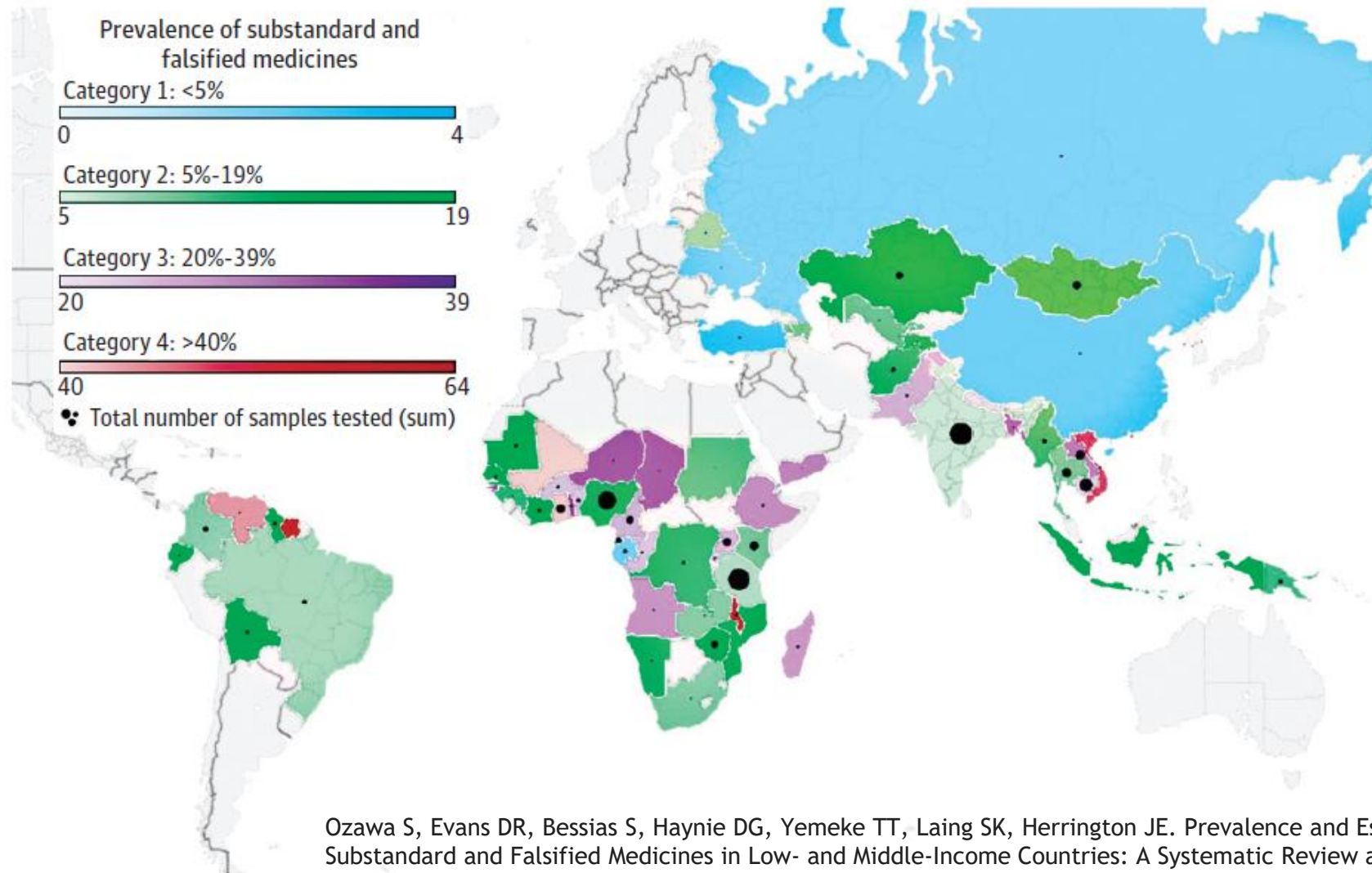


Quality of Medicines for Hypertensive Disorders of Pregnancy: A Systematic Review

Pete Lambert - Director, Monash Quality of Medicines Initiative, Monash University
Maternal Health Supplies Caucus

