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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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Keywords:	maternal immunization, maternal mortality, neonatal mortality, study protocol, maternal tetanus, neonatal tetanus



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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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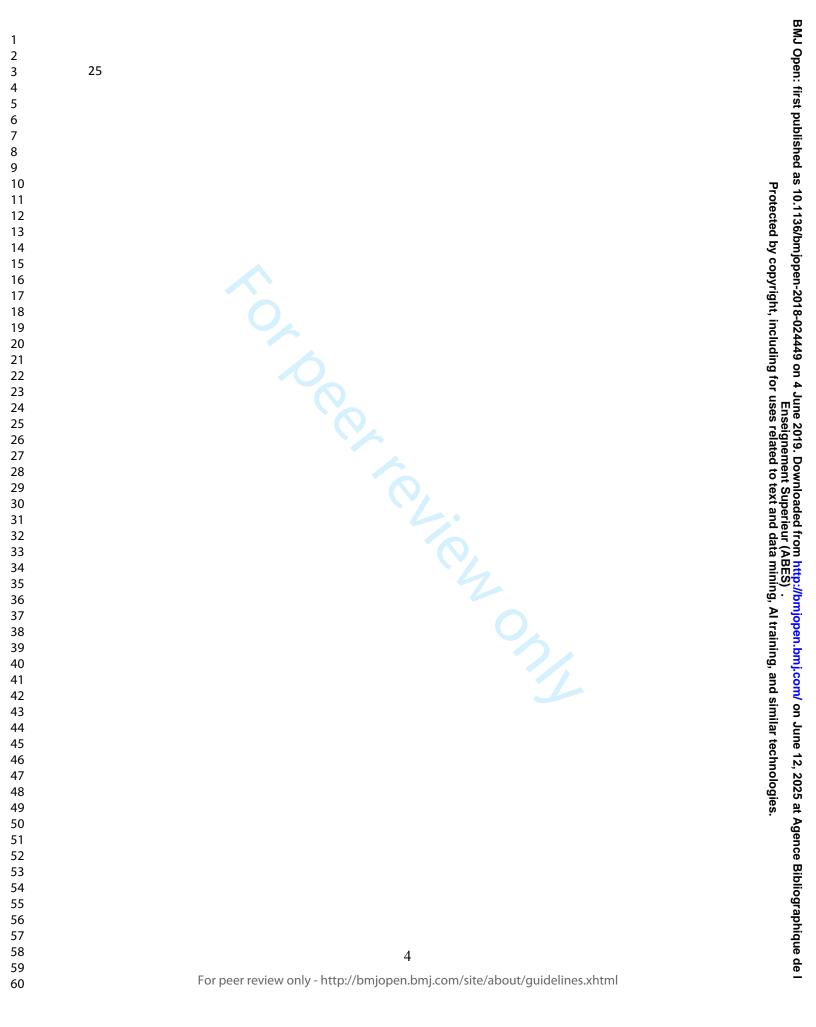
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1	ABSTRACT
2	Introduction. Maternal immunization (MI) is a safe and cost-effective way of preventing
3	neonatal tetanus, and is one of several strategies that aim to reduce the high global rates of
4	maternal and neonatal morbidity and mortality caused 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
22	submitted for publication in peer-reviewed journals that will be shared broadly among global

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- health decision makers, researchers, product developers, and country-level stakeholders.
 - Registration. Not applicable.



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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.
 - only indirectly through community health workers.



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51 INTRODUCTION

Vaccine-preventable diseases are a major cause of global child morbidity and mortality, particularly in low- and middle-income countries (LMICs).¹ 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.² 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.³⁻⁵

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.^{6,7} 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,⁹ and are recommended for pregnant women by the World Health Organization

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(WHO).^{6, 10-13} 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.¹⁴⁻¹⁸

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).¹⁹ 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.²⁰ 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.²¹

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;^{22, 23} 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. ²⁴
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.

