Promoting the Quality of Medicines Plus

USAID HSS Learning Series Webinar: Substandard and Falsified (SF) Medicines Burden Model

September 17, 2024

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Webinar Participation – Polls

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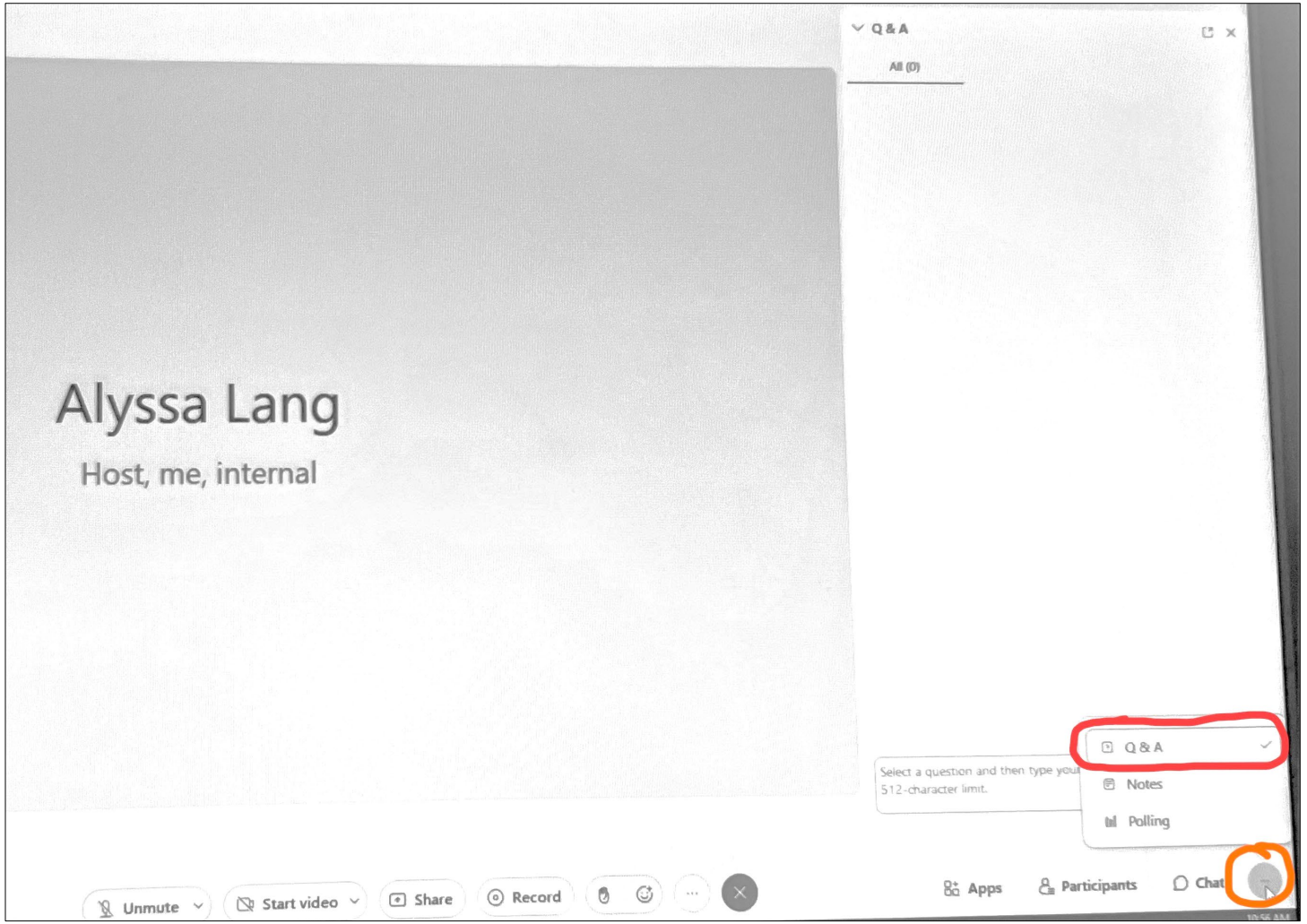

Agenda

- Welcome Remarks
- The Substandard and Falsified (SF) Medicines Burden Model – An Introduction
- Model Pilot in Kenya – SF Burden of Oxytocin on Post-Partum Hemorrhage
  - Discussion with Dr. Karima Wanga, of the Kenya Pharmacy and Poisons Board
- Development and Use of Two Prepopulated Models for Essential MNCH Medicines
- Launching the Pre-populated Models in Guinea
  - Discussion with Neimatu Adjabui, PQM+ West Africa Principal Program Manager
- Conclusion

