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# Modeling the Burden of Substandard and Falsified Oxytocin in Kenya

## Pilot Experience and Public Health Implications

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African Medicines Regulatory Harmonisation Programme

Promoting the Quality of Medicines Plus (PQM+)

# Agenda

- Introduction to the Model
- Kenya Pilot of the Model
- Methodology
- Results
- Conclusion

# Introduction to the Model: Why a Model?

- Substandard and falsified (SF) medicines are on the market in every country[1]
- One out of 10 tested samples are SF in low and middle-income countries (LMICs)[2]
- Countries may not know the burden of these SF medicines
- As countries better understand the burden, they will be able to make informed choices about investing to improve medicine quality

1. Substandard and falsified medical products. Geneva: World Health Organization; 2018.
2. 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.

# Methodology

## The SF Medicine Burden Model

- It is not possible to know the true burden, but the burden can be estimated using a model
- USAID OHS funded PQM+ to develop a user-friendly model that countries can use to estimate the burden of specific medicines
- In addition to USP, the team that developed the model included:
  - University of Washington (lead developer)
  - University of North Carolina-Chapel Hill (review; lit review; validation)
  - Harvard Pilgrim Healthcare (review)

# Model Overview

**Objective:** The primary aim of this generalized tool is to estimate the health and economic burden of any specific SF medical product

**Methods:** PQM+ uses a decision-tree model where we compare two scenarios:

*Scenario 1*: Real-world scenario that reflects the prevalence of SF medicines in a given country for a specific medicine

*Scenario 2* : Ideal-world scenario where there are no SF medicines

Comparing these two scenarios allows us to estimate the incremental health and economic burden of SF medicines

*Health outcomes:* Life-years, disability-adjusted life years (DALYs), quality-adjusted life-years (QALYs), death, and disease-specific outcomes

*Economic/societal outcomes*: Cost of retreatment and value of lost productivity from likely failed treatment or complications

**Assumptions:** The main driver of health burden from use of SF medicines is the relationship between medicine % of active pharmaceutical ingredient (API) and medicine efficacy

# Methodology

## How the Model Works

- Users input values for numerous parameters related to:
  - How many people are eligible to use the medicine each year
  - Where those people seek care
  - The quality of the medicine
  - Health outcomes for patients
    - With standard quality treatment
    - Without treatment
  - Costs of health outcomes and lost productivity
- The model assumes a relationship between medicine quality and medicine efficacy. Use of SF medicine leads to a decrement in treatment efficacy.

# How the Model Works (cont.)

Burden in an ideal scenario (i.e., all medicine is standard quality) − Burden in a real-world scenario (i.e., % of medicine is SF quality) = Incremental burden due to use of SF medicine

# The Model Estimates Two Major Classes of Outcomes:

**Health outcomes**:

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

**Economic/societal outcomes**:

- Cost of retreatment
- Value of lost productivity from failed treatment or complications from treatment

# Dealing with Data Uncertainty

- Data will not be perfect!
  - Users enter the likely values and ranges for each variable
- Users run one-way sensitivity analyses (OWSA) to:
  - Understand which parameters have the greatest impact on results
  - Estimate the range of possible results

# Important Points

- The model can be used for any medicine.
- The model is used to estimate burden for one medicine at a time.
- The model focuses on medicine quality only i.e. based on % of API; it does not reflect issues with medicine availability/stock-outs, poor prescribing practices, or poor patient adherence.

# The Process for Using the Model

1. A Working Group of key stakeholders is selected and oriented to the model.
2. The Working Group provides and agrees on values/ranges for the variables in the model.
3. A Model Manager enters the data and runs the sensitivity analyses.
4. The Working Group meets to review the results.
5. The Working Group determines next steps, if any, to address issues with the medicine's quality.

# Pilot in Kenya: Oxytocin to Treat Postpartum Hemorrhage

- Core group: Karim Wanga (head of post-market surveillance for Pharmacy & Poisons Board) and PQM+
- Larger working group included representatives from:
  - Ministry of Health
  - Kenya Medical Research Institute
  - Nairobi Metropolitan Services
  - University of Nairobi
- Piloted the model in FY2022

# The model assumes a relationship between medicine quality & efficacy.

| Medicine quality rating | % of required API | Reduction in efficacy | Medicine efficacy |
|---|---|---|---|
| Standard | 90 – 110% | 0% | 100% |
| Substandard and falsified (SS)-1 | 75 – 89% | 30% | 70% |
| SS-2 | 50 – 74% | 60% | 40% |
| SS-3 | < 50% | 100% | 0% |

# Basic Assumptions

- The model estimated the burden of SF oxytocin in Kenya for an annual cohort of approximately 1.6 million pregnant women.
- The model used a 7% prevalence of SF medicines - the midpoint between the two extremes of the range (0-13.6%) of recent quality testing of oxytocin in Kenya (Period; 2010- 2022)
- This model assumes the SF oxytocin has 75 – 89% of the required API, leading to a 30% reduction in efficacy.