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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	Data collection phase 3. 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
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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.²⁵

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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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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,

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. 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	351	Figure 1. Key health system features studied by the MIACSA project.
7 8 9	352	EPI = Expanded Programme on Immunization, ANC = antenatal care, AEFI = adverse events
10 11	353	following immunization, TT = tetanus toxoid.
12 13 14	354	
15 16 17	355	Figure 2. Study phase 1: List of indicators for the review of global databases.
18 19 20	356	CES = coverage evaluation survey, WUENIC = World Health Organization (WHO)/United
20 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	361	<i>influenzae</i> type B vaccine, Hib3 = third dose of <i>H. influenzae</i> type B vaccine, MCV1 = first
31 32	362	dose of measles-containing vaccine, MCV2 = second dose of measles-containing vaccine,
33 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	367	doses of tetanus toxoid vaccine, TT3 = third dose of tetanus toxoid vaccine, TT4 = fourth
44 45	368	dose of tetanus toxoid vaccine, TT5 = fifth dose of tetanus toxoid vaccine, RCV1 = first dose
46 47	369	of rubella-containing vaccine, RotaC = second or third dose of rotavirus vaccine depending
48 49 50	370	on number of doses recommended in national schedule, YFV = yellow fever vaccine.
50 51 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 12, 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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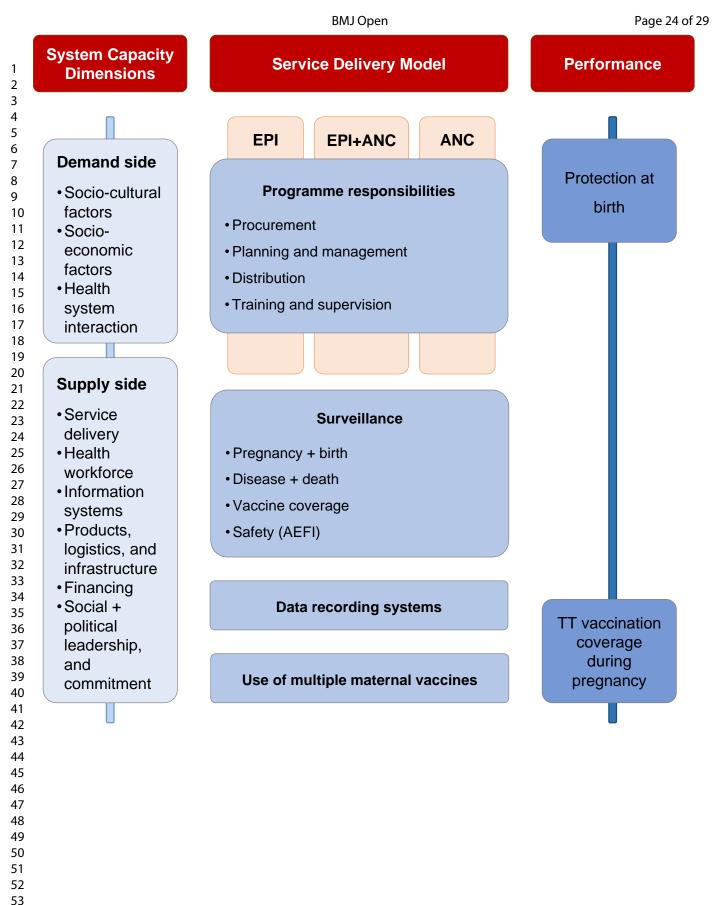
Key informant interviews, health facility visits, and focus group discussions will enable
observation and collection of further data on the variables from the previous study phases, in
particular at different levels of the health care system, and of socio-cultural and socioeconomic factors. End-users, 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

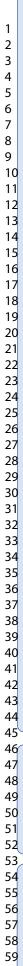
- Maternal, neonatal, and infant mortality;
- Stillbirth rates;
- Physician and midwife densities;
- Institutional deliveries;
- Coverage of a minimum of four ANC visits (ANC4+).

