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## The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, crosssectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, cross-sectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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\*\* The MIACSA expert advisory panel (EAP) consists of the following members: Flor M. Muñoz (chair), Michelle L. Giles (co-chair), Mercy Ahun, Martina Baye, Pradeep Haldar, Matthews Mathai, and Stephen Hodgins. Observers to EAP meetings included: Carsten Mantel, Elizabeth Mason, Sonja Mertens, Jayani Pathirana, Sarah Rendell. Additional WHO experts included: Emily Wootton, Laura Nic Lochlainn, Ahmadu Yakubu, and Sara Rendell. \*\*\* Last authors

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**Key words:** maternal immunization; maternal tetanus vaccination, maternal health; neonatal health; maternal tetanus; neonatal tetanus; maternal mortality; neonatal mortality; health care service delivery; antenatal care capacity; study protocol

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1	ABSTRACT
2	Introduction. Maternal immunization (MI) is a safe and cost-effective way of preventing
3	neonatal tetanus, and is one of several strategies that aim to reduce the high global rates of
4	maternal and neonatal morbidity and mortality caused by vaccine-preventable diseases.
5	Given the prospect of introducing new maternal vaccines in the near future, it is essential to
6	identify and understand current policies, practices, and unmet needs for introducing and/or
7	scaling up MI in low and middle income countries (LMICs).
8	Methods and analysis. The Maternal Immunization and Antenatal Care Situation Analysis
9	(MIACSA) is a mixed methods, cross-sectional study that will collect data in four phases: (1)
10	a review of global databases for selected health indicators in 136 LMICs; (2) a structured
11	online survey directed at Maternal, Newborn, and Child Health (MNCH) and Expanded
12	Programme on Immunization (EPI) focal points in all 136 LMICs; (3) semi-structured
13	telephone interviews of 30 selected LMICs; and (4) 10 week-long country visits, including
14	key informant interviews, health facility visits, and focus group discussions. The principal
15	analyses will assess correlations between the various aspects of MI delivery strategies and
16	proxy measures of health systems performance related to vaccine-preventable disease control.
17	The primary outcome will be a typology of existing MI delivery models, and secondary
18	outcomes will include country profiles of child and maternal health indicators, and an MI
19	gaps and needs analysis.
20	Ethics and dissemination. The protocol was approved by the World Health Organization
21	Ethics Review Committee. The results will be made available in a project report and

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submitted for publication in peer-reviewed journals that will be shared broadly among global 

health decision makers, researchers, product developers, and country-level stakeholders. 

Registration. Not applicable.



27 Streng

## Strengths and limitations of this study

28	•	The MIACSA study will provide a global overview and analysis of existing maternal
29		immunization (MI) delivery strategies in low- and middle-income countries (LMICs).
30	•	In order to optimise the assessment of MI delivery strategies in LMICs, data will be
31		collected in four phases: (1) a desktop review of relevant health indicators from global
32		sources, e.g. WHO and other UN databases, from 136 LMICs; (2) a structured online
33		survey directed at Maternal, Neonatal, and Child Health (MNCH) and Expanded
34		Programme on Immunization (EPI) programme managers and focal points in all 136
35		LMICs; (3) semi-structured telephone interviews of 30 selected LMICs; and (4) 10
36		week-long country visits, including key informant interviews, health facility visits, and
37		focus group discussions.
38	•	Strengths of the study include a mixed-methods design; a multidisciplinary approach
39		leveraging policy-level, academic, and implementers' experience; multi-level data
40		collection; a globally comprehensive analysis combined with in-depth information of a
41		subsample of LMICs; inter-sectoral collaboration between MNCH and EPI programmes,
42		and broad dissemination of results.
43	•	The results will provide evidence for a typology of MI delivery models in LMICs, and
44		identify capacity needs and key system changes, including policy adjustments required to
45		introduce new maternal vaccines and/or scale up existing MI in LMICs.

Limitations include the small number of countries and health care facilities visited within
 each country included in the study, thus precluding generalization of country visit
 findings to a national level, and the fact that the end-users' perspective will be captured
 only indirectly through community health workers.



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51 INTRODUCTION
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Vaccine-preventable diseases are a major cause of global child morbidity and mortality, particularly in low- and middle-income countries (LMICs).<sup>1</sup> Since the 1990s, public health interventions have more than halved under-five childhood mortality; however, reduction of stillbirths and of neonatal mortality (death in the first 28 days of life) has been slower.<sup>2</sup> This is in part due to the fact that most vaccines cannot be administered to newborns, who, being unable to develop protective responses due to limitations in their immune system, are left particularly vulnerable to infectious diseases. Vaccination of pregnant women, or maternal immunization (MI), has proven to be an effective strategy to reduce neonatal tetanus, and is a potential strategy to reduce the burden of other vaccine-preventable diseases in mothers and infants. Thus, MI is one of several strategies that aim to reach the third sustainable development goal of ending preventable maternal and newborn deaths.<sup>3-5</sup> 

Studies have shown that MI can effectively protect the mother, as well as her child, through transplacental transfer of maternal immunoglobulin G (IgG) to the foetus.<sup>6,7</sup> The Maternal and Neonatal Tetanus Elimination (MNTE) initiative has led the way in the implementation of MI, combining at least two doses of tetanus toxoid containing vaccine (TTCV) during pregnancy (TT2+) with the promotion of hygienic delivery and clean cord care practices, as well as vaccination of children and women of reproductive age, to eliminate maternal and neonatal tetanus as a public health problem. Between the late 1980s and 2015, the MNTE initiative reduced global tetanus-related neonatal mortality by 96%.8 

TTCV and inactivated influenza vaccines are considered safe and effective for use during
 pregnancy,<sup>9</sup> and are recommended for pregnant women by the World Health Organization

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(WHO).<sup>6, 10-13</sup> New vaccines, several of which are under development and evaluation, target
other important pathogens, such as group B streptococcus (GBS), and respiratory syncytial
virus (RSV), and may provide safe and cost-effective protection of mothers and their infants
through MI in the future.<sup>14-18</sup>

In order to identify the challenges of implementing current and new vaccines for MI, a better understanding is needed of the capabilities and limitations of existing delivery platforms, such as antenatal care (ANC) services and the Expanded Programme on Immunization (EPI).<sup>19</sup> The capacity of ANC services to deliver vaccines to pregnant women will require thorough assessment, as globally only 62% of women benefit from at least four ANC visits, i.e. the proportion of pregnant women who received 4 or more ANC visits during their last pregnancy (ANC4+), and in Sub-Saharan Africa and South Asia, ANC4+ coverage is only 52% and 46%, respectively.<sup>20</sup> Delivering vaccinations and other essential interventions to women at the necessary timely intervals during pregnancy, as well as documenting the coverage and outcomes of such interventions, requires a robust ANC platform with sufficient personnel and resources.<sup>21</sup> 

WHO recommends that pregnant women living in endemic areas are sufficiently immunised against tetanus in order to protect the women and their newborn infants. MI with TTCV is routine in many countries;<sup>22, 23</sup> however, progress of tetanus vaccination in LMICs has faced challenges leading to delays in elimination, and uptake among pregnant women of other vaccines, such as influenza and pertussis vaccines, has been low. As a part of EPI services, routine tetanus immunization during pregnancy has been complemented with supplementary vaccination activities in a majority of countries in order to reach high coverage and achieve

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99	MNTE goals. A better understanding of MI in the context of both ANC and EPI, including
100	implementation of guidelines and policies, ministerial responsibilities at national and
101	subnational levels, vaccine management including cold chain and logistics, vaccine
102	administration, staff capacity, social mobilisation, vaccine acceptance, and assessment of
103	vaccine safety, may help identify service delivery challenges as well as opportunities to
104	optimise current and future MI efforts. <sup>24</sup>
105	
106	Closer collaboration between ANC and EPI services could provide a unique and cost-
107	effective opportunity to further strengthen preventive health care measures for women and
108	children under each programme, by reducing missed opportunities for immunization,
109	including MI, as well as reinforcing the delivery of essential health care services.
110	
111	In view of recent product and policy developments, the WHO, supported by the Bill and
112	Melinda Gates Foundation, aims to identify the knowledge gaps in MI delivery strategies by
113	mapping the strengths and challenges of existing ANC and immunization services for
114	pregnant women in LMICs through the Maternal Immunization and Antenatal Care Situation
115	Analysis (MIACSA) project. The results will provide the evidence for a typology of MI
116	delivery models, as well as identify the capacity needs and key system changes required to
117	introduce new maternal vaccines and/or strengthen vaccine delivery for MI in LMICs.
118	Ultimately, the project aims to determine how existing health care services can be further
119	strengthened to improve maternal and neonatal outcomes, and how they could accommodate
120	new MI vaccines.

#### 122 METHODS AND ANALYSIS

#### 123 Study design and data collection.

Between November 2016 and December 2018, a mixed-methods, cross-sectional study will be carried out in four phases to assess key health system features related to the implementation of MI (Figure 1). An expert advisory panel (EAP) consisting of specialists in immunization, maternal and neonatal health, MI implementation and social sciences, will provide technical advice on the study design, the development of research questions and surveys, the data collection methods, and the results interpretation. In addition to following WHO standards for global monitoring surveys, all data collection tools and standard operating procedures will be reviewed and endorsed by the EAP. The surveys and country visits will be conducted in local languages when needed.

**Data collection phase 1.** The first phase will consist of collecting key health indicators of LMICs to create outlines of country profiles, focusing on ANC and EPI services. A desktop review of pre-defined health indicators (Figure 2) from 136 LMICs will be conducted from existing global data sources, including Demographic and Health Surveys (DHS)/Multiple Indicator Cluster Surveys (MICS), WHO/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, WHO/UNICEF Joint Reporting Forms (JRF), MNTE reports, and WHO Maternal, Newborn, Child, and Adolescent Health (MNCAH) policy survey. The indicators will focus on governance and policy environment, health systems performance, and immunization activities, including MI. Data from phase 1 will be compiled in a database for analysis of the study's research questions, and will inform the selection of countries for phase 3 (see below). 

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:	146	Data collection phase 2. The country profiles established in phase 1 will be completed and,
:	147	if needed, updated by an online survey with WHO Regional Offices, national Ministry of
	148	Health (MoH) focal points from Maternal, Newborn and Child Health (MNCH) and EPI
:	149	programmes and their WHO Country Office counterparts in all LMICs, using a structured
:	150	questionnaire (Figure 3). Data will be collected on service delivery models of maternal
	151	tetanus vaccination, including delivery platforms, programme funding, disease surveillance,
:	152	and vaccine safety surveillance. Data on maternal vaccines other than tetanus will be included
	153	when pertinent. A draft questionnaire will be piloted in advance of the survey. Non-
:	154	responders will be followed-up by telephone and email. Revisions following queries on
	155	missing, erroneous, or inconsistent data will be done at country level.
	156	
	157	<b>Data collection phase 3.</b> In order to understand how existing health care delivery services
	158	could be adapted to implement MI beyond tetanus immunization, further data will be
	159	collected on delivery platforms for maternal tetanus vaccination in LMICs. In-depth
	160	telephone interviews will be conducted with EPI and MNCH programme officers responsible
	161	for MI at the MoH in a sample of 30 countries, using a semi-structured questionnaire (Figure
:	162	4). The countries will be selected based on performance of MI as assessed by coverage of
:	163	maternal TTCV and ANC, geographic representation, and recommendations from WHO
	164	Regional Offices on MI priorities. The countries will be stratified into four groups; high and
:	165	low maternal tetanus vaccination performance measured as protection at birth (PAB), i.e. the
:	166	proportion of newborns protected at birth against neonatal tetanus, with a cut-off of 90%, and
:	167	high and low ANC performance (with a cut-off of the median ANC4+ coverage in countries
:	168	with available data). PAB was identified as a more reliable proxy measure than TT2+, as the
:	169	issue of not including already vaccinated women in the numerator used for estimating the
:	170	latter indicator would be avoided. The PAB cut-off level was set based on the target required
		11
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to attain and sustain MNTE, whereby >80% of pregnant women are immunized against
tetanus. The country selection will include a representation of all MI delivery models and
WHO regions, with a focus on Africa and South-East Asia where maternal and neonatal
mortality are highest, and will ensure inclusion of high performing countries in order to
include likely early adopters of new maternal vaccines and learning cases of best practices.

The interviews will collect data on the policy, governance, and funding environment for EPI and ANC programmes, ANC delivery, and maternal tetanus vaccination including monitoring and evaluation of results. The questionnaire will be shared with WHO country office focal points and MoH MNCH and EPI managers for compilation in advance of the teleconference, allowing for discussion and clarification when needed during the actual interview. Responses will be recorded using standard data entry procedures, and may be voice-recorded if consent is obtained by the interviewees. Any discordant responses will be attempted to be resolved by consensus, and incomplete responses will be followed up. A summary of key findings will be shared with the participants to confirm the responses were correctly captured. 

