2006

Guidelines for Drug Sampling

USP DQI Drug Quality Monitoring Program

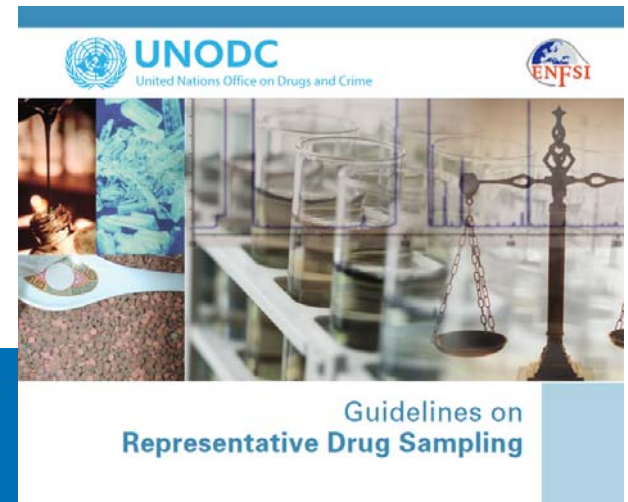
Use of the Basic Tests at the Peripheral Level

- UN United Nations Office on Drugs and Crime, 2009

- WHO, 2005, 2016

**WHO Expert Committee  
on Specifications  
for Pharmaceutical  
Preparations**

Fiftieth report



- MEDQUARG checklist, PLoS Medicine, 2009

OPEN ACCESS Freely available online

PLOS MEDICINE

Guidelines and Guidance


**Guidelines for Field Surveys of the Quality of  
Medicines: A Proposal**

Paul N. Newton\*, Sue J. Lee, Catherine Goodman, Facundo M. Fernández, Shunmay Yeung, Souly Phanouvong, Harparkash Kaur, Abdinasir A. Amin, Christopher J. M. Whitty, Gilbert O. Kokwaro, Niklas Lindegårdh, Patrick Lukulay, Lisa J. White, Nicholas P. J. Day, Michael D. Green, Nicholas J. White

# Study design

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## The importance of methodology


- Accuracy
  - Precision
  - Reliability
  - Generalizability
- 

# Steps to conduct MQ surveys

Initial Planning	Define Objectives	Human, Financial & Resource management	Methodology	Collection	Techniques to determine quality	Data & Information	Investigation of pharmaceutical products
	<p>Specify</p> <ul style="list-style-type: none"> <li>▪ Areas to be sampled</li> <li>▪ Pharmaceutical products</li> <li>▪ Medicine preparation type</li> <li>▪ Timing</li> <li>▪ Collection time</li> <li>▪ Definitions</li> </ul>	<ul style="list-style-type: none"> <li>▪ Survey management</li> <li>▪ Time Frame</li> <li>▪ Budget</li> </ul>	<p>1. Define</p> <ul style="list-style-type: none"> <li>▪ Sampling plan</li> <li>▪ Sampling frame</li> <li>▪ Sampling unit</li> <li>▪ Sample size</li> <li>▪ Outlet</li> <li>▪ Sample</li> <li>▪ Unit</li> </ul> <p>2. Sampling design</p> <ul style="list-style-type: none"> <li>• Convenience</li> <li>• Random</li> <li>• LQAS</li> <li>• Sentinel</li> <li>• No. Units to be collected</li> <li>• Dosage units sampling techniques</li> </ul>	<ul style="list-style-type: none"> <li>▪ Covert</li> <li>▪ Overt</li> <li>▪ Procedures for collection</li> </ul> <div style="border: 1px solid black; border-radius: 15px; padding: 5px; margin-top: 10px;"> <p>SOPs for:</p> <ul style="list-style-type: none"> <li>• Sample collection</li> <li>• Labelling</li> <li>• Transport</li> <li>• Storage</li> </ul> </div>	<ul style="list-style-type: none"> <li>▪ Assays to be conducted</li> <li>▪ Tests methods and specifications</li> <li>▪ Receipt &amp; testing of samples by laboratory</li> </ul> <div style="border: 1px solid black; border-radius: 15px; padding: 5px; margin-top: 10px;"> <p>SOPs for sample analysis</p> </div>	<ul style="list-style-type: none"> <li>▪ Data Management</li> <li>▪ Data analysis</li> <li>▪ Reporting</li> <li>▪ Publication</li> </ul>	
			<div style="border: 1px solid black; border-radius: 15px; padding: 5px; text-align: center;"> <p>Consider Ethics</p> </div>				

# Initial Planning-Objective

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- What is already known?
  - What medicines should be targeted and why?
  - Well-defined objectives
    - Are there PQM?
    - What is the proportion-- of PQM?of outlets selling PQM?
    - Changes over time?
    - ....
  - Definitions of Poor Quality, Falsified, Substandard
  - How do medicines reach patients?
- 

# Initial Planning-Objective

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- Well-defined time frame and resources available
- Where to sample?
- When to sample?
- Defining sampling unit: outlets/medicines
  - Are there PQM?
  - What is the prevalence?



