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Contextualized strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

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ABSTRACT

Introduction: Despite the unparalleled success of immunization in the control of vaccine preventable diseases, immunization coverage in South Africa remains suboptimal. While many evidence-based interventions have successfully improved vaccination coverage in other countries, they are not necessarily appropriate to the immunization needs, barriers, and facilitators of South Africa. The aim of this research is to investigate barriers and facilitators to optimal vaccination uptake, and develop contextualized strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa.

Methods: The study will employ a mixed-methods research design. It will be conducted over three iterative phases and use the Adopt, Contextualize, or Adapt (ACA) model as an overarching conceptual framework. Phase 1 will identify, and develop a sampling frame of, immunization stakeholders involved in the design, planning and implementation of childhood and HPV immunization programs in South Africa. Phase 2 will identify the main barriers and facilitators to, and solutions for, increasing vaccination coverage. This phase will comprise exploratory qualitative research with stakeholders and an overview of existing systematic reviews on interventions for improving vaccination coverage. Using the findings from Phase 2 and the ACA model, Phase 3 will develop a set of proposed interventions and implementation action plans for improving immunization coverage in South Africa. These plans will be discussed, revised and finalized through a series of participatory stakeholder workshops and an online questionnaire, conducted as part of Phase 3.

Ethics: Ethical approval will be obtained from the South African Medical Research Council. We will also obtain permission from the South African National Department of Health. No risks to participants are expected. Various steps will be taken to ensure the anonymity and confidentiality of participants.

Dissemination: The findings of the study will be shared at stakeholder workshops, the website of Cochrane South Africa, and academic publications and conferences.

Key words: South Africa, vaccination coverage, adoption, adaptation, contextualization, implementation science.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study will provide much-needed knowledge on barriers to, and solution for, optimal uptake of vaccination in South Africa by integrating global evidence on effective interventions with local knowledge on immunization needs, challenges and opportunities.
- Furthermore, it will develop contextualized strategies and implementation plans, in consultation with local stakeholders, to increase early childhood and adolescent vaccination coverage in South Africa.
- The qualitative research component of the study will be limited to the views and experiences of stakeholders involved in the design, planning and implementation of immunization programs; the views of the end-users of vaccination will be the focus of a subsequent study.
- The scope of the study does not include an evaluation of the implementation of these interventions, nor the measurement of the effectiveness of the interventions.

BACKGROUND

Despite the unparalleled success of immunization in the control of vaccine preventable diseases, immunization coverage in South Africa is suboptimal [1]. Not only has the country failed to reach internationally-set vaccination coverage targets, locally-set targets also remain unachieved. At the World Health Assembly in May 2012, all 194 WHO Member States, including South Africa, endorsed the Global Vaccine Action Plan and committed to achieving at least 90% national coverage with three doses of diphtheria-tetanus-pertussis (DTP3) containing vaccines in children under one year of age in all countries by 2015 [2]. South Africa had set a goal of achieving at least 92% DTP3 coverage by 2017 [3]. However, the South African Demographic and Health Survey conducted in 2016 found DTP3 coverage to be only 66% [4]. The low childhood immunization coverage in South Africa points to a serious situation which may see the country battle with the re-emergence of previously controlled infectious conditions including diphtheria, pertussis, and measles. There are already indications of re-emergence of these conditions in some parts of the country, including recent diphtheria and measles outbreaks in 2017 [5 6].

To ensure a sustainable improvement in vaccination coverage in South Africa, we need to identify what the main barriers are, and develop and implement effective and context-specific interventions to address these. There are many successful evidence-based interventions to increase immunization coverage in other countries. These include strategies directed at recipients of immunization services, healthcare providers or the health system, as well as multi-component strategies [7 8]. However, whilst

strategies to increase vaccination uptake may be effective in one setting, they are not necessarily applicable or effective elsewhere [7]. Irrespective of their effectiveness, immediate adoption of interventions from elsewhere is only likely to occur if health systems, health expenditure, disease epidemiology, workforce and training, and patient literacy and sharing are common between countries [7 8]. When this is not the situation, contextualization or adaptation of interventions may be required to ensure that they are locally relevant, and engage local people appropriately to enhance uptake [9]. Contextualization and adaptation involves building 'bridges' between the best evidence and effective local implementation, when best-available evidence recommendations cannot be immediately adopted [9 10]. Ultimately, in implementing interventions there is a need "to move from what works to what works where and why" [9].

Aims and objectives

The overarching aim of this research is to investigate barriers and facilitators to optimal uptake of vaccination services and develop contextualized strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa. The specific objectives are to:

1. Identify and compile a list of stakeholders who are involved in the planning, design and/or implementation of childhood and adolescent vaccination programmes in South Africa;
2. Consult with representative samples of these stakeholders to identify barriers and facilitators to, and solutions for, increasing vaccination coverage;
3. Conduct an overview of systematic reviews on effects of intervention for improving vaccination coverage worldwide;
4. Develop practical interventions and implementation plans for increasing vaccination coverage in South Africa, tailoring global evidence to local needs, barriers, and facilitators.

METHODS

This study will employ a mixed-methods research design, including exploratory qualitative research with immunization stakeholders, stakeholder participatory workshops, reviewing of the global literature and a structured questionnaire. It will consist of three iterative phases. The study will commence in February 2019 and end in February 2021.

[Insert Figure 1 here]

Overarching conceptual framework

We will draw on the Adopt, Contextualize, or Adapt (ACA) model developed by Dizon and colleagues [11] as the overarching conceptual framework for the study. This framework was developed and tested for use in low-and-middle income countries (LMICs) to better understand the gap between evidence-based recommendations and their local uptake. The ACA comprises 18 well-defined stages to identify barriers to intervention or guideline implementation and to guide discussions on implementing solutions to barriers. It considers the time frames for likely impact of solutions; with the assumption that longer term time frames are generally required when solutions necessitate change to policies, regulations, health systems or research. The use of the ACA model in the planned study is double sided, in that it will help to identify barriers for reaching all children and adolescents with life-saving vaccines and address local implementation of strategies that have been used elsewhere to increase coverage, thus ensuring that strategies are relevant to local situations.

Phase 1: Identification and sampling of immunization stakeholders

A draft list of stakeholder groups has already been developed by the project team, and will be updated iteratively and as necessary. This list was developed by the project team, drawing on their collective knowledge of the relevant stakeholders, scoping of the literature, team discussions, and the list generated from an earlier study among Expanded Program on Immunization (EPI) managers [1]. The methodology for developing the stakeholder list was guided by the methods used by the SAGE Allied Health study in identifying a complex multiple stakeholder allied health reference sample [12].

Stakeholders comprise people involved in any aspect of the design, planning and implementation of childhood and HPV immunization programs in South Africa. These include policy makers in national and provincial departments of health and education, programme and facility managers and bureaucrats, healthcare personnel and educators, academics or researchers, funders, members of professional associations, independent advisory bodies, non-Government Organizations (NGOs) and School Governing Bodies.

In this current study, we will not involve the beneficiaries, or end-users, of vaccination, such as patients and the wider public. We intend to build on the findings of this study to develop and implement a larger-

scale subsequent study to obtain the views, experiences and input of the end-users of vaccination, including patients and the wider public.

Both maximum variation and snowball sampling techniques will be used [13]. We have divided the stakeholder groups into clusters and estimated the number of people, and their potential roles, likely to be available in each cluster. The number of people we aim to speak to in each cluster will depend on the size of the cluster, and the likely heterogeneity of the people within the cluster. For example, in some stakeholder groups, such as the National Department of Health (NDoH), it appears that each person involved in immunization has a different role and will potentially bring a different perspective. Therefore, the estimated sample size is the same as the estimated number of people in the group. In other stakeholder groups, where there are many people doing similar work, we will sample approximately 10% (as appropriate across geographical areas). We anticipate a sample of approximately 140 people (either individually or in focus groups), however, sampling will continue until data saturation is reached.

In Table 1 *(See Supplementary File 1)* we outline the potentially-relevant stakeholder groups, the estimated number of people in each, and how we will approach the sampling for each group.

Phase 2: Identification of immunization coverage barriers and potential solutions

2.1. Qualitative research with immunization stakeholders

Recruitment

We will identify one key person in each stakeholder cluster who can assist us with recruitment of others. This may be someone at a national, provincial, regional or community level, who can assist in providing a short initial list of names of people who may be interested in participating, and who may know of others who might be interested in taking part in the study. Some members of our team are well known within the immunization community in South Africa and have a clear understanding of the stakeholders and the key players. Thus, they will commence the recruitment by identifying names of people in key positions, who are known to them, and who they believe could assist with recruitment of others.

Potential participants will be sent an email inviting them to take part in either interviews or focus group discussions. If no response is received within two weeks, we will follow-up the invitation with another

email and/or phone call. If we do not have a response at this stage, we will select another person in the same group (if possible) and initiate the invitation process.

Data collection

Semi-structured interviews or focus group discussions (FGDs) will be conducted with the sample of immunization stakeholders. The choice of an individual interview or FDG will be determined by the role, sensitivities, time constraints and knowledge of participants. It is envisaged that individual interviews will be conducted with participants in unique roles (where only that person can provide insights from that perspective). Focus groups will be conducted for efficiency when the views of a number of representatives of the same stakeholder group should be heard, where it is feasible to combine participants from one stakeholder group, and/or where hearing these views as a group will potentially increase the richness of understanding [14].

Interviews will be conducted face-to-face or telephonically at a date and time chosen by participants. Face-to-face interviews will take place at a location convenient to participants, which is conducive to a confidential exchange. The interviews will last between 45 and 60 minutes. Focus group will last 60-120 minutes and will each contain 6-10 participants, in line with methodological recommendations of appropriate focus group size.[32] The composition of focus groups will be stakeholder-specific, for example only nurses or only EPI managers. This will prevent the power-dynamics that exist between different stakeholder groups from potentially impacting on the discussions, and help ensure that more marginalized individuals can openly express their views and experiences.

Both the interviews and FGDs will be guided by a semi-structured topic guide *(See Supplementary File 2)* and conducted by two researchers who are trained in qualitative research methodologies and interviewing techniques. The interview guide has been developed by drawing on and integrating the insights obtained from a preliminary mapping of potential barriers and solutions to immunization coverage in South Africa conducted by the project team, a scoping review of the literature, team discussions, and the findings of two previous studies conducted by the Principal Investigator of this study [1 15]. The topic guide will explore the following topics: involvement in immunization programs; general views on the Expanded Program on Immunization (EPI) in South Africa; perspectives of the challenges of and solutions for the EPI program (including in relation to the healthcare system, healthcare providers, and service users/public); and views and experiences of the HPV vaccine and

school-based HPV vaccination program in South Africa. The guide will be flexible to ensure that participants can express what is important to them, and so learnings from previous interviews can be clarified and probed further.

With the permission of participants, all interviews and FGDs will be digitally recorded and field notes will be taken to ensure credibility and reliability of the information being collected. Data collection will continue until data saturation is reached.

Data management and analysis

Interviews and FDG recordings will be transcribed verbatim, and all personal identifying information will be removed from transcripts. The anonymized transcripts, together with field notes, will be downloaded into Nvivo, a software programme that aids with the management and analysis of qualitative data.

The data will be analyzed through a thematic analysis, using the phases described by Braun and Clarke [16]. Thematic analysis is a useful method for identifying and describing recurring patterns that are present in the data [16]. Two researchers will independently code 10 transcripts through line-by-line reading and with the aid of Nvivo to create a list of conceptual components ('opening coding'). These components will then be re-categorized into potential themes related to key immunization barriers and solutions ('selective coding'), and adapted into a coding framework to guide the analysis. The two researchers will compare their draft coding frameworks, and propose a standard and coherent coding framework. This will be presented to the project team for debate, clarification, and endorsement for all subsequent analyses. One researcher will then code the rest of the transcripts using this framework. Additional or revised codes will be developed iteratively as determined by the data and added to the coding framework. Throughout the research, the project team will meet regularly to discuss emerging findings and themes, and to use these to fine tune interview questions for subsequent interviews and FGDs. The final product of the analysis will be a 'conceptual map' which depicts the main barriers and potential solutions for increasing immunization coverage in South Africa.

2.2. Review of literature

We will conduct an overview of systematic reviews of interventions for improving vaccination coverage worldwide. The objective of the overview is to provide a broad synthesis of what is known from

up-to-date systematic reviews about the effectiveness of interventions for improving vaccination coverage.

We will develop a comprehensive search strategy for peer-reviewed literature, and search the following databases from inception to the date of the search: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effectiveness (DARE), PubMed, and PDQ-Evidence [17]. We will use standard Cochrane methods for the screening of search outputs, selection of reviews, data extraction, and assessment of methodological quality of included reviews [18 19]. For each included systematic review, we will prepare key messages, important background information, a summary of the findings of the review, and structured assessments of the relevance of the review for South Africa. The reviews will be organized using the logic framework we have previously developed for interventions aimed at improving vaccination coverage [8]

We will describe the characteristics of the included reviews in a table that will include the date of the last search, any important limitations, what the review authors searched for, and what they found. We will take into account all other relevant considerations besides the findings of the included reviews when drawing conclusions about implications for the immunization program in South Africa. This includes considerations related to the applicability of the findings, likely impacts on equity, and the values and preferences of South African immunization stakeholders.

Phase 3: Development of intervention recommendations and implementation action plans

Using the findings from Phase 2, together with the Adopt, Contextualize, or Adapt (ACA) decision-making process [11], the project team will develop a set of proposed interventions and implementation action plans for improving immunization coverage in South Africa.