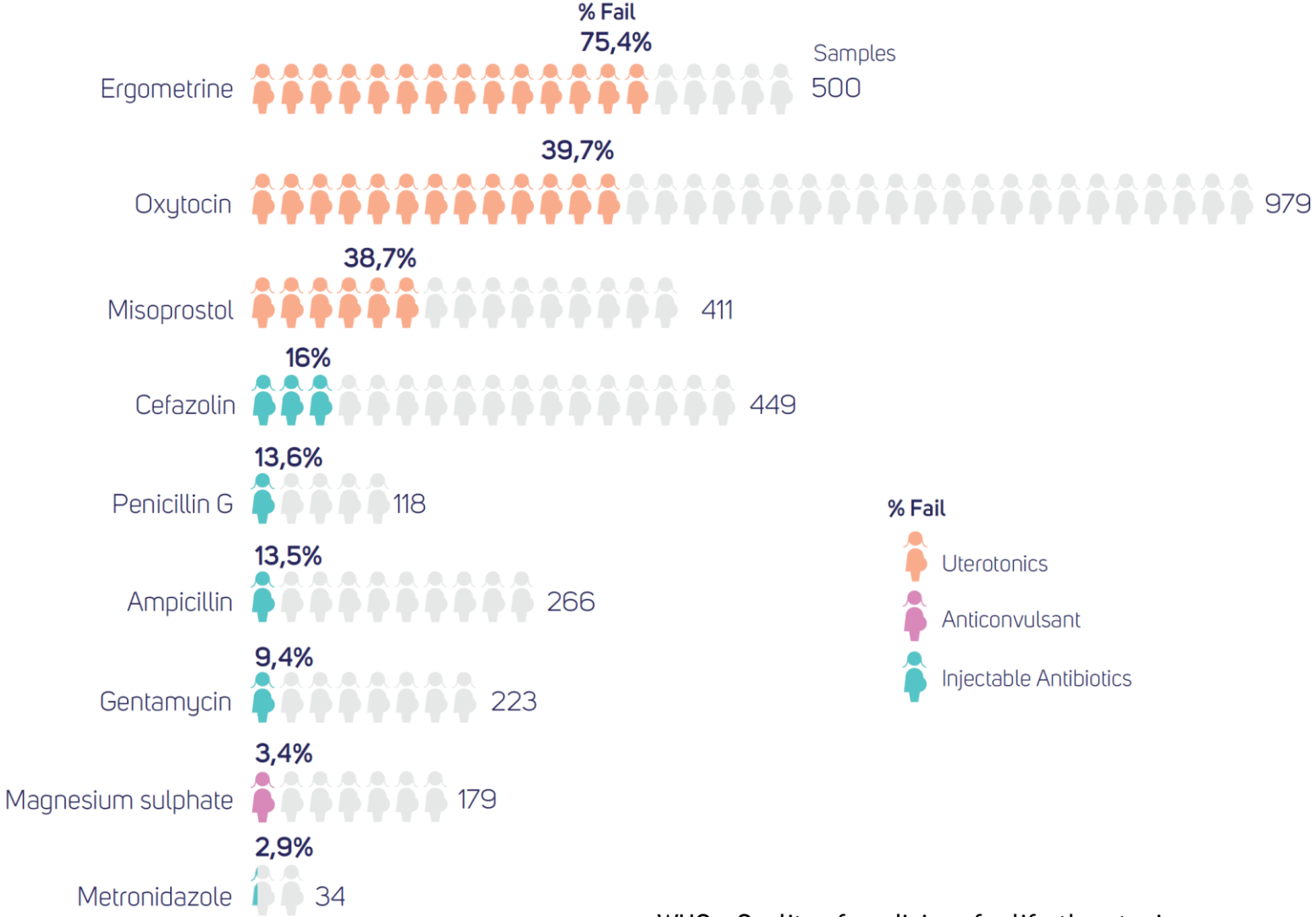
17 October 2023

Quality issues with medicines are a global problem, but predominate in LMICs



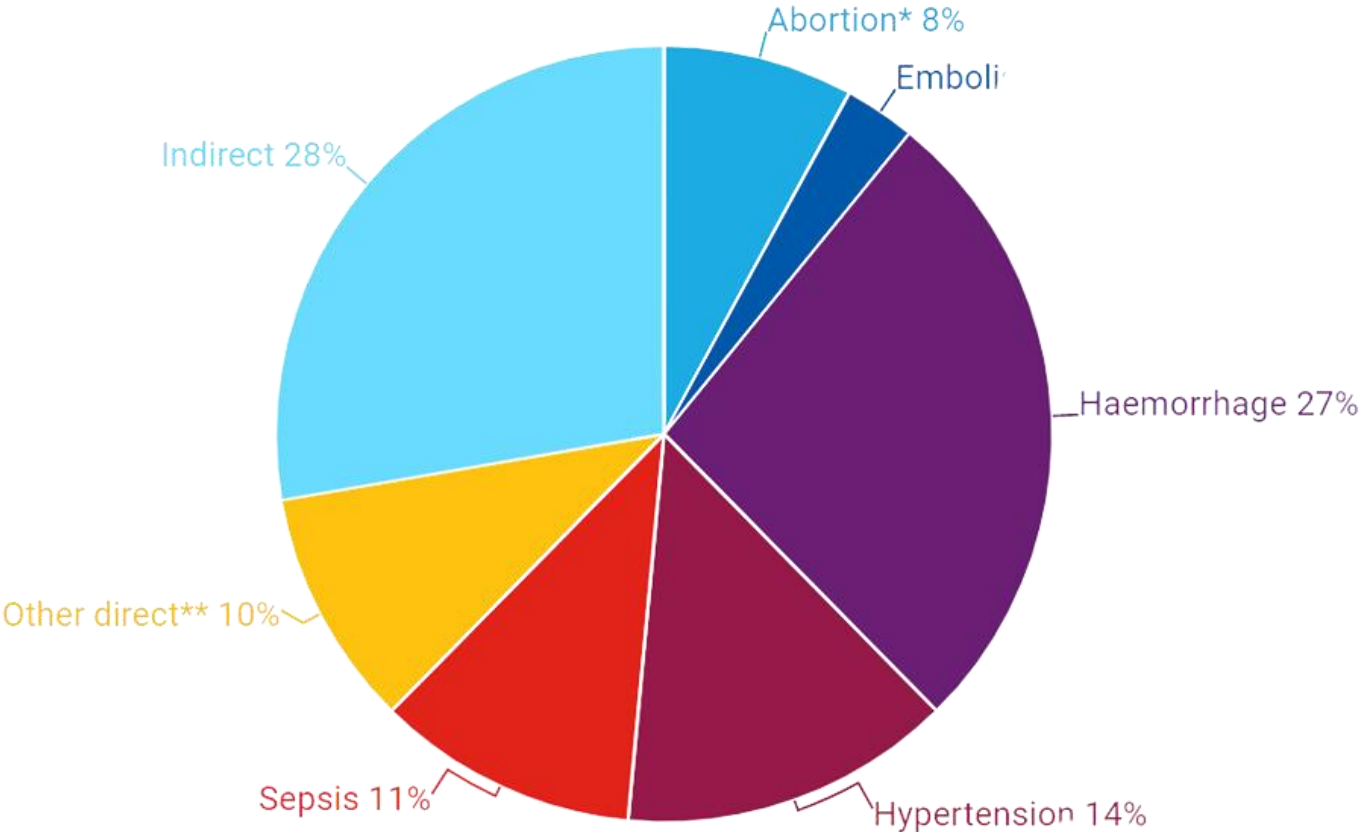
Ozawa S, Evans DR, Bessias S, Haynie DG, Yemeke TT, Laing SK, Herrington JE. Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. JAMA Netw Open. 2018

Quality issues are highly prevalent in obstetric medicines



WHO - Quality of medicines for life-threatening pregnancy complications in low- and middle-income countries: A systematic review (Torloni et al., 2020)

Pre-eclampsia/eclampsia is the second leading direct cause of maternal mortality



Say L et al., 'Global causes of maternal death: a WHO systematic analysis' Lancet Global Health. [http://dx.doi.org/10.1016/S2214-109X\(14\)70227-X](http://dx.doi.org/10.1016/S2214-109X(14)70227-X), May 6, 2014.