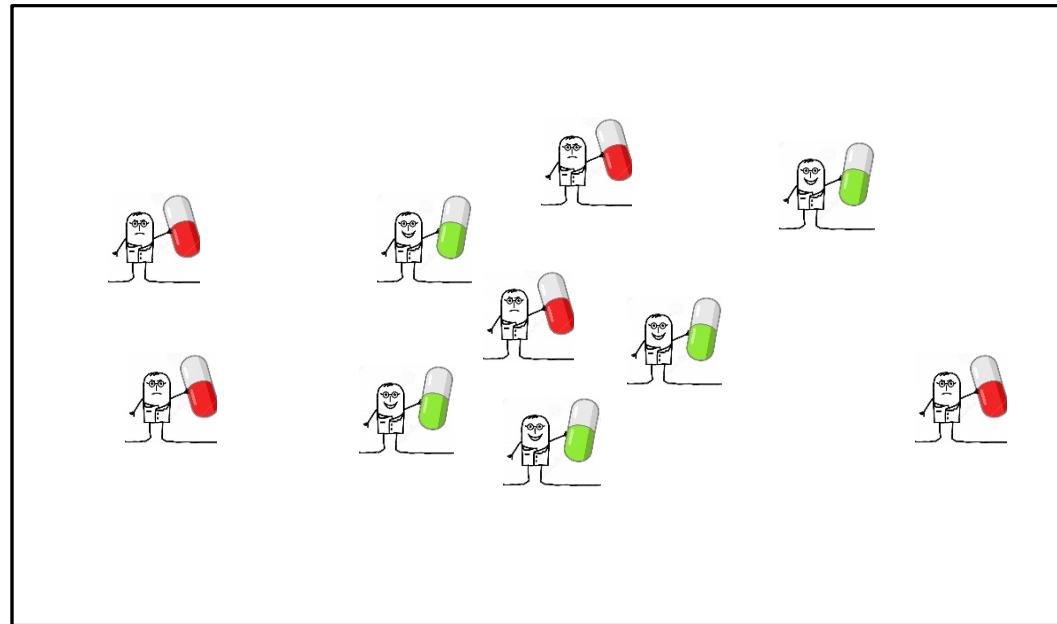
# Sampling plan – different strategies

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- Convenience
- Random
- LQAS
- Sentinel

# Methodology: sampling plan

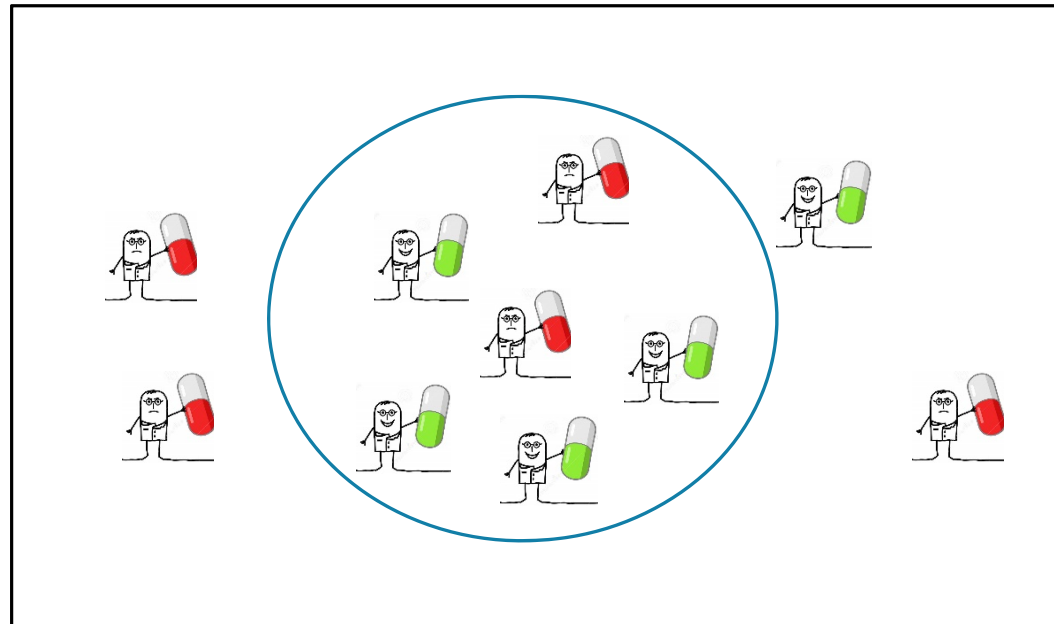
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# Methodology: sampling plan

