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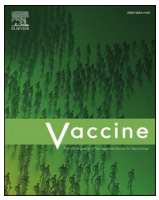

Vaccine stock-outs: A preventable health facility obstacle contributing to missed vaccinations in South African children

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ABSTRACT

In 2019 the National Department of Health (NDoH) conducted a national immunisation coverage survey of caregivers of children aged 24–35 months in all 52 districts of South Africa, and reported a national fully immunised under one year-old coverage of 83.9 %, and 76.8 % coverage for all vaccines scheduled up to 18 months of age. This retrospective, descriptive study was a secondary data analysis of 3576 validated Microsoft Excel® records containing the reasons for missed vaccinations collected by field workers during the 2019 national survey. The reason "vaccine out of stock" had been captured by field workers from children's vaccination cards, while other reasons given by caregivers had been captured either as pre-defined codes or free text. Free text reasons were analysed and additional codes created, and all reasons were categorised. In total, 3576 caregivers gave 8116 reasons for 8056 doses that had been missed by their children. Reasons related to health facility obstacles (HFOs) (67.9 %; 2429/3576) and personal obstacles (34.6 %; 1237/3576) constituted the major categories of reasons for missed vaccinations. Of all vaccines missed because of HFO-related reasons, 57.8 % (1403/2429) were missed because of vaccine stock-outs, affecting 39.2 % (1403/3576) of children. Other important HFOs included lack of access to vaccination services (24.5 %; 595/2429); and information about missed vaccinations and the need to return for catch-up not being shared with caregivers (17.1 %; 416/2429). These results were stratified by district and shared with the NDoH, who have initiated several projects in collaboration with other stakeholders, focusing mainly on building capacity for effective vaccine management to prevent vaccine stock-outs, and ensuring that all children are able to access vaccination services. The results of this study can be used as a baseline against which the success of future interventions emanating from these projects can be measured.

1. Introduction

National population-based immunisation coverage surveys are costly, but since they reach children whose caregivers may not access healthcare services contributing towards administrative data, they are necessary to identify and address gaps, thereby improving immunisation coverage. Together with official administrative coverage data reported by World Health Organization (WHO) member countries, the results of these surveys are used to calculate the annual WHO and United Nations Children's Fund Estimates (UNICEF) of National Immunization Coverage (WUENIC) [1]. From 27 June to 22 December 2019, the South African National Department of Health (NDoH) conducted a National

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Expanded Programme on Immunisation of South Africa (EPI-SA) population-based coverage survey of caregivers of children aged 24 to 35 months in all 52 districts of South Africa, which also captured data on reasons for missed vaccinations [2,3]. EPI-SA offers free routine infant immunisation services at public sector primary healthcare clinics throughout South Africa, with approximately 16 % of South African caregivers accessing these services through the private sector [4]. While additional vaccines are available through the private sector, and the private sector may have slightly different schedules for some vaccines, the children whose caregivers participated in this survey should have received birth doses of the bivalent oral polio vaccine (bOPV) and Bacille Calmette-Guérin vaccine (BCG), with another dose of bOPV given at 6 weeks; a hexavalent vaccine against diphtheria, tetanus, pertussis, polio, hepatitis B and *Haemophilus influenzae* type B (DTP-containing vaccine, abbreviated as DTP) at 6, 10 and 14 weeks, with a booster at 18 months; an oral rotavirus vaccine (RV) at 6 and 10 weeks; a pneumococcal conjugate vaccine (PCV) at 6 and 14 weeks, and at 9 months; and a measles-containing vaccine (MCV) at 6 and 12 months. At the time when these children were eligible for receiving either MCV1 or MCV2, there were no safety and effectiveness data on MeasBio® (the specific MCV vaccine used in EPI-SA at the time) when simultaneously administered with other vaccines, thus this vaccine was not administered at the same time as other vaccines.