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	Page 27 of 29 BMJ Open		
		Country context	
1 2 3	•	Overview	
5 4 5 6 7 8 9		 Integration of ANC and EPI organisation, i.e. national level coordination of maternal immunization, representation of maternal and newborn health care experts in NITAG; 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; Existence of national HMIS, completeness and mode of data collection, available data. 	
10 11 12 13 14 15 16		Funding of maternal tetanus immunization and ANC services	
		 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	•	 Coverage and quality of ANC, i.e. staffing, coverage, precision of estimate of gestational age, counselling, prevention and interventions, referral systems, and outreach services; Challenges to ANC delivery, e.g. staffing, equipment, infrastructure; Information used for planning and prioritisation, e.g. coverage, staffing, funding, user needs; ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up. 	
31 32 33		Tetanus vaccine delivery to pregnant women	
34 35		Overview	
36 37 38 39 40 41 42		 Type of vaccines delivered, i.e. TT, Td or other, frequency, any integration with ANC/EPI; Private providers of tetanus vaccination of pregnant women, available data; Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage; Current vaccination of pregnant women through ANC, staffing and challenges, e.g. infrastructure, cold chain, vaccine supply, skilled staff. 	
43 44		Vaccination of pregnant women outside ANC	
45 46 47 48 49		 Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing; Information used for planning and prioritisation of outreach services, e.g. ANC coverage, staffing, funding, user needs. 	
50 51		Recording of tetanus immunization during pregnancy	
52 53		• Policy, guidelines, operating procedures, with attention to immunization history and dosage.	
54 55 56		Maternal and neonatal tetanus surveillance	
50 57 58 59 60		 Existing neonatal and maternal tetanus surveillance systems, available data; Frequency of reporting, integration with other surveillance systems; For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml Existence, frequency and quality of monitoring. 	

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)

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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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.

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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.

$\begin{array}{c} 4\\ 5\\ 6\\ 7\\ 8\\ 9\\ 10\\ 11\\ 12\\ 13\\ 14\\ 15\\ 16\\ 17\\ 18\\ 19\\ 20\\ 21\\ 22\\ 23\\ 24\\ 25\\ 26\\ 27\\ 28\\ 29\\ 30\\ 31\\ 32\\ 33\\ 34\\ 35\\ 36\\ 37\\ 38\\ 39\\ 40\\ 41\\ 42\\ 43\\ 44\\ 45\\ 46\\ 47\\ 48\\ 49\\ 50\\ 51\\ 52\\ \end{array}$	Not applicable.
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ARTICLE SUMMARY

23	ARTICLE SUMMART		
26	Strengths and limitations of this study		
27	• The MIACSA study will provide a first time, comprehensive global overview and analysis		
28	of existing maternal immunization (MI) delivery strategies in low- and middle-income		
29	countries (LMICs).		
30	• The results will provide evidence to inform the development of a typology of MI delivery		
31	approaches in LMICs, and identify capacity needs and key system changes, including policy		
32	adjustments required to introduce new maternal vaccines and/or scale up existing MI in		
33	LMICs.		
34	• The study benefits from a mixed-methods design; a multidisciplinary approach leveraging		
35	policy-level, academic, and implementers' experience; multi-level data collection; a globally		
36	comprehensive analysis combined with in-depth information of a subsample of LMICs;		
37	inter-sectoral collaboration between MNCH and EPI programmes, and broad dissemination		
38	of results. Limitations include the small number of countries and health care facilities visited		
39	within each country included in the study, thus precluding generalization of country visit		
40	findings to a national level, and the fact that the end-users' perspective will be captured only		
41	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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45	INTRODUCTION
45	INTRODUCTION

Vaccine-preventable diseases are a major cause of global child morbidity and mortality, particularly in low- and middle-income countries (LMICs).¹ 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.² 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.³⁻⁵

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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.^{6,7} 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,⁹ and are recommended for pregnant women by the World Health Organization (WHO).^{6, 10-13} 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.¹⁴⁻¹⁸

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).¹⁹ 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.²⁰ 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.²¹

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;^{22, 23} 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

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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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METHODS AND ANALYSIS Patient and Public Involvement. The development of the research questions were influenced by an interdisciplinary group of international experts for the MIACSA project. The project did not include patients, but restricted itself to national level program managers and health facilities where health workers responded to interviews in their professional capacity. 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. Desk review of global data (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 desk review of pre-defined health indicators (Figure 2) from 136 LMICs will be

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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 12, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES).

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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