Data collection phase 4. Finally, in-country visits will be conducted in order to collect data on MI from key decision-makers and implementers at every level of the health care system, as well as to determine actual delivery, capacity and coordination of ANC and EPI services, on both supply and demand sides of the health care services (Figure 5). Ten countries will be selected based on high, medium, or low performance of MI systems as assessed by PAB and TT2+, a range of different MI delivery models (e.g. degree of coordination between EPI and ANC in MI delivery), and agreement by senior national and subnational MNCH and EPI staff for study visits. The final country selection will ensure representation of the range of MI

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delivery models, and will include high-performing countries, MNTE priority countries, and
countries with high ANC4+ coverage. Site visits will include ANC and EPI sites and session
observations, focus group discussions, and in-depth interviews. The week-long visits will be
piloted in two countries to adjust and refine the data collection tools and the standard
operating procedures, and data from these two countries will be included in the final analysis.

An initial joint focus group discussion will be held with national-level stakeholders, followed by key informant interviews with stakeholders pertinent to MI, ANC, and EPI services at subnational levels of the health care system, including decision and policy makers, technical and financial parties, and civil society, such as non-governmental organisations. The study will aim to conduct a total of twelve health facility visits taking into account a balance of geographical locations, urban and rural areas, and - if possible - different types of health facilities (e.g. small and larger health units). The country visits will be concluded with an on-site debriefing and joint data analysis with MoH MNCH and EPI focal points and other main country-level stakeholders. End-users, i.e. pregnant women, will not be interviewed as it would require a separate study design; however, their perspective will be indirectly included through the participation of community health workers at stakeholder meetings. 

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#### 213 Data analysis plan.

The principal analyses will assess correlations between the various documented aspects of MI
delivery platforms and metrics of health systems performance, i.e. PAB, ANC4+, and TT2+.
The primary outcome will be a typology of MI delivery models with indicators of high
performance and capacity to introduce new maternal vaccines and/or scale-up MI, based on
the analysis of quantitative data collected during the four project phases. Secondary outcomes

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will include country profiles of child and maternal health indicators with a special focus on MI and an MI gaps and needs analysis, based on intra- and cross-country analyses of qualitative data, according to themes generated from research questions and sub-themes generated from grounded analysis of data collected. The analyses will, where possible, take into consideration within-country heterogeneity, such as differences between urban and rural settings, and between various health system levels.

Furthermore, the data analyses will take into account the limitations of the study, including the reliability of the selected outcome measures, i.e. PAB and TT2+, potential biases introduced by the limited number of countries for which in-depth information will be available, i.e. through telephone interviews and in-country visits, selective sampling of in-country site visit locations, missing data, and the fact that the end-users' perspective will be captured only indirectly through community health workers. 

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### 233 ETHICS AND DISSEMINATION

Ethical considerations. The first three phases of the study are exempt from ethical
permission as participants will provide information on operations and administration of
public health services on a purely professional basis, and without disclosure of personidentifiable information. The protocol for the country visits was approved by the WHO
Research Ethics Review Committee (ERC.0002908).

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Country ownership will be ensured through transfer of responsibility for the data provision to
in-country focal points, and by joint, on-site analysis of the data collected during the country
visits with the main stakeholders. The study aims to contribute to the evidence needed to
ensure more equitable access to high-impact global health interventions, such as MI.<sup>25</sup>

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#### 245 Data management and dissemination.

The data will be managed and analysed by data clerks who were not part of the data
collection. Anonymised data from surveys and key informant interviews, excluding any
confidential information as identified by the in-country focal points, will be uploaded to a
publicly available data repository hosted by the WHO. Recordings from country interviews
will be transcribed before the qualitative analyses and destroyed at completion of the data
analyses.

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253 The results will be submitted for publication in peer-reviewed journals, as well as in a

254 MIACSA project report that will be shared widely with global health decision makers,

255 researchers, product developers, and implementers. The report and/or specific aspects of the

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data mining, Al training, and similar technologies

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project, will be presented at international stakeholder meetings, with the ultimate aim to establish a knowledge network of countries exploring MI implementation strategies. Further, the results will be shared through summaries on the WHO website and in public fora. Dissemination of the MIACSA results will aim to provide advice on best practices, policy requirements, capacity needs, and health system changes needed for successful introduction and integration of new maternal vaccines into national health systems, including ANC and EPI services, in LMICs. or open to the work

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## 331 AUTHORS' CONTRIBUTIONS

NR and PL designed the study; CM, EM, FMM, MLG, and the MIACSA expert advisory
panel group drafted the protocol with NR and PL; and all authors reviewed and approved the

334 final manuscript version.

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#### 347 COMPETING INTERESTS

348 The authors declare no competing interests.

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2 3 4	350	FIGURE LEGENDS
5 6 7	351	Figure 1. Key health system features studied by the MIACSA project.
8 9	352	EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events
10 11 12	353	following immunization, TT = tetanus toxoid.
13 14 15	354	
16 17	355	Figure 2. Study phase 1: List of indicators for the review of global databases.
19 20	356	CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United
21 22	357	Nations Children's Fund (UNICEF) estimates of national immunization coverage, BCG =
23 24	358	Bacillus Calmette-Guérin vaccine, DPT1 = first dose of diphtheria-pertussis-tetanus vaccine,
25 26	359	DPT3 = third dose of diphtheria-pertussis-tetanus vaccine, HepB1 = first dose of hepatitis B
27 28	360	vaccine, HepB3 = third dose of hepatitis B vaccine, Hib1 = first dose of <i>Haemophilus</i>
29 30 31	361	<i>influenzae</i> type B vaccine, Hib3 = third dose of <i>H. influenzae</i> type B vaccine, MCV1 = first
32 33	362	dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine,
34 35	363	PcV1 = first dose of pneumococcal conjugate vaccine, PcV3 = third dose of pneumococcal
36 37	364	conjugate vaccine, Pol1 = first dose of polio-containing vaccine, Pol3 = third dose of polio-
38 39	365	containing vaccine, TT1 = first dose of tetanus toxoid vaccine, TT1+ = at least one dose of
40 41	366	tetanus toxoid vaccine, TT2 = second dose of tetanus toxoid vaccine, TT2+ = at least two
42 43 44	367	doses of tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth
44 45 46	368	dose of tetanus toxoid vaccine, $TT5 = fifth$ dose of tetanus toxoid vaccine, $RCV1 = first$ dose
47 48	369	of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending
49 50	370	on number of doses recommended in national schedule, YFV = yellow fever vaccine.
52 53	371	
54 55 56 57	372	Figure 3. Study phase 2: Variables collected from online survey of 136 LMICs.

BMJ Open: first published as 10.1136/bmjopen-2018-024449 on 4 June 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

373	A structured questionnaire will be used to determine which service delivery platforms are in
374	place for tetanus vaccination of pregnant women in low- and middle-income countries
375	(LMICs), and to understand how existing health services could be adapted to implement
376	maternal immunization beyond tetanus vaccination. Internal validation questions are
377	incorporated in the questionnaire, and sources of data are requested, i.e. if administrative data
378	or personal estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization,
379	TT = tetanus toxoid, Td = tetanus-diphtheria, Tdap = tetanus-diphtheria-acellular pertussis,
380	AEFI = adverse events following immunization, TT2+ = at least 2 doses of tetanus toxoid
381	vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin
382	vaccine, OPV = oral polio vaccine, HBV = hepatitis B vaccine.
383	
384	Figure 4. Study phase 3: Variables collected from interviews of 30 selected LMICs.
385	A semi-structured questionnaire will be used to assess the preparedness of antenatal care
386	services for introducing (additional) immunizations for pregnant women in selected low- and
387	lower-middle income countries, and to understand the strengths and weaknesses of current
388	immunization to guide future planning. Internal validation questions are incorporated and
389	probing for further details will be done when deemed necessary by the interviewer(s).
390	Sources of data provided are requested, i.e. if administrative data or personal estimates. ANC
391	= antenatal care, EPI = Expanded Programme on Immunization, NITAG = National
392	Immunisation Technical Advisory Group, HMIS = Health management Information System,
393	TT = tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events following
394	immunization.
395	
396	Figure 5. Study phase 4: Country study analysis framework for 10 country visits.
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Key informant interviews, health facility visits, and focus group discussions will enable
observation and collection of further data on the variables from the previous study phases, in
particular at different levels of the health care system, and of socio-cultural and socioeconomic factors. End-users, i.e. pregnant women, will not be interviewed as it would require
a separate study design, and their perspective will be indirectly included through the

402 participation of community health workers at stakeholder meetings.

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# General

- World Bank income classification;
- Female literacy rate.

## **Health systems**

## General

- Health systems classification;
- Birth cohort (most recent year of available data);
- Target population of pregnant women.

Governance and policy environment

- Percentage of total expenditure on routine immunization financed by government funds;
- Existence of national immunization technical advisory group (NITAG);
- National policy on minimum antenatal care (ANC) visits;
- Eligibility for global vaccine alliance (GAVI) support.

## Health systems performance

- Maternal, neonatal, and infant mortality;
- Stillbirth rates;
- Physician and midwife densities;
- Institutional deliveries;
- Coverage of a minimum of four ANC visits (ANC4+).

Vaccination, including maternal immunization

- Number of confirmed tetanus and neonatal cases;
- Coverage of at least 2 doses of TT vaccine during pregnancy (TT2+);
- Tetanus toxoid (TT) vaccine as a proportion of CES and WUENIC vaccines, i.e. BCG, DPT1, DPT3, HepB1, HepB3, Hib1, Hib3, MCV1, MCV2, PAB, PcV1, PcV3, Pol1, Pol3, TT1, TT1+, TT2, TT2+, TT3 TT4, TT5, RCV1, RotaC, YFV;
- Proportion protected at birth from neonatal tetanus; i.e. protection at birth (PAB);
- TT containing vaccine(s) administered to pregnant women during routine visits;
- Most recent TT supplementary immunization activities (SIA), age range and size of target population, vaccination coverage, vaccine presentation, and year of next planned activity;
- Number of adverse events following immunization (AEFI);
- Maternal and Neonatal Tetanus Elimination (MNTE) status (year of elimination);
- Influenza vaccine administered to pregnant women;
- Pertussis vaccine administered to pregnant women.

### Immunization-associated activities

• Vitamin A supplementation.



# Service delivery models

Routine maternal tetanus vaccination

- Policy content and coverage data;
- Existing delivery models, e.g. facility-based ANC and EPI/immunization services, outreach services, and regular and ad hoc health campaigns;
- Type(s) of vaccines administered, i.e. TT, Td, Tdap (adult formulation).

Integrated health campaigns for maternal tetanus vaccination

- Programme management and coverage data;
- Existing campaigns integrated with vaccination, e.g. deworming, vitamin A, malaria, nutrition;
- Past and future schedules of integrated health campaigns.

EPI, ANC or other organisation of maternal tetanus vaccination

- National level planning and management;
- Training (rationale, safety and AEFI surveillance) and supervision of vaccinators;
- Vaccine procurement and distribution;
- Monitoring and evaluation, i.e. records (ANC or EPI-based personal, clinic, or electronic), frequency of performance assessment, monitoring indicators, e.g. TT2+, PAB.

Funding for maternal tetanus vaccination programme

• Domestic and external funding.

## Disease surveillance

- Maternal and neonatal tetanus, i.e. passive, sentinel, active, community-based;
- Other health indicators, i.e. congenital rubella syndrome, neonatal sepsis, neonatal mortality, maternal mortality, BCG at birth, OPV at birth, HBV at birth, other.

ANC capacity for maternal immunization

- Policy for ANC, i.e. number of visits, settings for ANC provision, i.e. government or private health facility/hospital, clinic, outreach programme;
- Any user fees for ANC and maternal immunization.

# Vaccine safety surveillance

- Surveillance of AEFI following immunization in general and maternal immunization;
- Any available surveillance data.

# Other maternal vaccines

- Routine maternal immunization, e.g. influenza, pertussis, or other;
- Programme\_management, i.e. EPI. ANC. or other responsible for planning, training, supervision, procurement, and distribution.

Pa	ae 27 d	of 29 BMJ Open
		Country context
1 2 2		Overview
3 4 5 6 7 8 9		<ul> <li>Integration of ANC and EPI organisation, i.e. national level coordination of maternal immunization, representation of maternal and newborn health care experts in NITAG;</li> <li>National policy and action plan for maternal immunization, and respective targets, i.e. coverage, completeness and timeliness of reports, how and why targets are/are not met;</li> <li>Existence of national HMIS, completeness and mode of data collection, available data.</li> </ul>
10 11		Funding of maternal tetanus immunization and ANC services
12 13 14 15 16	•	Domestic and external funding of ANC services and maternal immunization, user fees for ANC and tetanus vaccination, and impact of funding situation on ANC and/or maternal immunization, e.g. procurement, logistics, training, mobilisation, and/or administration.
17 18		Human resources
19 20		National and district level coordination and challenges for delivery.
21 22 23		Service delivery through ANC and the birth context
24 25 26 27 28 29 30	•	<ul> <li>Coverage and quality of ANC, i.e. staffing, coverage, precision of estimate of gestational age, counselling, prevention and interventions, referral systems, and outreach services;</li> <li>Challenges to ANC delivery, e.g. staffing, equipment, infrastructure;</li> <li>Information used for planning and prioritisation, e.g. coverage, staffing, funding, user needs;</li> <li>ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up.</li> </ul>
31 32 33 34		Tetanus vaccine delivery to pregnant women
35 36		Overview
37 38 39 40 41 42	•	<ul> <li>Type of vaccines delivered, i.e. TT, Td or other, frequency, any integration with ANC/EPI;</li> <li>Private providers of tetanus vaccination of pregnant women, available data;</li> <li>Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage;</li> <li>Current vaccination of pregnant women through ANC, staffing and challenges, e.g. infrastructure, cold chain, vaccine supply, skilled staff.</li> </ul>
45 44 45		Vaccination of pregnant women outside ANC
45 46 47 48 49		<ul> <li>Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing;</li> <li>Information used for planning and prioritisation of outreach services, e.g. ANC coverage, staffing, funding, user needs.</li> </ul>
50 51		Recording of tetanus immunization during pregnancy
52 53		• Policy, guidelines, operating procedures, with attention to immunization history and dosage.
54 55		Maternal and neonatal tetanus surveillance
50 57 58 59 60		<ul> <li>Existing neonatal and maternal tetanus surveillance systems, available data;</li> <li>Frequency of reporting, integration with other surveillance systems; For peer review only - http://bmiopen.bmj.com/site/about/guidelines.xhtml</li> <li>Existence, frequency and quality of monitoring.</li> </ul>

## Tetanus vaccine delivery to pregnant women, cont.

Surveillance of other diseases

• Maternal and neonatal mortality.