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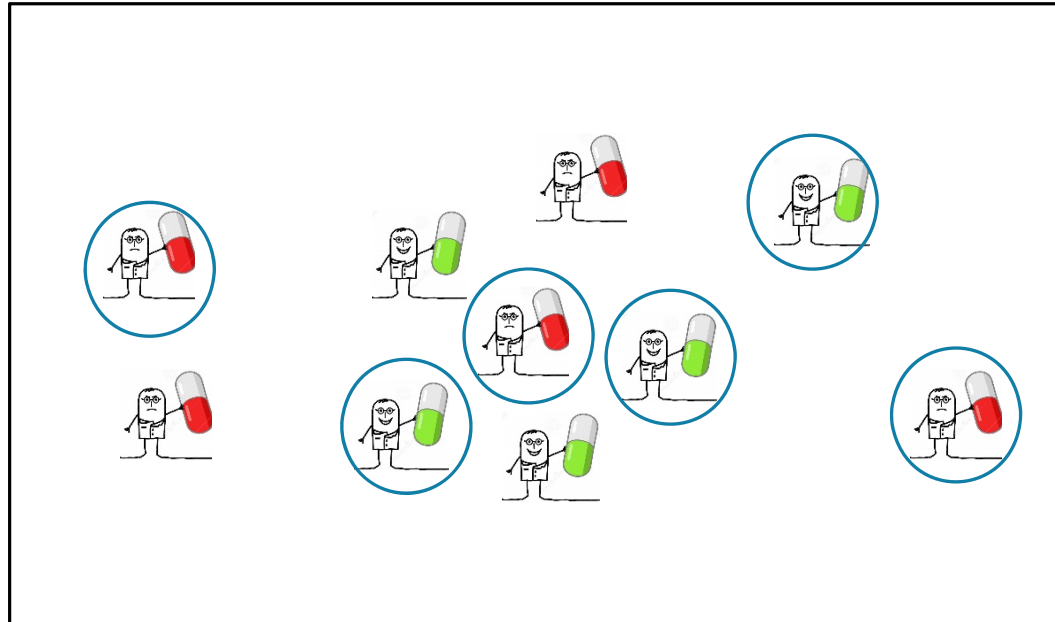
Convenience



# Methodology: sampling plan

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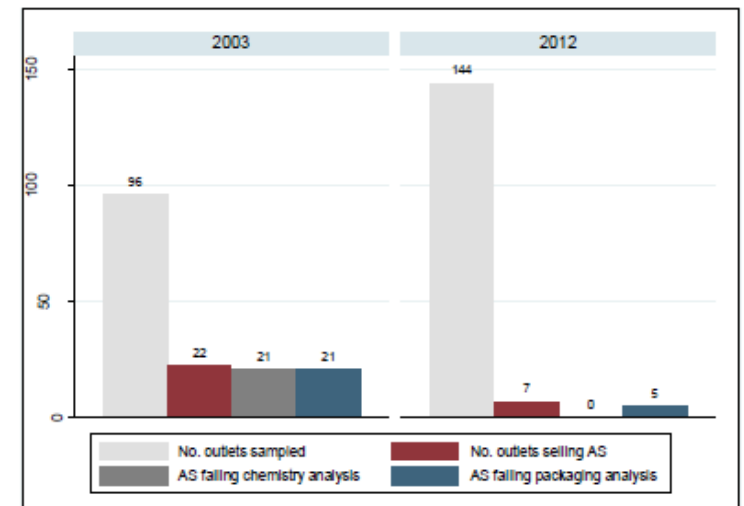
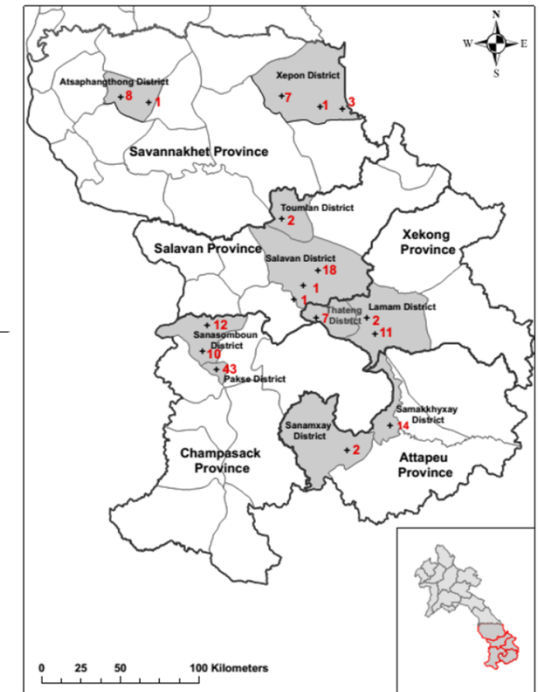
Random sampling