Welcome from Alison Collins, PQM+ AOR

Health Systems Advisor and Pharmaceutical and Supply Chain Systems Team Lead, USAID Bureau for Global Health, Office of Health Systems (OHS)

Alison Collins joined OHS in 2018 and currently serves as the Agreement Officer's Representative (AOR) for the Promoting the Quality of Medicines Plus (PQM+) program, providing technical support for HSS and pharmaceutical systems strengthening programming. She also serves as OHS' gender and youth point of contact. Prior to joining USAID, Alison supported HSS programs at Management Sciences for Health (MSH). Alison completed a dual MBA in Nonprofit Management and M.A. in Sustainable International Development at The Heller School for Social Policy and Management at Brandeis University.

USAID HSS Learning Series

- An initiative of USAID's Office of Health Systems to **convene HSS practitioners to share, learn, and use HSS evidence** to inform our collective efforts to support sustainable health system strengthening
- Upcoming Events:
  - October/November - Stay tuned for more information; coming soon!
  - December - "Government-led Contracting: A Sustainable Health Financing Solution" (USAID HS4TB Project)
- If you have a webinar idea that you would like to present as part of this series, please reach out to HSSlearning@usaid.gov for more information.

Health Systems Strengthening Learning Agenda

HSS Learning Agenda Question 3: What measurement tools, approaches, and data sources, from HSS or other fields, are most helpful in understanding interrelationships and interactions, and estimating impact of HSS interventions on health system outcomes and priority health outcomes?

The substandard and falsified medicine burden model can be used to estimate the health and economic burden of using poor quality medicines in the health system

Poor-quality medical products undermine global health progress

Medicines make up 3 of the top 10 sources of health system inefficiencies.
WHO estimates that 1 in 10 medical products is of poor quality. These products have numerous detrimental effects:

Health
increased mortality and morbidity, disease spread, antimicrobial resistance

Economic
increased out-of-pocket expenses, lost productivity, wasted health resources

Social
increased poverty, loss of confidence in health systems

Shared vision

PQM+ is a cooperative agreement between USAID and USP to sustainably strengthen medical product quality assurance systems in low-and middle-income countries.

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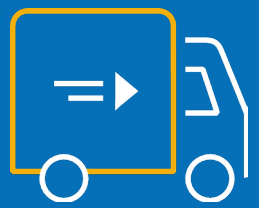
PQM+ Objectives

1

Improve **governance** for medical product quality assurance systems

2



Improve country and regional **regulatory systems** to assure the quality of medical products in the public and private sectors

3

Optimize and increase **financial resources** for medical product quality assurance

4

Increase **supply** of quality-assured essential medical products of public health importance

5

Advance global medical products quality assurance learning and operational agenda

Edward Abwao, Senior Technical Advisor, PQM+ Program, USP

Edward is a Kenya-based pharmacist with over 20 years of experience in the pharmaceutical field. He provides technical support for regulatory system strengthening activities in Kenya, the Intergovernmental Authority of Development (IGAD) and the East African Community (EAC), a regional economic community. He has also been involved in the regional harmonization initiatives in Africa, specifically in pharmacovigilance, post marketing surveillance, and clinical trials. Prior to joining the PQM+ program, Edward worked at the Pharmacy and Poisons Board of Kenya where he was the head of the clinical trials section. He holds a MSc in Medical Statistics from University of Nairobi and a MSc in Clinical Trials from the London School of Hygiene and Tropical Medicine.

The Substandard and Falsified (SF) Medicines Burden Model – An Introduction

What are substandard and falsified medicines and why should you care?

Substandard and falsified (SF) medicines are medicines that:	Have the wrong amount of active ingredient so they are ineffective Are falsified or otherwise deliberately counterfeit
Consequences of using SF medicines	• Failed treatment = poor health outcomes & wasted resources • Worst case scenario → mortality from poor quality medicine • Possible increase in resistance to antimicrobials • Loss of public trust in the health system

While U.S. Government programs that supply their own medicines, such as PEPFAR or PMI, provide quality-assured products, some medicines on the local market may not be quality assured. These affect public health and erode gains from these programs.

How big a problem are SF medicines?

Presence of Substandard and Falsified Medicines

A World Health Organization (WHO) study (2017)* estimated the prevalence of SF medicines globally to be 10.5% of medicines in LMICs.

However, WHO considers this statistic an underestimate.