3.1. Stakeholder workshops

The list of interventions and draft implementation plans will be sent to all stakeholders who took part in interviews and FGDs, as well as to the head of each stakeholder group for comment. Thereafter, stakeholder workshops will be convened. Questions and comments on the draft implementation plans will be invited prior to the workshops. Modifications will be made to the draft implementation plan prior to the workshop, and the revised plan will be circulated several days before the workshop to allow

participants to familiarize themselves with changes. An accompanying document will outline the modifications that were made and why they were made.

One main workshop will be held at the South African Medical Research Council (SAMRC), and at least one workshop will be held in each province after this. All those who participated in interviews and FGDs, as well as to the head of each stakeholder group, will be invited to attend a workshop. Using a range of participatory methodologies [20], the modified implementation plan will be discussed, further revised and endorsed at the main workshop, and this document will be presented and endorsed at each subsequent workshop. Not only with the workshops acknowledge stakeholders' valuable participation in the research, they will also help facilitate 'buy-in' for proposed implementation strategies. That is, stakeholders will potentially become change agents on the ground, who can assist in implementing and improving uptake of recommended interventions [21].

3.2. Online questionnaire

Individuals from stakeholder groups (outlined in Phase 1) who did not take part in interviews or FGDs will be given an opportunity to provide input on the recommended interventions and implementation action plans through an online questionnaire. Specific targeted approaches (including emails, telephone calls, postal mail, editorials or advertisements in professional newsletters and journals, website alerts and other social media outlets such as twitter and Facebook) will be used to alert people in the stakeholder groups about the questionnaire and to invite them to provide input.

Individuals will be invited to download the summary document and implementation plans from a link hosted on the Cochrane South Africa website. Feedback on the implementation plans will be invited for a six-week period, using a structured questionnaire delivered by an electronic SurveyMonkey form. Survey Monkey is an efficient electronic tool that captures large datasets safely and quickly. It also collates findings into a MS Excel spreadsheet. The questionnaire will be linked directly to the implementation plans for ease of questionnaire completion. It will ask for input on the feasibility and acceptability of the implementation plans and whether the timeframe of the plans is achievable. Respondents will also be asked to identify potential barriers to successful implementation of the plans, and if possible, to identify ways to resolve them. We anticipate no more than 10 questions on the implementation plans, and another 1-2 questions on barriers and facilitators. Where possible, questions will have drop-down menus to aid completion. Feedback will be anonymous.

The feedback will be summarized descriptively for each question, using the appropriate statistics (percentages, or mean values). The findings will be posted on the Cochrane South Africa website within two months of the closure of the consultation period, and will be held there whilst the implementation plans are being rolled out. In this way, stakeholders can have immediate access to the plans and feedback as required.

ETHICAL CONSIDERATIONS

Ethical approval will be obtained from the South African Medical Research Council (SAMRC). We will also obtain permission from the South African National Department of Health.

The study process will comply with the requirements of the latest version of the Declaration of Helsinki (7th revision, 2013). Verbal and written information about the study will be provided to all participants taking part in interviews and FGDs. The consent form will make explicit the following aspects: the voluntary nature of participation, that there will be no negative consequences if they decide not to participate and that they will be asked explicitly for permission for the interview to be digitally recorded and that this is also voluntary. Written consent will be obtained from all research participants before proceeding with interviews or focus groups. All participants who complete the structured questionnaire will be provided with an online study information sheet as part of the electronic SurveyMonkey form, and will be required to provide online consent before proceeding with the questionnaire. All feedback on the questionnaire will be anonymous.

Details from interviews and FGDs will be entered into a study-specific database on the day of collection (stakeholder group, participant ID etc.). Study data, including audio-recordings, will be stored on password-protected computers and shared with the study team only. All digital recorders on recorders will be destroyed following safe storage and transcription, and identifying information will be removed from all transcripts. Reports of the findings will not identify individual participants. Participant anonymity and confidentiality will thus be ensured.

No risks to participants or researchers are expected. All potential participants for interviews or focus groups are not considered as vulnerable individuals or groups. However, participants may be uncomfortable expressing criticisms of vaccination programs. Where there is this potential, and where

potential participants identify concerns, we will reassure participants of the steps that will be taken to ensure confidentiality. For participants in focus groups, we will remind participants at the outset that while the researchers undertake to maintain confidentiality, we cannot guarantee that other focus group participants will. At the start of the focus group, we will discuss the importance of maintaining confidentiality by everyone involved after the focus group, but will explain that there is an inherent risk of breaches of confidentiality in this method. We will ensure participants are aware of this risk.

DISSEMINATION OF FINDINGS

The findings of the study will be shared with people in the stakeholder groups, at the consultation workshops and through the online questionnaire and Cochrane South Africa website. In addition, at the end of the study, a project report of the main study findings will be shared with all stakeholders who took part in interviews, focus groups and/or consultation workshops. The findings will also be communicated through academic publications and conferences. Reporting of the qualitative data will adhere to the Consolidated criteria for reporting qualitative research (COREQ)[22] guidelines; the overview of systematic reviews protocol and full review will adhere to the Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P)[23] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[24] approaches respectively.

AUTHORS' CONTRIBUTIONS

The study was initially conceived by CW. The methods were designed by all authors, over a number of meetings. The background to the research was provided by CW, NN, DN, and methods advice was provided by SC and KD. The manuscript was drafted by KG, PM, SC and CW, and all authors contributed to versions of the manuscript and approved the final draft.

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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

FIGURE LEGEND

Figure 1: Study phases

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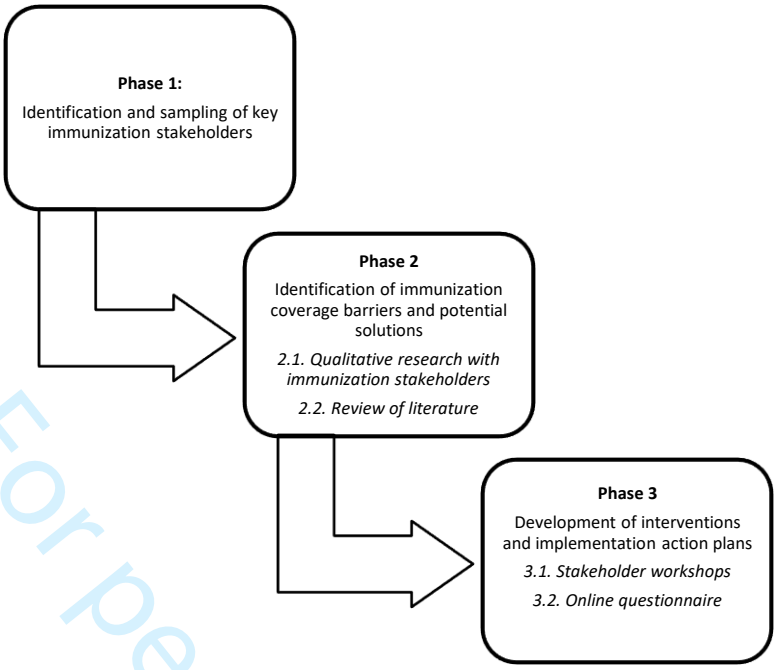

Table 1. Stakeholder groups and sample sizes

Stakeholders	Who	Predicted number	Cluster interview sample
National Department of Health	Individuals	12	12
Provincial Department of Health	Individuals	24	18
District and Facility Levels	Individuals	150	27
District Clinical Specialist Teams	Individuals	30	6
Pharmacies or Hospitals	Individuals providing pharmacy-specific services	20	12
Individual Vaccinators	Individuals	30	12
Non-Governmental Organization	Individuals providing NGO-specific immunization services	10	8
National Advisory Group on Immunisation	Individuals	12	6
WH O	Individual	6	2
UNICEF	Individual in an immunization role	1	1
PATH	Individuals in immunization roles	15	2
Health Systems Trust	Individuals in immunization roles	15	2
PEPFAR	Individuals in projects linked to PEPFAR (e.g. Right To Care, Broad Reach)	51	5
National Certification Committee for Polo Eradication	Individuals in immunization roles	6	1
Saving Babies	Individuals in immunization roles	8	1
PMTCT Working Group	Individuals in immunization roles	12	1
Paediatric Working Group	Individuals in immunization roles	12	1
Paediatric Management Group	Individuals in immunization roles	1	1
SA Paediatric Association (SAPA)	Individuals in immunization roles	1	1
Public Health Association of South Africa	Individuals in immunization roles	1	1
South African Medical Association	Individuals in immunization roles	1	1
Federation of Infectious Diseases Societies of Southern Africa	Individuals in immunization roles	1	1
South African Vaccination and Immunisation Centre	Individuals in immunization roles	4	1

Centre for Vaccines and Immunology, National Institute of Communicable Diseases	Individuals in immunization roles	2	1
National Vaccinators' Forum	Individuals in immunization roles	8	1
Amayeza- Independent Trainer on Vaccination	Spokesperson	1	1
African Local Initiative for Vaccinology Expertise	Spokesperson	2	1
Vaccines for Africa	Spokesperson	2	1
GSK	Spokesperson	1	1
Sanofi Pasteur	Spokesperson	2	1
BIOVAC	Spokesperson	2	1
Pfizer	Spokesperson	1	1
Association of early Childhood Development Centres	Representatives	4	2
Department of Education	School Health Coordinators: National and Provincial level	4	2
School Governing Bodies	Chairperson (individual) or spokesperson	4	2
Parent Association	Chairperson (individual) or spokesperson	4	2
Total		**460**	**140**

Draft Interview and Focus Group Topic Guide

Demographic information
Official title:
Organisation/Place of work:
Location:
Gender:

Part 1: Involvement in immunization programmes

1. Can you describe what your current involvement is in Immunization programme(s) in South Africa?

Probes:

- How long have you worked in the area of vaccination/immunization?
- Possible functions/roles?
- Are you involved/have experience with both childhood and pre-adolescent/adolescent vaccination programmes in the country?

Part 2: General views of the Expanded Programme on Immunisation (EPI) in South Africa

2. What do you see as the central goals of the national Expanded Programme on Immunization (EPI) in South Africa?

Probes:

- Have these goals changed over time?

3. What do you think is currently working well with the EPI programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting (where appropriate)
- What do you think have been the enabling factors underpinning these successes? *(Probes: Political, structural, ideological, financial?)*

4. Do think the national EPI programme is generally meeting its central goals?

Probes:

- Why/why not?
- If answered that EPI Programme(s) are NOT achieving set goals, ask the following:
  - Do you think the current performance of the EPI Programme is a serious national challenge?
  - Do you think managers and especially senior managers of the DOH (at all levels) view the poor/under performance of EPI as a serious challenge that should be urgently addressed?

    If yes: Are their actions in line with this view?

    If yes: Can you give us examples of these actions which demonstrate the urgency with which they view this situation?

Part 3: Specific challenges of and solutions for the EPI programme

I would now like us to talk about some of the challenges currently facing the EPI programme, and your thoughts about how these might be addressed.

Healthcare system

5. What are your views and experiences of the public primary health facilities where vaccinations are provided? What kind of challenges exist in these health facilities for the vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- Management structures?
- Management approach? The focus of managers and what they prioritise (and not)?
- Health information systems (is vaccine recording and reporting maintained)?
- Financial resources?
- Availability of staff (shortages/high turnovers)?
- Availability of vaccine education/information materials?
- Availability of initiatives to advocate for immunization?
- Availability of approaches to mobilise communities/public to vaccinate children e.g. social media
- Existence of approaches that attempt to link EPI (services, planning and mode of operation) to other apparently more successful programmes or programmes that may have a wider coverage e.g. PMTCT?
- Waiting times in the clinics?
- Mixed queues?
- Operating times?
- Treatment and attitude of Health Care Providers (Vaccinators and other HCP)?
- Attitude of non-Health Professionals such as clerks and others.
- Others (specify)

6. What do you think could be done to address some of these challenges?

Probe:

- Who should be tasked with addressing these challenges?

7. Do you see shortages of vaccines as a significant issue nationally and in your local setting?

Probes:

- Why/why not?
- If yes: Can you provide a specific example of this challenge?
- If yes: Where do you think the problem lies (*e.g. vaccine procurement, storage, distribution/delivery)?*
- Are you aware of any attempts or intervention measures by the DOH (at any level: national, province or district) to address the challenge of vaccine shortages? If yes, how successful do you think these attempts have been?
- Do you have any ideas on how to overcome the challenge of vaccine shortages? Who should be tasked with addressing this challenge?

8. Who are the main role-players/stakeholders involved in EPI programme(s) in South Africa?

Probes:

- Is there sufficient communication/collaboration between stakeholders? Why/ why not? What could be done to improve this?
- Is there sufficient advocacy/social mobilization amongst stakeholders? Why/ why not? What could be done to improve this?
- Are community leaders/groups sufficiently involved in the EPI? Why/ why not? How do you think these stakeholders be more involved?

9. Can you tell me a bit about the relationship between the public and private health sectors in terms of the EPI programme?

Probes

- Is there any collaboration/interaction between them? Why/why not?
- Do you see this as a problem? Why/why not?
- If seen as a problem: what could be done to increase collaboration/interaction?
- According to your knowledge either in terms of policy or in terms of practice and experience: "Are Private or NGO vaccinators able to access state vaccines for their clients, free of charge?" If yes, do they provide feedback on data of doses given?

Healthcare providers

10. What are your views about health care providers (HCP) administering vaccines in public health facilities? Do you think there are any challenges in relation to HCPs for vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- General attitudes and behavior of health care providers *(e.g. friendly/helpful/rude)?*
- Knowledge about vaccines and vaccination?
- Knowledge and experiences with the conditions that the vaccines prevent?
- Perceptions of vaccines and vaccination?
- Perceptions of the importance of communicating with caregivers about vaccination?
- Use opportunities to assess the vaccination status of the child?
- Sufficient skills/training?
- Do they vaccinate their own children/grandchildren or take special interest to help ensure that children of close relatives are vaccinated?
- How do they access vaccination for their own children/grandchildren or relatives? Through private or public institutions?