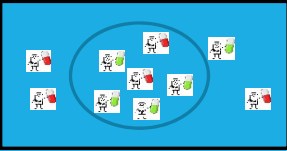
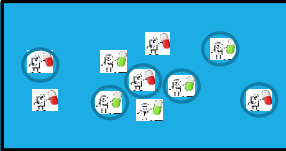
# Random sampling

## Example

- Random sampling
- Stratification urban/rural district
- Private sector
- Mystery shopper methodology
- Antimalarials bought in 76.4% (110) outlets



# Methodology: sampling plan

	Convenience 	Randomized 
<u>Advantages</u>	<ul style="list-style-type: none"> <li>-<b>Simple</b></li> <li>-Relatively inexpensive</li> <li>-Do <b>not require complete lists</b> of outlets in a define area</li> <li>-May provide a <b>signal</b></li> </ul>	<ul style="list-style-type: none"> <li>-With sufficient sample <b>size=reliable estimates</b> with confidence intervals</li> <li>-Evaluation of interventions are valid</li> <li><b>Comparison</b> of estimates <b>through time</b></li> </ul>
<u>Disadvantages</u>	<ul style="list-style-type: none"> <li>-Prone to <b>bias</b></li> <li>-Depending on <b>collector's choice</b></li> <li>-Prevalence estimates <b>cannot be generalized to other areas</b></li> </ul>	<ul style="list-style-type: none"> <li>-Large sample size needed = <b>additional costs</b> in labour and time</li> <li>-<b>Require comprehensive lists</b> of outlets</li> </ul>

# Lot quality assurance sampling strategy (LQAS)

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- To determine whether the prevalence of outlets selling PQM exceeds a certain threshold within an area ('lot')
- Most economical as a first step
- Level of risk of non inspecting each item
  - Risk of accepting a 'bad' lot = consumer risk
  - Risk of non-accepting a 'good lot' = provider risk
- Accept or reject an entire lot after inspecting a randomly selected sample


# LQAS

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## **Advantages**

- Requires smaller sample size= reduces time and costs
- NB: sampling can stop once the number of outlets with PQM is exceeded
- Useful in routine surveillances
- Changes through time
- To decide whether larger-scale surveys are required
- Information translatable into policy

## **Disadvantages**

- Requires random sampling
  - No estimate of exact prevalence of PQM
- 



# LQAS

## *Saudi Arabia example*

- **Objective:** % pharmacies (according to the category of pharmacy) selling PQ amoxicillin
- **Lot** = category of pharmacy (independent or chain)
- Upper and lower rate threshold predefined as 20% and 5%
- Consumer and provider risks predefined at 0.05 and 0.10
- N° of randomly selected pharmacies in each lot: **36**
- Sale of PQM in > 3 pharmacies within a 'lot' implied a prevalence of > 20%

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### The Quality of Medicines in Community Pharmacies in Riyadh, Saudi Arabia: A Lot Quality Assurance Sampling (LQAS)-Based Survey