PQM+ has supported risk-based post-marketing surveillance studies in 21 countries across Africa and Asia, and failure rates for individual medicines have ranged from 0 – 48%. **

*A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization; 2017. License: CC BY-NC-SA 3.0 IGO.

**Note that these failure rates are from risk-based post-marketing surveillance and thus are not generalizable to the entire country.

Poll Question # 1

Multiple choice poll – please select one answer.

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Do you ever hear about poor quality medicines in your country?

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Poll # 1 Results

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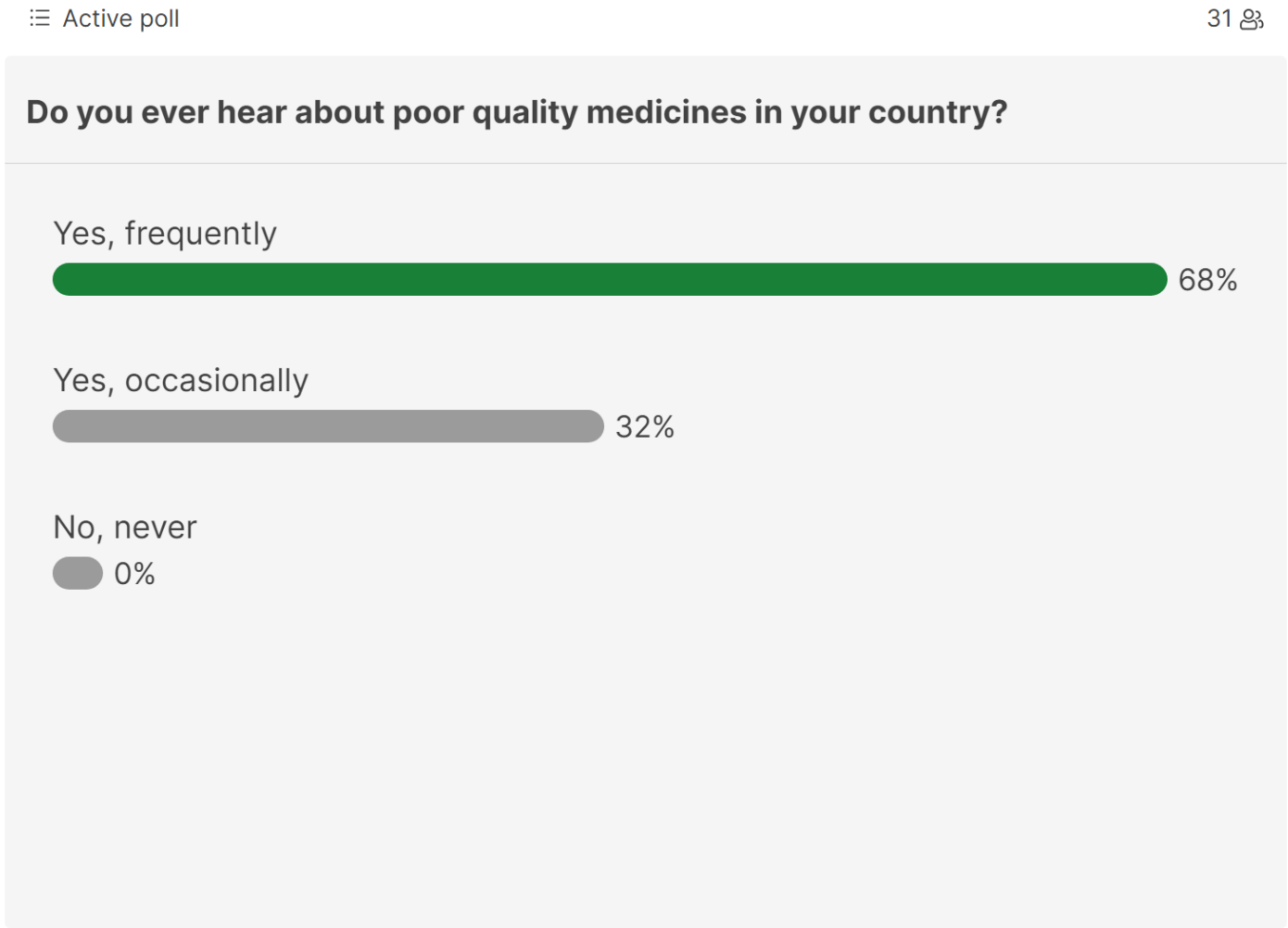

Poll Question # 2

Multiple choice poll – select multiple choices as relevant

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What public health programs do you think might be most affected by the SF medicines?