1 2 3		
4 5	250	be conducted to assess the goodness of fit and create the final model.
6 7	251	
 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 	252	Global online survey (phase 2)
	253	The variables are based on the online survey as described above. For a summary of the included
	254	components see Figure 3. Data from the online survey will be checked for completeness and
	255	consistency and coded to reflect skip patterns. The complete data set for analyses will include
	256	PAB from phase 1 (desk review database) and will be linked with the database containing
	257	responses for the global online questionnaire Descriptive analyses will be conducted including
	258	summary measures. Bivariate analyses will be conducted to assess the associations between the
	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 31 32 33 34 35 36 37 38 39 40 41	261	relationship between the responses in the online questionnaire and high coverage of PAB $\geq=90\%$
	262	independently . These models will be created as described in phase 1. A two-sided p-value of
	263	0.05 will be considered as significant.
	264	
	265	Telephone conferences (quantitative analyses, phase 3)
	266	The primary objective is to provide descriptive information about maternal immunization
42 43	267	services and its organization (Figure 4).
44 45	268	Data from this phase will be checked for completeness and consistency and coded to reflect skip
46 47 48	269	patterns. Descriptive analyses will be conducted including summary measures.
49 50	270	
51 52	271	Qualitative analyses based on country visits and telephone conferences (phase 4)
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272	Ten countries will be visited to conduct qualitative interviews at national and subnational level.
273	Resulting qualitative information and from these visits as well as from telephone interview
274	conducted in the previous phase will be used in a thematic analysis applied by trained qualitative
275	data analysts to the following qualitative data sources: comments and free-text responses to
276	telephone interview questions (phase 3), semi-structured interviews with community health
277	workers (phase 4), comments and free-text response to stakeholder and facility manager
278	interviews (phase 4), comments provided during debrief sessions with national level stakeholders
279	in-country (phase 4). Thematic analysis will be applied to intra-case and cross-case analysis.
280	First, an intra-case analysis will organize and reduce qualitative findings within each country
281	along two criteria: (1) relevance of finding to research questions and (2) relative frequency of
282	finding across data sources. Second, a cross-case analysis will organize findings across countries
283	into themes generated from research questions and sub-themes generated from grounded analysis
284	of data collected. Two qualitative data analysts will co-organize and reduce intra-country
285	findings. For cross-country findings, qualitative analysts will independently generate themes and
286	sub-themes for cross-case analysis and will then resolve any inter-coder divergence in themes
287	and sub-themes based on relevance of theme to data source, relevance of theme to research
288	questions and robustness of theme relative to alternative themes. See figure 4 and 5 for the
289	included components.

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 12, 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.²⁵

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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

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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

³⁸₃₉ 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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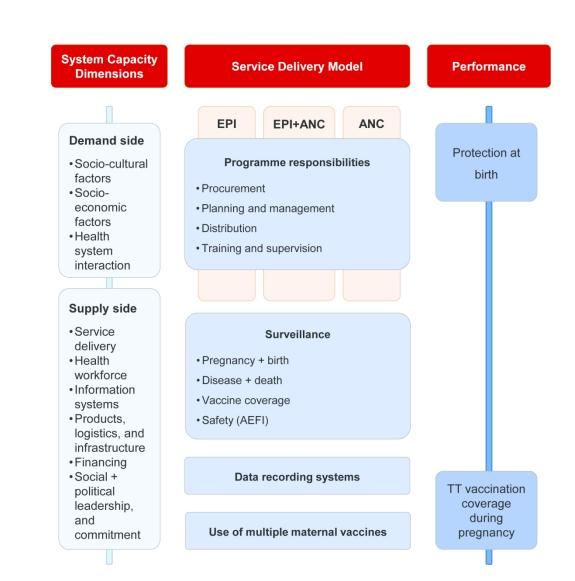
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Figure 3. Study phase 2: Variables collected from online survey of 136 LMICs.

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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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2 3 4	477	
5 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 22	484	community health workers at stakeholder meetings.
22 23 24		community health workers at stakeholder meetings.
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 $\label{eq:EPI} \mbox{EPI} = \mbox{Expanded Programme on Immunization, ANC} = \mbox{antenatal care, AEFI} = \mbox{adverse events following} \\ \mbox{immunization, TT} = \mbox{tetanus toxoid.}$