Quality of Medicines for Hypertensive Disorders of Pregnancy

Data presented comes from ongoing PhD program at Monash by Pooja Maharjan

1. Systematic review of studies assessing the quality of medicines for hypertensive disorders of pregnancy
2. Post-marketing surveillance of quality of medicines for hypertensive disorders of pregnancy targeting five countries
3. If quality deficiencies are found, a health economic evaluation of the potential impact of these poor quality medicines.



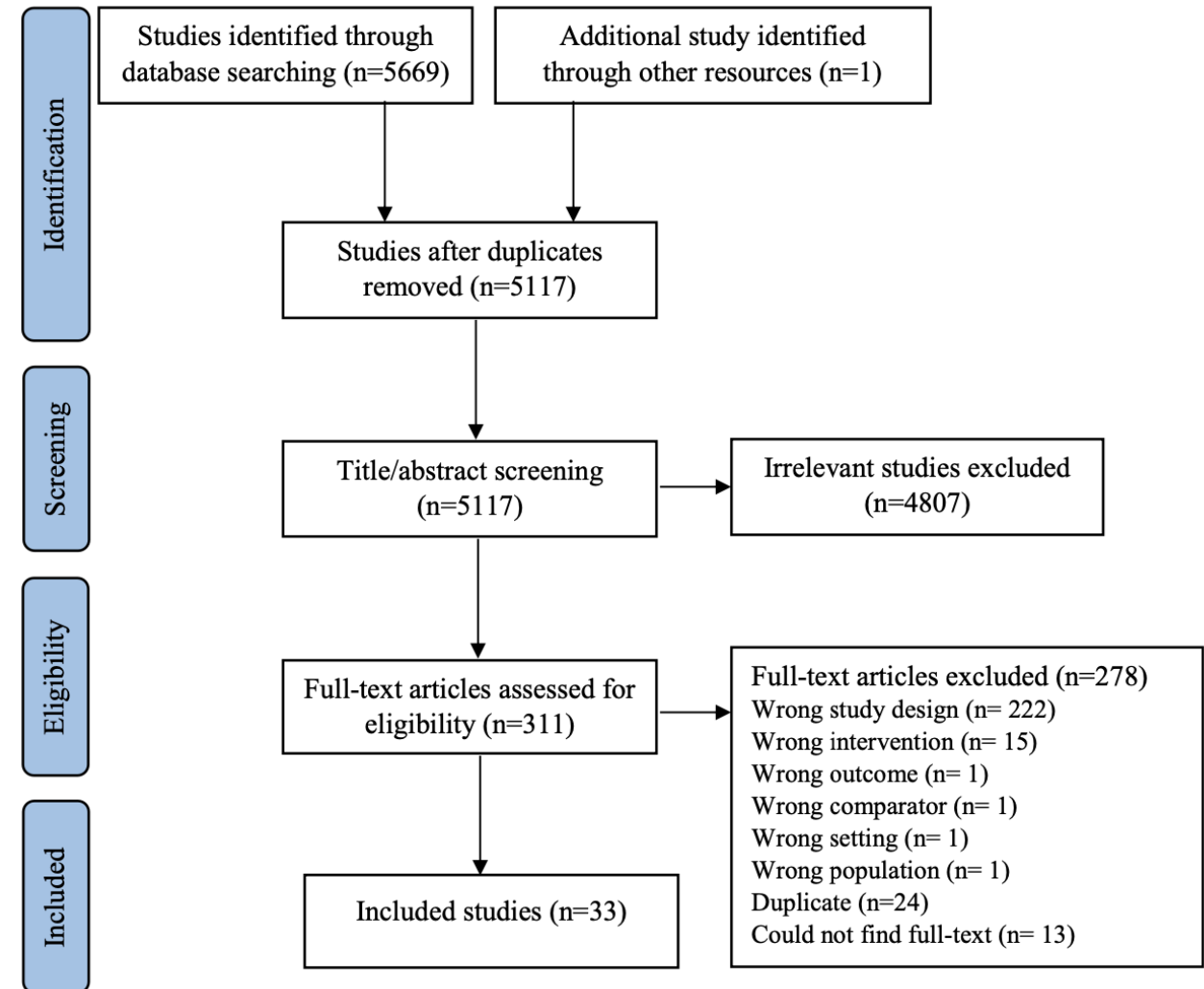
Systematic Review of Quality of Medicines for Hypertensive Disorders of Pregnancy