11. What do you think should be done to improve the attitudes and behavior of HCP?

Probe

- Who should be tasked with dealing with these issues?

12. What do you think should be done to improve the knowledge/skills of health care providers?

Probe:

- Who should be tasked with doing this?

Service users/public

13. What is your sense of the general level of knowledge amongst the public about childhood vaccines, immunisation services and the conditions that these prevent?

Probes:

- Are there gaps in knowledge? If yes: what kinds of gaps?
- Do you think people know about the benefits of childhood vaccines?
- What sources do people go to for information about childhood vaccination? *e.g. Internet; social media networks; health care workers; friends/family; schools; religious leaders?*
- Which sources do you think people perceive as being trustworthy/untrustworthy?

14. What do you think influences people' decision about whether to vaccinate their children or not?

Probes:

- What doubts, fears, concerns (if any) about vaccines and vaccination services do you think people might have that could prevent them from deciding to vaccinate their children? *(e.g. concerns about vaccine quality, safety, contra-indications, risks etc.)*
- What negative attitudes or beliefs (if any) about vaccines and vaccination do you think people might have that could prevent them from deciding to vaccinate their children? *(ask if they have heard any specific stories/rumours)*
- Where might these negative attitudes/beliefs/concerns come from? (*e.g. religion, cultural norms & practices, traditional leaders, anti-vac lobbying, media)*
- What role (if any) do you think a lack of trust in the health care system, healthcare providers and/or government might play in people's decision to vaccinate their children? *(e.g. lack of trust in providers' competence; perceptions of poor quality of care; manner in which providers treat them and their children etc.)*
- Do you think people face any practical challenges that could prevent them from choosing or accessing vaccination? *(e.g cost, travel, language or cultural differences, clinic opening hours, vaccine stock-outs etc.)*
- Are there any other factors, that we haven't already discussed, that you think might prevent people from accepting and taking-up childhood vaccination?

15. Want to you think could be done to make parents more likely to vaccinate their children according to the EPI schedule?

Probes:

- How can vaccination services best enable, support and motivate childhood vaccination?
- What channels do you think would be most effective in promoting childhood vaccination?
- Who should promote vaccination? *(e.g. health care workers, teachers, community leaders, media)*
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? Media- radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials- posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?

16. We have spoken about various different challenges facing the EPI programme in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current EPI programme, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Do you think there are different priorities for different Provinces?

Part 4: HPV Vaccine

I would now like to talk a bit about the HPV vaccine and vaccination in South Africa.

17. What is your overall impression of the school HPV vaccination programme?

Probes:

- Is the programme successful or not successful? Why?
- Who is involved with the programme? Is there collaboration between the stakeholders? Why/why not?

- Have you received any feedback about the programme *(e.g. from parents/girls? teachers? those delivering the programme? others?)*

18. What do you think is currently working well with the programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting
- What do you think have been the enabling factors underpinning these successes? *(Probe: Political, structural, ideological, financial?)*

Main challenges and potential solutions

19. Currently the HPV Vaccination Programme is delivered in a campaign like approach- vaccination teams visit schools twice a year and targeted children come at the same time to line up for this vaccine. What are your thoughts about this approach?

Probes

- What are the strengths and weaknesses of this approach? *(and probe for specific examples in local setting)*
- Do you think parents/girls/teachers are happy with this approach? Why/why not? *(and probe for specific examples in local setting)*
- What alternative delivery mechanisms (if any) do you think might be more effective?

20. Currently the programme does not include private schools and the HPV vaccine is not available at public health facilities. What are your thoughts about this?

Probes

- What kinds of problems, if any, do you think these absences might be generating?
- Should the programme be extended to private schools? Why/why not? If yes: how should it be incorporated in private schools?
- Should the HPV vaccine be made available at public health facilities? Why/why not? If yes: what would be needed to operationalize this?

21. What do you think influences parents' and girls' decision to take-up the HPV vaccine?

Probes:

- To what extent do you think parents and girls think that the HPV vaccine is necessary? Do you think they know about the reasons for/benefits of the vaccine? Why/why not?
- Do you think parents and girls trust the HPV vaccine to protect their health? Why/why not?
- What doubts, fears, concerns (if any) do you think parents and girls might have about the HPV vaccine? What do you think might be the sources of these concerns/beliefs? *(e.g. cultural norms, community practices/traditions, anti-vac lobbying, social media, internet)*
- What role (if any) do you think a lack of trust in health system, healthcare providers and decision makers might play in parents and girls concerns and beliefs about the HPV vaccines and vaccination?
- Are there any other factors, that we have not already discussed, that you think might influence parents and girls decision to accept the HPV vaccine?

22. Figures suggest that there is a significant drop in uptake from the 1st to the 2nd dose. Why do you think this might be so?

23. What do you think could be done to encourage parents and girls to consent to the HPV vaccine within the school programme?

Probes:

- Is information about the HPV vaccine and vaccination programme currently provided to parents of targeted girls and and these girls? Do you think further information and communication channels are needed?
- Is information about the HPV vaccine and vaccination programme provided to parents on non targeted girls?
- What channels do you think would be most effective in promoting the HPV vaccination?
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? media (radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials (posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?
- Who should be involved with education and communication activities (*e.g. health care workers, teachers, community leaders, media)*
- What would help parents and girls complete the vaccine series i.e. return for the second dose?

24. What are your views about health care providers (HCPs) and the HPV vaccine and vaccination services?

Probes

- What are HCPs general attitudes and behaviours towards the HPV vaccine and providing vaccination for HPV*?*
- Do you think HCPs know about the HPV vaccine?
- Do you think HCPs know about the conditions the HPV vaccine prevents?
- Do you think HCPs vaccinate their own children/grandchildren for HPV or take special interest to help ensure that children of close relatives are vaccinated for HPV?

25. We have spoken about various different challenges facing HPV vaccination in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current HPV vaccination programme in South Africa, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Are there different priorities for different Provinces?

Part 5: Closing

This has been a very informative interview. Thank you so much for your time.

Is there anything we haven't covered that you would like to add? Is there anything you would like to say in closing?

Do you know of anyone else who could provide important insights as a key informant and might be interested in participating in the study?

If yes: can you provide us with their contact details so we can get in touch with them?

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Contextualized strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

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Contextualized strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

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ABSTRACT

Introduction: Despite the unparalleled success of immunization in the control of vaccine preventable diseases, immunization coverage in South Africa remains suboptimal. While many evidence-based interventions have successfully improved vaccination coverage in other countries, they are not necessarily appropriate to the immunization needs, barriers, and facilitators of South Africa. The aim of this research is to investigate barriers and facilitators to optimal vaccination uptake, and develop contextualized strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa.

Methods: The study will employ a mixed-methods research design. It will be conducted over three iterative phases and use the Adopt, Contextualize, or Adapt (ACA) model as an overarching conceptual framework. Phase 1 will identify, and develop a sampling frame of, immunization stakeholders involved in the design, planning and implementation of childhood and human papillomavirus immunization programmes in South Africa. Phase 2 will identify the main barriers and facilitators to, and solutions for, increasing vaccination coverage. This phase will comprise exploratory qualitative research with stakeholders and a review of existing systematic reviews on interventions for improving vaccination coverage. Using the findings from Phase 2 and the ACA model, Phase 3 will develop a set of proposed interventions and implementation action plans for improving immunization coverage in South Africa. These plans will be discussed, revised and finalized through a series of participatory stakeholder workshops and an online questionnaire, conducted as part of Phase 3.

Ethics: Ethical approval was obtained from the South African Medical Research Council (EC018-11/2018). We will also obtain permission from the South African National Department of Health. No risks to participants are expected. Various steps will be taken to ensure the anonymity and confidentiality of participants.

Dissemination: The findings of the study will be shared at stakeholder workshops, the website of Cochrane South Africa, and academic publications and conferences.

Key words: South Africa, vaccination coverage, adoption, adaptation, contextualization, implementation science.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our mixed-methods and theory-informed approach will facilitate the triangulation of data thus strengthening the credibility and reliability of the findings. This approach will also help develop a more holistic and comprehensive understanding of the barriers and facilitators to vaccination uptake than could be gained from single methodologies.

- Our rigorous maximum variation sampling approach will enable engagement with a heterogenous group of relevant stakeholders and could potentially provide maximum diversity of responses and experiences with which to address our research questions.

- Complementary research competencies and experiences among the research team will help strengthen the rigour of the study interpretations.

- Our sample is limited to stakeholders involved in the design, planning and implementation of immunization programmes, with the exclusion of potentially relevant decision-makers outside the field of immunization and the end-users of vaccinations. While the views of the latter will be the focus of a subsequent study, exclusion of these important stakeholders is a limitation of this current study.

- The scope of our study does not include an evaluation of the implementation of interventions, nor the measurement of the effectiveness of the interventions, another potential limitation of the study.

BACKGROUND

Despite the unparalleled success of immunization in the control of vaccine preventable diseases, immunization coverage in South Africa is suboptimal [1]. Not only has the country failed to reach internationally-set vaccination coverage targets, locally-set targets also remain unachieved. At the World Health Assembly in May 2012, all 194 WHO Member States, including South Africa, endorsed the Global Vaccine Action Plan and committed to achieving at least 90% national coverage with three doses of diphtheria-tetanus-pertussis (DTP3) containing vaccines in children under one year of age in all countries by 2015 [2]. South Africa had set a goal of achieving at least 92% DTP3 coverage by 2017 [3].

However, the South African Demographic and Health Survey conducted in 2016 found DTP3 coverage to be only 66% [4]. The low childhood immunization coverage in South Africa points to a serious situation which may see the country battle with the re-emergence of previously controlled infectious conditions including diphtheria, pertussis, and measles. There are already indications of re-emergence of these conditions in some parts of the country, including diphtheria and measles outbreaks in 2017 [5 6].

To ensure a sustainable improvement in vaccination coverage in South Africa, we need to identify what the main barriers are, and develop and implement effective and context-specific interventions to address these. There are many successful evidence-based interventions to increase immunisation coverage in other countries. These include strategies directed at recipients of immunisation services, healthcare providers or the health system, as well as multi-component strategies [7 8]. However, whilst strategies to increase vaccination uptake may be effective in one setting, they are not necessarily applicable or effective elsewhere [7]. Irrespective of their effectiveness, immediate adoption of interventions from elsewhere is only likely to occur if health systems, health expenditure, disease epidemiology, workforce and training, and patient literacy and sharing are common between countries [7 8]. When this is not the situation, contextualization or adaptation of interventions may be required to ensure that they are locally relevant, and engage local people appropriately to enhance uptake [9]. Contextualization and adaptation involves building 'bridges' between the best evidence and effective local implementation, when best-available evidence recommendations cannot be immediately adopted [9 10]. Ultimately, in implementing interventions there is a need "to move from what works to what works where and why" [9].

South Africa's immunisation programme

Currently the National Department of Health's Expanded Programme on Immunisation of South Africa targets 11 diseases: polio, measles, tuberculosis, diphtheria, pertussis, tetanus, *Haemophilus influenzae* type b, hepatitis B, rotavirus diarrhoea, pneumococcal infection, and cervical cancer (see Table 1). Vaccines against the first 10 diseases are provided free of charge to infants and children at all public healthcare facilities. Since 2014, cervical cancer has been targeted through a school-based human papillomavirus (HPV) vaccination programme, with two doses (six months apart, administered during one-month campaigns) of the bivalent HPV vaccine offered free of charge to grade four girls aged nine years or more in public sector schools. In addition to the vaccines listed in Table 1, vaccines targeting influenza, rubella, mumps, varicella (chickenpox), meningococcal meningitis, hepatitis A and genital

warts (the quadrivalent HPV vaccine prevents cervical cancer and genital warts) are available in the private sector.

Table 1: Expanded Programme on Immunisation Schedule in South Africa

Age of child	Vaccines scheduled
At birth	Bacille Calmette-Guérin (BCG)
	Oral polio vaccine (OPV) (0)
6 weeks	OPV (1)
	Rotavirus vaccine (RV) (1)
	Diphtheria, tetanus and acellular pertussis vaccine + inactivated polio vaccine + *Haemophilus influenzae* type b vaccine + hepatitis B vaccine combined (DTaP-IPV-Hib-HepB) (1)
	Pneumococcal conjugate vaccine (PCV) (1)
10 weeks	DTaP-IPV-Hib-HepB (2)
14 weeks	RV (2)
	DTaP-IPV-Hib-HepB (3)
	PCV (2)
6 months	Measles vaccine (1)
9 months	PCV (3)
12 months	Measles vaccine (2)
18 months	DTaP-IPV-Hib-HepB (4)
6 years	Tetanus and reduced-strength diphtheria vaccine (Td) vaccine
≥9 years	Human papillomavirus (HPV) vaccine (1 and 2, 6 months apart)
12 years	Td vaccine

Aims and objectives

The overarching aim of this research is to investigate barriers and facilitators to optimal uptake of vaccination services and develop contextualized strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa. The specific objectives are to:

1. Identify and compile a list of stakeholders who are involved in the planning, design and/or implementation of childhood and adolescent vaccination programmes in South Africa;
2. Consult with representative samples of these stakeholders to identify barriers and facilitators to, and solutions for, increasing vaccination coverage;
3. Identify and review relevant in-country immunisation-related documentation, including (but not limited to) legislation and policies relevant to immunization;

4. Conduct a review of systematic reviews on effects of interventions for improving vaccination coverage;
5. Develop practical interventions and implementation plans for increasing vaccination coverage in South Africa, tailoring global evidence to local needs, barriers, and facilitators.