This national survey included 17,180 children who had a Road to Health Booklet (RtHB), the official home-based record where vaccinations and other health indicators are recorded by health facility staff. It reported a national fully immunised under one year-old coverage of 83.9 %, which is below the global coverage target of 90 %; and 76.8 % coverage for all vaccines scheduled up to 18 months of age [3]. Previous South African studies investigating infant immunisation coverage and reasons for missed vaccinations, have reported reasons related to health facility obstacles (HFOs) as major drivers of suboptimal coverage [5–10]. While reasons related to vaccine hesitancy have been identified as the major drivers of low human papillomavirus (HPV) vaccine coverage in South Africa [11,12], they have not featured prominently in South African infant immunisation coverage studies [5–10]. Other reasons that were identified in previous South African infant immunisation coverage studies include those related to personal obstacles, lack of motivation and lack of information [5–10]. Thus, this study used the "reasons for missed vaccinations" data collected during the national 2019 survey, in order to understand the reasons for missed vaccinations on a national scale.

2. Materials and methods

2.1. Study design and study population

This retrospective, descriptive study was a secondary data analysis of the "reasons for missed vaccination" data collected for the 2019 national EPI-SA coverage survey, conducted by the University of the Witwatersrand, Vaccines and Infectious Diseases Analytics (Wits-VIDA) Research Unit in collaboration with the NDoH and the National Institute for Communicable Diseases (NICD) [3]. Of all children whose RtHBs indicated they had missed one or more vaccination/s, one or more reason/s for missed vaccination/s had been captured for 3576, with these records having been validated by Wits-VIDA data capturers using photographs taken of RtHBs by fieldworkers. The study population thus consisted of 3576 validated Microsoft Excel® records containing data on the reasons for missed vaccinations. Data on reasons for missed vaccinations consisted of pre-defined codes captured by the field workers during data collection, including a code for "other" when the reason did not fit under any other pre-defined code. The code for "vaccine out of stock" was captured when the vaccinator had recorded this reason on the RtHB, while all other reasons were collected from caregivers. Since the questionnaire required field workers to capture all reasons provided by caregivers, there were often two or more reasons captured for missing a specific vaccine dose. When a reason did not fit under any pre-defined code, field workers captured their interpretation of what the caregiver told them for these "other" reasons, using free text data truncated at 50 characters, including spaces.

2.2. Coding of free text data

A content analysis approach associated with qualitative research was used to generate quantifiable data from the free text data, as an extension to the predefined codes captured by field workers when reasons for missed doses were provided. The first author (NMM) carefully reviewed the free text summaries captured by the field workers to gain an understanding of the data and identify commonalities between reasons, which were then coded. Consensus was then reached with three co-authors (JCM, ZI and RJB), on a set of codes to be used (coding framework). Thereafter NMM used the coding framework to code all free text data, in additional fields added to capture the final codes in the database.

2.3. Categorisation of reason codes

Original codes and new free text data codes were grouped by NMM into categories for reasons related to HFOs, vaccine hesitancy and other categories. Consensus was then reached with JCM, ZI and RJB on a set of categories, and the codes that needed to be included within each category. Thereafter, additional formula-based summary fields were created in the database to categorise all codes.

2.4. Data analysis

Microsoft Excel® data were imported into Epi Info™ 7.2.5.0 (Centers for Disease Control and Prevention, USA) for descriptive data analysis. This included analysing the frequency distributions of reasons and reason categories, stratified by districts.

2.5. Ethical considerations

The database provided by the NDoH for this study did not contain data on personal identifiers. Before conducting the study, ethical clearance was obtained from the Sefako Makgatho University Research Ethics Committee (SMUREC/P/258/2021;PG).

3. Results

3.1. Reasons for missed vaccinations

Field workers had selected "other reasons" for 103 missed birth doses and 1517 missed vaccines scheduled from 6 weeks to 18 months, with free text reasons being captured for 95 and 1364 respectively of these "other" reasons (i.e. 1459 free text reasons were included in the qualitative analysis). A few field workers did not seem to be aware that they had to summarise the reasons within a 50-character limit, resulting in a few reasons being unclear (eg.: "The child stopped to take his vaccines because he w"). Other field workers seemed to over-summarise, resulting in text being captured that was unrelated to a reason (eg.: "Children are twins"). Also, some field workers captured judgemental interpretations of the reasons given by caregivers (eg.: "The mother was lazy and making excuse"). Analysis of these free text reasons resulted in the creation of new reasons codes.