# Health-Seeking Behavior Parameters

| Parameter | Base case | Range |
|---|---|---|
| Eligible population (pregnant women in Kenya annually) | 1,599,306 | (1,507,450 - 1,723,692) |
| Percentage of population who seek care (percentage of health facility deliveries) | 75% | (67 - 79) |
| Percentage of population who receive care in the public sector (percentage of deliveries in the public sector) | 71% | (69 - 74) |
| Percentage of population who receive care in the private sector (percentage of deliveries in the private sector) | 17% | (15 - 18) |
| Percentage of population who receive care in other sectors, if applicable (percentage of deliveries in the faith-based sector) | 13% | (11 - 14) |
| Proportion of hospitals in public sector | 40% | N/A |
| Proportion of public health centers in public sector | 60% | N/A |
| Proportion of hospitals in private sector | 46% | N/A |
| Proportion of private pharmacies in private sector | 21% | N/A |
| Proportion of "other locations" in private sector, if applicable (proportion of doctors'/clinical officers' clinics) | 33% | N/A |
| Percentage of healthcare providers who up dose when using SF medicines | 50% | (0 - 50) |

# Epidemiological & Medicine Quality Parameters

| Parameter | | Base Case | Range |
|---|---|---|---|
| **Epidemiological Parameters** | | | |
| 15 | Mother's mean childbearing age | 28.6 | (14 - 50) |
| 16 | Expectation of life at age 25-29 | 47.47 | (30.44 - 56.83) |
| **Medicine Quality** | | | |
| 17 | Prevalence of standard quality medicines | 93% | (86 - 100) |
| 18 | Prevalence of SF1 medicines | 7% | (0 - 14) |
| 19 | Prevalence of SF2 medicines | 0% | N/A |
| 20 | Prevalence of SF3 medicines | 0% | N/A |

# Costs – Values Provided for 30 Cost-Related Variables

| Parameter | Base Case | Range |
|---|---|---|
| National average drug cost per dose | $0.39 | (0.03 - 1.35) |
| National average unit cost of mild PPH management | $77.61 | (50 - 500) |
| National average unit cost of hysterectomy management | $663 | (500 - 1,663.25) |
| National average unit cost of severe PPH management | $1343 | (77.61 - 1,611) |
| Productivity loss due to days of missed work (per day) | $5.5 | (2.39 - 7) |
| GDP per capita | $1,838.21 | |

# Results

The model estimates that, due to use of SF oxytocin, every year in Kenya there are:

| | |
|---|---|
| Additional cases of mild PPH | 2,005 |
| Additional cases of severe PPH | 489 |
| Additional hysterectomies | 26 |
| Additional deaths | 26 |
| Life-years lost | 420 |

# Results

## Estimated Economic Burden from Use of SF Oxytocin in Kenya for One Year

| Total Economic Burden | | |
|---|---|---|
| **Health system** | | $937,050.22 |
| **Productivity losses** | | $302,071.16 |
| from missed days of work | ($21,728.85) | |
| from premature death | ($280,342.31) | |
| **TOTAL ECONOMIC COSTS** | | **$1,239,121.37** |

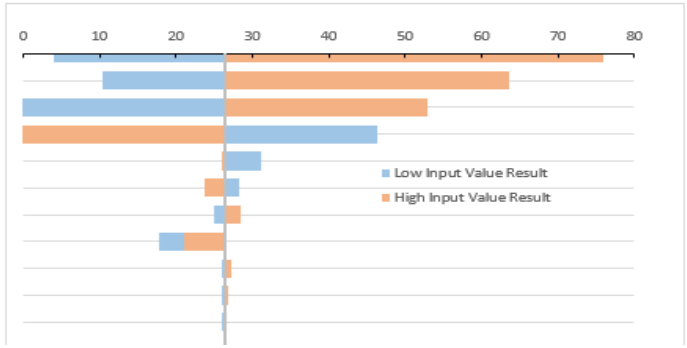
# Results

## Sensitivity Analyses

- A one-way sensitivity analysis (OWSA) examined the sensitivity of the model to changes in its inputs (i.e., the low and high input values for each variable).
- Included a range or a confidence interval for key variables.
- Allows one to examine the effect that each variable has on the model's results, one variable at a time (with all other variables held constant).
- Generates tornado diagrams that show:
  - The spread of the model results depending on the low and high input value of each model input
  - Which model input has the most effect on the results