METHODS

This study will employ a mixed-methods research design, including exploratory qualitative research with immunization stakeholders, stakeholder participatory workshops, reviewing of the global literature and a structured questionnaire. It will consist of three iterative phases. The study will commence in July 2019 and end in July 2021. An overview of the study phases is depicted in Figure 1.

[Insert Mono Image_Figure 1 here]

Overarching conceptual framework

We will draw on the Adopt, Contextualize, or Adapt (ACA) model developed by Dizon and colleagues [11] as the overarching conceptual framework for the study. This framework was developed and tested for use in low-and-middle income countries (LMICs) to better understand the gap between evidence-based recommendations and their local uptake. The ACA comprises 18 well-defined stages to identify barriers to intervention or guideline implementation and to guide discussions on implementing solutions to barriers. It considers the time frames for likely impact of solutions; with the assumption that longer term time frames are generally required when solutions necessitate change to policies, regulations, health systems or research. The use of the ACA model in the planned study is double sided, in that it will help to identify barriers for reaching all children and adolescents with life-saving vaccines and address local implementation of strategies that have been used elsewhere to increase coverage, thus ensuring that strategies are relevant to local situations.

Phase 1: Identification and sampling of immunization stakeholders

A draft list of stakeholder groups has already been developed by the project team, and will be updated iteratively and as necessary. This list was developed by the project team, drawing on their collective knowledge of the relevant stakeholders, scoping of the literature, team discussions, and the list generated from an earlier study among Expanded Programme on Immunisation (EPI) managers [1]. The

methodology for developing the stakeholder list was guided by the methods used by the SAGE Allied Health study in identifying a complex multiple stakeholder allied health reference sample [12].

Stakeholders comprise people involved in any aspect of the design, planning and implementation of childhood and HPV immunization programs in South Africa. These include policy makers in national and provincial departments of health and education, programme and facility managers and bureaucrats, healthcare personnel and educators, academics or researchers, funders, members of professional associations, independent advisory bodies, non-Government Organizations (NGOs) and School Governing Bodies.

Both maximum variation and snowball sampling techniques will be used [13]. We have divided the stakeholder groups into clusters and estimated the number of people, and their potential roles, likely to be available in each cluster. The number of people we aim to speak to in each cluster will depend on the size of the cluster, and the likely heterogeneity of the people within the cluster. For example, in some stakeholder groups, such as the National Department of Health (NDoH), it appears that each person involved in immunization has a different role and will potentially bring a different perspective. Therefore, the estimated sample size is the same as the estimated number of people in the group. In other stakeholder groups, where there are many people doing similar work, we will sample approximately 10% (as appropriate across geographical areas). We anticipate a sample of approximately 140 people (either individually or in focus groups), however, sampling will continue until data saturation is reached.

In Table 1 *(See Supplementary File 1)* we outline the potentially-relevant stakeholder groups, the estimated number of people in each, and how we will approach the sampling for each group.

Patient and Public Involvement

In the current study we have not involved patients in the design and do not plan to involve them in the recruitment and conduct of the study. The beneficiaries, or end-users, of vaccination, such as patients and the wider public will also not be included as participants in the study. Previous research in South Africa has identified that the vast majority of missed opportunities for vaccinations are caused by health facility obstacles [14-16], and thus we felt it pertinent to start with understanding the 'provider-perspective'. We intend to build on the findings of this study to develop and implement a larger-scale

subsequent study to obtain the views, experiences and input of the end-users of vaccination, including patients and the wider public.

The results of the study will be disseminated to participants through a variety of mechanisms, including at the consultation workshops, through the online questionnaire and Cochrane South Africa website and through a project report of the main study findings which will be shared with all stakeholders who took part in interviews, focus groups and/or consultation workshops (See more details under 'Dissemination of Findings)

Phase 2: Identification of immunization coverage barriers and potential solutions

2.1. Qualitative research with immunization stakeholders

Recruitment

We will identify one key person in each stakeholder cluster who can assist us with recruitment of others. This may be someone at a national, provincial, regional or community level, who can assist in providing a short initial list of names of people who may be interested in participating, and who may know of others who might be interested in taking part in the study. Some members of our team are well known within the immunization community in South Africa and have a clear understanding of the stakeholders and the key players. Thus, they will commence the recruitment by identifying names of people in key positions, who are known to them, and who they believe could assist with recruitment of others.

Potential participants will be sent an email inviting them to take part in either interviews or focus group discussions. If no response is received within two weeks, we will follow-up the invitation with another email and/or phone call. If we do not have a response at this stage, we will select another person in the same group (if possible) and initiate the invitation process.

Data collection

Semi-structured interviews or focus group discussions (FGDs) will be conducted with the sample of immunization stakeholders. The choice of an individual interview or FDG will be determined by the role, sensitivities, time constraints and knowledge of participants. It is envisaged that individual interviews will be conducted with participants in unique roles (where only that person can provide insights from that perspective). Focus groups will be conducted for efficiency when the views of a number of

representatives of the same stakeholder group should be heard, where it is feasible to combine participants from one stakeholder group, and/or where hearing these views as a group will potentially increase the richness of understanding [17].

Interviews will be conducted face-to-face or telephonically at a date and time chosen by participants. Face-to-face interviews will take place at a location convenient to participants, which is conducive to a confidential exchange. The interviews will last between 45 and 60 minutes. Focus group will last 60-120 minutes and will each contain 6-10 participants, in line with methodological recommendations of appropriate focus group size [18]. The composition of focus groups will be stakeholder-specific, for example only nurses or only EPI managers. This will prevent the power-dynamics that exist between different stakeholder groups from potentially impacting on the discussions, and help ensure that more marginalized individuals can openly express their views and experiences.

Both the interviews and FGDs will be guided by a semi-structured topic guide *(See Supplementary File 2)* and conducted by two researchers who are trained in qualitative research methodologies and interviewing techniques. The interview guide has been developed by drawing on and integrating the insights obtained from a preliminary mapping of potential barriers and solutions to immunization coverage in South Africa conducted by the project team, a scoping review of the literature, team discussions, and the findings of two previous studies conducted by the Principal Investigator of this study [1 19]. The topic guide will explore the following topics: involvement in immunization programs; general views on the EPI in South Africa; perspectives of the challenges of and solutions for the EPI program (including in relation to the healthcare system, healthcare providers, and service users/public); and views and experiences of the HPV vaccine and school-based HPV vaccination program in South Africa. The guide will be flexible to ensure that participants can express what is important to them, and so learnings from previous interviews can be clarified and probed further.

With the permission of participants, all interviews and FGDs will be digitally recorded and field notes will be taken to ensure credibility and reliability of the information being collected. Data collection will continue until data saturation is reached.

Data management and analysis

Interviews and FDG recordings will be transcribed verbatim, and all personal identifying information will be removed from transcripts. The anonymized transcripts, together with field notes, will be downloaded into Nvivo, a software programme that aids with the management and analysis of qualitative data.

The data will be analyzed through a thematic analysis, using the phases described by Braun and Clarke [20]. Thematic analysis is a useful method for identifying and describing recurring patterns that are present in the data [20]. Two researchers will independently code 10 transcripts through line-by-line reading and with the aid of Nvivo to create a list of conceptual components ('opening coding'). These components will then be re-categorized into potential themes related to key immunization barriers and solutions ('selective coding'), and adapted into a coding framework to guide the analysis. The two researchers will compare their draft coding frameworks, and propose a standard and coherent coding framework. This will be presented to the project team for debate, clarification, and endorsement for all subsequent analyses. One researcher will then code the rest of the transcripts using this framework. Additional or revised codes will be developed iteratively as determined by the data and added to the coding framework. Throughout the research, the project team will meet regularly to discuss emerging findings and themes, and to use these to fine tune interview questions for subsequent interviews and FGDs. The final product of the analysis will be a 'conceptual map' which depicts the main barriers and potential solutions for increasing immunization coverage in South Africa.

2.2. Review of literature

We will identify and review relevant in-country EPI-related documentation, including legislation and policies relevant to immunization, including EPI policy documents; broader health plans (e.g. the National Health Insurance, National Development Plan, Vision 2030); National Immunisation Technical Advisory Group reports and meeting minutes (where available); reports of stock-outs, and any other relevant documents. We will use these documents to obtain information on the context of immunization in South Africa and reported barriers and facilitators, to supplement the findings from our qualitative research with stakeholders.

We will also conduct a review of systematic reviews of interventions for improving vaccination coverage worldwide. The objective of the review is to provide a broad synthesis of what is known from up-to-date systematic reviews about the effectiveness of interventions for improving vaccination coverage.

We will develop a comprehensive search strategy for peer-reviewed literature, and search the following databases from inception to the date of the search: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effectiveness (DARE), PubMed, and PDQ-Evidence [21]. We will use standard Cochrane methods for the screening of search outputs, selection of reviews, data extraction, and assessment of methodological quality of included reviews [22 23]. For each included systematic review, we will prepare key messages, important background information, a summary of the findings of the review, and structured assessments of the relevance of the review for South Africa. The reviews will be organized using the logic framework we have previously developed for interventions aimed at improving vaccination coverage [8]

We will describe the characteristics of the included reviews in a table that will include the date of the last search, any important limitations, what the review authors searched for, and what they found. We will take into account all other relevant considerations besides the findings of the included reviews when drawing conclusions about implications for the immunization program in South Africa. This includes considerations related to the applicability of the findings, likely impacts on equity, and the values and preferences of South African immunization stakeholders.

Phase 3: Development of intervention recommendations and implementation action plans

Using the findings from Phase 2, together with the Adopt, Contextualize, or Adapt (ACA) decision-making process [11], the project team will develop a set of proposed interventions and implementation action plans for improving immunization coverage in South Africa.

3.1. Stakeholder workshops

The list of interventions and draft implementation plans will be sent to all stakeholders who took part in interviews and FGDs, as well as to the head of each stakeholder group for comment. Thereafter, stakeholder workshops will be convened. Questions and comments on the draft implementation plans will be invited prior to the workshops. Modifications will be made to the draft implementation plan prior to the workshop, and the revised plan will be circulated several days before the workshop to allow participants to familiarize themselves with changes. An accompanying document will outline the modifications that were made and why they were made.

One main workshop will be held at the South African Medical Research Council (SAMRC), and at least one workshop will be held in each province after this. All those who participated in interviews and FGDs, as well as to the head of each stakeholder group, will be invited to attend a workshop. Using a range of participatory methodologies [24], the modified implementation plan will be discussed, further revised and endorsed at the main workshop, and this document will be presented and endorsed at each subsequent workshop. Not only with the workshops acknowledge stakeholders' valuable participation in the research, they will also help facilitate 'buy-in' for proposed implementation strategies. That is, stakeholders will potentially become change agents on the ground, who can assist in implementing and improving uptake of recommended interventions [25].

3.2. Online questionnaire

Individuals from stakeholder groups (outlined in Phase 1) who did not take part in interviews or FGDs will be given an opportunity to provide input on the recommended interventions and implementation action plans through an online questionnaire. Specific targeted approaches (including emails, telephone calls, postal mail, editorials or advertisements in professional newsletters and journals, website alerts and other social media outlets such as twitter and Facebook) will be used to alert people in the stakeholder groups about the questionnaire and to invite them to provide input.

Individuals will be invited to download the summary document and implementation plans from a link hosted on the Cochrane South Africa website. Feedback on the implementation plans will be invited for a six-week period, using a structured questionnaire delivered by an electronic SurveyMonkey form. Survey Monkey is an efficient electronic tool that captures large datasets safely and quickly. It also collates findings into a MS Excel spreadsheet. The questionnaire will be linked directly to the implementation plans for ease of questionnaire completion. It will ask for input on the feasibility and acceptability of the implementation plans and whether the timeframe of the plans is achievable. Respondents will also be asked to identify potential barriers to successful implementation of the plans, and if possible, to identify ways to resolve them. We anticipate no more than 10 questions on the implementation plans, and another 1-2 questions on barriers and facilitators. Where possible, questions will have drop-down menus to aid completion. Feedback will be anonymous.

The feedback will be summarized descriptively for each question, using the appropriate statistics (percentages, or mean values). The findings will be posted on the Cochrane South Africa website within

two months of the closure of the consultation period, and will be held there whilst the implementation plans are being rolled out. In this way, stakeholders can have immediate access to the plans and feedback as required.

ETHICAL CONSIDERATIONS

Ethical approval has been obtained from the South African Medical Research Council (SAMRC) (EC018-11/2018). We will also obtain permission from the South African National Department of Health.

The study process will comply with the requirements of the latest version of the Declaration of Helsinki (7th revision, 2013). Verbal and written information about the study will be provided to all participants taking part in interviews and FGDs. The consent form will make explicit the following aspects: the voluntary nature of participation, that there will be no negative consequences if they decide not to participate and that they will be asked explicitly for permission for the interview to be digitally recorded and that this is also voluntary. Written consent will be obtained from all research participants before proceeding with interviews or focus groups. All participants who complete the structured questionnaire will be provided with an online study information sheet as part of the electronic SurveyMonkey form, and will be required to provide online consent before proceeding with the questionnaire. All feedback on the questionnaire will be anonymous.

Details from interviews and FGDs will be entered into a study-specific database on the day of collection (stakeholder group, participant ID etc.). Study data, including audio-recordings, will be stored on password-protected computers and shared with the study team only. All digital recorders on recorders will be destroyed following safe storage and transcription, and identifying information will be removed from all transcripts. Reports of the findings will not identify individual participants. Participant anonymity and confidentiality will thus be ensured.