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Poll # 2 Results

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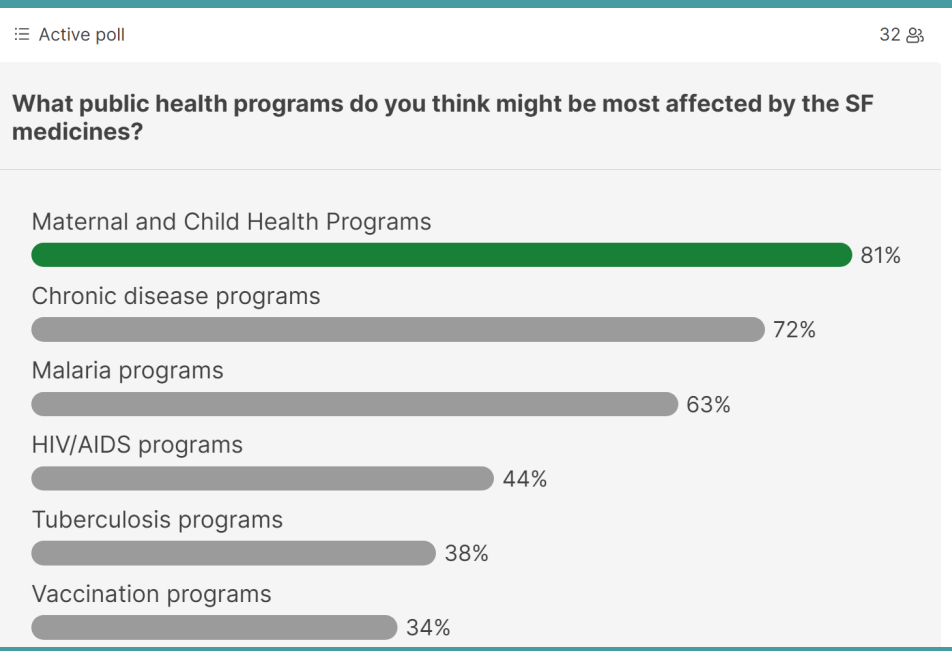

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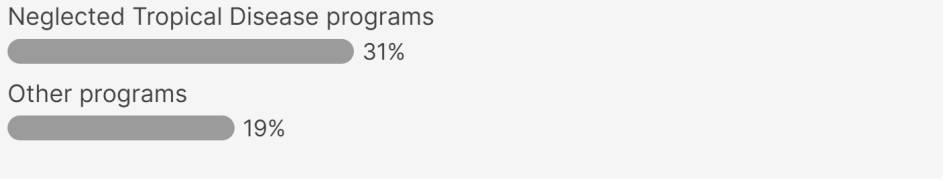


Other programs included:

- Infectious diseases programs

What does use of SF medicines cost a country?

Answer:

We don't really know

- **WHO estimated* the incremental deaths due to SF medicines for two diseases:**
  - Approximately 2.1%-4.9% of total malaria deaths in sub-Saharan Africa are due to SF antimalarials
  - In the most likely scenario, the presence of SF antibiotics results in 8,688 - 72,430 additional deaths from severe childhood pneumonia
- **Countries can't readily translate the WHO estimates** into their own contexts to know the burden in their countries
- Countries might also have **other medicines of concern**.

*A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.

Amanda Lewin, PhD., Senior Technical Advisor, PQM+ Program, USP

Amanda Lewin, Ph.D. provides technical assistance to national medical regulatory agencies, local manufacturers, and local contract research organizations (CRO) to help increase the supply of quality medicines. Her focus is supporting the conduct, review, and inspection of bioavailability/ bioequivalence studies and supporting other aspects related to the evaluation of safety and efficacy for pharmaceuticals. Prior to joining PQM+, Amanda was a Lead Pharmacologist at the U.S. FDA in the Office of Study Integrity and Surveillance (OSIS). Amanda earned her Ph.D. in Pharmacology from Georgetown University, her M.S. in Forensic Toxicology from The George Washington University, and her B.S. in chemistry from the University of California, Santa Barbara.