Target Medicines

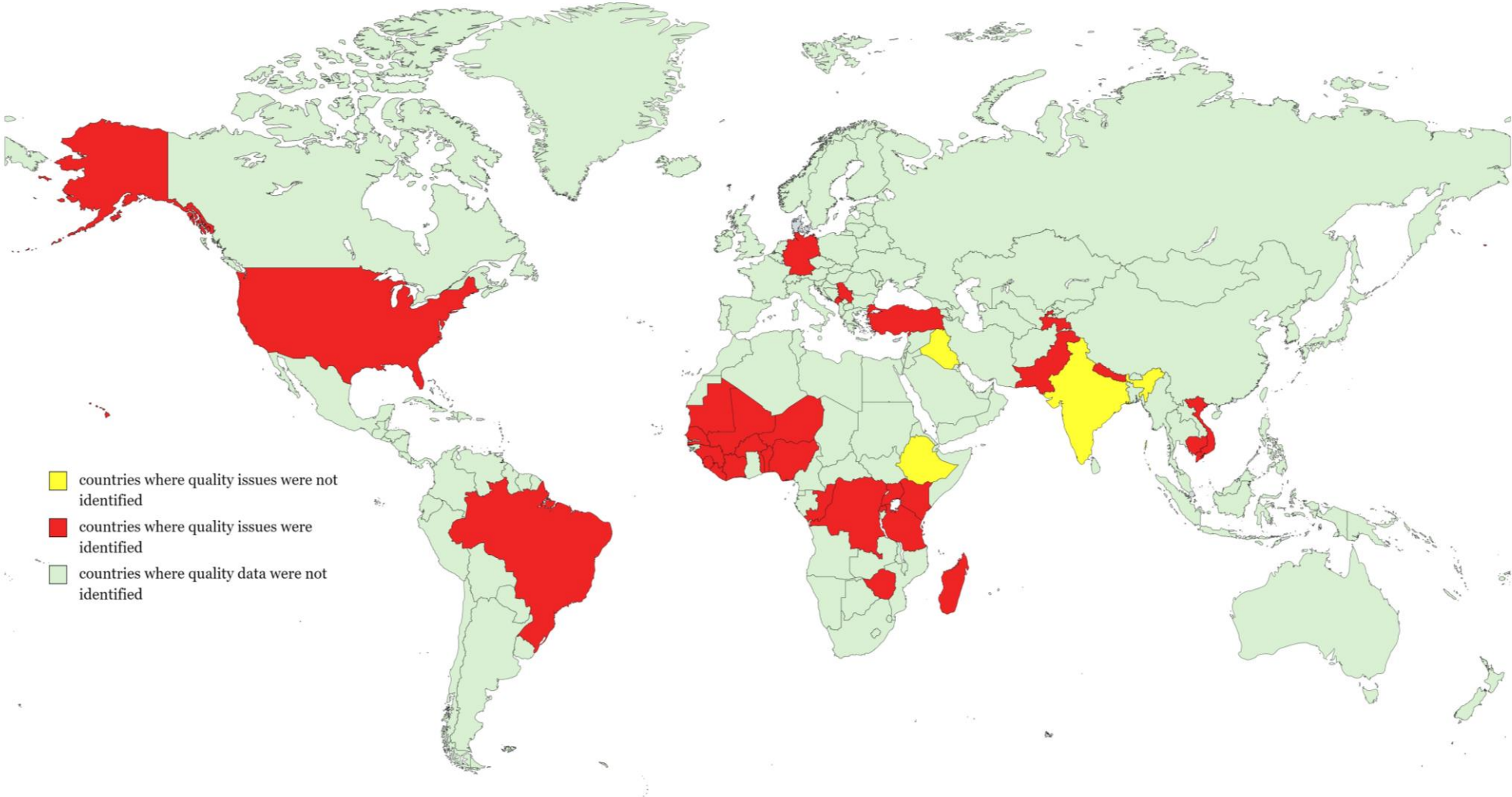
Drug	Indication
Calcium	Prevention of pre-eclampsia
Aspirin	Prevention of pre-eclampsia
Labetalol	Management of hypertension
Nifedipine	Management of hypertension
Methyldopa	Management of hypertension
Hydralazine	Management of hypertension
Amlodipine	Management of postpartum hypertension
Enalapril	Management of postpartum hypertension
Magnesium Sulphate	Prevention and management of eclamptic seizures