No risks to participants or researchers are expected. All potential participants for interviews or focus groups are not considered as vulnerable individuals or groups. However, participants may be uncomfortable expressing criticisms of vaccination programs. Where there is this potential, and where potential participants identify concerns, we will reassure participants of the steps that will be taken to ensure confidentiality. For participants in focus groups, we will remind participants at the outset that while the researchers undertake to maintain confidentiality, we cannot guarantee that other focus

group participants will. At the start of the focus group, we will discuss the importance of maintaining confidentiality by everyone involved after the focus group, but will explain that there is an inherent risk of breaches of confidentiality in this method. We will ensure participants are aware of this risk.

DISSEMINATION OF FINDINGS

The findings of the study will be shared with people in the stakeholder groups, at the consultation workshops and through the online questionnaire and Cochrane South Africa website. In addition, at the end of the study, a project report of the main study findings will be shared with all stakeholders who took part in interviews, focus groups and/or consultation workshops. The findings will also be communicated through academic publications and conferences. Reporting of the qualitative data will adhere to the Consolidated criteria for reporting qualitative research (COREQ)[26] guidelines; and the reporting of the review of systematic reviews will adhere to the "Preferred Reporting Items for Systematic Reviews and Meta-analyses' protocols (PRISMA-P)[27] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[28] for the protocol and full review respectively.

AUTHORS' CONTRIBUTIONS

The study was conceived by CW. SC led the design of the qualitative components of the study. KD and JD developed the overarching conceptual framework and the sampling approach. NN and DN developed the list of stakeholder groups, with input from PM and RB; NN, DN, PM and RB worked together to develop the methodology for phase 3 of the study. The manuscript was drafted by CW and SC. All authors reviewed and provided critical input to manuscript drafts and provided final approval.

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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

FIGURE LEGEND

Figure 1: Study phases

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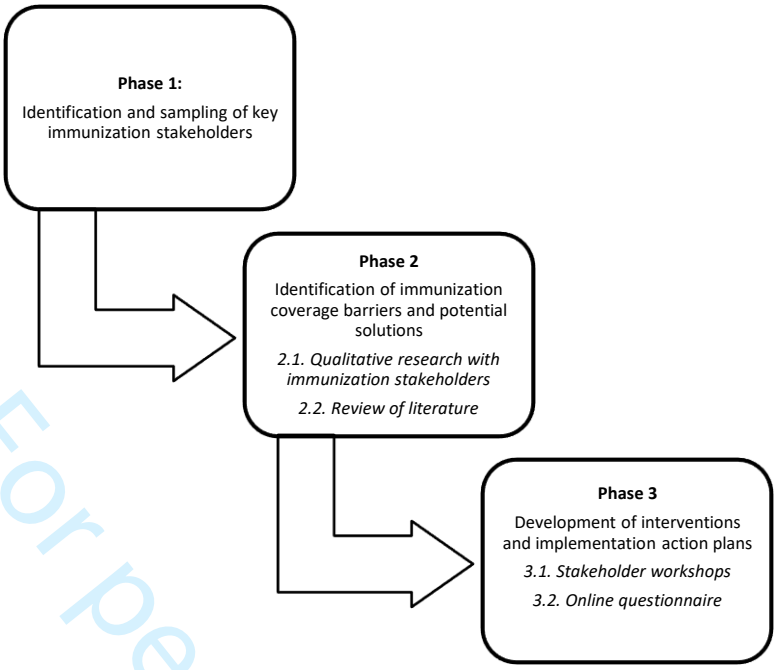

Table 1. Stakeholder groups and sample sizes

Stakeholders	Who	Predicted number	Cluster interview sample
National Department of Health	Individuals	12	12
Provincial Department of Health	Individuals	24	18
District and Facility Levels	Individuals	150	27
District Clinical Specialist Teams	Individuals	30	6
Pharmacies or Hospitals	Individuals providing pharmacy-specific services	20	12
Individual Vaccinators	Individuals	30	12
Non-Governmental Organization	Individuals providing NGO-specific immunization services	10	8
National Advisory Group on Immunisation	Individuals	12	6
WH O	Individual	6	2
UNICEF	Individual in an immunization role	1	1
PATH	Individuals in immunization roles	15	2
Health Systems Trust	Individuals in immunization roles	15	2
PEPFAR	Individuals in projects linked to PEPFAR (e.g. Right To Care, Broad Reach)	51	5
National Certification Committee for Polo Eradication	Individuals in immunization roles	6	1
Saving Babies	Individuals in immunization roles	8	1
PMTCT Working Group	Individuals in immunization roles	12	1
Paediatric Working Group	Individuals in immunization roles	12	1
Paediatric Management Group	Individuals in immunization roles	1	1
SA Paediatric Association (SAPA)	Individuals in immunization roles	1	1
Public Health Association of South Africa	Individuals in immunization roles	1	1
South African Medical Association	Individuals in immunization roles	1	1
Federation of Infectious Diseases Societies of Southern Africa	Individuals in immunization roles	1	1
South African Vaccination and Immunisation Centre	Individuals in immunization roles	4	1

Centre for Vaccines and Immunology, National Institute of Communicable Diseases	Individuals in immunization roles	2	1
National Vaccinators' Forum	Individuals in immunization roles	8	1
Amayeza- Independent Trainer on Vaccination	Spokesperson	1	1
African Local Initiative for Vaccinology Expertise	Spokesperson	2	1
Vaccines for Africa	Spokesperson	2	1
GSK	Spokesperson	1	1
Sanofi Pasteur	Spokesperson	2	1
BIOVAC	Spokesperson	2	1
Pfizer	Spokesperson	1	1
Association of early Childhood Development Centres	Representatives	4	2
Department of Education	School Health Coordinators: National and Provincial level	4	2
School Governing Bodies	Chairperson (individual) or spokesperson	4	2
Parent Association	Chairperson (individual) or spokesperson	4	2
Total		**460**	**140**

Draft Interview and Focus Group Topic Guide

Demographic information
Official title:
Organisation/Place of work:
Location:
Gender:

Part 1: Involvement in immunization programmes

1. Can you describe what your current involvement is in Immunization programme(s) in South Africa?

Probes:

- How long have you worked in the area of vaccination/immunization?
- Possible functions/roles?
- Are you involved/have experience with both childhood and pre-adolescent/adolescent vaccination programmes in the country?

Part 2: General views of the Expanded Programme on Immunisation (EPI) in South Africa

2. What do you see as the central goals of the national Expanded Programme on Immunization (EPI) in South Africa?

Probes:

- Have these goals changed over time?

3. What do you think is currently working well with the EPI programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting (where appropriate)
- What do you think have been the enabling factors underpinning these successes? *(Probes: Political, structural, ideological, financial?)*

4. Do think the national EPI programme is generally meeting its central goals?

Probes:

- Why/why not?
- If answered that EPI Programme(s) are NOT achieving set goals, ask the following:
  - Do you think the current performance of the EPI Programme is a serious national challenge?
  - Do you think managers and especially senior managers of the DOH (at all levels) view the poor/under performance of EPI as a serious challenge that should be urgently addressed?

    If yes: Are their actions in line with this view?

    If yes: Can you give us examples of these actions which demonstrate the urgency with which they view this situation?

Part 3: Specific challenges of and solutions for the EPI programme

I would now like us to talk about some of the challenges currently facing the EPI programme, and your thoughts about how these might be addressed.

Healthcare system

5. What are your views and experiences of the public primary health facilities where vaccinations are provided? What kind of challenges exist in these health facilities for the vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- Management structures?
- Management approach? The focus of managers and what they prioritise (and not)?
- Health information systems (is vaccine recording and reporting maintained)?
- Financial resources?
- Availability of staff (shortages/high turnovers)?
- Availability of vaccine education/information materials?
- Availability of initiatives to advocate for immunization?
- Availability of approaches to mobilise communities/public to vaccinate children e.g. social media
- Existence of approaches that attempt to link EPI (services, planning and mode of operation) to other apparently more successful programmes or programmes that may have a wider coverage e.g. PMTCT?
- Waiting times in the clinics?
- Mixed queues?
- Operating times?
- Treatment and attitude of Health Care Providers (Vaccinators and other HCP)?
- Attitude of non-Health Professionals such as clerks and others.
- Others (specify)

6. What do you think could be done to address some of these challenges?

Probe:

- Who should be tasked with addressing these challenges?

7. Do you see shortages of vaccines as a significant issue nationally and in your local setting?

Probes:

- Why/why not?
- If yes: Can you provide a specific example of this challenge?
- If yes: Where do you think the problem lies (*e.g. vaccine procurement, storage, distribution/delivery)?*
- Are you aware of any attempts or intervention measures by the DOH (at any level: national, province or district) to address the challenge of vaccine shortages? If yes, how successful do you think these attempts have been?
- Do you have any ideas on how to overcome the challenge of vaccine shortages? Who should be tasked with addressing this challenge?

8. Who are the main role-players/stakeholders involved in EPI programme(s) in South Africa?

Probes:

- Is there sufficient communication/collaboration between stakeholders? Why/ why not? What could be done to improve this?
- Is there sufficient advocacy/social mobilization amongst stakeholders? Why/ why not? What could be done to improve this?
- Are community leaders/groups sufficiently involved in the EPI? Why/ why not? How do you think these stakeholders be more involved?

9. Can you tell me a bit about the relationship between the public and private health sectors in terms of the EPI programme?

Probes

- Is there any collaboration/interaction between them? Why/why not?
- Do you see this as a problem? Why/why not?
- If seen as a problem: what could be done to increase collaboration/interaction?
- According to your knowledge either in terms of policy or in terms of practice and experience: "Are Private or NGO vaccinators able to access state vaccines for their clients, free of charge?" If yes, do they provide feedback on data of doses given?

Healthcare providers

10. What are your views about health care providers (HCP) administering vaccines in public health facilities? Do you think there are any challenges in relation to HCPs for vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- General attitudes and behavior of health care providers *(e.g. friendly/helpful/rude)?*
- Knowledge about vaccines and vaccination?
- Knowledge and experiences with the conditions that the vaccines prevent?
- Perceptions of vaccines and vaccination?
- Perceptions of the importance of communicating with caregivers about vaccination?
- Use opportunities to assess the vaccination status of the child?
- Sufficient skills/training?
- Do they vaccinate their own children/grandchildren or take special interest to help ensure that children of close relatives are vaccinated?
- How do they access vaccination for their own children/grandchildren or relatives? Through private or public institutions?

11. What do you think should be done to improve the attitudes and behavior of HCP?

Probe

- Who should be tasked with dealing with these issues?

12. What do you think should be done to improve the knowledge/skills of health care providers?

Probe:

- Who should be tasked with doing this?

Service users/public

13. What is your sense of the general level of knowledge amongst the public about childhood vaccines, immunisation services and the conditions that these prevent?

Probes:

- Are there gaps in knowledge? If yes: what kinds of gaps?
- Do you think people know about the benefits of childhood vaccines?
- What sources do people go to for information about childhood vaccination? *e.g. Internet; social media networks; health care workers; friends/family; schools; religious leaders?*
- Which sources do you think people perceive as being trustworthy/untrustworthy?

14. What do you think influences people' decision about whether to vaccinate their children or not?

Probes:

- What doubts, fears, concerns (if any) about vaccines and vaccination services do you think people might have that could prevent them from deciding to vaccinate their children? *(e.g. concerns about vaccine quality, safety, contra-indications, risks etc.)*
- What negative attitudes or beliefs (if any) about vaccines and vaccination do you think people might have that could prevent them from deciding to vaccinate their children? *(ask if they have heard any specific stories/rumours)*
- Where might these negative attitudes/beliefs/concerns come from? (*e.g. religion, cultural norms & practices, traditional leaders, anti-vac lobbying, media)*
- What role (if any) do you think a lack of trust in the health care system, healthcare providers and/or government might play in people's decision to vaccinate their children? *(e.g. lack of trust in providers' competence; perceptions of poor quality of care; manner in which providers treat them and their children etc.)*
- Do you think people face any practical challenges that could prevent them from choosing or accessing vaccination? *(e.g cost, travel, language or cultural differences, clinic opening hours, vaccine stock-outs etc.)*
- Are there any other factors, that we haven't already discussed, that you think might prevent people from accepting and taking-up childhood vaccination?

15. Want to you think could be done to make parents more likely to vaccinate their children according to the EPI schedule?

Probes:

- How can vaccination services best enable, support and motivate childhood vaccination?
- What channels do you think would be most effective in promoting childhood vaccination?
- Who should promote vaccination? *(e.g. health care workers, teachers, community leaders, media)*
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? Media- radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials- posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?

16. We have spoken about various different challenges facing the EPI programme in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current EPI programme, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Do you think there are different priorities for different Provinces?

Part 4: HPV Vaccine

I would now like to talk a bit about the HPV vaccine and vaccination in South Africa.

17. What is your overall impression of the school HPV vaccination programme?

Probes:

- Is the programme successful or not successful? Why?
- Who is involved with the programme? Is there collaboration between the stakeholders? Why/why not?

- Have you received any feedback about the programme *(e.g. from parents/girls? teachers? those delivering the programme? others?)*

18. What do you think is currently working well with the programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting
- What do you think have been the enabling factors underpinning these successes? *(Probe: Political, structural, ideological, financial?)*

Main challenges and potential solutions

19. Currently the HPV Vaccination Programme is delivered in a campaign like approach- vaccination teams visit schools twice a year and targeted children come at the same time to line up for this vaccine. What are your thoughts about this approach?

Probes

- What are the strengths and weaknesses of this approach? *(and probe for specific examples in local setting)*
- Do you think parents/girls/teachers are happy with this approach? Why/why not? *(and probe for specific examples in local setting)*
- What alternative delivery mechanisms (if any) do you think might be more effective?

20. Currently the programme does not include private schools and the HPV vaccine is not available at public health facilities. What are your thoughts about this?