PQM+ (funded by USAID, and partnered with the University of Washington) developed the SF medicine burden model to help country stakeholders estimate the burden in their country

The model is applied by medicine and by indication

Example: amoxicillin for childhood pneumonia

Users input basic data like:

- Rates of SF medicine
- Population eligible to use the medicine annually
- Care seeking behavior
- Probability the specified medicine is received
- Probabilities for different health outcomes with and without treatment
- Costs of treatment for health outcomes if initial treatment fails

The model estimates two major classes of outcomes:

Health outcomes:

- Deaths
- Life-years
- Disability-adjusted life years (DALYs)
- Quality-adjusted life-years (QALYs)
- Disease-specific outcomes

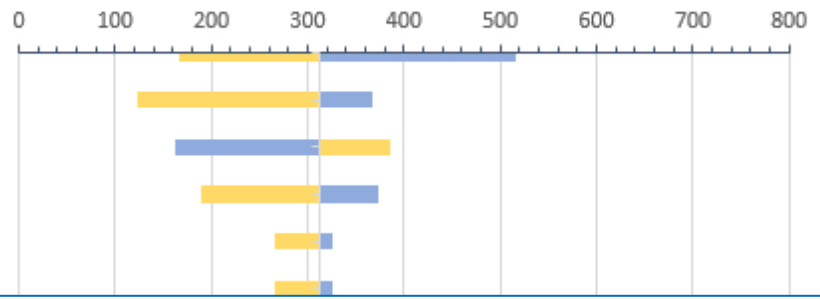
Economic/societal outcomes:

- Cost of additional treatment
- Value of lost productivity from failed treatment or complications from treatment
- Value of lost productivity due to death

What results does the model generate?

- The model generates a base case for the outcomes and a range to reflect data uncertainty
- One-way sensitivity analyses show which parameters have the greatest impact on the outcome of interest to help stakeholders interpret the results.

Example one-way sensitivity analysis tornado diagram showing parameters with the greatest impact on an outcome



Parameter
Lifetime probability of condition-related death without treatment
Proportion of Substandard and Falsified Medicines 3 in the Real-world Scenario
Lifetime probability of condition-related death with treatment
Proportion of Substandard and Falsified Medicines 1 in the Real-world Scenario
Proportion of Substandard and Falsified Medicines 3 at Public Hospitals in the Real-world Scenario
Proportion of Substandard and Falsified Medicines 3 at Public Health Centers in the Real-world Scenario

Model Pilot in Kenya – SF Burden of Oxytocin on Post-Partum Hemorrhage

Stakeholders in Kenya had ongoing concerns about the quality of oxytocin

- Lack of efficacy leading to frequent up-dosing
- Failed treatment was costly:
  - Mild PPH
  - Severe PPH
  - Hysterectomy
  - Death

Process for using the model in Kenya

- Identified appropriate stakeholders to collect the information and data points needed to use the model
- Oriented stakeholders
- Stakeholders collected needed data points from already available literature and internal government sources; entered these data points into the model
- Stakeholders met to review the results and plan next steps

Kenya results – assuming 7% of oxytocin is SF; 1.2 million pregnant women deliver in healthcare facilities, for a year's worth of SF Oxytocin:

Health burden

- 2,005 additional cases of mild PPH
- 488 additional cases of severe PPH
- 25 additional hysterectomies
- 26 additional deaths
- 420 life-years lost

Societal/economic burden

$ 937,050 direct healthcare costs

$ 302,071 in productivity losses:

- $21,729 from missed work
- $280,342 from premature death

TOTAL: $1,239,121

Karim Wanga, Senior Principal Regulatory Officer, Pharmacy and Poisons Board

Karim Wanga is a Senior Principal Regulatory Officer at the Pharmacy and Poisons Board, in the department of product safety. He has worked with PPB for over ten years across several regulatory functions, which include regulatory inspections, pharmacovigilance and post-marketing surveillance. He also supports the medicines regulation harmonization (MRH) program at the Inter-governmental Authority on Development (IGAD) as a pharmaceutical expert.

He has special interest in drug utilization studies and medicines regulatory sciences.

Karim Wanga is a pharmacist by training and graduated with a Master's of Pharmacy in Pharmacoepidemiology and Pharmacovigilance from the University of Nairobi. He is also a fellow in Anti-Microbial Resistance (AMR) from the London School of Hygiene and Tropical Medicine.

Development and Use of Two Prepopulated Models for Essential MNCH Medicines

Lessons from Kenya pilot that led to pre-populated templates

Challenge:

It was very hard to get good data on the probability of different health outcomes from failed treatment.

Solutions:

Created pre-populated templates with health outcome probabilities from the literature

- For oxytocin for PPH
- For amoxicillin for childhood pneumonia

Challenge:

It was very hard to get good data for many parameters.

