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Protocol for a systematic review of peer-reviewed literature on the impact and process indicators of elimination of mother-to-child transmission of HIV, syphilis, and hepatitis B in middle income non European Union countries in the World Health Organisation European Region, 2018-2022

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ADMINISTRATIVE INFORMATION

Support - No specific funding, part of routine activities of the World Health Organization Collaborating Centre for HIV Strategic Information.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 May 2024 and was last updated on 20 May 2024.

INTRODUCTION

Review question / Objective What impact and process indicators of elimination of mother-to-child transmission of HIV, syphilis and hepatitis B are available in the published literature for the middle-income non European Union countries of the World Health Organisation (WHO) European Region and Kosovo for the period 2018-2022 and what is the progress towards the triple elimination targets?

Condition being studied WHO and member states have committed to the triple elimination of mother-to-child transmission (EMTCT) of HIV, syphilis, and hepatitis B virus (HBV) as a public health priority. Given the similar pathways of mother-to-child transmission (MTCT) of these infections and the potential for integrating interventions via antenatal, delivery, and postnatal

services, there is an opportunity for focused efforts to end all three types of transmission. In 2021, the WHO issued a new version of impact and process targets for the validation of the triple EMTCT. The purpose of the elimination targets is to ensure the availability of quality reproductive and maternal and child health services to reduce and control the transmission of HIV, syphilis, and HBV between mothers and their offspring, and to provide the best available treatment to the mother, such that incidence is reduced to a very low level.

METHODS

Participant or population Pregnant women and their children in Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, Republic of Moldova, Russian Federation, Serbia, Tajikistan, Turkey,

Turkmenistan, Ukraine, and Uzbekistan. We will also include data for Kosovo.

Intervention Both interventional and non-interventional studies will be included.

Comparator Studies with and without comparators will be included.

Study designs to be included Cross-sectional/prevalence, cohort, randomised control trials, or case-control study design.

Eligibility criteria Inclusion criteria

(1) Cross-sectional/prevalence, cohort, randomised control trials, or case-control study design

(2) Conducted in middle income non European Union countries in the WHO European Region or in Kosovo

(3) Reported on an HIV, syphilis or HBV EMTCT-related indicator of interest

Exclusion criteria:

(1) Reports which do not include primary data

(2) Reports published prior to 2018

(3) Reports of studies conducted outside of the countries of interest or Kosovo

(4) Sample from populations not specifically including pregnant women or children.

Information sources We explored the most recent data (from 2018 – 2022) available through WHO, The Joint United Nations Programme on HIV/AIDS (UNAIDS), The United Nations Children's Fund (UNICEF) and United Nations Development Programme (UNDP) databases. We will systematically search the following databases for published articles:

- MEDLINE (via Ovid)

- Scopus

- Web of Science Core Collection

We will restrict our searches to articles published from January 2018 onwards. We will also screen references of included reports for eligible publications. We will not search for unpublished studies. We will apply no language restrictions.

The methods for this systematic review of published literature are adapted from: Bell et al. Progress towards triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Pacific Island Countries and Territories: a systematic review. *Lancet Reg Health West Pac.* 2023;35:100740. doi: 10.1016/j.lanwpc.2023.100740.

Main outcome(s) HIV

- Impact: Population case rate of new paediatric HIV infections due to MTCT per 100 000 live births; MTCT rate of HIV

- Process: ANC coverage (at least one visit (ANC-1)); Coverage of HIV testing of pregnant women; ART coverage of pregnant women living with HIV

Syphilis

- Impact: Case rate of congenital syphilis per 100 000 live births

- Process: ANC coverage (at least one visit (ANC-1)); Coverage of syphilis testing of pregnant women among those who had at least one ANC visit; Adequate syphilis treatment of syphilis-seropositive pregnant women

Hepatitis B

- Impact: Prevalence of HBsAg in children ≤5 years old; MTCT rate

- Process: coverage of maternal HBsAg testing; coverage with antivirals for eligible HBsAg-positive pregnant women for countries in which these are relevant for elimination validation.

Data on HepB3 vaccine coverage and HepB-BD coverage will not be extracted as these are available through WHO/UNICEF Estimates of National Immunization Coverage (WUENIC), and their methodology also includes systematic reviews of published literature.

Data management Study selection

- Two reviewers will independently apply eligibility criteria and select studies for inclusion in the systematic review

- Disagreements will be resolved and documented by a third researcher

Data extraction

- One reviewer will extract data and the second reviewer will verify for accuracy

- Disagreements in individual judgements will be resolved and documented by a third researcher

- Data extraction sheet in Microsoft Excel will be designed and piloted for this purpose.

We will extract article information (lead author, year of publication, country) as well as information on study design, year of study, province/region (if relevant), setting population, sample size, indicator descriptor and the estimate. For studies with multiple indicators, we will include data for each indicator. We will not contact study authors for clarification or missing data.

Quality assessment / Risk of bias analysis Two reviewers will independently assess quality of included articles using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (<https://www.nhlbi.nih.gov/health-topics/study-qualityassessment-tools>). We will assess the quality according to 14 criteria and give an overall quality rating of good, fair or poor. Disagreements will be resolved and documented by a third researcher.

Strategy of data synthesis We will perform a narrative synthesis of the results.

Subgroup analysis We will not perform subgroup analyses, but will present the values for each indicator, per study and per country.

Sensitivity analysis We will not perform sensitivity analyses.

Language restriction We will apply no language restrictions.

Country(ies) involved Croatia.

Other relevant information The methods for this systematic review of published literature are adapted from: Bell et al. Progress towards triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Pacific Island Countries and Territories: a systematic review. *Lancet Reg Health West Pac.* 2023;35:100740. doi: 10.1016/j.lanwpc.2023.100740.

Keywords EMTCT; Elimination of mother-to-child transmission; Europe; HIV; Hepatitis B; Syphilis.

Contributions of each author

Author 1 - Jelena Barbaric - Screening, data extraction, quality assessment.

Author 2 - Ivana Bozicevic - Screening, data extraction, quality assessment.

Author 3 - Helena Markulin - Information Specialist, search strategies, searches.