Vaccine safety surveillance systems

• Existence of training, surveillance of vaccination of pregnant women on AEFI, available data.

Other vaccines than tetanus in pregnancy

• Policy, partners, and delivery mechanisms for vaccines to pregnant women other than tetanus, e.g. influenza, pertussis, yellow fever, and meningococcus A, available data;

• Main barriers for introducing additional vaccines for pregnant women, by administration level;

 Potential interventions to support uptake of maternal vaccinations, e.g. elimination of user fees, client/provider communication, availability of medicines.

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# Supply side (health system)

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# Service delivery

- Integration of antenatal care (ANC) and Expanded Programme on Immunization;
- Accessibility, outreach services;
- Costs of services;
- Availability, supply chain;
- Quality and mode of delivery;
- Cultural appropriateness;
- Follow-up, e.g. mobile technology;
- Function of referral system.

## Health care workers

- Education, professional skills;
- Workload, working conditions;
- Professional attitudes (non-discriminatory);
- Communication skills;
- Role of community health workers.

# Information

- Actionable health information system;
- Demand side information campaigns.

# Medical products, vaccines, technology

- Safety;
- Supply chain skills, documentation.

## Financing

- Domestic, external funding;
- Devolution of health services planning and financing;
- Results-based approaches.

# Leadership, governance

- Partnerships;
- Political priorities;
- Health system organisation, e.g. level of decentralisation;
- Accountability mechanisms;
- Community participation.

# Demand side (pregnant women)

# Socio-cultural and -economic factors

- Socio-economic status;
- General health literacy;
- Knowledge about maternal vaccination;
- Mobility, security;

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- Personal characteristics, i.e. age, marital status, parity;
- Culture, religion.

# Health systems interaction

- Reception of adequate information;
- Distance to health facility;
- Direct and indirect costs of services;
- Transport, infrastructure (safety, accessibility);
- Opportunity costs, i.e. time spent at facility;
- Clarity of procedures;
- Communication (trust);
- Non-discrimination;
- Community outreach.

## The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, crosssectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, cross-sectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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**Key words:** maternal immunization; maternal tetanus vaccination, maternal health; neonatal health; maternal tetanus; neonatal tetanus; maternal mortality; neonatal mortality; health care service delivery; antenatal care capacity; study protocol

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## ABSTRACT

Introduction. Maternal immunization (MI) is a safe and cost-effective way of preventing
neonatal tetanus, and is one of several strategies that aim to reduce the high global rates of
maternal and neonatal morbidity and mortality caused by vaccine-preventable diseases. Given
the prospect of introducing new maternal vaccines in the near future, it is essential to identify
and understand current policies, practices, and unmet needs for introducing and/or scaling up MI
in low and middle income countries (LMICs).

Methods and analysis. The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) is a mixed methods, cross-sectional study that will collect data in four phases: (1) a review of global databases for selected health indicators in 136 LMICs; (2) a structured online survey directed at Maternal, Newborn, and Child Health (MNCH) and Expanded Programme on Immunization (EPI) focal points in all 136 LMICs; (3) semi-structured telephone interviews of 30 selected LMICs; and (4) 10 week-long country visits, including key informant interviews, health facility visits, and focus group discussions. The principal analyses will assess correlations between the various aspects of MI delivery strategies and proxy measures of health systems performance related to vaccine-preventable disease control. The primary outcome will be a typology of existing MI delivery models, and secondary outcomes will include country profiles of child and maternal health indicators, and an MI gaps and needs analysis. 

Ethics and dissemination. The protocol was approved by the World Health Organization Ethics
Review Committee. The results will be made available in a project report and submitted for
publication in peer-reviewed journals that will be shared broadly among global health decision
makers, researchers, product developers, and country-level stakeholders.
$1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \\ 9 \\ 10 \\ 11 \\ 12 \\ 13 \\ 14 \\ 15 \\ 16 \\ 17 \\ 18 \\ 19 \\ 20 \\ 21 \\ 22 \\ 23 \\ 24 \\ 25 \\ 26 \\ 27 \\ 28 \\ 29 \\ 30 \\ 31 \\ 32 \\ 33 \\ 34 \\ 35 \\ 36 \\ 37 \\ 38 \\ 940 \\ 41 \\ 42 \\ 43 \\ 44 \\ 546 \\ 47 \\ 48 \\ 950 \\ 51 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ $	23	Registration. Not applicable.
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26 Strengths and limitations of this study

The MIACSA study will provide a first time, comprehensive global overview and analysis
 of existing maternal immunization (MI) delivery strategies in low- and middle-income
 countries (LMICs).

The results will provide evidence to inform the development of a typology of MI delivery
 approaches in LMICs, and identify capacity needs and key system changes, including policy
 adjustments required to introduce new maternal vaccines and/or scale up existing MI in
 LMICs.

The study benefits from a mixed-methods design; a multidisciplinary approach leveraging policy-level, academic, and implementers' experience; multi-level data collection; a globally comprehensive analysis combined with in-depth information of a subsample of LMICs; inter-sectoral collaboration between MNCH and EPI programmes, and broad dissemination of results. Limitations include the small number of countries and health care facilities visited within each country included in the study, thus precluding generalization of country visit findings to a national level, and the fact that the end-users' perspective will be captured only indirectly through community health workers.

42 Data on maternal immunization service delivery collected through an online survey targeting all
43 low and middle income countries, will be analysed within the limitations of validity of data
44 collected.

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#### **INTRODUCTION**

Vaccine-preventable diseases are a major cause of global child morbidity and mortality, particularly in low- and middle-income countries (LMICs).<sup>1</sup> Since the 1990s, public health interventions have more than halved under-five childhood mortality; however, reduction of stillbirths and of neonatal mortality (death in the first 28 days of life) has been slower.<sup>2</sup> This is in part due to the fact that most vaccines cannot be administered to newborns, who, being unable to develop protective responses due to limitations in their immune system, are left particularly vulnerable to infectious diseases. Vaccination of pregnant women, or maternal immunization (MI), has proven to be an effective strategy to reduce neonatal tetanus, and is a potential strategy to reduce the burden of other vaccine-preventable diseases in mothers and infants. Thus, MI is one of several strategies that aim to reach the third sustainable development goal of ending preventable maternal and newborn deaths.<sup>3-5</sup> 

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Studies have shown that MI can effectively protect the mother, as well as her child, through transplacental transfer of maternal immunoglobulin G (IgG) to the foetus.<sup>6,7</sup> The Maternal and Neonatal Tetanus Elimination (MNTE) initiative has led the way in the implementation of MI, combining at least two doses of tetanus toxoid containing vaccine (TTCV) during pregnancy (TT2+) with the promotion of hygienic delivery and clean cord care practices, as well as vaccination of children and women of reproductive age, to eliminate maternal and neonatal tetanus as a public health problem. Between the late 1980s and 2015, the MNTE initiative reduced global tetanus-related neonatal mortality by 96%.8 

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TTCV and inactivated influenza vaccines are considered safe and effective for use during pregnancy,<sup>9</sup> and are recommended for pregnant women by the World Health Organization (WHO).<sup>6, 10-13</sup> New vaccines, several of which are under development and evaluation, target other important pathogens, such as group B streptococcus (GBS), and respiratory syncytial virus (RSV), and may provide safe and cost-effective protection of mothers and their infants through MI in the future.<sup>14-18</sup>

In order to identify the challenges of implementing current and new vaccines for MI, a better understanding is needed of the capabilities and limitations of existing delivery platforms, such as antenatal care (ANC) services and the Expanded Programme on Immunization (EPI).<sup>19</sup> The capacity of ANC services to deliver vaccines to pregnant women will require thorough assessment, as globally only 62% of women benefit from at least four ANC visits, i.e. the proportion of pregnant women who received 4 or more ANC visits during their last pregnancy (ANC4+), and in Sub-Saharan Africa and South Asia, ANC4+ coverage is only 52% and 46%, respectively.<sup>20</sup> Delivering vaccinations and other essential interventions to women at the necessary timely intervals during pregnancy, as well as documenting the coverage and outcomes of such interventions, requires a robust ANC platform with sufficient personnel and resources.<sup>21</sup> 

WHO recommends that pregnant women living in endemic areas are sufficiently immunised against tetanus in order to protect the women and their newborn infants. MI with TTCV is routine in many countries;<sup>22, 23</sup> however, progress of tetanus vaccination in LMICs has faced challenges leading to delays in elimination, and uptake among pregnant women of other

vaccines, such as influenza and pertussis vaccines, has been low. As a part of EPI services, routine tetanus immunization during pregnancy has been complemented with supplementary vaccination activities in a majority of countries in order to reach high coverage and achieve MNTE goals. A better understanding of MI in the context of both ANC and EPI, including implementation of guidelines and policies, ministerial responsibilities at national and subnational levels, vaccine management including cold chain and logistics, vaccine administration, staff capacity, social mobilisation, vaccine acceptance, and assessment of vaccine safety, may help identify service delivery challenges as well as opportunities to optimise current and future MI efforts.24

99 Closer collaboration between ANC and EPI services could provide a unique and cost-effective 100 opportunity to further strengthen preventive health care measures for women and children under 101 each programme, by reducing missed opportunities for immunization, including MI, as well as 102 reinforcing the delivery of essential health care services.

In view of recent product and policy developments, the WHO, supported by the Bill and Melinda
Gates Foundation, aims to identify the knowledge gaps in MI delivery strategies by mapping the
strengths and challenges of existing ANC and immunization services for pregnant women in
LMICs through the Maternal Immunization and Antenatal Care Situation Analysis (MIACSA)
project. The results will provide the evidence for a typology of MI delivery models, as well as
identify the capacity needs and key system changes required to introduce new maternal vaccines
and/or strengthen vaccine delivery for MI in LMICs. Ultimately, the project aims to identify and

understand current MI and ANC related policies, practices and the need for strengthening both
immunization and maternal child health care services , and how they could accommodate new
MI vaccines.

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2 3 4	115	METHODS AND ANALYSIS
5 6 7	116	Patient and Public Involvement.
8 9	117	The development of the research questions were influenced by an interdisciplinary group of
10 11	118	international experts for the MIACSA project. The project did not include patients, but restricted
12 13 14	119	itself to national level program managers and health facilities where health workers responded to
15 16	120	interviews in their professional capacity.
17 18	121	
19 20 21	122	
22 23	123	Study design and data collection
24 25 26	124	Between November 2016 and December 2018, a mixed-methods, cross-sectional study will be
27 28	125	carried out in four phases to assess key health system features related to the implementation of
29 30 31	126	MI (Figure 1). An expert advisory panel (EAP) consisting of specialists in immunization,
32 33	127	maternal and neonatal health, MI implementation and social sciences, will provide technical
34 35	128	advice on the study design, the development of research questions and surveys, the data
36 37	129	collection methods, and the results interpretation. In addition to following WHO standards for
38 39 40	130	global monitoring surveys, all data collection tools and standard operating procedures will be
41 42	131	reviewed and endorsed by the EAP. The surveys and country visits will be conducted in local
43 44	132	languages when needed.
45 46 47 48	133	
49 50	134	Desk review of global data (Data collection phase 1). The first phase will consist of collecting
51 52	135	key health indicators of LMICs to create outlines of country profiles, focusing on ANC and EPI
53 54 55 56	136	services. A desk review of pre-defined health indicators (Figure 2) from 136 LMICs will be
57 58 59		10

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conducted from existing global data sources, including Demographic and Health Surveys (DHS)/Multiple Indicator Cluster Surveys (MICS), WHO/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, WHO/UNICEF Joint Reporting Forms (JRF), MNTE reports, and WHO Maternal, Newborn, Child, and Adolescent Health (MNCAH) policy survey. The indicators will focus on governance and policy environment, health systems performance, and immunization activities, including MI. Data from phase 1 will be compiled in a database for analysis of the study's research questions, and will inform the selection of countries for phase 3 (see below). 