Solutions:

- Identified the best sources of relevant data and pre-populated regional models with those.
- Identified best globally-recognized sources of relevant country statistics.

Prepopulated Template Model for SF Oxytocin and Amoxicillin

Applicable data was identified to create two prepopulated template models

- Burden of SF amoxicillin for childhood pneumonia in Southeast Asia and Africa
- Burden of SF oxytocin for the prevention and treatment of postpartum hemorrhage in Africa

Regional or low- and middle-income specific data were used for inputs such as:

- GDP Per Capita (USD)
- Average Expenditure on Health (USD)
- Life Expectation at Birth (Years)
- Mortality Rates
- Probability for Disease-Specific Outcomes
- Proportion of SF medicines
- Costs of Treatment

Regional results for use of SF oxytocin for PPH in Africa (per 1 million births)

	Base Case	Range
Economic Burden due to SF Oxytocin (in US dollars)		
Health system	$450,000	-
Productivity losses (from premature death)	$1,200,000	-
from missed days of work	$6,000	-
TOTAL ECONOMIC COSTS	**$1,700,000**	**$0.4 – $3.6 million**
Health Burden due to SF Oxytocin		
Incremental deaths	17	2 – 38
Life years lost due to pre-mature deaths	385	37 – 874
Additional cases of mild PPH	4,269	100 – 12,585
Additional cases of severe PPH	328	23 – 757
Additional cases of hysterectomy	15	3 – 32

Regional results for use of SF amoxicillin for childhood pneumonia in SE Asia (per 1 million cases)

	Base Case	Range
Economic Burden due to SF Amoxicillin (in US dollars)		
Health system	$770,000	-
Productivity losses	$8,900,000	-
from missed days of work (caregiver)	*$400,000*	-
from premature death	*$8,500,000*	-
TOTAL ECONOMIC COSTS	**$9,600,000**	**$5 – $15 million**
Health Burden due to SF Amoxicillin		
Incremental deaths	**144**	**67 – 235**
Life years lost due to pre-mature deaths	3,851	1,797 – 6,289
Additional cases of severe pneumonia	6,472	3,116 – 11,266
Additional cases of very severe pneumonia	1,103	527 – 1,918

Regional results for use of SF amoxicillin for childhood pneumonia in Africa (per 1 million cases)

	Base Case	Range
Economic burden due to SF Amoxicillin (in US dollars)		
Health system	$3,300,000	-
Productivity losses	$12,200,000	-
from missed days of work (caregiver)	*$300,000*	-
from premature death	*$11,900,000*	-
TOTAL ECONOMIC COSTS	**$15,500,000**	**$10 – $23 million**
Health burden due to SF Amoxicillin		
Incremental deaths	**214**	**114 – 353**
Life years lost due to pre-mature deaths	5,412	2,886 – 8,930
Additional cases of severe pneumonia	5,534	3,035 – 9,104
Additional cases of very severe pneumonia	2,213	1,214 – 3,641

Launching the Pre-populated Models in Guinea

Focus of upcoming work in Guinea

- Used the model template for amoxicillin to treat childhood pneumonia in Africa.
- Adjusted available data inputs to represent the context in Guinea, most importantly:
  - SF rates of amoxicillin in Guinea
  - Eligible population in Guinea

	Base Case
Economic Burden due to SF Amoxicillin (in US dollars)	
Health System	$156,000
Productivity losses	$575,000
TOTAL ECONOMIC COSTS	**$731,000**
Health Burden due to SF Amoxicillin	
Incremental deaths	**10**
Life years lost due to pre-mature deaths	255
Additional cases of severe pneumonia	261
Additional cases of very severe pneumonia	104

Two processes for using the model:

Kenya approach: engage group of stakeholders from the outset to collect the data inputs, run the model, review results, and promote action.

- The stakeholders start with an empty model.

Alternative approach: small team uses the prepopulated model to get a very rough estimate, then use that estimate to interest stakeholders in improving the estimate and taking action.

- The small team starts with the prepopulated model.

Neimatu Adjabui - PMP, ASQ-CQA, CMQ/OE, PQM+ Principal Program Manager, West Africa, USP

Neimatu is a pharmaceutical systems expert with close to 20 years' experience in pharmaceutical Quality Management Systems (QMS), medical products regulation, including harmonization, local pharmaceutical manufacturing and donor-funded program management. She joined USP in 2013 and has served in various roles. She is currently the principal program manager for West Africa managing PQM+ technical assistance projects funded by USAID in seven countries. Prior to joining USP, she worked in a WHO GMP compliant pharmaceutical manufacturing plant in Ghana as a quality control manager and later as acting Quality Assurance and regulatory affairs manager. Neimatu is a PMI certified Project Management Professional, ASQ Certified Manager of Quality/Organizational Excellence, an ASQ Certified Quality Auditor (CQA) and an ISO 17025:2017 Lead Assessor. She has an honors BSc. in Chemistry from the University of Toronto, Canada and an MSc. in Pharmaceutical Sciences from Kingston University, UK.