Overall, 8116 reasons were captured for 8056 missed doses. The coded reasons (i.e. original coded reasons and coded free text data) were categorised into seven main categories (Table 1). The reasons belonging to six of these categories are listed in the footnotes of Table 1, while the reasons belonging to the HFO category are fully described in Table 2.

Some caregivers gave more than one reason for a missed vaccine. In some instances, these reasons belonged to the same category, while in

Table 1
Frequency distribution of categories of reasons provided by caregivers.

	Birth doses[a]		Doses given at 6 weeks to 18 months[b]		All vaccines[c]	
Reasons category	n[d]	%[d]	n[d]	%[d]	n[d]	%[d]
Healthy facility obstacles	307	82.7	2230	66.0	2429	67.9
[e]Personal obstacles	35	9.4	1217	36.0	1237	34.6
[f]Unknown	21	5.7	125	3.7	139	3.9
[g]Vaccine hesitancy	7	1.9	89	2.6	91	2.5
[h]Lack of motivation	2	0.5	47	1.4	49	1.4
[i]Unclear	2	0.5	11	0.3	13	0.4
[j]Lack of information	0	0.0	5	0.1	5	0.1

[a] 472 reasons given for 460 missed doses by 371 caregivers.
[b] 7 644 reasons given for 7596 missed doses by 3377 caregivers.
[c] 8 116 reasons given for 8056 missed doses by 3576 caregivers.
[d] Percentages and n are based on the number of caregivers. When more than one reason was given by a caregiver, these sometimes belonged to the same or different categories, thus the total reasons are greater than the number of caregivers.
[e] Personal obstacles: Forgetting to take the child; having no one to take child to the clinic; lost RtHB; new RtHB does not have these vaccines recorded and unsure if they were received; from another country where this vaccine is not given; vaccine not given in the private sector; illness; hospitalisation; parent is a drug addict.
[f] Unknown: The caregiver being interviewed did not know why the child had missed vaccination/s.
[g] Vaccine hesitancy: Refusal by one or both parents; religion prohibits vaccination; postponed (the child is not yet two years old; the child will be taken at a later date; the child will be taken when he turns three; the child will be taken as soon as possible).
[h] Lack of motivation: Judgemental interpretations by field workers (mother lazy, does not care, negligent); tired of going to the clinic; does not want to go to the clinic; stopped going to the clinic; does not see the importance; it was raining.
[i] Unclear: Incomplete because of truncation at 50 characters; text unrelated to a reason.
[j] Lack of information: Judgemental interpretation by field worker ("The caregiver was and still ignorant"); did not know where to go; nothing was explained to her. This differs from "Information not given by clinic", which has been categorised as a HFO.

Table 2
Frequency distribution of reasons related to health facility obstacles.

	Birth doses[a]		Doses given at 6 weeks to 18 months[b]		All vaccines[c]	
Reasons	n[d]	%[d]	n[d]	%[d]	n[d]	%[d]
Vaccine out of stock	203	66.1	1260	56.5	1403	57.8
[e]Information not given by clinic	0	0	416	18.7	416	17.1
No clinic nearby	0	0	207	9.3	207	8.5
[f]Clinic not open after working hours	1	0.3	197	8.8	198	8.2
Vaccinator not on duty	0	0	164	7.4	164	6.8
Dose given but not recorded	10	3.3	93	4.2	100	4.1
No one offered the baby a vaccine	80	26.1	0	0	80	3.3
Facility provides poor services	1	0.3	65	2.9	65	2.7
[g]The card was lost / not with me at the time	0	0	42	1.9	42	1.7
[h]Health facility closed on day of visit	0	0	26	1.2	26	1.1
Birth was out of hospital	21	6.8	0	0	21	0.9
I was asked to pay for vaccination	1	0.3	0	0	1	0
[i]Child brought back too soon	0	0	1	0	1	0