Probes

- What kinds of problems, if any, do you think these absences might be generating?
- Should the programme be extended to private schools? Why/why not? If yes: how should it be incorporated in private schools?
- Should the HPV vaccine be made available at public health facilities? Why/why not? If yes: what would be needed to operationalize this?

21. What do you think influences parents' and girls' decision to take-up the HPV vaccine?

Probes:

- To what extent do you think parents and girls think that the HPV vaccine is necessary? Do you think they know about the reasons for/benefits of the vaccine? Why/why not?
- Do you think parents and girls trust the HPV vaccine to protect their health? Why/why not?
- What doubts, fears, concerns (if any) do you think parents and girls might have about the HPV vaccine? What do you think might be the sources of these concerns/beliefs? *(e.g. cultural norms, community practices/traditions, anti-vac lobbying, social media, internet)*
- What role (if any) do you think a lack of trust in health system, healthcare providers and decision makers might play in parents and girls concerns and beliefs about the HPV vaccines and vaccination?
- Are there any other factors, that we have not already discussed, that you think might influence parents and girls decision to accept the HPV vaccine?

22. Figures suggest that there is a significant drop in uptake from the 1st to the 2nd dose. Why do you think this might be so?

23. What do you think could be done to encourage parents and girls to consent to the HPV vaccine within the school programme?

Probes:

- Is information about the HPV vaccine and vaccination programme currently provided to parents of targeted girls and and these girls? Do you think further information and communication channels are needed?
- Is information about the HPV vaccine and vaccination programme provided to parents on non targeted girls?
- What channels do you think would be most effective in promoting the HPV vaccination?
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? media (radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials (posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?
- Who should be involved with education and communication activities (*e.g. health care workers, teachers, community leaders, media)*
- What would help parents and girls complete the vaccine series i.e. return for the second dose?

24. What are your views about health care providers (HCPs) and the HPV vaccine and vaccination services?

Probes

- What are HCPs general attitudes and behaviours towards the HPV vaccine and providing vaccination for HPV*?*
- Do you think HCPs know about the HPV vaccine?
- Do you think HCPs know about the conditions the HPV vaccine prevents?
- Do you think HCPs vaccinate their own children/grandchildren for HPV or take special interest to help ensure that children of close relatives are vaccinated for HPV?

25. We have spoken about various different challenges facing HPV vaccination in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current HPV vaccination programme in South Africa, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Are there different priorities for different Provinces?

Part 5: Closing

This has been a very informative interview. Thank you so much for your time.

Is there anything we haven't covered that you would like to add? Is there anything you would like to say in closing?

Do you know of anyone else who could provide important insights as a key informant and might be interested in participating in the study?

If yes: can you provide us with their contact details so we can get in touch with them?

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Contextualised strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

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Contextualised strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

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ABSTRACT

Introduction: Despite the unparalleled success of immunisation in the control of vaccine preventable diseases, immunisation coverage in South Africa remains suboptimal. While many evidence-based interventions have successfully improved vaccination coverage in other countries, they are not necessarily appropriate to the immunisation needs, barriers, and facilitators of South Africa. The aim of this research is to investigate barriers and facilitators to optimal vaccination uptake, and develop contextualised strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa.

Methods: The study will employ a mixed-methods research design. It will be conducted over three iterative phases and use the Adopt, Contextualise, or Adapt (ACA) model as an overarching conceptual framework. Phase 1 will identify, and develop a sampling frame of, immunisation stakeholders involved in the design, planning and implementation of childhood and human papillomavirus immunisation programmes in South Africa. Phase 2 will identify the main barriers and facilitators to, and solutions for, increasing vaccination coverage. This phase will comprise exploratory qualitative research with stakeholders and a review of existing systematic reviews on interventions for improving vaccination coverage. Using the findings from Phase 2 and the ACA model, Phase 3 will develop a set of proposed interventions and implementation action plans for improving immunisation coverage in South Africa. These plans will be discussed, revised and finalised through a series of participatory stakeholder workshops and an online questionnaire, conducted as part of Phase 3.

Ethics: Ethical approval was obtained from the South African Medical Research Council (EC018-11/2018). No risks to participants are expected. Various steps will be taken to ensure the anonymity and confidentiality of participants.

Dissemination: The study findings will be shared at stakeholder workshops, the website of Cochrane South Africa, and academic publications and conferences.

Key words: South Africa, vaccination coverage, adoption, adaptation, contextualisation, implementation science.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our mixed-methods and theory-informed approach will facilitate the development of a more holistic and comprehensive understanding of the barriers and facilitators to vaccination uptake than could be gained from single methodologies and atheoretical approaches.
- Our rigorous maximum variation sampling approach will enable engagement with a heterogenous group of relevant stakeholders and could potentially provide maximum diversity of responses and experiences with which to address our research questions.
- Complementary research competencies and experiences among the research team will help strengthen the rigour of the study interpretations.
- Our sample is limited to stakeholders involved in the design, planning and implementation of immunisation programmes, with the exclusion of potentially relevant decision-makers outside the field of immunisation and the end-users of vaccinations.
- The scope of our study does not include an evaluation of the implementation of interventions, nor the measurement of the effectiveness of the interventions, another potential limitation of the study.

BACKGROUND

Despite the unparalleled success of immunisation in the control of vaccine preventable diseases, immunisation coverage in South Africa is suboptimal [1]. Not only has the country failed to reach internationally-set vaccination coverage targets, locally-set targets also remain unachieved. At the World Health Assembly in May 2012, all 194 WHO Member States, including South Africa, endorsed the Global Vaccine Action Plan and committed to achieving at least 90% national coverage with three doses of diphtheria-tetanus-pertussis (DTP3) containing vaccines in children under one year of age in all countries by 2015 [2]. South Africa had set a goal of achieving at least 92% DTP3 coverage by 2017 [3]. However, the South African Demographic and Health Survey conducted in 2016 found DTP3 coverage to be only 66% [4]. The low childhood immunisation coverage in South Africa points to a serious situation which may see the country battle with the re-emergence of previously controlled infectious conditions

including diphtheria, pertussis, and measles. There are already indications of re-emergence of these conditions in some parts of the country, including recent diphtheria and measles outbreaks [5 6].

To ensure a sustainable improvement in vaccination coverage in South Africa, we need to identify what the main barriers are, and develop and implement effective and context-specific interventions to address these. There are many successful evidence-based interventions to increase immunisation coverage in other countries. These include strategies directed at recipients of immunisation services, healthcare providers or the health system, as well as multi-component strategies [7 8]. However, whilst strategies to increase vaccination uptake may be effective in one setting, they are not necessarily applicable or effective elsewhere [7]. Irrespective of their effectiveness, immediate adoption of interventions from elsewhere is only likely to occur if health systems, health expenditure, disease epidemiology, workforce and training, and patient literacy and sharing are common between countries [7 8]. When this is not the situation, contextualisation or adaptation of interventions may be required to ensure that they are locally relevant, and engage local people appropriately to enhance uptake [9]. Contextualisation and adaptation involve building 'bridges' between the best evidence and effective local implementation, when best-available evidence recommendations cannot be immediately adopted [9 10]. Ultimately, in implementing interventions there is a need "to move from what works to what works where and why" [9].

South Africa's immunisation programme

Currently the National Department of Health's Expanded Programme on Immunisation of South Africa targets 11 diseases: polio, measles, tuberculosis, diphtheria, pertussis, tetanus, *Haemophilus influenzae* type b, hepatitis B, rotavirus diarrhoea, pneumococcal infection, and cervical cancer (see Table 1). Vaccines against the first 10 diseases are provided free of charge to infants and children at all public healthcare facilities. Since 2014, cervical cancer has been targeted through a school-based human papillomavirus (HPV) vaccination programme, with two doses (six months apart, administered during one-month campaigns) of the bivalent HPV vaccine offered free of charge to grade four girls aged nine years or more in public sector schools. In addition to the vaccines listed in Table 1, vaccines targeting influenza, rubella, mumps, varicella (chickenpox), meningococcal meningitis, hepatitis A and genital warts (the quadrivalent HPV vaccine prevents cervical cancer and genital warts) are available in the private sector in South Africa.

Table 1: Expanded Programme on Immunisation Schedule in South Africa

Age of child	Vaccines scheduled
At birth	Bacille Calmette-Guérin (BCG)
	Oral polio vaccine (OPV) (0)
6 weeks	OPV (1)
	Rotavirus vaccine (RV) (1)
	Diphtheria, tetanus and acellular pertussis vaccine + inactivated polio vaccine + *Haemophilus influenzae* type b vaccine + hepatitis B vaccine combined (DTaP-IPV-Hib-HepB) (1)
	Pneumococcal conjugate vaccine (PCV) (1)
10 weeks	DTaP-IPV-Hib-HepB (2)
14 weeks	RV (2)
	DTaP-IPV-Hib-HepB (3)
	PCV (2)
6 months	Measles vaccine (1)
9 months	PCV (3)
12 months	Measles vaccine (2)
18 months	DTaP-IPV-Hib-HepB (4)
6 years	Tetanus and reduced-strength diphtheria vaccine (Td) vaccine
≥9 years	Human papillomavirus (HPV) vaccine (1 and 2, 6 months apart)
12 years	Td vaccine

Aims and objectives

The overarching aim of this research is to investigate barriers and facilitators to optimal uptake of vaccination services and develop contextualised strategies and implementation plans to increase childhood and adolescent vaccination coverage in South Africa. The specific objectives are to:

1. Identify and compile a list of stakeholders who are involved in the planning, design and/or implementation of childhood and adolescent vaccination programmes in South Africa;
2. Consult with representative samples of these stakeholders to identify barriers and facilitators to, and solutions for, increasing vaccination coverage;
3. Identify and review relevant in-country immunisation-related documentation, including (but not limited to) legislation and policies relevant to immunisation;
4. Conduct a review of systematic reviews on effects of interventions for improving vaccination coverage;
5. Develop practical interventions and implementation plans for increasing vaccination coverage in South Africa, tailoring global evidence to local needs, barriers, and facilitators.

METHODS

This study will employ a mixed-methods research design, including exploratory qualitative research with immunisation stakeholders, stakeholder participatory workshops, reviewing of the global literature and a structured questionnaire. It will consist of three iterative phases. The study will commence in July 2019 and end in July 2021. An overview of the study phases is depicted in Figure 1.

[Insert Mono Image_Figure 1 here]

Overarching conceptual framework

We will draw on the Adopt, Contextualise, or Adapt (ACA) model developed by Dizon and colleagues [11] as the overarching conceptual framework for the study. This framework was developed and tested for use in low-and-middle income countries (LMICs) to better understand the gap between evidence-based recommendations and their local uptake. The ACA comprises 18 well-defined stages to identify barriers to intervention or guideline implementation and to guide discussions on implementing solutions to barriers. It considers the time frames for likely impact of solutions; with the assumption that longer term time frames are generally required when solutions necessitate change to policies, regulations, health systems or research. The use of the ACA model in the planned study is double sided, in that it will help to identify barriers for reaching all children and adolescents with life-saving vaccines and address local implementation of strategies that have been used elsewhere to increase coverage, thus ensuring that strategies are relevant to local situations.

Phase 1: Identification and sampling of immunisation stakeholders

A draft list of stakeholder groups has already been developed by the project team and will be updated iteratively and as necessary. This list was developed by the project team, drawing on their collective knowledge of the relevant stakeholders, scoping of the literature, team discussions, and the list generated from an earlier study among Expanded Programme on Immunisation (EPI) managers [1]. The methodology for developing the stakeholder list was guided by the methods used by the South African Guidelines Excellence (SAGE) Allied Health study in identifying a complex multiple stakeholder allied health reference sample [12].

Stakeholders comprise people involved in any aspect of the design, planning, and implementation of childhood and HPV immunisation programmes in South Africa. These include policy makers in national and provincial departments of health and education, programme and facility managers and bureaucrats, healthcare personnel and educators, academics or researchers, funders, members of professional associations, independent advisory bodies, Non-Governmental Organisations (NGOs), and School Governing Bodies.

Both maximum variation and snowball sampling techniques will be used [13]. We have divided the stakeholder groups into clusters and estimated the number of people, and their potential roles, likely to be available in each cluster. The number of people we aim to speak to in each cluster will depend on the size of the cluster, and the likely heterogeneity of the people within the cluster. For example, in some stakeholder groups, such as the South African National Department of Health, it appears that each person involved in immunisation has a different role and will potentially bring a different perspective. Therefore, the estimated sample size is the same as the estimated number of people in the group. In other stakeholder groups, where there are many people doing similar work, we will sample approximately 10% (as appropriate across geographical areas). We anticipate a sample of approximately 140 people (either individually or in focus groups), however, sampling will continue until data saturation is reached.

In Table 1 *(See Supplementary File 1)* we outline the potentially-relevant stakeholder groups, the estimated number of people in each, and how we will approach the sampling for each group.

Patient and public involvement

In the current study we have not involved patients in the design and do not plan to involve them in the recruitment and conduct of the study. The beneficiaries or end-users of vaccination and the wider public will also not be included as participants in the study. Previous research in South Africa has identified that the vast majority of missed opportunities for vaccinations are caused by health facility obstacles [14-16], and thus we felt it pertinent to start with understanding the 'provider-perspective'. We intend to build on the findings of this study to develop and implement a larger-scale subsequent study to obtain the views, experiences and input of the end-users of vaccination, including patients and the wider public.