Poll Question # 3

Multiple choice poll – please select one response

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Would your country benefit from estimating burden of using SF oxytocin for PPH or amoxicillin?

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Poll # 3 Response

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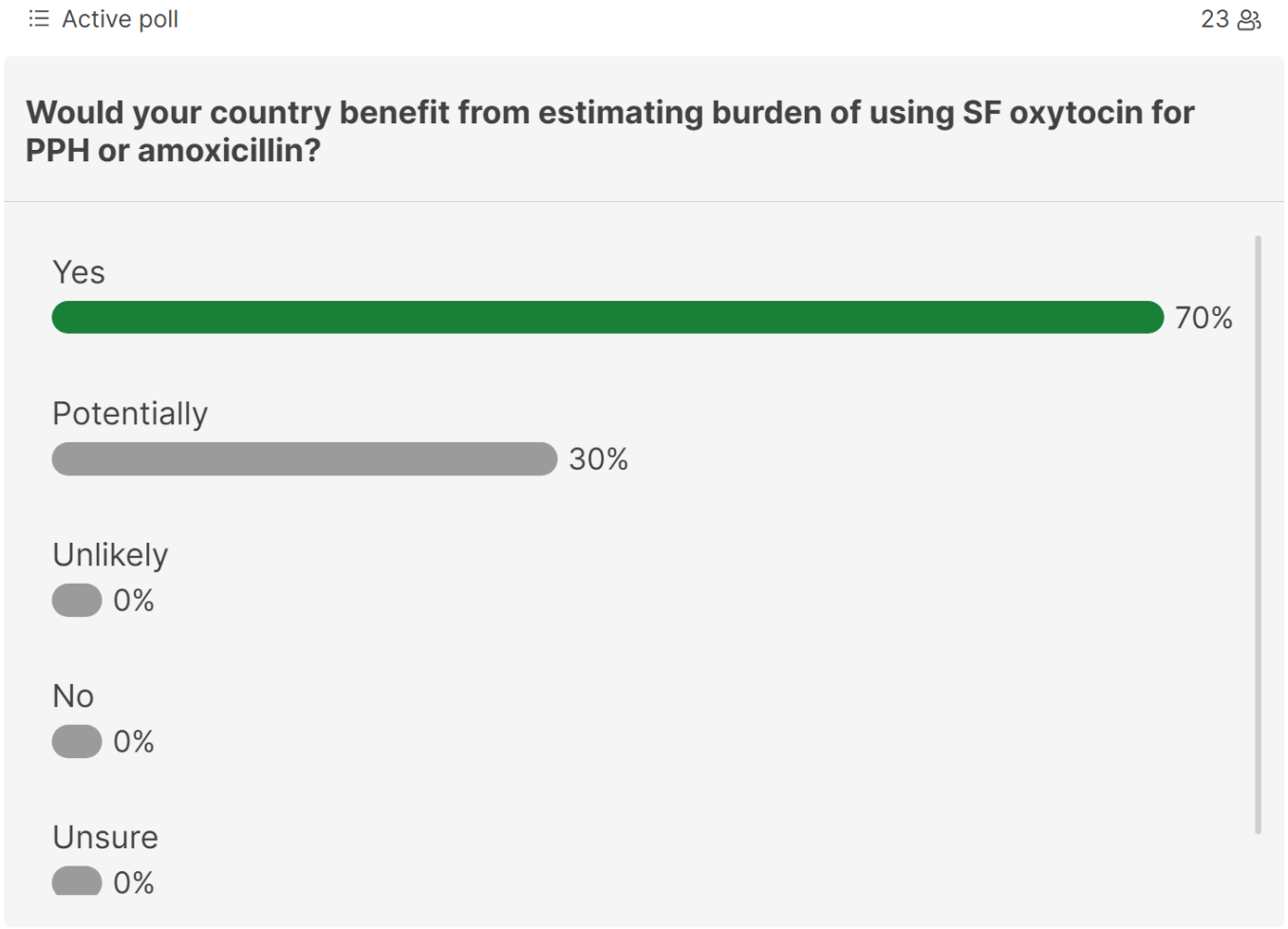

Poll Question # 4

Word cloud poll – type in any answer that applies

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Are there other medicines whose quality is of major concern in your country?