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 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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6	Comvies delliveru medale
7	Service delivery models
8	Routine maternal tetanus vaccination
9	Policy content and coverage data;
10	Existing delivery models, e.g. facility-based ANC and EPI/immunization services, outreach
11 12	 services, and regular and ad hoc health campaigns; Type(s) of vaccines administered, i.e. TT, Td, Tdap (adult formulation).
12	
	Integrated health campaigns for maternal tetanus vaccination
14 15	Programme management and coverage data;
15	 Existing campaigns integrated with vaccination, e.g. deworming, vitamin A, malaria, nutrition; Past and future schedules of integrated health campaigns.
	- Past and future schedules of integrated health campaigns.
17 18	EPI, ANC or other organisation of maternal tetanus vaccination
18 19	 National level coordination planning and management;
20	 Training (rationale, safety and AEFI surveillance) and supervision of vaccinators;
20	 Vaccine procurement and distribution; Monitoring and evaluation, i.e. records (ANC or EPI-based personal, clinic, or electronic),
21	frequency of performance assessment, monitoring indicators, e.g. TT2+, PAB.
22	Funding for maternal tetanus vaccination programme
23	
25	Domestic and external funding.
26	Disease surveillance
27	Maternal and neonatal tetanus, i.e. passive, sentinel, active, community-based;
28	Other health indicators, i.e. congenital rubella syndrome, neonatal sepsis, neonatal
29	mortality, maternal mortality, BCG at birth, OPV at birth, HBV at birth, other.
30	ANC capacity for maternal immunization
31	Policy for ANC, i.e. number of visits, settings for ANC provision, i.e. government or private
32	health facility/hospital, clinic, outreach programme;Any user fees for ANC and maternal immunization.
33	
34	
35	Vaccine safety surveillance
36	 Surveillance of AEFI following immunization in general and maternal immunization;
37	 Surveniance of AET following infindinzation in general and maternal infindinzation, Any available surveillance data.
38	
39	
40	Other maternal vaccines
41	• Routine maternal immunization, e.g. influenza, pertussis, or other;
42	 Programme management, i.e. EPI, ANC, or other responsible for planning, training, supervision, procurement, and distribution.
43	supervision, procurement, and distribution.
44	
45	A structured questionnaire will be used to determine which service delivery platforms are in place for
46	tetanus vaccination of pregnant women in low- and middle-income countries (LMICs), and to understand
47	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
48	requested, i.e. if administrative data or personal estimates. ANC = antenatal care, EPI = Expanded
49	Programme on Immunization, $TT =$ tetanus toxoid, $Td =$ tetanus-diphtheria, $Tdap =$ tetanus-diphtheria-
50	acellular pertussis, AEFI = adverse events following immunization, TT2+ = at least 2 doses of tetanus toxoi
51	vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin vaccine, OPV = oral
52	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	immunization, representation of maternal and newborn health care experts in NITAG; National policy and action plan for maternal immunization, and respective targets, i.e.
10	coverage, completeness and timeliness of reports, how and why targets are/are not met;
12	Existence of national HMIS, completeness and mode of data collection, available data.
12	 Funding of maternal tetanus immunization and ANC services 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
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	 Information used for planning and prioritisation, e.g. coverage, staffing, funding, user needs; ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up.
21	The reading is the set in the set of the period of the period of the set of t
22	Tetanus vaccine delivery to pregnant women
23	Overview
24	 Type of vaccines delivered, i.e. TT, Td or other, frequency, any integration with ANC/EPI;
25	 Private providers of tetanus vaccination of pregnant women, available data; Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage;
26	Current vaccination of pregnant women through ANC, staffing and challenges, e.g.
27	infrastructure, cold chain, vaccine supply, skilled staff. Vaccination of pregnant women outside ANC
28	Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing;
29	 Information used for planning and prioritisation of outreach services, e.g. ANC coverage,
30	staffing, funding, user needs.
31	Recording of tetanus immunization during pregnancy
32	Policy, guidelines, operating procedures, with attention to immunization history and dosage.
33	Maternal and neonatal tetanus surveillance
34	 Existing neonatal and maternal tetanus surveillance systems, available data; Frequency of reporting, integration with other surveillance systems;
35	Existence, frequency and quality of monitoring.
36	Surveillance of other diseases
37	Maternal and neonatal mortality.
•••	Vaccine safety surveillance systems
38	Existence of training, surveillance of vaccination of pregnant women on AEFI, available data.
39	Other vaccines than tetanus in pregnancy
40	Policy, partners, and delivery mechanisms for vaccines to pregnant women other than
41	tetanus, e.g. influenza, pertussis, yellow fever, and meningococcus A, available data; Main barriers for introducing additional vaccines for pregnant women, by administration level;
42	 Potential interventions to support uptake of maternal vaccinations, e.g. elimination of user fees, client/provider communication, availability of medicines.
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	ructured questionnaire will be used to assess the preparedness of antenatal care services for
10 acustula	ng (additional) immunizations for pregnant women in selected low- and lower-middle income
4/	s, and to understand the strengths and weaknesses of current immunization to guide future
	nternal validation questions are incorporated and probing for further details will be done when essary by the interviewer(s). Sources of data provided are requested, i.e. if administrative data
	al estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization, NITAG =
	munisation Technical Advisory Group, HMIS = Health management Information System, $TT =$
	anus toxoid, $Td =$ tetanus-diphtheria, AEFI = adverse events following immunization.
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Supply side (health system)	Demand side (pregnant women)
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;	 Demand side (pregnant women) Socio-cultural and -economic factors Socio-economic status; General health literacy; Knowledge about maternal vaccination; Mobility, security; 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.
 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. 	