[a] 317 HFO-related reasons given by 307 caregivers.
[b] 2471 HFO-related reasons given by 2230 caregivers.
[c] 2724 HFO-related reasons given by 2429 caregivers.
[d] Percentages and n are based on the number of caregivers. Since more than one health facility-related reason was given by some caregivers, the totals are greater than the number of caregivers.
[e] Includes: Follow-up date not given; no explanation given about the need to return (because child did not receive all scheduled vaccines but caregiver was not made aware of this; because vaccine is out of stock; because MCV cannot be given at the same time).
[f] Includes: Mother at work; mother in matric / at school; inconvenient clinic hours; mother too busy; time constraints.
[g] Caregiver either turned away at clinic, or reluctant to attend and be turned away without child's RtHB.
[h] Not included with "Clinic not open after working hours" because the day of the week and time of the visits were not recorded.
[i] Child turned away at 7 months as 2nd dose of MCV is given at 12 months. However, the child subsequently received vaccines at 9 months and 18 months, and was never caught up with 2nd dose of MCV.

other instances, these reasons belonged to different categories. In addition, children missed different vaccines for different reasons belonging to different categories. As a result, reasons related to HFOs were also reported by 60.0 % (3/5) of caregivers reporting reasons related to lack of information; 36.7 % (18/49) of caregivers reporting reasons related to lack of motivation; 25.0 % (309/1237) of caregivers reporting reasons related to personal obstacles; 22.0 % (20/91) of caregivers reporting reasons related to vaccine hesitancy; 16.5 % (23/139) of caregivers who did not know why the child had missed vaccine doses; and 7.7 % (1/13) of caregivers reporting reasons that were not clearly captured by field workers.

HFOs accounted for most missed vaccinations for which reasons were given (Table 1), with vaccine stock-outs accounting for most vaccinations that were missed because of HFOs (Table 2), and 23.2 % (1866/8056) of overall missed doses for which reasons were given. Of all children who had never been vaccinated and whose caregivers gave reasons, 84.3 % (333/395) missed vaccinations because of HFOs, with vaccine stock-outs accounting for 63.1 % (210/333) of HFOs. Of all children, 39.2 % (1403/3576) missed ≥1 vaccine dose/s because of vaccine stock-outs. Further details of specific vaccines that were missed

Table 3
Frequency distribution of all missed vaccinations and those caused by vaccine stock-outs.

		Children who missed ≥ 1 vaccine dose/s[a]		Caregivers giving reasons for missed vaccine dose/s[b]		Reason for missed vaccine dose: Vaccine out of stock[c]	
Scheduled age	Vaccine	n	%	n	%	n	%
Birth	Bacille Calmette-Guérin (BCG)	762	19.3	318	41.7	167	52.5
	Bivalent oral polio vaccine (bOPV)0	813	20.6	142	17.5	61	43.0
6 weeks	bOPV1	1063	26.9	347	32.6	144	41.5
	Rotavirus vaccine (RV)1	952	24.1	226	23.7	67	29.6
	Pneumococcal conjugate vaccine (PCV)1	894	22.7	174	19.5	50	28.7
	DTP-containing vaccine[d] (DTP)1	1061	26.9	350	33.0	151	43.1
10 weeks	DTP2	1133	28.7	429	37.9	127	29.6
	RV2	1123	28.5	420	37.4	89	21.2
14 weeks	PCV2	1024	26.0	309	30.2	55	17.8
	DTP3	1247	31.6	545	43.7	163	29.9
6 months	Measles vaccine (MCV)1	1271	32.2	566	44.5	96	17.0
9 months	PCV3	1474	37.4	781	53.0	147	18.8
12 months	MCV2	2048	51.9	1375	67.1	1	0.1
18 months	DTP4	2723	69.0	2074	76.2	548	26.4

[a] Denominator based on total number of children who had missed ≥1 vaccinations ($n = 3946$).
[b] Denominator based on total number of the specific vaccination that was missed.
[c] Denominator based on total number of caregivers who gave reasons for specific missed vaccinations.
[d] Hexavalent vaccine against diphtheria, tetanus, pertussis, polio, hepatitis B and *Haemophilus influenzae* type B (Hib) (DTaP-IPV-HepB-Hib).