Global online survey (Data collection phase 2). The country profiles established in phase 1 will be completed and, if needed, updated by an online survey with WHO Regional Offices, national Ministry of Health (MoH) focal points from Maternal, Newborn and Child Health (MNCH) and EPI programmes and their WHO Country Office counterparts in all LMICs, using a structured questionnaire (Figure 3). Data will be collected on service delivery models of maternal tetanus vaccination, including delivery platforms, programme funding, disease surveillance, and vaccine safety surveillance. Data on maternal vaccines other than tetanus will be included when pertinent. A draft questionnaire will be piloted in advance of the survey. Non-responders will be followed-up by telephone and email. Revisions following queries on missing, erroneous, or inconsistent data will be done at country level.

Telephone interviews (Data collection phase 3). In order to understand how existing health
care delivery services could be adapted to implement MI beyond tetanus immunization, further

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data will be collected on delivery platforms for maternal tetanus vaccination in LMICs. In-depth telephone interviews will be conducted with EPI and MNCH programme officers responsible for MI at the MoH in a sample of 30 countries, using a semi-structured questionnaire (Figure 4). The countries will be selected based on performance of MI as assessed by coverage of maternal TTCV and ANC, geographic representation, and recommendations from WHO Regional Offices on MI priorities. The countries will be stratified into four groups; high and low maternal tetanus vaccination performance measured as protection at birth (PAB), i.e. the proportion of newborns protected at birth against neonatal tetanus, with a cut-off of 90%, and high and low ANC performance (with a cut-off of the median ANC4+ coverage in countries with available data). PAB was identified as a more reliable proxy measure than TT2+, as the issue of not including already vaccinated women in the numerator used for estimating the latter indicator would be avoided. The PAB cut-off level was set based on the target required to attain and sustain MNTE, whereby >80% of pregnant women are immunized against tetanus. The country selection will include a representation of all MI delivery models and WHO regions, with a focus on Africa and South-East Asia where maternal and neonatal mortality are highest, and will ensure inclusion of high performing countries in order to include likely early adopters of new maternal vaccines and learning cases of best practices.

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The interviews will collect data on the policy, governance, and funding environment for EPI and ANC programmes, ANC delivery, and maternal tetanus vaccination including monitoring and evaluation of results. The questionnaire will be shared with WHO country office focal points and MoH MNCH and EPI managers for compilation in advance of the teleconference, allowing for discussion and clarification when needed during the actual interview. Responses will be recorded

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using standard data entry procedures, and may be voice-recorded if consent is obtained by the interviewees. Any discordant responses will be attempted to be resolved by consensus, and incomplete responses will be followed up. A summary of key findings will be shared with the participants to confirm the responses were correctly captured. Country visits (data collection phase 4). Finally, in-country visits will be conducted in order to collect data on MI from key decision-makers and implementers at every level of the health care system, as well as to determine actual delivery, capacity and coordination of ANC and EPI services, on both supply and demand sides of the health care services (Figure 5). Ten countries will be selected based on high, medium, or low performance of MI systems as assessed by PAB and TT2+, a range of different MI delivery models (e.g. degree of coordination between EPI and ANC in MI delivery), and agreement by senior national and subnational MNCH and EPI staff for study visits. The final country selection will ensure representation of the range of MI delivery models, and will include high-performing countries, MNTE priority countries, and countries with high ANC4+ coverage. Site visits will include ANC and EPI sites and session observations, focus group discussions, and in-depth interviews. The week-long visits will be piloted in two countries to adjust and refine the data collection tools and the standard operating procedures, and data from these two countries will be included in the final analysis. An initial joint focus group discussion will be held with national-level stakeholders, followed by key informant interviews with stakeholders pertinent to MI, ANC, and EPI services at subnational levels of the health care system, including decision and policy makers, technical and 

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financial parties, and civil society, such as non-governmental organisations. The study will aim to conduct a total of twelve health facility visits taking into account a balance of geographical locations, urban and rural areas, and - if possible - different types of health facilities (e.g. small and larger health units). The country visits will be concluded with an on-site debriefing and joint data analysis with MoH MNCH and EPI focal points and other main country-level stakeholders. End-users, i.e. pregnant women, will not be interviewed as it would require a separate study design; however, their perspective will be indirectly included through the participation of community health workers at stakeholder meetings. 

# 213 Data analysis plan

The cross-sectional data analyses will be carried out over four data collection 4 phases (desk review of global data, online questionnaire and indepth country interviews, and country visits). The first three will yield quantitative data. The last two data collection phases will also provide an in-depth qualitative analyses of data collected from a select number of countries. Below we describe the analyses for each phase. BMJ Open: first published as 10.1136/bmjopen-2018-024449 on 4 June 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES).

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9 219 0 <sup>1</sup> 220

# 220 Desk review of global data(phase 1)

The MIACSA project will conduct a desk review of global databases (Joint reporting form
(JRF), United Nations (UN) mortality reports, Demographic health survey (DHS), Multiple
Cluster Indicators Survey (MICS), WHO MNCAH policy survey database, maternal and
neonatal tetanus elimination (MNTE) database, WHO/UNICEF Estimates of National
Immunization Coverage (WUENIC)) targeting 136 low- and middle income countries (LMIC).
The primary outcome variable (dependant variable) to asses MI performance will be PAB (cut-

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off level <90% and  $\geq 90\%$ ) and the independent variables will include country economic level, immunization coverage, mortality, service coverage, available ANC and vaccination policies and availability of a national immunization advisory committee (Figure 2). We will first asses the database for completeness of data. We will also conduct a sensitivity analysis based on imputation of data based on available predictors for countries with missing data on PAB. Results from the complete case analysis will be compared with the sensitivity analysis to explore bias due to missing data. We will conduct bivariate analyses to assess whether the dependant variables are associated with the independent variables. We will also do multivariable analyses within subgroups, since vaccinations may differ by other factors (e.g., WHO Regions; GAVI status; World Bank income level; MNTE; female literacy rate). For continuous variables we will first assess the normality using the Shapiro-Wilk test. If needed, we will make appropriate transformations to normalize the data or group them into categories as necessary. We will then compare the distributions of the variables by groups with two-sided chi-square (categorical variables) or t-tests (continuous variables) or the equivalent non-parametric tests (e.g., Fisher's exact or Wilcoxon/Kruskal-Wallis), as appropriate. A two-sided p-value of 0.05 will be considered as significant. To create a multivariable model, we will include all variables that are significantly associated with the dependant variable and those variables which have shown association within the available literature. We will then asses for collinearity and remove one of the variables if collinearity is found. We will also assess for interactions and will create interaction terms to be included in the model if any interactions are found. Both forward and backward elimination will

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3 4 5	250	be conducted to assess the goodness of fit and create the final model.
5 6 7	251	
, 8 9	252	Global online survey (phase 2)
10 11	253	The variables are based on the online survey as described above. For a summary of the included
12 13	254	components see Figure 3. Data from the online survey will be checked for completeness and
14 15 16	255	consistency and coded to reflect skip patterns. The complete data set for analyses will include
17 18	256	PAB from phase 1 (desk review database) and will be linked with the database containing
19 20	257	responses for the global online questionnaire Descriptive analyses will be conducted including
21 22 23	258	summary measures. Bivariate analyses will be conducted to assess the associations between the
24 25	259	questionnaire variables and the dependant variable PAB and the significance of the relationship
26 27	260	will be tested with Fisher's Exact test. Logistic regression models will be used to assess the
28 29 30	261	relationship between the responses in the online questionnaire and high coverage of PAB >=90%
31 32	262	independently . These models will be created as described in phase 1. A two-sided p-value of
33 34	263	0.05 will be considered as significant.
35 36 27	264	
37 38 39	265	Telephone conferences (quantitative analyses, phase 3)
40 41	266	The primary objective is to provide descriptive information about maternal immunization
42 43	267	services and its organization (Figure 4).
44 45 46	268	Data from this phase will be checked for completeness and consistency and coded to reflect skip
40 47 48	269	patterns. Descriptive analyses will be conducted including summary measures.
49 50	270	
51 52 53 54 55 56	271	Qualitative analyses based on country visits and telephone conferences (phase 4)
57 58		16
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Ten countries will be visited to conduct qualitative interviews at national and subnational level. Resulting qualitative information and from these visits as well as from telephone interview conducted in the previous phase will be used in a thematic analysis applied by trained qualitative data analysts to the following qualitative data sources: comments and free-text responses to telephone interview questions (phase 3), semi-structured interviews with community health workers (phase 4), comments and free-text response to stakeholder and facility manager interviews (phase 4), comments provided during debrief sessions with national level stakeholders in-country (phase 4). Thematic analysis will be applied to intra-case and cross-case analysis. First, an intra-case analysis will organize and reduce qualitative findings within each country along two criteria: (1) relevance of finding to research questions and (2) relative frequency of finding across data sources. Second, a cross-case analysis will organize findings across countries into themes generated from research questions and sub-themes generated from grounded analysis of data collected. Two qualitative data analysts will co-organize and reduce intra-country findings. For cross-country findings, qualitative analysts will independently generate themes and sub-themes for cross-case analysis and will then resolve any inter-coder divergence in themes and sub-themes based on relevance of theme to data source, relevance of theme to research questions and robustness of theme relative to alternative themes. See figure 4 and 5 for the included components. 

- 291 Consolidated data analysis

To inform the development of a typology of MI delivery models approaches in LMICs
quantitative and qualitative data analysis results will be consolidated in a global analysis of MI
and ANC service delivery approaches in countries as well as individual country profiles that

shall support countries to conduct self-assessments of their MI and ANC systems strengths and
capacity gaps. Based on the advice of the project's advisory group, a checklist approach will be
considered to provide a profiling for countries with sufficient data available, including indicators
on policy and governance, financing, programme management, service delivery systems and
demand side issues. Ultimately, such a profiling shall help countries and other MI stakeholders to
identify the needs for targeted support to strengthen existing MI programmes or to reach
readiness to introduce future programmes.

### 303 Limitations

The data analyses will take into account the limitations of the study, including the reliability of the selected outcome measures, i.e. PAB, potential biases introduced by the limited number of countries for which in-depth information will be available, i.e. through telephone interviews and in-country visits, selective sampling of in-country site visit locations, missing data, and the fact that the end-users' perspective will be captured only indirectly through facility and community based health workers. BMJ Open: first published as 10.1136/bmjopen-2018-024449 on 4 June 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES).

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# ETHICS AND DISSEMINATION

Ethical considerations. The first three phases of the study are exempt from ethical permission
as participants will provide information on operations and administration of public health
services on a purely professional basis, and without disclosure of person-identifiable
information. The protocol for the country visits was approved by the WHO Research Ethics
Review Committee (ERC.0002908).

Country ownership will be ensured through transfer of responsibility for the data provision to incountry focal points, and by joint, on-site analysis of the data collected during the country visits with the main stakeholders. The study aims to contribute to the evidence needed to ensure more equitable access to high-impact global health interventions, such as MI.<sup>25</sup>

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# 323 Data management and dissemination

The data will be managed and analysed by data clerks who were not part of the data collection. Anonymised data from surveys and key informant interviews, excluding any confidential information as identified by the in-country focal points, will be uploaded to a publicly available data repository hosted by the WHO. Recordings from country interviews will be transcribed before the qualitative analyses and destroyed at completion of the data analyses.

The results will be submitted for publication in peer-reviewed journals, as well as in a MIACSA project report that will be shared widely with global health decision makers, researchers, product Page 21 of 33

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developers, and implementers. The report and/or specific aspects of the project, will be presented
at international stakeholder meetings, with the ultimate aim to establish a knowledge network of
countries exploring MI implementation strategies. Further, the results will be shared through
summaries on the WHO website and in public fora.

To ensure wide distribution of the project findings to the international scientific community and national stakeholders involved in maternal immunization, findings will be also shared at the end of the project through a a large stakeholder convening. At this meeting, key aspects of maternal tetanus vaccination service delivery mechanisms and antenatal care capacities identified in select countries will be discussed to enable exchange of lessons learnt between select participating countries and to discuss generalizable lessons learnt that may improve maternal immunization service delivery through an integrated platform considering Immunization and Maternal Child Health Care mechanisms. Dissemination of the MIACSA results will aim to provide advice on best practices, policy requirements, capacity needs, and health system changes needed for successful introduction and integration of new maternal vaccines into national health systems, including ANC and EPI 

<sup>38</sup><sub>39</sub> 347 services, in LMICs.

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#### **AUTHORS' CONTRIBUTIONS** 413

NR and PL designed the study with inputs from TD and JH; CM, EM, FMM, MLG, TD, JH, AM 414 415 and the MIACSA expert advisory panel group drafted the protocol with NR and PL; and all 416 authors reviewed and approved the final manuscript version.

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- 429 **COMPETING INTERESTS** 
  - The authors declare no competing interests. 430

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Figure 1. Key health system features studied by the MIACSA project. 

**FIGURE LEGENDS** 

EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events following immunization, TT = tetanus toxoid. 

Figure 2. Study phase 1: List of indicators for the review of global databases. 

CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, BCG = Bacillus Calmette-Guérin vaccine, DPT1 = first dose of diphtheria-pertussis-tetanus vaccine, DPT3 = third dose of diphtheria-pertussis-tetanus vaccine, HepB1 = first dose of hepatitis B vaccine, HepB3 = third dose of hepatitis B vaccine, Hib1 = first dose of *Haemophilus influenzae* type B vaccine, Hib3 = third dose of *H. influenzae* type B vaccine, MCV1 = first dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine, PcV1 = first dose of pneumococcal conjugate vaccine, PcV3 = third dose of pneumococcal conjugate vaccine, Pol1 = first dose of polio-containing vaccine, Pol3 = third dose of polio-containing vaccine, TT1 = first dose of tetanus toxoid vaccine, TT1+ = at least one dose of tetanus toxoid vaccine, TT2 = second dose of tetanus toxoid vaccine, TT2+ = at least two doses of tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth dose of tetanus toxoid vaccine, TT5 = fifth dose of tetanus toxoid vaccine, RCV1 = first dose of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending on number of doses recommended in national schedule, YFV = yellow fever vaccine. 

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Figure 3. Study phase 2: Variables collected from online survey of 136 LMICs. 

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A structured questionnaire will be used to determine which service delivery platforms are in place for tetanus vaccination of pregnant women in low- and middle-income countries (LMICs), and to understand how existing health services could be adapted to implement maternal immunization beyond tetanus vaccination. Internal validation questions are incorporated in the questionnaire, and sources of data are requested, i.e. if administrative data or personal estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization, TT = tetanus toxoid, Td = tetanus-diphtheria, Tdap = tetanus-diphtheria-acellular pertussis, AEFI = adverse events following immunization, TT2+ = at least 2 doses of tetanus toxoid vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin vaccine, OPV = oral polio vaccine, HBV = hepatitis B vaccine. Figure 4. Study phase 3: Variables collected from interviews of 30 selected LMICs. A semi-structured questionnaire will be used to assess the preparedness of antenatal care services for introducing (additional) immunizations for pregnant women in selected low- and lower-middle income countries, and to understand the strengths and weaknesses of current immunization to guide future planning. Internal validation questions are incorporated and probing for further details will be done when deemed necessary by the interviewer(s). Sources of data provided are requested, i.e. if administrative data or personal estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization, NITAG = National Immunisation Technical Advisory Group, HMIS = Health management Information System, TT = tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events following immunization.

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1 2		
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6 7	478	Figure 5. Study phase 4: Country study analysis framework for 10 country visits.
8 9 10	479	Key informant interviews, health facility visits, and focus group discussions will enable
11 12	480	observation and collection of further data on the variables from the previous study phases, in
13 14 15	481	particular at different levels of the health care system, and of socio-cultural and socio-economic
16 17	482	factors. End-users, i.e. pregnant women, will not be interviewed as it would require a separate
18 19	483	study design, and their perspective will be indirectly included through the participation of
20 21	484	community health workers at stakeholder meetings.
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EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events following immunization, TT = tetanus toxoid.

#### General

- World Bank income classification;
- Female literacy rate.

#### Health systems

#### General

· Health systems classification;

- Birth cohort (most recent year of available data);
- Target population of pregnant women.

Governance and policy environment

- Percentage of total expenditure on routine immunization financed by government funds;
- · Existence of national immunization technical advisory group (NITAG);
- National policy on minimum antenatal care (ANC) visits;
- · Eligibility for global vaccine alliance (GAVI) support.

Health systems performance

- · Maternal, neonatal, and infant mortality;
- Stillbirth rates;
- · Physician and midwife densities;
- Institutional deliveries;
- · Coverage of a minimum of four ANC visits (ANC4+).

Vaccination, including maternal immunization

- · Number of confirmed tetanus and neonatal cases;
- Coverage of at least 2 doses of TT vaccine during pregnancy (TT2+);
- Tetanus toxoid (TT) vaccine as a proportion of CES and WUENIC vaccines, i.e. BCG, DPT1, DPT3, HepB1, HepB3, Hib1, Hib3, MCV1, MCV2, PAB, PcV1, PcV3, Pol1, Pol3, TT1, TT1+, TT2, TT2+, TT3 TT4, TT5, RCV1, RotaC, YFV;
- Proportion protected at birth from neonatal tetanus; i.e. protection at birth (PAB);
- TT containing vaccine(s) administered to pregnant women during routine visits;
- Most recent TT supplementary immunization activities (SIA), age range and size of target population, vaccination coverage, vaccine presentation, and year of next planned activity;
   Number of adverse events following immunization (AEFI):
- Maternal and Neonatal Totanus Elimination (MNTE) status (year of elimination):
- Maternal and Neonatal Tetanus Elimination (MNTE) status (year of elimination);
- Influenza vaccine administered to pregnant women;
   Pertussis vaccine administered to pregnant women.
- Immunization-associated activities
- Vitamin A supplementation.

Figure 2. Study phase 1: List of indicators for the review of global databases. CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, BCG = Bacillus Calmette-Guérin vaccine, DPT1 = first dose of diphtheria-pertussis-tetanus vaccine, DPT3 = third dose of diphtheria-pertussis-tetanus vaccine, HepB1 = first dose of hepatitis B vaccine, Hib3 = third dose of hepatitis B vaccine, MCV1 = first dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine, PcV3 = third dose of pneumococcal conjugate vaccine, Pol1 = first dose of polio-containing vaccine, Pol3 = third dose of tetanus toxoid vaccine, TT1 = at least one dose of tetanus toxoid vaccine, TT2 = second dose of tetanus toxoid vaccine, TT2 + = at least two doses of

tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth dose of tetanus toxoid vaccine, TT5 = fifth dose of tetanus toxoid vaccine, RCV1 = first dose of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending on number of doses recommended in national schedule, YFV = yellow fever vaccine.

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	Service delivery medele
	Service delivery models
	Routine maternal tetanus vaccination
	Policy content and coverage data;
	Existing delivery models, e.g. facility-based ANC and EPI/immunization services, outreach
	<ul> <li>services, and regular and ad hoc health campaigns;</li> <li>Type(s) of vaccines administered, i.e. TT_Td_Tdan (adult formulation).</li> </ul>
	Integrated health campaigns for maternal tetanus vaccination
	Programme management and coverage data;
	<ul> <li>Existing campaigns integrated with vaccination, e.g. deworming, vitamin A, malaria, nutrition;</li> <li>Past and future schedules of integrated health campaigns.</li> </ul>
	EPI, ANC or other organisation of maternal tetanus vaccination
	National level coordination planning and management;
	<ul> <li>Training (rationale, safety and AEFI surveillance) and supervision of vaccinators;</li> <li>Vaccine programment and distribution;</li> </ul>
	<ul> <li>Vaccine procurement and distribution;</li> <li>Monitoring and evaluation, i.e. records (ANC or EPI-based personal, clinic, or electronic),</li> </ul>
	frequency of performance assessment, monitoring indicators, e.g. TT2+, PAB.
	Funding for maternal tetanus vaccination programme
	Domestic and external funding
	Disease surveillance
	Maternal and neonatal tetanus, i.e. passive, sentinel, active, community-based;
	<ul> <li>Other health indicators, i.e. congenital rubella syndrome, neonatal sepsis, neonatal mortality, maternal mortality, BCG at birth, OPV at birth, HBV at birth, other.</li> </ul>
	ANC capacity for maternal immunization
	<ul> <li>Policy for ANC, i.e. number of visits, settings for ANC provision, i.e. government or private health facility/hospital_clinic_outreach programme;</li> </ul>
	Any user fees for ANC and maternal immunization.
	Vaccine safety surveillance
	<ul> <li>Surveillance of AEFI following immunization in general and maternal immunization;</li> </ul>
	Any available surveillance data.
	Other maternal vaccines
	Douting maternal immunization or influenza portugais or other
	<ul> <li>Programme management, i.e. EPI, ANC, or other responsible for planning, training,</li> </ul>
	supervision, procurement, and distribution.
	A structured questionnaire will be used to determine which service delivery platforms are
	tetanus vaccination of pregnant women in low- and middle-income countries (LMICs), and t
	how existing health services could be adapted to implement maternal immunization beyo
	vaccination. Internal validation questions are incorporated in the questionnaire, and source
	requested, i.e. if administrative data or personal estimates. ANC = antenatal care, EPI =
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	vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin vaccir
	polio vaccine, HBV = hepatitis B vaccine.

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7	Country context	
8	Overview	
9	Integration of ANC and EPI organisation, i.e. national level coordination of maternal	
10	<ul> <li>immunization, representation of maternal and newborn health care experts in NITAG;</li> <li>National policy and action plan for maternal immunization, and respective targets, i.e.</li> </ul>	
10	coverage, completeness and timeliness of reports, how and why targets are/are not met;	
17	Existence of national ninic, completeness and indue of data conection, available data.	
12	Demostic and external funding of AVC services and maternal immunization, user face for	
15	ANC and tetanus vaccination, and impact of funding situation on ANC and/or maternal	
14	immunization, e.g. procurement, logistics, training, mobilisation, and/or administration.	
15	Human resources	
16	National and district level coordination and challenges for delivery.	
17	Service delivery through ANC and the birth context	
18	Coverage and quality of ANC, i.e. staffing, coverage, precision of estimate of gestational	
19	age, counselling, prevention and interventions, referral systems, and outreach services; Challenges to ANC delivery e.g. staffing, equipment, infrastructure;	
20	<ul> <li>Information used for planning and prioritisation, e.g. coverage, staffing, funding, user needs;</li> </ul>	
21	ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up.	
22	Tetanus vaccine delivery to pregnant women	
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25	<ul> <li>Type of vaccines delivered, i.e. T1, Id or other, frequency, any integration with ANC/EPI;</li> <li>Private providers of tetanus vaccination of pregnant women, available data;</li> </ul>	
25	<ul> <li>Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage;</li> <li>Current vaccination of pregnant women through ANC, staffing and challenges, e.g.</li> </ul>	
20	infrastructure, cold chain, vaccine supply, skilled staff.	
27	Vaccination of pregnant women outside ANC	
28	<ul> <li>Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing;</li> <li>Information used for planning and prioritisation of outreach services, e.g. ANC coverage.</li> </ul>	
29	staffing, funding, user needs.	
30	Recording of tetanus immunization during pregnancy	
31	Policy, guidelines, operating procedures, with attention to immunization history and dosage.	
32	Maternal and neonatal tetanus surveillance	
33	<ul> <li>Existing neonatal and maternal tetanus surveillance systems, available data;</li> </ul>	
34	<ul> <li>Frequency of reporting, integration with other surveillance systems;</li> <li>Existence, frequency and quality of monitoring.</li> </ul>	
35		
36	Surveillance of other diseases	
37	Maternal and neonatal mortality.	
38	Vaccine safety surveillance systems	
39	Existence of training, surveillance of vaccination of pregnant women on AEFI, available data.	
40	Other vaccines than tetanus in pregnancy	
41	<ul> <li>Policy, partners, and delivery mechanisms for vaccines to pregnant women other than tetanus, e.g. influenza, partnersis, vallow favor, and maningococcus a qualitable data;</li> </ul>	
42	<ul> <li>Main barriers for introducing additional vaccines for pregnant women, by administration level;</li> </ul>	
72 /3	<ul> <li>Potential interventions to support uptake of maternal vaccinations, e.g. elimination of user fees, client/provider communication, availability of medicines.</li> </ul>	
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44 45	A comi attractured questionnaire will be used to person the property and the second	tonatal care convision for
45	A semi-structured questionnaire will be used to assess the preparedness of an introducing (additional) immunizations for program women in selected low as	nd lower-middle income
46	countries, and to understand the strengths and weaknesses of current immur	na lower-minute mcome
4/	planning. Internal validation questions are incorporated and prohing for further	details will be done when
48	deemed necessary by the interviewer(s). Sources of data provided are requested	, i.e. if administrative data
49	or personal estimates. ANC = antenatal care, EPI = Expanded Programme on	Immunization, NITAG =
50	National Immunisation Technical Advisory Group, HMIS = Health management I	nformation System, TT =
51	tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events followir	ng immunization.
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Supply side (health system)	Demand side (pregnant women)
Service delivery	Socio-cultural and -economic factors
Service delivery	Socio-cultural and -economic factors <ul> <li>Socio-economic status;</li> <li>General health literacy;</li> <li>Knowledge about maternal vaccination;</li> <li>Mobility, security;</li> <li>Personal characteristics, i.e. age, marital status, parity;</li> <li>Culture, religion.</li> <li>Health systems interaction</li> <li>Reception of adequate information;</li> <li>Distance to health facility;</li> <li>Direct and indirect costs of services;</li> <li>Transport, infrastructure (safety, accessibility);</li> <li>Opportunity costs, i.e. time spent at facility;</li> <li>Clarity of procedures;</li> <li>Communication (trust);</li> <li>Non-discrimination;</li> <li>Community outreach.</li> </ul>
<ul> <li>Medical products, vaccines, technology</li> <li>Safety;</li> <li>Supply chain skills, documentation</li> </ul>	
<ul> <li>Financing</li> <li>Domestic, external funding;</li> <li>Devolution of health services planning and financing;</li> <li>Results-based approaches.</li> </ul>	
Leadership, governance <ul> <li>Partnerships;</li> <li>Political priorities;</li> <li>Health system organisation, e.g. level of decentralisation;</li> <li>Accountability mechanisms;</li> <li>Community participation.</li> </ul>	

Key informant interviews, health facility visits, and focus group discussions will enable observation and collection of further data on the variables from the previous study phases, in particular at different levels of the health care system, and of socio-cultural and socio-economic factors. End-users, i.e. pregnant women, will not be interviewed as it would require a separate study design, and their perspective will be indirectly included through the participation of community health workers at stakeholder meetings.