The results of the study will be disseminated to participants through a variety of mechanisms, including at the consultation workshops, through the online questionnaire and Cochrane South Africa website and through a project report of the main study findings which will be shared with all stakeholders who took part in interviews, focus groups and/or consultation workshops (See more details under 'Dissemination of Findings)

Phase 2: Identification of immunisation coverage barriers and potential solutions

2.1. Qualitative research with immunisation stakeholders

Recruitment

We will identify one key person in each stakeholder cluster who can assist us with recruitment of others. This may be someone at a national, provincial, regional or community level, who can assist in providing a short initial list of names of people who may be interested in participating, and who may know of others who might be interested in taking part in the study. Some members of our team are well known within the immunisation community in South Africa and have a clear understanding of the stakeholders and the key players. Thus, they will commence the recruitment by identifying names of people in key positions, who are known to them, and who they believe could assist with recruitment of others. We will also obtain, from the South African National Department of Health (NDoH), permission to conduct interviews with NDoH stakeholders and support with identifying and contacting such stakeholders.

Potential participants will be sent an email inviting them to take part in either interviews or focus group discussions. If no response is received within two weeks, we will follow-up the invitation with another email and/or phone call. If we do not have a response at this stage, we will select another person in the same group (if possible) and initiate the invitation process.

Data collection

Semi-structured interviews or focus group discussions (FGDs) will be conducted with the sample of immunisation stakeholders. The choice of an individual interview or FDG will be determined by the role, sensitivities, time constraints and knowledge of participants. It is envisaged that individual interviews will be conducted with participants in unique roles (where only that person can provide insights from that perspective). Focus groups will be conducted for efficiency when the views of a number of representatives of the same stakeholder group should be heard, where it is feasible to combine

participants from one stakeholder group, and/or where hearing these views as a group will potentially increase the richness of understanding [17].

Interviews will be conducted face-to-face or telephonically at a date and time chosen by participants. Face-to-face interviews will take place at a location convenient to participants, which is conducive to a confidential exchange. The interviews will last between 45 and 60 minutes. FGDs will last 60-120 minutes and will each contain 6-10 participants, in line with methodological recommendations of appropriate focus group size [18]. The composition of focus groups will be stakeholder-specific, for example only nurses or only EPI managers. This will prevent the power-dynamics that exist between different stakeholder groups from potentially impacting on the discussions, and help ensure that more marginalided individuals can openly express their views and experiences.

Both the interviews and FGDs will be guided by a semi-structured topic guide *(See Supplementary File 2)* and conducted by two researchers who are trained in qualitative research methodologies and interviewing techniques. The interview guide has been developed by drawing on and integrating the insights obtained from a preliminary mapping of potential barriers and solutions to immunisation coverage in South Africa conducted by the project team, a scoping review of the literature, team discussions, and the findings of two previous studies conducted by the Principal Investigator of this study [1 19]. The topic guide will explore the following topics: involvement in immunisation programmes; general views on the EPI in South Africa; perspectives of the challenges of and solutions for the EPI programme (including in relation to the healthcare system, healthcare providers, and service users/public); and views and experiences of the HPV vaccine and school-based HPV vaccination programme in South Africa. The guide will be flexible to ensure that participants can express what is important to them, and so learnings from previous interviews can be clarified and probed further.

With the permission of participants, all interviews and FGDs will be digitally recorded and field notes will be taken to ensure credibility and reliability of the information being collected. Data collection will continue until data saturation is reached.

Data management and analysis

Interview and FGD recordings will be transcribed verbatim, and all personal identifying information will be removed from transcripts. The anonymised transcripts, together with field notes, will be downloaded into Nvivo, a software programme that aids with the management and analysis of qualitative data.

The data will be analysed through a thematic analysis, using the phases described by Braun and Clarke [20]. Thematic analysis is a useful method for identifying and describing recurring patterns that are present in the data [20]. Two researchers will independently code 10 transcripts through line-by-line reading and with the aid of Nvivo to create a list of conceptual components ('opening coding'). These components will then be re-categorised into potential themes related to key immunisation barriers and solutions ('selective coding'), and adapted into a coding framework to guide the analysis. The two researchers will compare their draft coding frameworks, and propose a standard and coherent coding framework. This will be presented to the project team for debate, clarification, and endorsement for all subsequent analyses. One researcher will then code the rest of the transcripts using this framework. Additional or revised codes will be developed iteratively as determined by the data and added to the coding framework. Throughout the research, the project team will meet regularly to discuss emerging findings and themes, and to use these to fine tune interview questions for subsequent interviews and FGDs. The final product of the analysis will be a 'conceptual map' which depicts the main barriers and potential solutions for increasing immunisation coverage in South Africa.

2.2. Review of literature

We will identify and review relevant in-country EPI-related documentation, including legislation and policies relevant to immunisation, including EPI policy documents; broader health plans (e.g. the National Health Insurance, National Development Plan, Vision 2030); National Immunisation Technical Advisory Group reports and meeting minutes (where available); reports of stock-outs, and any other relevant documents. We will also identify and review legislation and policy-documents indirectly relevant to immunisation, for example those related to school health and school standard operating procedures, data security and sharing and digital health, amongst others. We will use both these directly and indirectly relevant documents to obtain information on the context of immunisation in South Africa and reported barriers and facilitators, to supplement the findings from our qualitative research with stakeholders.

We will also conduct a review of systematic reviews of interventions for improving vaccination coverage worldwide. The objective of the review is to provide a broad synthesis of what is known from up-to-date systematic reviews about the effectiveness and costs of interventions for improving vaccination coverage.

We will develop a comprehensive search strategy for peer-reviewed literature, and search the following databases from inception to the date of the search: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effectiveness (DARE), PubMed, and PDQ-Evidence [21]. We will use standard Cochrane methods for the screening of search outputs, selection of reviews, data extraction, and assessment of methodological quality of included reviews [22 23]. For each included systematic review, we will prepare key messages, important background information, a summary of the findings of the review, and structured assessments of the relevance of the review for South Africa. The reviews will be organised using the logic framework we have previously developed for interventions aimed at improving vaccination coverage [8]

We will describe the characteristics of the included reviews in a table that will include the date of the last search, any important limitations, what the review authors searched for, and what they found. We will take into account all other relevant considerations besides the findings of the included reviews when drawing conclusions about implications for the immunisation programme in South Africa. This includes considerations related to the applicability of the findings, likely impacts on equity, and the values and preferences of South African immunisation stakeholders.

Phase 3: Development of intervention recommendations and implementation action plans

Using the findings from Phase 2, together with the Adopt, Contextualise, or Adapt (ACA) decision-making process [11], the project team will develop a set of proposed interventions and implementation action plans for improving immunisation coverage in South Africa. We will also undertake a preliminary costing of each proposed intervention and accompanying implementation plan.

3.1. Stakeholder workshops

The list of interventions, draft implementation plans, and preliminary costs will be sent to all stakeholders who took part in interviews and FGDs, as well as to the head of each stakeholder group for comment. Thereafter, stakeholder workshops will be convened. Questions and comments on the draft

implementation plans will be invited prior to the workshops. Modifications will be made to the draft implementation plan prior to the workshop, and the revised plan will be circulated several days before the workshop to allow participants to familiarise themselves with changes. An accompanying document will outline the modifications that were made and why they were made.

One main workshop will be held at the South African Medical Research Council (SAMRC) Head Office in Cape Town, and at least one workshop will be held in each province after this. All those who participated in interviews and FGDs, as well as to the head of each stakeholder group, will be invited to attend a workshop. Using a range of participatory methodologies [24], the modified implementation plan will be discussed, further revised and endorsed at the main workshop, and this document will be presented and endorsed at each subsequent workshop. Not only will the workshops acknowledge stakeholders' valuable participation in the research, they will also help facilitate 'buy-in' for proposed implementation strategies. That is, stakeholders will potentially become change agents on the ground, who can assist in implementing and improving uptake of recommended interventions [25].

3.2. Online questionnaire

Individuals from stakeholder groups (outlined in Phase 1) who did not take part in interviews or FGDs will be given an opportunity to provide input on the recommended interventions and implementation action plans through an online questionnaire. Specific targeted approaches (including emails, telephone calls, postal mail, editorials or advertisements in professional newsletters and journals, website alerts and other social media outlets such as twitter and Facebook) will be used to alert people in the stakeholder groups about the questionnaire and to invite them to provide input.

Individuals will be invited to download the summary document and implementation plans from a link hosted on the Cochrane South Africa website. Feedback on the implementation plans will be invited for a six-week period, using a structured questionnaire delivered by an electronic SurveyMonkey form. Survey Monkey is an efficient electronic tool that captures large datasets safely and quickly. It also collates findings into a Microsoft Excel spreadsheet. The questionnaire will be linked directly to the implementation plans for ease of questionnaire completion. It will ask for input on the feasibility and acceptability of the implementation plans and whether the timeframe of the plans is achievable. Respondents will also be asked to identify potential barriers to successful implementation of the plans, and if possible, to identify ways to resolve them. We anticipate no more than 10 questions on the

implementation plans, and another 1-2 questions on barriers and facilitators. Where possible, questions will have drop-down menus to aid completion. Feedback will be anonymous.

The feedback will be summarised descriptively for each question, using the appropriate statistics (percentages, or mean values). The findings will be posted on the Cochrane South Africa website within two months of the closure of the consultation period, and will be held there whilst the implementation plans are being rolled out. In this way, stakeholders can have immediate access to the plans and feedback as required.

ETHICAL CONSIDERATIONS

Ethical approval has been obtained from the SAMRC (EC018-11/2018). The study process will comply with the requirements of the latest version of the Declaration of Helsinki (7th revision, 2013). Verbal and written information about the study will be provided to all participants taking part in interviews and FGDs. The consent form will make explicit the following aspects: the voluntary nature of participation, that there will be no negative consequences if they decide not to participate and that they will be asked explicitly for permission for the interview to be digitally recorded and that this is also voluntary. Written consent will be obtained from all research participants before proceeding with interviews or focus groups. All participants who complete the structured questionnaire will be provided with an online study information sheet as part of the electronic SurveyMonkey form, and will be required to provide online consent before proceeding with the questionnaire. All feedback on the questionnaire will be anonymous.

Details from interviews and FGDs will be entered into a study-specific database on the day of collection (stakeholder group, participant ID etc.). Study data, including audio-recordings, will be stored on password-protected computers and shared with the study team only. All digital recorders on recorders will be destroyed following safe storage and transcription, and identifying information will be removed from all transcripts. Reports of the findings will not identify individual participants. Participant anonymity and confidentiality will thus be ensured.

No risks to participants or researchers are expected. All potential participants for interviews or focus groups are not considered as vulnerable individuals or groups. However, participants may be uncomfortable expressing criticisms of vaccination programmes. Where there is this potential, and

where potential participants identify concerns, we will reassure participants of the steps that will be taken to ensure confidentiality. For participants in focus groups, we will remind participants at the outset that while the researchers undertake to maintain confidentiality, we cannot guarantee that other focus group participants will. At the start of the focus group, we will discuss the importance of maintaining confidentiality by everyone involved after the focus group, but will explain that there is an inherent risk of breaches of confidentiality in this method. We will ensure participants are aware of this risk.

DISSEMINATION OF FINDINGS

The findings of the study will be shared with people in the stakeholder groups, at the consultation workshops, and through the online questionnaire and Cochrane South Africa website. In addition, at the end of the study, a project report of the main study findings will be shared with all stakeholders who took part in interviews, focus groups, and/or consultation workshops. The findings will also be communicated through academic publications and conferences. Reporting of the qualitative data will adhere to the Consolidated criteria for reporting qualitative research (COREQ)[26] guidelines; and the reporting of the review of systematic reviews will adhere to the "Preferred Reporting Items for Systematic Reviews and Meta-analyses' protocols (PRISMA-P)[27] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[28] for the protocol and full review respectively.

AUTHORS' CONTRIBUTIONS

The study was conceived by CW. SC led the design of the qualitative components of the study. KG and JD developed the overarching conceptual framework and the sampling approach. NN and DN developed the list of stakeholder groups, with input from CW, PM, and RB. NN, DN, PM, and RB worked together to develop the methodology for phase 3 of the study. The manuscript was drafted by CW and SC. All authors reviewed and provided critical input to manuscript drafts and provided final approval.