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Poll # 4 Response

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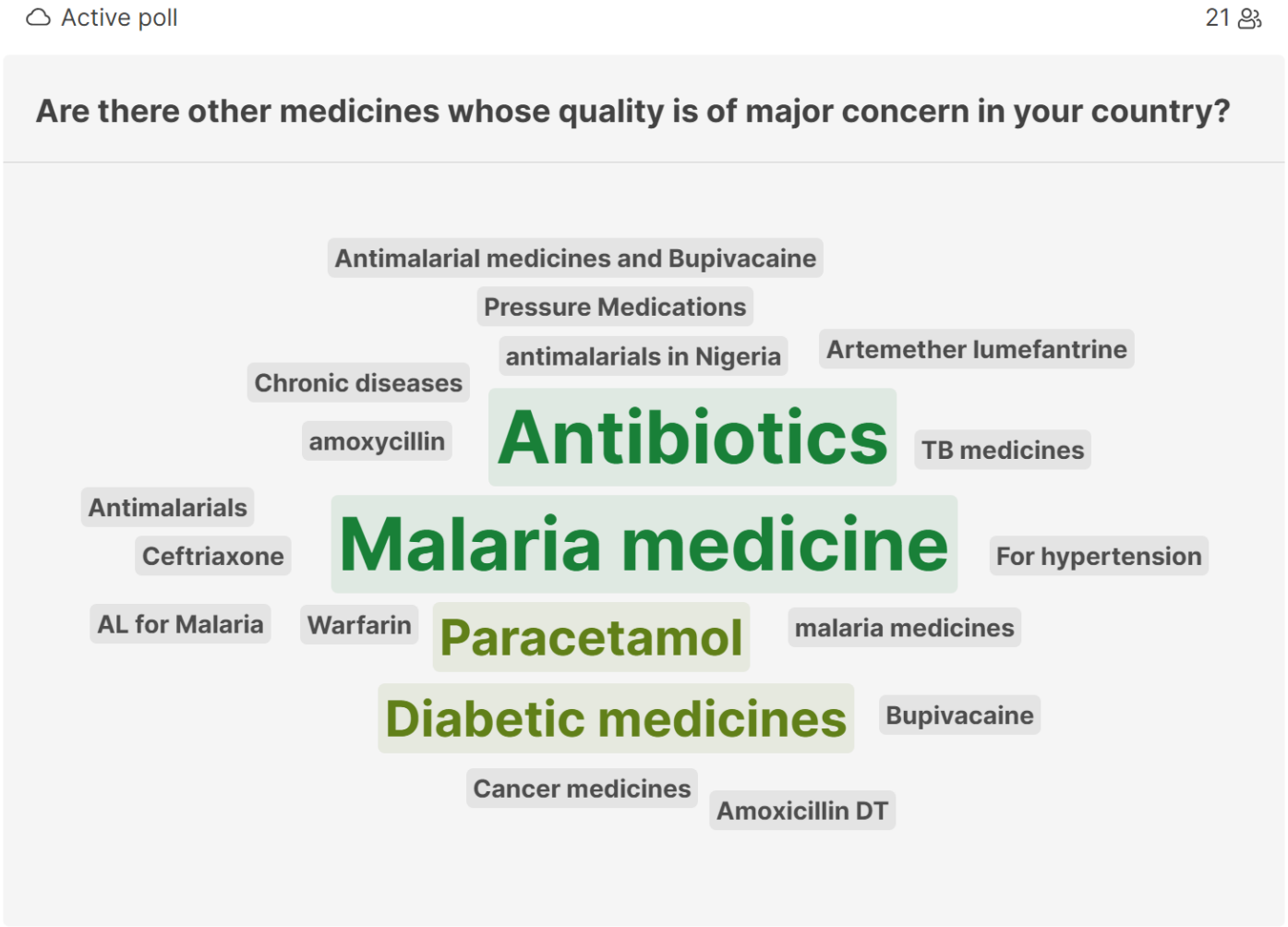

Conclusion

SF medicines are in the market.

SF medicines impose a heavy burden. Poor quality medicines erode progress with two other health system building blocks: service delivery and financing.

The burden is largely unrecognized, but it can be estimated.

The estimated burden can be used to advocate for increased efforts to improve medicine quality.

Promoting the Quality of Medicines Plus

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