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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Secondary Subject Heading:	Global health, Public health
Keywords:	maternal immunization, maternal mortality, neonatal mortality, study protocol, maternal tetanus, neonatal tetanus

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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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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

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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.

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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3 4	26	AR	ARTICLE SUMMARY			
5 6	27	Str	Strengths and limitations of this study			
7						
8 9	28	•	The MIACSA study provides a first time, comprehensive global overview and analysis			
10 11 12	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	36	•	End-users' perspective is captured only indirectly through community health workers.			
28 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	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).¹ 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.² 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.³⁻⁵

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.^{6,7} 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,⁹ and are recommended for pregnant women by the World Health Organization

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(WHO).^{6, 10-13} 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.¹⁴⁻¹⁸ 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).¹⁹ 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.²⁰ 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.²¹

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;^{22, 23} 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.²⁴ Closer collaboration between ANC and EPI services could provide a unique and costeffective opportunity to further strengthen preventive health care measures for women and

children under each programme, by reducing missed opportunities for immunization, 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.

1 2		
2 3 4 5	111	METHODS AND ANALYSIS
6 7	112	Patient and Public Involvement.
8 9 10 11 12	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
12 13 14	115	restricted itself to national level program managers and health facilities where health workers
15 16	116	responded to interviews in their professional capacity.
17 18	117	
19 20 21	118	
22 23	119	Study design and data collection
24		
25 26	120	Between November 2016 and December 2018, a mixed-methods, cross-sectional study will
27 28 29 30 31 32 33 34 35 36 37	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
38 39 40	126	WHO standards for global monitoring surveys, all data collection tools and standard
41 42	127	operating procedures will be reviewed and endorsed by the EAP. The surveys and country
43 44	128	visits will be conducted in local languages when needed.
45 46 47	129	
48		
49 50	130	Desk review of global data (Data collection phase 1). The first phase will consist of collecting
51 52	131	key health indicators of LMICs to create outlines of country profiles, focusing on ANC and
53 54 55	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 8 9 10 11 12 13 14	184	Country visits (data collection phase 4). Finally, in-country visits will be conducted in
	185	order to collect data on MI from key decision-makers and implementers at every level of the
	186	health care system, as well as to determine actual delivery, capacity and coordination of ANC
	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
27 28	193	countries, MNTE priority countries, and countries with high ANC4+ coverage. Site visits will
29 30 31 32 33 34 35	194	include ANC and EPI sites and session observations, focus group discussions, and in-depth
	195	interviews. The week-long visits will be piloted in two countries to adjust and refine the data
	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 42 43	198	
	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
48 49 50 51 52 53 54 55 56 57	202	and financial parties, and civil society, such as non-governmental organisations. The study
	203	will aim to conduct a total of twelve health facility visits taking into account a balance of
	204	geographical locations, urban and rural areas, and - if possible - different types of health
	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.		
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 22	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 32 33 34 35 36 37	218	Desk review of global data (phase 1)		
	219	The MIACSA project will conduct a desk review of global databases (Joint reporting form		
	220	(JRF), United Nations (UN) mortality reports, Demographic health survey (DHS), Multiple		
	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 50 51 52 53 54 55 56 57 58	226	(cut-off level <90% and \geq 90%) and the independent variables will include country economic		
	227	level, immunization coverage, mortality, service coverage, available ANC and vaccination		
	228	policies and availability of a national immunization advisory committee (Figure 2).		
	229	We will first asses the database for completeness of data. We will also conduct a sensitivity		
	230	analysis based on imputation of data based on available predictors for countries with missing		
59 60	231	data on PAB. Results from the complete case analysis will be compared with the sensitivity		

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,

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analysis to explore bias due to missing data.