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#### ABSTRACT

**Objectives:** To classify community pharmacies (CPs) in Riyadh, Saudi Arabia, in terms of the quality of medicines sold by them, using a lot quality assurance sampling (LQAS) technique with a predefined threshold. **Methods:** Riyadh CPs were divided into 2 categories ("lots" for the purpose of LQAS), i.e., chain and independent CPs. Upper and lower rate thresholds for CPs that sell low-quality medicines were predefined as 20% and 5%, respectively. Consumer and provider risks were predefined as 0.05 and 0.10, respectively. The calculated number of randomly selected CPs required in each lot was 36. Thus, sale of low-quality medicines in >3 CPs implies a prevalence of >20% of such CPs according to LQAS. A randomly selected brand of amoxicillin (selected as a quality indicator of medicines because it is both widely counterfeited and heat-sensitive) was purchased from each pharmacy by a "mystery shopper", checked for authenticity, and analyzed for drug content and content uniformity using a validated HPLC method. **Results:** Substandard amoxicillin was purchased in 9 pharmacies (4 chains and 5 independent). Both lots were thus rejected as unacceptable, which may indicate that consumers in Riyadh are at risk of purchasing substandard medicines at CPs. **Conclusions:** The quality of medicines sold in CPs in Riyadh did not meet our acceptability criterion, and appropriate intervention by decision makers is recommended. LQAS proved to be a practical, economical, and statistically valid sampling method for surveying the quality of medicines. It should enable decision makers to allocate resources for improvement more efficiently.

**Keywords:** Amoxicillin; Antibiotic; Quality of Medicines; Lot Quality Assurance Sampling; Saudi Arabia; Community Pharmacy

# Sentinel Site Monitoring

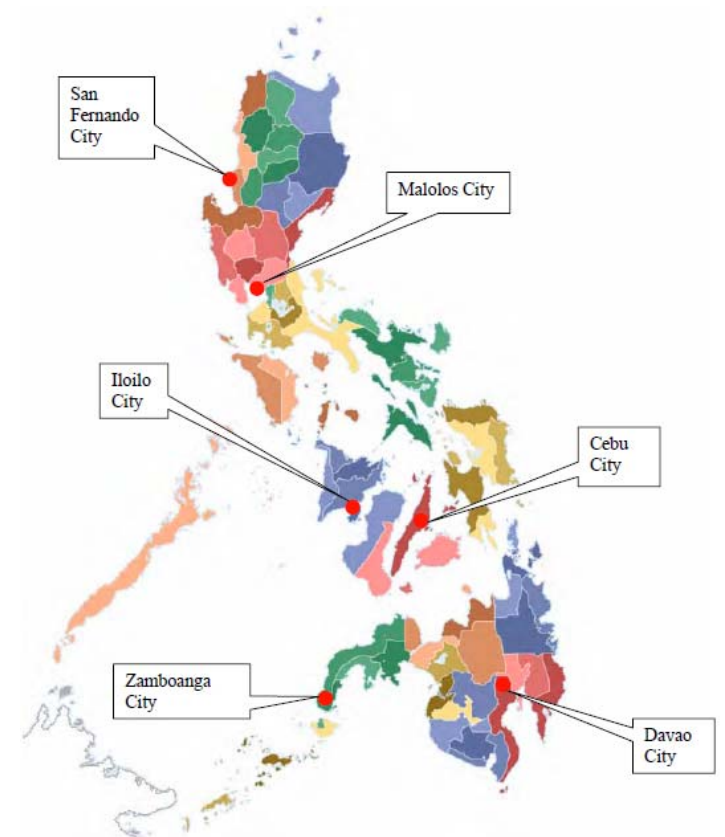
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## Advantages

- Longitudinal changes can be followed through time

## Disadvantages

- Outlet staff may realize that they are being sampled and change their behaviour accordingly



# Sample collection

## *Overt vs mystery shopper*

	Overt	Mystery shopper
<b><u>Main points</u></b>	Identity and purpose of the buyer is <b>known</b> by the establishment	Identity and purpose of the buyer is <b>unknown</b> by the establishment Nationals of the country
<b><u>Advantages</u></b>	<ul style="list-style-type: none"><li>-Only possible method in some circumstances (e.g. public establishment)</li><li>-More info on the medicines (structures questionnaire)</li></ul>	<ul style="list-style-type: none"><li>-Seller behavior not under influence</li><li>-To measure real-life quality of service, compliance with the regulation</li></ul>
<b><u>Disadvantages</u></b>	<ul style="list-style-type: none"><li>-Influence what medicines are offered for sale</li></ul>	<ul style="list-style-type: none"><li>-If too many units are requested = suspicions</li><li>-Expired medicines more likely to be sold</li><li>-Info on medicines limited, debriefing forms</li></ul>

# Other considerations

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- SOP are important
  - Storage and transport of medicines
  - Labelling
- Number of samples to collect
  - 30 units per batch?
    - Enough for a fair battery of tests
    - Too many units asked = suspicions from the seller
    - Not enough units in the outlet....



# Conclusion

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Robust evidence - transparency - consistency

- Conditioned by good quality methodology

-- contribute to future interventions

# Acknowledgments

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