# The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, crosssectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study protocol: A multi-regional, cross-sectional analysis of maternal immunization delivery strategies to reduce maternal and neonatal morbidity and mortality

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\*\* The MIACSA expert advisory panel (EAP) consists of the following members: Flor M. Muñoz (chair), Michelle L. Giles (co-chair), Mercy Ahun, Martina Baye, Pradeep Haldar, and Matthews Mathai. Observers to EAP meetings included: Carsten Mantel, Elizabeth Mason,

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Sonja Mertens, Jayani Pathirana, Sarah Rendell. Additional WHO experts included: Emily Wootton, Laura Nic Lochlainn, Ahmadu Yakubu, and Sara Rendell.

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**Key words:** maternal immunization; maternal tetanus vaccination, maternal health; neonatal health; maternal tetanus; neonatal tetanus; maternal mortality; neonatal mortality; health care service delivery; antenatal care capacity; study protocol

## ABSTRACT

Introduction. Maternal immunization (MI) is a safe and cost-effective way of preventing
neonatal tetanus, and is one of several strategies that aim to reduce the high global rates of
maternal and neonatal morbidity and mortality caused by vaccine-preventable diseases.
Given the prospect of introducing new maternal vaccines in the near future, it is essential to
identify and understand current policies, practices, and unmet needs for introducing and/or
scaling up MI in low and middle income countries (LMICs).

Methods and analysis. The Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) is a mixed methods, cross-sectional study that will collect data in four phases: (1) a review of global databases for selected health indicators in 136 LMICs; (2) a structured online survey directed at Maternal, Newborn, and Child Health (MNCH) and Expanded Programme on Immunization (EPI) focal points in all 136 LMICs; (3) semi-structured telephone interviews of 30 selected LMICs; and (4) 10 week-long country visits, including key informant interviews, health facility visits, and focus group discussions. The principal analyses will assess correlations between the various aspects of MI delivery strategies and proxy measures of health systems performance related to vaccine-preventable disease control. The primary outcome will be a typology of existing MI delivery models, and secondary outcomes will include country profiles of child and maternal health indicators, and an MI gaps and needs analysis.

20 Ethics and dissemination. The protocol was approved by the World Health Organization
21 Ethics Review Committee. The results will be made available in a project report and
22 submitted for publication in peer-reviewed journals that will be shared broadly among global
23 health decision makers, researchers, product developers, and country-level stakeholders.

**Registration.** Not applicable.

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2 3	26	AR	RTICLE SUMMARY
5 6	27	Str	engths and limitations of this study
7 8 9	28	•	The MIACSA study provides a first time, comprehensive global overview and analysis
10 11	29		of existing maternal immunization (MI) delivery strategies in low- and middle-income
12 13 14	30		countries (LMICs).
15 16	31	•	The study benefits from a mixed-methods design; a multidisciplinary approach
17 18	32		leveraging policy-level, academic, and implementers' experience.
19 20 21	33	•	Limitations include the small number of countries and health care facilities visited within
22 23	34		each country included in the study, precluding generalization of country visit findings to
24 25	35		a national level.
26 27 28	36	•	End-users' perspective is captured only indirectly through community health workers.
29 30	37		Data on maternal immunization service delivery collected through an online survey
31 32	38		targeting all low and middle income countries, is analysed within the limitations of the
33         34         35         36         37         38         39         40         41         42         43         44         45         46         47         48         49         50         51         52         53         54         55         56         57         58         59         60	39		validity of data collected.

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### 40 INTRODUCTION

Vaccine-preventable diseases are a major cause of global child morbidity and mortality, particularly in low- and middle-income countries (LMICs).<sup>1</sup> Since the 1990s, public health interventions have more than halved under-five childhood mortality; however, reduction of stillbirths and of neonatal mortality (death in the first 28 days of life) has been slower.<sup>2</sup> This is in part due to the fact that most vaccines cannot be administered to newborns, who, being unable to develop protective responses due to limitations in their immune system, are left particularly vulnerable to infectious diseases. Vaccination of pregnant women, or maternal immunization (MI), has proven to be an effective strategy to reduce neonatal tetanus, and is a potential strategy to reduce the burden of other vaccine-preventable diseases in mothers and infants. Thus, MI is one of several strategies that aim to reach the third sustainable development goal of ending preventable maternal and newborn deaths.<sup>3-5</sup> 

Studies have shown that MI can effectively protect the mother, as well as her child, through transplacental transfer of maternal immunoglobulin G (IgG) to the foetus.<sup>6,7</sup> The Maternal and Neonatal Tetanus Elimination (MNTE) initiative has led the way in the implementation of MI, combining at least two doses of tetanus toxoid containing vaccine (TTCV) during pregnancy (TT2+) with the promotion of hygienic delivery and clean cord care practices, as well as vaccination of children and women of reproductive age, to eliminate maternal and neonatal tetanus as a public health problem. Between the late 1980s and 2015, the MNTE initiative reduced global tetanus-related neonatal mortality by 96%.8 

TTCV and inactivated influenza vaccines are considered safe and effective for use during
 pregnancy,<sup>9</sup> and are recommended for pregnant women by the World Health Organization

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(WHO).<sup>6, 10-13</sup> New vaccines, several of which are under development and evaluation, target other important pathogens, such as group B streptococcus (GBS), and respiratory syncytial virus (RSV), and may provide safe and cost-effective protection of mothers and their infants through MI in the future.<sup>14-18</sup> In order to identify the challenges of implementing current and new vaccines for MI, a better understanding is needed of the capabilities and limitations of existing delivery platforms, such as antenatal care (ANC) services and the Expanded Programme on Immunization (EPI).<sup>19</sup> The capacity of ANC services to deliver vaccines to pregnant women will require thorough assessment, as globally only 62% of women benefit from at least four ANC visits, i.e. the proportion of pregnant women who received 4 or more ANC visits during their last pregnancy (ANC4+), and in Sub-Saharan Africa and South Asia, ANC4+ coverage is only 52% and 46%, respectively.<sup>20</sup> Delivering vaccinations and other essential interventions to women at the necessary timely intervals during pregnancy, as well as documenting the coverage and outcomes of such interventions, requires a robust ANC platform with sufficient 

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79 personnel and resources.<sup>21</sup>

81 WHO recommends that pregnant women living in endemic areas are sufficiently immunised 82 against tetanus in order to protect the women and their newborn infants. MI with TTCV is 83 routine in many countries;<sup>22, 23</sup> however, progress of tetanus vaccination in LMICs has faced 84 challenges leading to delays in elimination, and uptake among pregnant women of other 85 vaccines, such as influenza and pertussis vaccines, has been low. As a part of EPI services, 86 routine tetanus immunization during pregnancy has been complemented with supplementary 87 vaccination activities in a majority of countries in order to reach high coverage and achieve

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MNTE goals. A better understanding of MI in the context of both ANC and EPI, including implementation of guidelines and policies, ministerial responsibilities at national and subnational levels, vaccine management including cold chain and logistics, vaccine administration, staff capacity, social mobilisation, vaccine acceptance, and assessment of vaccine safety, may help identify service delivery challenges as well as opportunities to optimise current and future MI efforts.<sup>24</sup>

95 Closer collaboration between ANC and EPI services could provide a unique and cost96 effective opportunity to further strengthen preventive health care measures for women and
97 children under each programme, by reducing missed opportunities for immunization,
98 including MI, as well as reinforcing the delivery of essential health care services.

In view of recent product and policy developments, the WHO, supported by the Bill and Melinda Gates Foundation, aims to identify the knowledge gaps in MI delivery strategies by mapping the strengths and challenges of existing ANC and immunization services for pregnant women in LMICs through the Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) project. The results will provide the evidence for a typology of MI delivery models, as well as identify the capacity needs and key system changes required to introduce new maternal vaccines and/or strengthen vaccine delivery for MI in LMICs. Ultimately, the project aims to identify and understand current MI and ANC related policies, practices and the need for strengthening both immunization and maternal child health care services, and how they could accommodate new MI vaccines.

2 3 4 5 6 7 8 9 10 11 2 13 14 15 16 7 8 9 10 11 2 13 14 15 16 7 8 9 20 22 32 4 5 6 7 8 9 0 11 2 12 23 4 5 6 7 8 9 0 11 2 23 4 5 6 7 8 9 0 11 2 23 4 5 6 7 8 9 0 11 2 23 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 11 2 2 3 4 5 6 7 8 9 0 1 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	111	METHODS AND ANALYSIS
	112	Patient and Public Involvement.
	113	The development of the research questions were influenced by an interdisciplinary group of
	114	international experts for the MIACSA project. The project did not include patients, but
	115	restricted itself to national level program managers and health facilities where health workers
	116	responded to interviews in their professional capacity.
	117	
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	119	Study design and data collection
	120	Between November 2016 and December 2018, a mixed-methods, cross-sectional study will
	121	be carried out in four phases to assess key health system features related to the
	122	implementation of MI (Figure 1). An expert advisory panel (EAP) consisting of specialists in
	123	immunization, maternal and neonatal health, MI implementation and social sciences, will
	124	provide technical advice on the study design, the development of research questions and
	125	surveys, the data collection methods, and the results interpretation. In addition to following
	126	WHO standards for global monitoring surveys, all data collection tools and standard
	127	operating procedures will be reviewed and endorsed by the EAP. The surveys and country
	128	visits will be conducted in local languages when needed.
	129	
	130	Desk review of global data (Data collection phase 1). The first phase will consist of collecting
	131	key health indicators of LMICs to create outlines of country profiles, focusing on ANC and
	132	EPI services. A desk review of pre-defined health indicators (Figure 2) from 136 LMICs will
56 57	133	be conducted from existing global data sources, including Demographic and Health Surveys
58 59 60	134	(DHS)/Multiple Indicator Cluster Surveys (MICS), WHO/United Nations Children's Fund

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(UNICEF) estimates of national immunization coverage, WHO/UNICEF Joint Reporting
Forms (JRF), MNTE reports, and WHO Maternal, Newborn, Child, and Adolescent Health
(MNCAH) policy survey. The indicators will focus on governance and policy environment,
health systems performance, and immunization activities, including MI. Data from phase 1
will be compiled in a database for analysis of the study's research questions, and will inform
the selection of countries for phase 3 (see below).

Global online survey (Data collection phase 2). The country profiles established in phase 1 will be completed and, if needed, updated by an online survey with WHO Regional Offices, national Ministry of Health (MoH) focal points from Maternal, Newborn and Child Health (MNCH) and EPI programmes and their WHO Country Office counterparts in all LMICs, using a structured questionnaire (Figure 3). Data will be collected on service delivery models of maternal tetanus vaccination, including delivery platforms, programme funding, disease surveillance, and vaccine safety surveillance. Data on maternal vaccines other than tetanus will be included when pertinent. A draft questionnaire will be piloted in advance of the survey. Non-responders will be followed-up by telephone and email. Revisions following queries on missing, erroneous, or inconsistent data will be done at country level. 

Telephone interviews (Data collection phase 3). In order to understand how existing health
care delivery services could be adapted to implement MI beyond tetanus immunization,
further data will be collected on delivery platforms for maternal tetanus vaccination in
LMICs. In-depth telephone interviews will be conducted with EPI and MNCH programme
officers responsible for MI at the MoH in a sample of 30 countries, using a semi-structured
questionnaire (Figure 4). The countries will be selected based on performance of MI as

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assessed by coverage of maternal TTCV and ANC, geographic representation, and recommendations from WHO Regional Offices on MI priorities. The countries will be stratified into four groups; high and low maternal tetanus vaccination performance measured as protection at birth (PAB), i.e. the proportion of newborns protected at birth against neonatal tetanus, with a cut-off of 90%, and high and low ANC performance (with a cut-off of the median ANC4+ coverage in countries with available data). PAB was identified as a more reliable proxy measure than TT2+, as the issue of not including already vaccinated women in the numerator used for estimating the latter indicator would be avoided. The PAB cut-off level was set based on the target required to attain and sustain MNTE, whereby >80% of pregnant women are immunized against tetanus. The country selection will include a representation of all MI delivery models and WHO regions, with a focus on Africa and South-East Asia where maternal and neonatal mortality are highest, and will ensure inclusion of high performing countries in order to include likely early adopters of new maternal vaccines and learning cases of best practices. 

The interviews will collect data on the policy, governance, and funding environment for EPI and ANC programmes, ANC delivery, and maternal tetanus vaccination including monitoring and evaluation of results. The questionnaire will be shared with WHO country office focal points and MoH MNCH and EPI managers for compilation in advance of the teleconference, allowing for discussion and clarification when needed during the actual interview. Responses will be recorded using standard data entry procedures, and may be voice-recorded if consent is obtained by the interviewees. Any discordant responses will be attempted to be resolved by consensus, and incomplete responses will be followed up. A summary of key findings will be shared with the participants to confirm the responses were correctly captured. 