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 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 >=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

307 data, and the fact that the end-users' perspective will be captured only indirectly through 308 facility and community based health workers.	1 2	
308 facility and community based health workers.	2	data, and the fact that the end-users' perspective will be captured only indirectly through
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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.²⁵

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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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24 25	423	specialists of the Expert Advisory Panel for their valuable advice and guidance on				
26 27 28	424	development of the protocol methodology. The authors also wish to thank Dr. Peter Mark				
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31 32 33	426	the public or patients in the project development.				
34 35 36	427					
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42 43 44	430	OPP1156378.				
45 46 47	431					
48 49 50	432	COMPETING INTERESTS				
51 52 53	433	The authors declare no competing interests.				
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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 LMICs.
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459	A structured questionnaire will be used to determine which service delivery platforms are in
460	place for tetanus vaccination of pregnant women in low- and middle-income countries
461	(LMICs), and to understand how existing health services could be adapted to implement
462	maternal immunization beyond tetanus vaccination. Internal validation questions are
463	incorporated in the questionnaire, and sources of data are requested, i.e. if administrative data
464	or personal estimates. ANC = antenatal care, EPI = Expanded Programme on Immunization,
465	TT = tetanus toxoid, Td = tetanus-diphtheria, Tdap = tetanus-diphtheria-acellular pertussis,
466	AEFI = adverse events following immunization, TT2+ = at least 2 doses of tetanus toxoid
467	vaccine during pregnancy, PAB = protection at birth, BCG = Bacillus Calmette-Guérin
468	vaccine, OPV = oral polio vaccine, HBV = hepatitis B vaccine.
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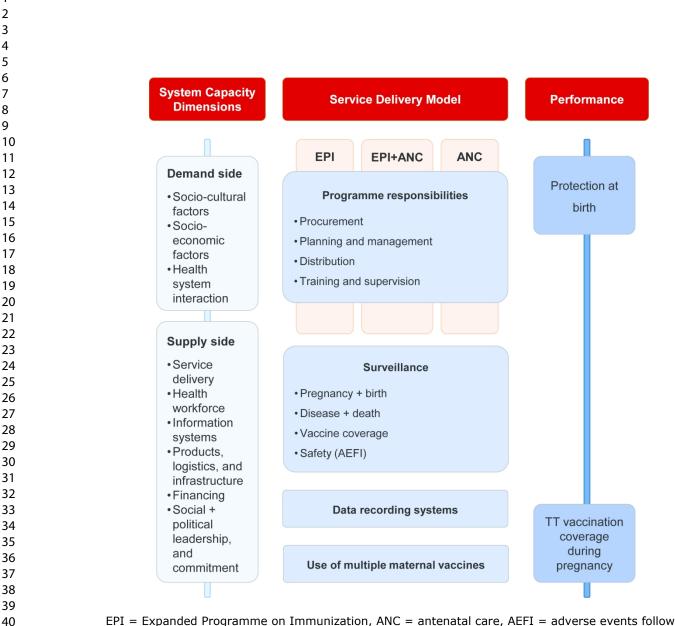
70 Figure 4. Study phase 3: Variables collected from interviews of 30 selected LMICs.

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 81

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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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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.

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, 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, 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+ = 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 vaccina	ation
 Policy content and coverage data; 	ity-based ANC and EPI/immunization services, outreach nealth campaigns;
Integrated health campaigns for	maternal tetanus vaccination
 Programme management and cov Existing campaigns integrated with Past and future schedules of integrated 	vaccination, e.g. deworming, vitamin A, malaria, nutrition;
EPI, ANC or other organisation o	f maternal tetanus vaccination
Vaccine procurement and distribut Monitoring and evaluation, i.e. reco	I surveillance) and supervision of vaccinators;
Funding for maternal tetanus vac	cination programme
Domestic and external funding.	
Disease surveillance	
Other health indicators, i.e. conget	. passive, sentinel, active, community-based; nital rubella syndrome, neonatal sepsis, neonatal at birth, OPV at birth, HBV at birth, other.
ANC capacity for maternal immu	nization
 Policy for ANC, i.e. number of visit health facility/hospital, clinic, outre Any user fees for ANC and matern 	
Vaccine safety surveillanc	e
	nunization in general and maternal immunization;
Other maternal vaccines	
 Routine maternal immunization, e. Programme management, i.e. EPI supervision, procurement, and dis 	, ANC, or other responsible for planning, training,
tetanus vaccination of pregnant women in low how existing health services could be adapt vaccination. Internal validation questions are requested, i.e. if administrative data or per Programme on Immunization, TT = tetanus to acellular pertussis, AEFI = adverse events follow vaccine during pregnancy, PAB = protection at	etermine which service delivery platforms are in place for - and middle-income countries (LMICs), and to understand ed to implement maternal immunization beyond tetanus incorporated in the questionnaire, and sources of data are sonal estimates. ANC = antenatal care, EPI = Expanded oxoid, Td = tetanus-diphtheria, Tdap = tetanus-diphtheria- ving immunization, TT2+ = at least 2 doses of tetanus toxoid to birth, BCG = Bacillus Calmette-Guérin vaccine, OPV = oral HBV = hepatitis B vaccine.