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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

FIGURE LEGEND

Figure 1: Study phases

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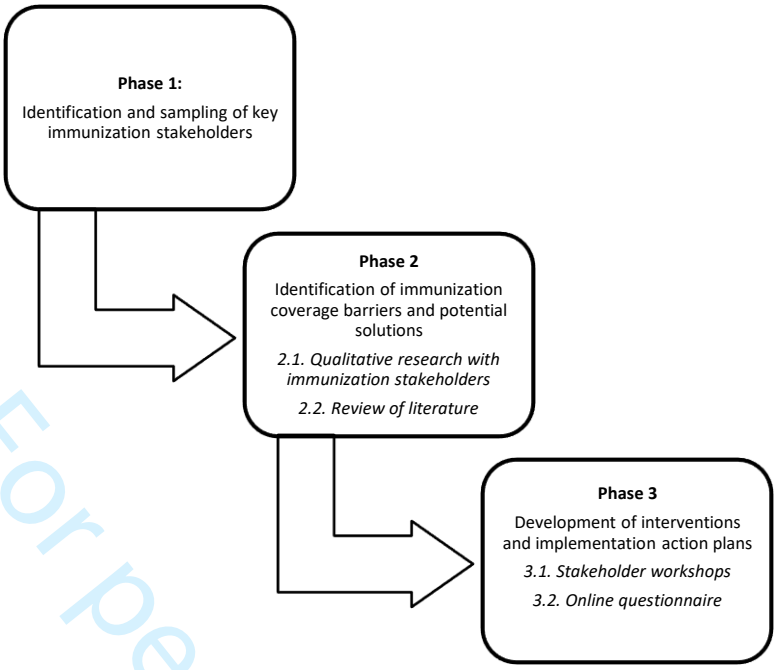

Table 1. Stakeholder groups and sample sizes

Stakeholders	Who	Predicted number	Cluster interview sample
National Department of Health	Individuals	12	12
Provincial Department of Health	Individuals	24	18
District and Facility Levels	Individuals	150	27
District Clinical Specialist Teams	Individuals	30	6
Pharmacies or Hospitals	Individuals providing pharmacy-specific services	20	12
Individual Vaccinators	Individuals	30	12
Non-Governmental Organization	Individuals providing NGO-specific immunization services	10	8
National Advisory Group on Immunisation	Individuals	12	6
WH O	Individual	6	2
UNICEF	Individual in an immunization role	1	1
PATH	Individuals in immunization roles	15	2
Health Systems Trust	Individuals in immunization roles	15	2
PEPFAR	Individuals in projects linked to PEPFAR (e.g. Right To Care, Broad Reach)	51	5
National Certification Committee for Polo Eradication	Individuals in immunization roles	6	1
Saving Babies	Individuals in immunization roles	8	1
PMTCT Working Group	Individuals in immunization roles	12	1
Paediatric Working Group	Individuals in immunization roles	12	1
Paediatric Management Group	Individuals in immunization roles	1	1
SA Paediatric Association (SAPA)	Individuals in immunization roles	1	1
Public Health Association of South Africa	Individuals in immunization roles	1	1
South African Medical Association	Individuals in immunization roles	1	1
Federation of Infectious Diseases Societies of Southern Africa	Individuals in immunization roles	1	1
South African Vaccination and Immunisation Centre	Individuals in immunization roles	4	1

Centre for Vaccines and Immunology, National Institute of Communicable Diseases	Individuals in immunization roles	2	1
National Vaccinators' Forum	Individuals in immunization roles	8	1
Amayeza- Independent Trainer on Vaccination	Spokesperson	1	1
African Local Initiative for Vaccinology Expertise	Spokesperson	2	1
Vaccines for Africa	Spokesperson	2	1
GSK	Spokesperson	1	1
Sanofi Pasteur	Spokesperson	2	1
BIOVAC	Spokesperson	2	1
Pfizer	Spokesperson	1	1
Association of early Childhood Development Centres	Representatives	4	2
Department of Education	School Health Coordinators: National and Provincial level	4	2
School Governing Bodies	Chairperson (individual) or spokesperson	4	2
Parent Association	Chairperson (individual) or spokesperson	4	2
Total		**460**	**140**

Contextualized strategies to increase childhood and adolescent vaccination coverage in South Africa: A mixed-methods study [protocol]

Draft Interview and Focus Group Topic Guide

Demographic information
Official title:
Organisation/Place of work:
Location:
Gender:

Part 1: Involvement in immunization programmes

1. Can you describe what your current involvement is in Immunization programme(s) in South Africa?

Probes:

- How long have you worked in the area of vaccination/immunization?
- Possible functions/roles?
- Are you involved/have experience with both childhood and pre-adolescent/adolescent vaccination programmes in the country?

Part 2: General views of the Expanded Programme on Immunisation (EPI) in South Africa

2. What do you see as the central goals of the national Expanded Programme on Immunization (EPI) in South Africa?

Probes:

- Have these goals changed over time?

3. What do you think is currently working well with the EPI programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting (where appropriate)
- What do you think have been the enabling factors underpinning these successes? *(Probes: Political, structural, ideological, financial?)*

4. Do think the national EPI programme is generally meeting its central goals?

Probes:

- Why/why not?
- If answered that EPI Programme(s) are NOT achieving set goals, ask the following:
  - Do you think the current performance of the EPI Programme is a serious national challenge?
  - Do you think managers and especially senior managers of the DOH (at all levels) view the poor/under performance of EPI as a serious challenge that should be urgently addressed?
    If yes: Are their actions in line with this view?
    If yes: Can you give us examples of these actions which demonstrate the urgency with which they view this situation?

Part 3: Specific challenges of and solutions for the EPI programme

I would now like us to talk about some of the challenges currently facing the EPI programme, and your thoughts about how these might be addressed.

Healthcare system

5. What are your views and experiences of the public primary health facilities where vaccinations are provided? What kind of challenges exist in these health facilities for the vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- Management structures?
- Management approach? The focus of managers and what they prioritise (and not)?
- Health information systems (is vaccine recording and reporting maintained)?
- Financial resources?
- Availability of staff (shortages/high turnovers)?
- Availability of vaccine education/information materials?
- Availability of initiatives to advocate for immunization?
- Availability of approaches to mobilise communities/public to vaccinate children e.g. social media
- Existence of approaches that attempt to link EPI (services, planning and mode of operation) to other apparently more successful programmes or programmes that may have a wider coverage e.g. PMTCT?
- Waiting times in the clinics?
- Mixed queues?
- Operating times?
- Treatment and attitude of Health Care Providers (Vaccinators and other HCP)?
- Attitude of non-Health Professionals such as clerks and others.
- Others (specify)

6. What do you think could be done to address some of these challenges?

Probe:

- Who should be tasked with addressing these challenges?

7. Do you see shortages of vaccines as a significant issue nationally and in your local setting?

Probes:

- Why/why not?
- If yes: Can you provide a specific example of this challenge?
- If yes: Where do you think the problem lies (*e.g. vaccine procurement, storage, distribution/delivery)?*
- Are you aware of any attempts or intervention measures by the DOH (at any level: national, province or district) to address the challenge of vaccine shortages? If yes, how successful do you think these attempts have been?
- Do you have any ideas on how to overcome the challenge of vaccine shortages? Who should be tasked with addressing this challenge?

8. Who are the main role-players/stakeholders involved in EPI programme(s) in South Africa?

Probes:

- Is there sufficient communication/collaboration between stakeholders? Why/ why not? What could be done to improve this?
- Is there sufficient advocacy/social mobilization amongst stakeholders? Why/ why not? What could be done to improve this?

- Are community leaders/groups sufficiently involved in the EPI? Why/ why not? How do you think these stakeholders be more involved?

9. Can you tell me a bit about the relationship between the public and private health sectors in terms of the EPI programme?

Probes

- Is there any collaboration/interaction between them? Why/why not?
- Do you see this as a problem? Why/why not?
- If seen as a problem: what could be done to increase collaboration/interaction?
- According to your knowledge either in terms of policy or in terms of practice and experience: "Are Private or NGO vaccinators able to access state vaccines for their clients, free of charge?" If yes, do they provide feedback on data of doses given?

Healthcare providers

10. What are your views about health care providers (HCP) administering vaccines in public health facilities? Do you think there are any challenges in relation to HCPs for vaccination programmes?

Probes: ask for specific examples of their experience of the following nationally AND in their local setting (where appropriate)

- General attitudes and behavior of health care providers *(e.g. friendly/helpful/rude)?*
- Knowledge about vaccines and vaccination?
- Knowledge and experiences with the conditions that the vaccines prevent?
- Perceptions of vaccines and vaccination?
- Perceptions of multiple injections and the introduction of more vaccines?
- Perceptions of the importance of communicating with caregivers about vaccination?
- Use opportunities to assess the vaccination status of the child?
- Sufficient skills/training?
- Do they vaccinate their own children/grandchildren or take special interest to help ensure that children of close relatives are vaccinated?
- How do they access vaccination for their own children/grandchildren or relatives? Through private or public institutions?

11. What do you think should be done to improve the attitudes and behavior of HCP?

Probe

- Who should be tasked with dealing with these issues?

12. What do you think should be done to improve the knowledge/skills of health care providers?

Probe:

- Who should be tasked with doing this?

Service users/public

13. What is your sense of the general level of knowledge amongst the public about childhood vaccines, immunisation services and the conditions that these prevent?

Probes:

- Are there gaps in knowledge? If yes: what kinds of gaps?
- Do you think people know about the benefits of childhood vaccines?

- What sources do people go to for information about childhood vaccination? *e.g. Internet; social media networks; health care workers; friends/family; schools; religious leaders?*
- Which sources do you think people perceive as being trustworthy/untrustworthy?

14. What do you think influences people' decision about whether to vaccinate their children or not?

Probes:

- What doubts, fears, concerns (if any) about vaccines and vaccination services do you think people might have that could prevent them from deciding to vaccinate their children? *(e.g. concerns about vaccine quality, safety, contra-indications, risks etc.)*
- What negative attitudes or beliefs (if any) about vaccines and vaccination do you think people might have that could prevent them from deciding to vaccinate their children? *(ask if they have heard any specific stories/rumours)*
- Where might these negative attitudes/beliefs/concerns come from? (*e.g. religion, cultural norms & practices, traditional leaders, anti-vac lobbying, media)*
- What role (if any) do you think a lack of trust in the health care system, healthcare providers and/or government might play in people's decision to vaccinate their children? *(e.g. lack of trust in providers' competence; perceptions of poor quality of care; manner in which providers treat them and their children etc.)*
- Do you think people face any practical challenges that could prevent them from choosing or accessing vaccination? *(e.g cost, travel, language or cultural differences, clinic opening hours, vaccine stock-outs etc.)*
- Are there any other factors, that we haven't already discussed, that you think might prevent people from accepting and taking-up childhood vaccination?

15. Want to you think could be done to make parents more likely to vaccinate their children according to the EPI schedule?

Probes:

- How can vaccination services best enable, support and motivate childhood vaccination?
- What channels do you think would be most effective in promoting childhood vaccination?
- Who should promote vaccination? *(e.g. health care workers, teachers, community leaders, media)*
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? Media- radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials- posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?

16. We have spoken about various different challenges facing the EPI programme in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current EPI programme, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Do you think there are different priorities for different Provinces?

Part 4: HPV Vaccine

I would now like to talk a bit about the HPV vaccine and vaccination in South Africa.

17. What is your overall impression of the school HPV vaccination programme?

Probes:

- Is the programme successful or not successful? Why?
- Who is involved with the programme? Is there collaboration between the stakeholders? Why/why not?
- Have you received any feedback about the programme *(e.g. from parents/girls? teachers? those delivering the programme? others?)*

18. What do you think is currently working well with the programme?

Probes:

- Ask for specific example(s) of strengths nationally and in their local setting
- What do you think have been the enabling factors underpinning these successes? *(Probe: Political, structural, ideological, financial?)*

Main challenges and potential solutions

19. Currently the HPV Vaccination Programme is delivered in a campaign like approach- vaccination teams visit schools twice a year and targeted children come at the same time to line up for this vaccine. What are your thoughts about this approach?

Probes

- What are the strengths and weaknesses of this approach? *(and probe for specific examples in local setting)*
- Do you think parents/girls/teachers are happy with this approach? Why/why not? *(and probe for specific examples in local setting)*
- What alternative delivery mechanisms (if any) do you think might be more effective?

20. Currently the programme does not include private schools and the HPV vaccine is not available at public health facilities. What are your thoughts about this?

Probes

- What kinds of problems, if any, do you think these absences might be generating?
- Should the programme be extended to private schools? Why/why not? If yes: how should it be incorporated in private schools?
- Should the HPV vaccine be made available at public health facilities? Why/why not? If yes: what would be needed to operationalize this?

21. What do you think influences parents' and girls' decision to take-up the HPV vaccine?

Probes:

- To what extent do you think parents and girls think that the HPV vaccine is necessary? Do you think they know about the reasons for/benefits of the vaccine? Why/why not?
- Do you think parents and girls trust the HPV vaccine to protect their health? Why/why not?
- What doubts, fears, concerns (if any) do you think parents and girls might have about the HPV vaccine? What do you think might be the sources of these concerns/beliefs? *(e.g. cultural norms, community practices/traditions, anti-vac lobbying, social media, internet)*
- What role (if any) do you think a lack of trust in health system, healthcare providers and decision makers might play in parents and girls concerns and beliefs about the HPV vaccines and vaccination?
- Are there any other factors, that we have not already discussed, that you think might influence parents and girls decision to accept the HPV vaccine?

22. Figures suggest that there is a significant drop in uptake from the 1st to the 2nd dose. Why do you think this might be so?

23. What do you think could be done to encourage parents and girls to consent to the HPV vaccine within the school programme?

Probes:

- Is information about the HPV vaccine and vaccination programme currently provided to parents of targeted girls and and these girls? Do you think further information and communication channels are needed?
- Is information about the HPV vaccine and vaccination programme provided to parents on non targeted girls?
- What channels do you think would be most effective in promoting the HPV vaccination?
- What formats should be used? (*e.g. advocacy visits? dialogue meetings? media (radio announcements, jingles on TV, information in newspapers/magazines)? education and communication materials (posters, billboards, banners, pamphlets)*
- What content should the information include? Should this content be the same across the country or different for different settings?
- Who should be involved with education and communication activities (*e.g. health care workers, teachers, community leaders, media)*
- What would help parents and girls complete the vaccine series i.e. return for the second dose?

24. What are your views about health care providers (HCPs) and the HPV vaccine and vaccination services?

Probes

- What are HCPs general attitudes and behaviours towards the HPV vaccine and providing vaccination for HPV*?*
- Do you think HCPs know about the HPV vaccine?
- Do you think HCPs know about the conditions the HPV vaccine prevents?
- Do you think HCPs vaccinate their own children/grandchildren for HPV or take special interest to help ensure that children of close relatives are vaccinated for HPV?

25. We have spoken about various different challenges facing HPV vaccination in the country. In summary, what for you are the most pressing issues that should be prioritized? In other words, if you could change 3 things about the current HPV vaccination programme in South Africa, what would these be?

Probes:

- Why do you perceive these to be the most important?
- Are there different priorities for different Provinces?

Part 5: Closing

This has been a very informative interview. Thank you so much for your time.

Is there anything we haven't covered that you would like to add? Is there anything you would like to say in closing?

Do you know of anyone else who could provide important insights as a key informant and might be interested in participating in the study?
If yes: can you provide us with their contact details so we can get in touch with them?