# Sensitivity Analysis Results: Impact of Parameter Ranges on Incremental Deaths

| One-Way Sensitivity | Select: | Outcome: | Live Result: | Run One-Way |
|---|---|---|---|---|
| | | Incremental Deaths | 26.5 | |




| Parameter | Low Input Value | High Input Value | Low Input Value Result | High Input Value Result | Spread |
|---|---|---|---|---|---|
| Probability of Severe PPH without treatment | 0.01845 | 0.0974 | 4.118623021 | 75.93426934 | 71.81564632 |
| Mortality risk from PPH | 0.021 | 0.13 | 10.32940547 | 63.57671577 | 53.2473103 |
| Proportion of Substandard and Falsified Medicines 1 in the Real-world Scena | 0 | 0.14 | 0 | 52.90030157 | 52.90030157 |
| Treatment Effect of Substandard and Falsified Medicines 1 (API: 75-90%) | 0.3 | 1 | 46.28776388 | 0 | 46.28776388 |
| Proportion of Healthcare Providers who increase dose to achieve full effect | 0.41 | 0.51 | 31.21117793 | 25.92114777 | 5.290030157 |
| Probability of Severe PPH with treatment | 0.012 | 0.017 | 28.26941985 | 23.72124719 | 4.548172661 |
| Population Eligible | 1130587.5 | 1292769 | 24.93098869 | 28.50731087 | 3.576322171 |
| Percentage of Population that seeks care | 0.67 | 0.793 | 17.72160103 | 20.97496957 | 3.253368547 |
| Percentage of Population that receives care in the Public Sector | 0.6873 | 0.7389 | 25.95210406 | 27.31908337 | 1.366979314 |
| Percentage of Population that receives care in the Private Sector | 0.1477 | 0.1765 | 25.9649811 | 26.72437713 | 0.759396037 |
| Percentage of Population that receives care at Faith-based sector | 0.1134 | 0.1362 | 26.07572635 | 26.67691488 | 0.601188529 |
| Probability of Hysterectomy with treatment | 0.001 | 0.0028 | 26.46430066 | 26.37940143 | 0.084899223 |

- Incremental deaths base case: 27 deaths per year
- Probability of severe PPH without treatment has the largest impact on incremental deaths: **Range: 4 – 76 incremental deaths**
- Mortality risk of PPH has the second largest impact on incremental deaths: Range: **10 – 64 incremental deaths**
- Proportion of SF medicines 1 in the real-world scenario is the third largest impact on incremental deaths: Range **0- 53 incremental deaths**

# Most Influential Parameters on Outcomes

| Outcome (column A) | Most influential parameter (column B) | Range of parameter (Column C) | Range of Outcome (Column D) |
|---|---|---|---|
| Economic burden | Probability of severe PPH without treatment | 1.85-9.74% | **$ 442,897 - $ 3,003,462** economic burden |
| Incremental cases of severe PPH | | | **75 – 1405** additional cases of severe PPH |
| Incremental cases of mild PPH | Probability of mild PPH without treatment | 0.123- 0.464 | **51 – 5795** additional cases of mild PPH |
| Incremental number of hysterectomies | Proportion of SF medicines 1 in the real-world scenario | 0 - 0.14 | **0– 51** additional hysterectomies |
| Incremental deaths | Probability of severe PPH without treatment | 0.01845- 0.0974 | **4 – 76** additional hysterectomies |
| Life-years lost | Probability of severe PPH without treatment | 0.01845- 0.0974 | **65 - 1204** life-years lost |

# Conclusions

- The burden of SF oxytocin in Kenya was substantial in 2019, however recent studies (2022) have shown improved compliance (100%)
- ***The SF model (quality data of oxytocin for period 2010-2022); produced the following results***
- More than 2,000 cases of PPH (2,004 mild and 488 severe)
- 26 additional deaths (and life-years lost from those)
- SF oxytocin probably leads to more than $1.2 million per year in economic costs.
  - The estimated burden could be substantially lower or as high as $3 million per year.
- The model can be used by countries and NMRAs to estimate the burden of SF medicines in their markets

# Acknowledgment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# Thank you!

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