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6	Country context	
/	country context	
8	Overview	
9	 Integration of ANC and EPI organisation, i.e. national level coordination of maternal immunization, representation of maternal and newborn health care experts in NITAG; 	
10	 National policy and action plan for maternal immunization, and respective targets, i.e. 	
11	 coverage, completeness and timeliness of reports, how and why targets are/are not met; Existence of national HMIS, completeness and mode of data collection, available data. 	
12	Funding of maternal tetanus immunization and ANC services	
13	Domestic and external funding of ANC services and maternal immunization, user fees for	
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	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	 Information used for planning and prioritisation, e.g. coverage, staffing, funding, user needs 	;
21	ANC records, i.e. verbal, written, electronic, and personal or facility-based, follow-up.	
22	Tetanus vaccine delivery to pregnant women	
23		
24	Overview	
25	 Type of vaccines delivered, i.e. TT, Td or other, frequency, any integration with ANC/EPI; Private providers of tetanus vaccination of pregnant women, available data; 	
	 Existing quality of TT vaccine cold chain, and ANC services' capacity for vaccine storage; Current vaccination of pregnant women through ANC, staffing and challenges, e.g. 	
26	infrastructure, cold chain, vaccine supply, skilled staff.	
27	Vaccination of pregnant women outside ANC	
28	Primary, secondary and tertiary clinical settings for vaccination of pregnant women, staffing	B C C C C C C C C C C C C C C C C C C C
29	 Information used for planning and prioritisation of outreach services, e.g. ANC coverage, staffing, funding, user needs. 	
30	Recording of tetanus immunization during pregnancy	
31	 Policy, guidelines, operating procedures, with attention to immunization history and dosage 	
32		
33	Maternal and neonatal tetanus surveillance	
34	 Existing neonatal and maternal tetanus surveillance systems, available data; Frequency of reporting, integration with other surveillance systems; 	
35	 Existence, frequency and quality of monitoring. 	
	Surveillance of other diseases	
36	Maternal and neonatal mortality.	
37	Vaccine safety surveillance systems	
38	 Existence of training, surveillance of vaccination of pregnant women on AEFI, available data 	a
39	Other vaccines than tetanus in pregnancy	
40	Policy, partners, and delivery mechanisms for vaccines to pregnant women other than	
41	tetanus, e.g. influenza, pertussis, yellow fever, and meningococcus A, available data;	
42	 Main barriers for introducing additional vaccines for pregnant women, by administration lev Potential interventions to support uptake of maternal vaccinations, e.g. elimination of user 	el;
43	fees, client/provider communication, availability of medicines.	
44		
45	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	
46	countries, and to understand the strengths and weaknesses of current imr	
47	planning. Internal validation questions are incorporated and probing for furth	
48	deemed necessary by the interviewer(s). Sources of data provided are request	
49	or personal estimates. ANC = antenatal care, EPI = Expanded Programme	
50	National Immunisation Technical Advisory Group, HMIS = Health managemen	
51	tetanus toxoid, Td = tetanus-diphtheria, AEFI = adverse events follo	
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data =

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Supply side (health system)	Demand side (pregnant women)
Service delivery	Socio-cultural and -economic factors
 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. 	 Socio-economic status; General health literacy; Knowledge about maternal vaccination; Mobility, security; Personal characteristics, i.e. age, marital status, parity; Culture, religion. Health systems interaction
 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; 	 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.
 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. 	

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.