Systematic Review of Quality of Medicines for Hypertensive Disorders of Pregnancy (HDoP)

- Aim: Synthesise available evidence on quality of medicines for HDoP.
- Searches conducted on six databases (PUBMED, MEDLINE, EMBASE, CINAHL, ProQuest and Cochrane Library)
- Search included peer-reviewed and grey literature
- Studies were agnostic to indication
- Two reviewers independently assessed the studies for inclusion using the Medicine Quality Assessment Reporting Guidelines tool



Systematic Review of Quality of Medicines for Hypertensive Disorders of Pregnancy - Results



Systematic Review of Quality of Medicines for Hypertensive Disorders of Pregnancy - Results

Drug	No. of studies	No. of samples	Countries from which samples were collected	No. (%) of studies identifying quality issues	Prevalance of failed samples per study (%)	Quality issues identified
Calcium	5	85	USA, Brazil, Pakistan	5 (100%)	10.0% – 88.9%	API content, heavy metals
Aspirin	8	1510	USA, Nigeria, Iraq, Brazil, Yugoslavia, Cambodia	6 (75%)	0.0% - 92.7%	API content, related substances, dissolution testing, physical parameters
Nifedipine	2	170	Nigeria, Germany	2 (100%)	60.3% – 74.5%	API content, impurities
Methyldopa	3	27	Nigeria, Rwanda, Brazil	2 (67%)	0.0% - 50.0%	API content
Hydralazine	1	16	USA	1 (100%)	75%	Impurities
Amlodipine	7	605	India, Nigeria, Nepal, Cambodia, Multi-Country (10 African countries)	5 (71%)	0.0% - 30.0%	API content (incl. counterfeit), physical parameters
Enalapril	3	14	Brazil, Turkiye	3 (100%)	100%	API content, impurities, physical parameters
Magnesium Sulphate	5	1355	USA, Nigeria Ethiopia, UNCoLS (10 countries)	4 (80%)	0.0% - 44.4%	Fungal contamination, API content, pH

Quality of Medicines for Hypertensive Disorders of Pregnancy

Summary

- 29/33 (88%) Studies found evidence of poor quality medicines (with varying prevalence)
- Quality issues not limited to LMICs
- Products tested came from a range of source countries
- Most common deficiencies were low API content and impurities/related substances
- Limited information in the studies as to root cause of quality deficiencies however there are clearly issues of manufacturing quality and some evidence of degradation (e.g. aspirin)

Quality of Medicines for Hypertensive Disorders of Pregnancy

Next steps

- Paper currently under journal review
- Abstract available - Maharjan et al, Pharmacy Education, 23(6) 429-430, 2023
- Post-marketing surveillance of quality of medicines for hypertensive disorders of pregnancy targeting five countries:
 - Ghana, Ethiopia, Malawi, Nigeria and Nepal
 - Supported by USAID GHSC-PSM
 - Targeting aspirin, magnesium sulphate and most commonly used antihypertensive in each country
 - Urban vs rural, private vs public, supply chain from point of entry, regulatory status
 - Where possible, inclusion of root cause analysis
 - To be conducted 2023-2024
- If quality deficiencies are found, a health economic evaluation of the potential impact of these poor quality medicines will be conducted.

Acknowledgements



Prof. Josh Vogel
Dr Annie McDougall
Meghna Prasannan Ponganam



Pooja Maharjan
Prof. Michelle McIntosh