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2 3 4 5	183	
6 7	184	Country visits (data collection phase 4). Finally, in-country visits will be conducted in
8 9	185	order to collect data on MI from key decision-makers and implementers at every level of the
10 11 12	186	health care system, as well as to determine actual delivery, capacity and coordination of ANC
13 14	187	and EPI services, on both supply and demand sides of the health care services (Figure 5). Ten
15 16	188	countries will be selected based on high, medium, or low performance of MI systems as
17 18 19	189	assessed by PAB and TT2+, a range of different MI delivery models (e.g. degree of
20 21	190	coordination between EPI and ANC in MI delivery), and agreement by senior national and
22 23	191	subnational MNCH and EPI staff for study visits. The final country selection will ensure
24 25 26	192	representation of the range of MI delivery models, and will include high-performing
20 27 28	193	countries, MNTE priority countries, and countries with high ANC4+ coverage. Site visits will
29 30	194	include ANC and EPI sites and session observations, focus group discussions, and in-depth
31 32 22	195	interviews. The week-long visits will be piloted in two countries to adjust and refine the data
35 34 35	196	collection tools and the standard operating procedures, and data from these two countries will
36 37	197	be included in the final analysis.
38 39 40 41	198	
42 43	199	An initial joint focus group discussion will be held with national-level stakeholders, followed
44 45	200	by key informant interviews with stakeholders pertinent to MI, ANC, and EPI services at
46 47 48	201	subnational levels of the health care system, including decision and policy makers, technical
49 50	202	and financial parties, and civil society, such as non-governmental organisations. The study
51 52	203	will aim to conduct a total of twelve health facility visits taking into account a balance of
53 54 55	204	geographical locations, urban and rural areas, and - if possible - different types of health
56 57	205	facilities (e.g. small and larger health units). The country visits will be concluded with an on-
58 59 60	206	site debriefing and joint data analysis with MoH MNCH and EPI focal points and other main

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2 3 4	207	country-level stakeholders. End-users, i.e. pregnant women, will not be interviewed as it
5 6	208	would require a separate study design; however, their perspective will be indirectly included
7 8 9	209	through the participation of community health workers at stakeholder meetings.
9 10 11 12	210	
13 14 15	211	Data analysis plan
16 17	212	The cross-sectional data analyses will be carried out over four data collection 4 phases (desk
18 19	213	review of global data, online questionnaire and indepth country interviews, and country
20 21	214	visits). The first three will yield quantitative data. The last two data collection phases will
22 23 24	215	also provide an in-depth qualitative analyses of data collected from a select number of
25 26	216	countries. Below we describe the analyses for each phase.
27 28	217	
29 30 31	218	Desk review of global data (phase 1)
32 33	219	The MIACSA project will conduct a desk review of global databases (Joint reporting form
34 35	220	(JRF), United Nations (UN) mortality reports, Demographic health survey (DHS), Multiple
36 37	221	Cluster Indicators Survey (MICS), WHO MNCAH policy survey database, maternal and
38 39 40	222	neonatal tetanus elimination (MNTE) database, WHO/UNICEF Estimates of National
41 42	223	Immunization Coverage (WUENIC)) targeting 136 low- and middle income countries
43 44	224	(LMIC).
45 46 47	225	The primary outcome variable (dependant variable) to asses MI performance will be PAB
47 48 49	226	(cut-off level <90% and $\geq$ 90%) and the independent variables will include country economic
50 51	227	level, immunization coverage, mortality, service coverage, available ANC and vaccination
52 53	228	policies and availability of a national immunization advisory committee (Figure 2).
54 55		
56	229	We will first asses the database for completeness of data. We will also conduct a sensitivity
56 57 58	229 230	We will first asses the database for completeness of data. We will also conduct a sensitivity analysis based on imputation of data based on available predictors for countries with missing

We will conduct bivariate analyses to assess whether the dependant variables are associated

with the independent variables. We will also do multivariable analyses within subgroups,

since vaccinations may differ by other factors (e.g., WHO Regions; GAVI status; World

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analysis to explore bias due to missing data. 

Bank income level; MNTE; female literacy rate). For continuous variables we will first assess the normality using the Shapiro-Wilk test. If needed, we will make appropriate transformations to normalize the data or group them into categories as necessary. We will then compare the distributions of the variables by groups with two-sided chi-square (categorical variables) or t-tests (continuous variables) or the equivalent non-parametric tests (e.g., Fisher's exact or Wilcoxon/Kruskal-Wallis), as appropriate. A two-sided p-value of 0.05 will be considered as significant. To create a multivariable model, we will include all variables that are significantly associated with the dependant variable and those variables which have shown association within the available literature. We will then asses for collinearity and remove one of the variables if collinearity is found. We will also assess for interactions and will create interaction terms to be included in the model if any interactions are found. Both forward and backward elimination will be conducted to assess the goodness of fit and create the final model. **Global online survey (phase 2)** The variables are based on the online survey as described above. For a summary of the included components see Figure 3. Data from the online survey will be checked for completeness and consistency and coded to reflect skip patterns. The complete data set for analyses will include PAB from phase 1 (desk review database) and will be linked with the database containing responses for the global online questionnaire. Descriptive analyses will 

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257	be conducted including summary measures. Bivariate analyses will be conducted to assess
258	the associations between the questionnaire variables and the dependant variable PAB and the
259	significance of the relationship will be tested with Fisher's Exact test. Logistic regression
260	models will be used to assess the relationship between the responses in the online
261	questionnaire and high coverage of PAB $\geq=90\%$ independently. These models will be created
262	as described in phase 1. A two-sided p-value of 0.05 will be considered as significant.
263	
264	Telephone conferences (quantitative analyses, phase 3)
265	The primary objective is to provide descriptive information about maternal immunization
266	services and its organization (Figure 4).
267	Data from this phase will be checked for completeness and consistency and coded to reflect
268	skip patterns. Descriptive analyses will be conducted including summary measures.
269	
270	Qualitative analyses based on country visits and telephone conferences (phase 4)
271	Ten countries will be visited to conduct qualitative interviews at national and subnational
272	level. Resulting qualitative information and from these visits as well as from telephone
273	interview conducted in the previous phase will be used in a thematic analysis applied by
274	trained qualitative data analysts to the following qualitative data sources: comments and free-
275	text responses to telephone interview questions (phase 3), semi-structured interviews with
276	community health workers (phase 4), comments and free-text response to stakeholder and
277	facility manager interviews (phase 4), comments provided during debrief sessions with
278	national level stakeholders in-country (phase 4). Thematic analysis will be applied to intra-
279	case and cross-case analysis. First, an intra-case analysis will organize and reduce qualitative
280	findings within each country along two criteria: (1) relevance of finding to research questions
281	and (2) relative frequency of finding across data sources. Second, a cross-case analysis will

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organize findings across countries into themes generated from research questions and subthemes generated from grounded analysis of data collected. Two qualitative data analysts will co-organize and reduce intra-country findings. For cross-country findings, qualitative analysts will independently generate themes and sub-themes for cross-case analysis and will then resolve any inter-coder divergence in themes and sub-themes based on relevance of theme to data source, relevance of theme to research questions and robustness of theme relative to alternative themes. See figure 4 and 5 for the included components.

290 Consolidated data analysis

To inform the development of a typology of MI delivery models approaches in LMICs quantitative and qualitative data analysis results will be consolidated in a global analysis of MI and ANC service delivery approaches in countries as well as individual country profiles that shall support countries to conduct self-assessments of their MI and ANC systems strengths and capacity gaps. Based on the advice of the project's advisory group, a checklist approach will be considered to provide a profiling for countries with sufficient data available. including indicators on policy and governance, financing, programme management, service delivery systems and demand side issues. Ultimately, such a profiling shall help countries and other MI stakeholders to identify the needs for targeted support to strengthen existing MI programmes or to reach readiness to introduce future programmes. 

# 302 Limitations

The data analyses will take into account the limitations of the study, including the reliability of the selected outcome measures, i.e. PAB, potential biases introduced by the limited number of countries for which in-depth information will be available, i.e. through telephone interviews and in-country visits, selective sampling of in-country site visit locations, missing

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2 3	307	data and the fact that the end-users' perspective will be captured only indirectly through
4 5	507	data, and the fact that the end users' perspective will be captured only mencerry through
6	308	facility and community based health workers.
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# ETHICS AND DISSEMINATION

Ethical considerations. The first three phases of the study are exempt from ethical permission as participants will provide information on operations and administration of public health services on a purely professional basis, and without disclosure of personidentifiable information. The protocol for the country visits was approved by the WHO Research Ethics Review Committee (ERC.0002908).

Country ownership will be ensured through transfer of responsibility for the data provision to in-country focal points, and by joint, on-site analysis of the data collected during the country visits with the main stakeholders. The study aims to contribute to the evidence needed to ensure more equitable access to high-impact global health interventions, such as MI.<sup>25</sup>

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# 322 Data management and dissemination

The data will be managed and analysed by data clerks who were not part of the data collection. Anonymised data from surveys and key informant interviews, excluding any confidential information as identified by the in-country focal points, will be uploaded to a publicly available data repository hosted by the WHO. Recordings from country interviews will be transcribed before the qualitative analyses and destroyed at completion of the data analyses.

The results will be submitted for publication in peer-reviewed journals, as well as in a

331 MIACSA project report that will be shared widely with global health decision makers,

332 researchers, product developers, and implementers. The report and/or specific aspects of the

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project, will be presented at international stakeholder meetings, with the ultimate aim to establish a knowledge network of countries exploring MI implementation strategies. Further, the results will be shared through summaries on the WHO website and in public fora. To ensure wide distribution of the project findings to the international scientific community and national stakeholders involved in maternal immunization, findings will be also shared at the end of the project through a large stakeholder convening. At this meeting, key aspects of maternal tetanus vaccination service delivery mechanisms and antenatal care capacities identified in select countries will be discussed to enable exchange of lessons learnt between select participating countries and to discuss generalizable lessons learnt that may improve maternal immunization service delivery through an integrated platform considering Immunization and Maternal Child Health Care mechanisms. Dissemination of the MIACSA results will aim to provide advice on best practices, policy requirements, capacity needs, and health system changes needed for successful introduction and integration of new maternal vaccines into national health systems, including ANC and EPI services, in LMICs. 

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2 3 4 5	415	AUTHORS' CONTRIBUTIONS
5 6 7	416	NR and PL designed the study with inputs from TD and JH; CM, EM, FMM, MLG, TD, JH,
8 9	417	AM and the MIACSA expert advisory panel group drafted the protocol with NR and PL; and
10 11 12	418	all authors reviewed and approved the final manuscript version.
13 14 15	419	
16 17 18	420	ACKNOWLEDGMENTS
19 20 21	421	The investigators wish to thank the EPI and MNCH focal points at the regional and national
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51 52 53	433	The authors declare no competing interests.
54 55 56 57 58 59 60	434	

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#### **FIGURE LEGENDS**

Figure 1. Key health system features studied by the MIACSA project. 

EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events following immunization, TT = tetanus toxoid. 

> Figure 2. Study phase 1: List of indicators for the review of global databases.

CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, BCG = Bacillus Calmette-Guérin vaccine, DPT1 = first dose of diphtheria-pertussis-tetanus vaccine, DPT3 = third dose of diphtheria-pertussis-tetanus vaccine, HepB1 = first dose of hepatitis B vaccine, HepB3 = third dose of hepatitis B vaccine, Hib1 = first dose of Haemophilus *influenzae* type B vaccine, Hib3 = third dose of *H. influenzae* type B vaccine, MCV1 = first dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine, PcV1 = first dose of pneumococcal conjugate vaccine, PcV3 = third dose of pneumococcalconjugate vaccine, Pol1 = first dose of polio-containing vaccine, Pol3 = third dose of polio-containing vaccine, TT1 = first dose of tetanus toxoid vaccine, TT1+= at least one dose of tetanus toxoid vaccine, TT2 = second dose of tetanus toxoid vaccine, TT2+= at least two doses of tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth dose of tetanus toxoid vaccine, TT5 = fifth dose of tetanus toxoid vaccine, RCV1 = first dose of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending on number of doses recommended in national schedule, YFV = yellow fever vaccine.

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458 Figure 3. Study phase 2: Variables collected from online survey of 136 LMI
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59	A structured questionnaire will be used to determine which service delivery platforms are in
60	place for tetanus vaccination of pregnant women in low- and middle-income countries
61	(LMICs), and to understand how existing health services could be adapted to implement
62	maternal immunization beyond tetanus vaccination. Internal validation questions are
63	incorporated in the questionnaire, and sources of data are requested, i.e. if administrative data
64	or personal estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization,
65	TT = tetanus toxoid, Td = tetanus-diphtheria, Tdap = tetanus-diphtheria-acellular pertussis,
66	AEFI = adverse events following immunization, TT2+ = at least 2 doses of tetanus toxoid
67	vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin
68	vaccine, OPV = oral polio vaccine, HBV = hepatitis B vaccine.
69	

# 70 Figure 4. Study phase 3: Variables collected from interviews of 30 selected LMICs.

A semi-structured questionnaire will be used to assess the preparedness of antenatal care 71 services for introducing (additional) immunizations for pregnant women in selected low- and 72 73 lower-middle income countries, and to understand the strengths and weaknesses of current immunization to guide future planning. Internal validation questions are incorporated and 74 probing for further details will be done when deemed necessary by the interviewer(s). 75 Sources of data provided are requested, i.e. if administrative data or personal estimates. ANC 76 = antenatal care, EPI = Expanded Programme on Immunization, NITAG = National 77 Immunisation Technical Advisory Group, HMIS = Health management Information System, 78 TT = tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events following 79 immunization. 80

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# 482 Figure 5. Study phase 4: Country study analysis framework for 10 country visits.

Key informant interviews, health facility visits, and focus group discussions will enable observation and collection of further data on the variables from the previous study phases, in particular at different levels of the health care system, and of socio-cultural and socio-economic factors. End-users, i.e. pregnant women, will not be interviewed as it would require a separate study design, and their perspective will be indirectly included through the nunity heatu. participation of community health workers at stakeholder meetings.



EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events following immunization, TT = tetanus toxoid.

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- World Bank income classification;
- Female literacy rate.

#### Health systems

#### General

· Health systems classification;

- · Birth cohort (most recent year of available data);
  - Target population of pregnant women.

Governance and policy environment

- Percentage of total expenditure on routine immunization financed by government funds;
- · Existence of national immunization technical advisory group (NITAG);
- National policy on minimum antenatal care (ANC) visits;
- Eligibility for global vaccine alliance (GAVI) support.

Health systems performance

- · Maternal, neonatal, and infant mortality;
- Stillbirth rates;
- Physician and midwife densities;
- Institutional deliveries;
- Coverage of a minimum of four ANC visits (ANC4+).

Vaccination, including maternal immunization

- · Number of confirmed tetanus and neonatal cases;
- Coverage of at least 2 doses of TT vaccine during pregnancy (TT2+);
- Tetanus toxoid (TT) vaccine as a proportion of CES and WUENIC vaccines, i.e. BCG, DPT1, DPT3, HepB1, HepB3, Hib1, Hib3, MCV1, MCV2, PAB, PcV1, PcV3, Pol1, Pol3, TT1, TT1+, TT2, TT2+, TT3 TT4, TT5, RCV1, RotaC, YFV;
- Proportion protected at birth from neonatal tetanus; i.e. protection at birth (PAB);
- TT containing vaccine(s) administered to pregnant women during routine visits;
- Most recent TT supplementary immunization activities (SIA), age range and size of target population, vaccination coverage, vaccine presentation, and year of next planned activity;
   Number of adverse events following immunization (AEFI):
- Maternal and Neonatal Tetanus Elimination (MNTE) status (year of elimination);
- Influenza vaccine administered to pregnant women;
- Pertussis vaccine administered to pregnant women.
- Immunization-associated activities
- Vitamin A supplementation.

Figure 2. Study phase 1: List of indicators for the review of global databases. CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United Nations Children's Fund (UNICEF) estimates of national immunization coverage, BCG = Bacillus Calmette-Guérin vaccine, DPT1 = first dose of diphtheria-pertussis-tetanus vaccine, DPT3 = third dose of diphtheria-pertussis-tetanus vaccine, HepB1 = first dose of hepatitis B vaccine, Hib3 = third dose of hepatitis B vaccine, MCV1 = first dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine, Pol3 = third dose of pneumococcal conjugate vaccine, Pol1 = first dose of polio-containing vaccine, Pol3 = third dose of tetanus toxoid vaccine, TT1 = at least one dose of tetanus toxoid vaccine, TT2 = second dose of tetanus toxoid vaccine, TT2 + = at least two doses of

tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth dose of tetanus toxoid vaccine, TT5 = fifth dose of tetanus toxoid vaccine, RCV1 = first dose of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending on number of doses recommended in national schedule, YFV = yellow fever vaccine.

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	Service delivery models	
	Routine maternal tetanus vaccination	
	<ul> <li>Policy content and coverage data;</li> <li>Existing delivery models, e.g. facility-based ANC and EPI/immunization services, outreach services, and regular and ad hoc health campaigns;</li> <li>Type(s) of vaccines administered, i.e. TT, Td, Tdap (adult formulation).</li> </ul>	
	Integrated health campaigns for maternal tetanus vaccination	
	<ul> <li>Programme management and coverage data;</li> <li>Existing campaigns integrated with vaccination, e.g. deworming, vitamin A, malaria, nutrition;</li> <li>Past and future schedules of integrated health campaigns.</li> </ul>	
	EPI, ANC or other organisation of maternal tetanus vaccination	
	<ul> <li>National level coordination planning and management;</li> <li>Training (rationale, safety and AEFI surveillance) and supervision of vaccinators;</li> <li>Vaccine procurement and distribution;</li> <li>Monitoring and evaluation, i.e. records (ANC or EPI-based personal, clinic, or electronic),</li> </ul>	
	frequency of performance assessment, monitoring indicators, e.g. TT2+, PAB.	
	Domestic and external funding.	
	Disease surveillance	
	<ul> <li>Maternal and neonatal tetanus, i.e. passive, sentinel, active, community-based;</li> <li>Other health indicators, i.e. congenital rubella syndrome, neonatal sepsis, neonatal mortality, maternal mortality, BCG at birth, OPV at birth, HBV at birth, other.</li> </ul>	
	ANC capacity for maternal immunization	
	<ul> <li>Policy for ANC, i.e. number of visits, settings for ANC provision, i.e. government or private health facility/hospital, clinic, outreach programme;</li> <li>Any user fees for ANC and maternal immunization.</li> </ul>	
	Vaccine safety surveillance	
	<ul> <li>Surveillance of AEFI following immunization in general and maternal immunization;</li> <li>Any available surveillance data.</li> </ul>	
	Other maternal vaccines	
	<ul> <li>Routine maternal immunization, e.g. influenza, pertussis, or other;</li> <li>Programme management, i.e. EPI, ANC, or other responsible for planning, training, supervision, procurement, and distribution.</li> </ul>	
A structured ques tetanus vaccination how existing hea vaccination. Intern requested, i.e. if Programme on Imn acellular pertussis, AE vaccine during preg	stionnaire will be used to determine which service delivery platforms a of pregnant women in low- and middle-income countries (LMICs), ar lth services could be adapted to implement maternal immunization b al validation questions are incorporated in the questionnaire, and sou administrative data or personal estimates. ANC = antenatal care, EP nunization, TT = tetanus toxoid, Td = tetanus-diphtheria, Tdap = tet EFI = adverse events following immunization, TT2+ = at least 2 dose nancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin var polio vaccine, HBV = hepatitis B vaccine.	are in place for nd to understand eyond tetanus irces of data are VI = Expanded anus-diphtheria- s of tetanus toxoid ccine, OPV = oral

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6		
7	Country context	
8	Overview	
9	<ul> <li>Integration of ANC and EPI organisation, i.e. national level coordination of maternal immunication, concrete the organization of maternal and neutrons health area expected in NITAC;</li> </ul>	
10	<ul> <li>National policy and action plan for maternal immunization, and respective targets, i.e.</li> </ul>	
11	<ul> <li>coverage, completeness and timeliness of reports, how and why targets are/are not met;</li> <li>Existence of national HMIS, completeness and mode of data collection, available data.</li> </ul>	
12	Funding of maternal tetanus immunization and ANC services	
13	<ul> <li>Domestic and external funding of ANC services and maternal immunization, user fees for</li> </ul>	
14	ANC and tetanus vaccination, and impact of funding situation on ANC and/or maternal immunization, e.g. procurement, logistics, training, mobilisation, and/or administration.	
15	Human resources	
16	<ul> <li>National and district level coordination and challenges for delivery.</li> </ul>	
17		
18	Service delivery through ANC and the birth context	
10	<ul> <li>Coverage and quality of ANC, i.e. staffing, coverage, precision of estimate of gestational and counselling, prevention and interventions, referral systems, and outreach services;</li> </ul>	
20	<ul> <li>Challenges to ANC delivery, e.g. staffing, equipment, infrastructure;</li> </ul>	
20	<ul> <li>Information used for planning and prioritisation, e.g. coverage, stafting, funding, user needs;</li> <li>ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up.</li> </ul>	
21		
22	Tetanus vaccine delivery to pregnant women	
23	Overview	
24	<ul> <li>Type of vaccines delivered, i.e. TT, Td or other, frequency, any integration with ANC/EPI;</li> <li>Bringto providers of tatenue vaccingtion of program upmas, qualitable data;</li> </ul>	
25	<ul> <li>Finite providers of relations vaccination of pregnant women, available data,</li> <li>Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage;</li> </ul>	
26	<ul> <li>Current vaccination of pregnant women through ANC, staffing and challenges, e.g. infrastructure, cold chain, vaccine supply, skilled staff.</li> </ul>	
27	Vaccination of pregnant women outside ANC	
28	Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing;	
29	<ul> <li>Information used for planning and prioritisation of outreach services, e.g. ANC coverage, staffing, funding, user needs.</li> </ul>	
30	Recording of tetanus immunization during pregnancy	
31	Policy, guidelines, operating procedures, with attention to immunization history and dosage.	
32	Maternal and neonatal tetanus surveillance	
33	Existing register and maternal tetranus surveillance systems, available data:	
34	<ul> <li>Frequency of reporting, integration with other surveillance systems;</li> <li>Evidence frequency and walks of prosterior.</li> </ul>	
35	Existence, requercy and quality or monitoring.	
36	Surveillance of other diseases	
37	Maternal and neonatal mortality.	
38	Vaccine safety surveillance systems	
39	Existence of training, surveillance of vaccination of pregnant women on AEFI, available data.	
40	Other vaccines than tetanus in pregnancy	
41	<ul> <li>Policy, partners, and delivery mechanisms for vaccines to pregnant women other than tetanus, e.g. influenza, partners, values fever, and maniprocessure. A available data</li> </ul>	
42	<ul> <li>Main barriers for introducing additional vaccines for pregnant women, by administration level;</li> </ul>	
13	<ul> <li>Potential interventions to support uptake or maternal vaccinations, e.g. elimination or user fees, client/provider communication, availability of medicines.</li> </ul>	
43		)
44	A comi-structured questionnaire will be used to access the proparedness of an	tonatal caro convicos for
4J 46	introducing (additional) immunizations for pregnant women in selected low-	nd lower-middle income
40	countries, and to understand the strengths and weaknesses of current immu	nization to guide future
47	planning. Internal validation questions are incorporated and probing for further	details will be done when
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49	or personal estimates. ANC = antenatal care, EPI = Expanded Programme on	Immunization, NITAG =
50	National Immunisation Technical Advisory Group, HMIS = Health management I	Information System, $TT =$
51	tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events following	ng immunization.
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data =

Supply side (health system)	Demand side (pregnant women)
Service delivery	Socio-cultural and -economic factors
<ul> <li>Integration of antenatal care (ANC) and Expanded Programme on Immunization;</li> <li>Accessibility, outreach services;</li> <li>Costs of services;</li> <li>Availability, supply chain;</li> <li>Quality and mode of delivery;</li> <li>Cultural appropriateness;</li> <li>Eollowup, e.g. mobile technology;</li> </ul>	<ul> <li>Socio-economic status;</li> <li>General health literacy;</li> <li>Knowledge about maternal vaccination;</li> <li>Mobility, security;</li> <li>Personal characteristics, i.e. age, marital status, parity;</li> <li>Culture, religion.</li> </ul>
Function of referral system.	Health systems interaction
Health care workers <ul> <li>Education, professional skills;</li> <li>Workload, working conditions;</li> <li>Professional attitudes (non-discriminatory);</li> <li>Communication skills;</li> <li>Role of community health workers.</li> </ul>	<ul> <li>Reception of adequate information;</li> <li>Distance to health facility;</li> <li>Direct and indirect costs of services;</li> <li>Transport, infrastructure (safety, accessibility);</li> <li>Opportunity costs, i.e. time spent at facility</li> <li>Clarity of procedures;</li> <li>Clarity of procedures;</li> </ul>
Information	Non-discrimination;
<ul><li>Actionable health information system;</li><li>Demand side information campaigns.</li></ul>	Community outreach.
Medical products, vaccines, technology	
<ul><li>Safety;</li><li>Supply chain skills, documentation.</li></ul>	
Financing	
<ul> <li>Domestic, external funding;</li> <li>Devolution of health services planning and financing;</li> <li>Results-based approaches.</li> </ul>	
Leadership, governance	
<ul> <li>Partnerships;</li> <li>Political priorities;</li> <li>Health system organisation, e.g. level of decentralisation;</li> <li>Accountability mechanisms;</li> </ul>	

Key informant interviews, health facility visits, and focus group discussions will enable observation and collection of further data on the variables from the previous study phases, in particular at different levels of the health care system, and of socio-cultural and socio-economic factors. End-users, i.e. pregnant women, will not be interviewed as it would require a separate study design, and their perspective will be indirectly included through the participation of community health workers at stakeholder meetings.