Table 4
Frequency distribution of vaccine doses missed because information was not provided by the clinic ($n = 792$ doses).

		Vaccine missed because information not given by clinic	
Scheduled age	Vaccine	n	%
6 weeks	bOPV1	29	3.7
	RV1	22	2.8
	PCV1	15	1.9
	DTP1	34	4.3
10 weeks	DTP2	50	6.3
	RV2	42	5.3
14 weeks	PCV2	25	3.2
	DTP3	65	8.2
6 months	MCV1	73	9.2
9 months	PCV3	80	10.1
12 months	MCV2	147	18.6
18 months	DTP4	210	26.5

because of vaccine stock-outs are provided in Table 3. Of all children who missed at least one of their birth doses because of vaccine stock-outs, 12.1 % (25/203) missed both BCG and bOPV0 for this reason. Of all children who missed at least one of their vaccines scheduled from 6 weeks to 18 months because of stock-outs, 30.0 % (378/1260) missed more than one of these vaccines for this reason.

The second-most important HFO-related reason was that information was not given to the caregiver by clinic staff. This reason was classified as a HFO in this study, and not as "lack of information", to differentiate between a general lack of awareness about immunisation or not knowing where to go to receive vaccinations, versus caregivers whose children had received other vaccinations, but were not told that their child had missed a vaccine, or that they should bring the child back for follow-up vaccinations. In many instances, children who missed vaccinations without their caregivers being informed, had received vaccinations scheduled at older ages. For example, of all children whose caregivers were not informed that their child had missed DTP3 (scheduled at 14 weeks), 66.2 % (43/65) had received at least one of the later vaccines, with 60 % (39/65) having received MCV1 (scheduled at 6 months); 55.4 % (36/65) having received PCV3 (scheduled at 9 months); 52.3 % (34/65) having received MCV2 (scheduled at 12 months); and 50.8 % (33/65) having received DTP4 (scheduled at 18 months). Also, of all children whose caregivers were not informed that their child had missed MCV1, 47.9 % (35/73) had received at least one of the later vaccines, with 38.4 % (28/73) having received PCV3; 28.8 % (21/73) having received MCV2; and 28.8 % (21/73) having received DTP4. In addition, of all children whose caregivers were not informed that their child had missed PCV3, 27.5 % (22/80) had received at least one of the later vaccines, with 21.3 % (17/80) having received MCV2, and 13.8 % (11/80) having received DTP4. In total, 792 doses were missed by 416 children whose caregivers were not informed that their children needed to receive these doses. See Table 4 for further details.

Four of the HFO reasons implied lack of access to vaccination services, including "clinic not open after working hours", "no clinic nearby", "health facility closed on day of visit" and "vaccinator not on duty", thus were grouped in a "lack of access" sub-category. These reasons collectively accounted for 24.5 % (595/2429) of children who missed ≥1 vaccination because of HFOs.

4. Discussion

This is the second South African study to report the reasons for missed vaccinations at national level; however, it is the first South African study based on a large representative sample of over 3000 children who had missed one or more vaccinations. Almost 70 % of missed vaccinations were reportedly due to HFOs, a finding that is supported by previous South African studies investigating infant immunisation coverage and reasons for missed vaccinations in seven provinces: Western Cape, Eastern Cape, Limpopo, North West, KwaZulu Natal, Mpumalanga and Gauteng [5–10]. Of all vaccines missed because of HFO-related reasons, 57.8 % were missed because of vaccine stock-outs, affecting 39.2 % of children. BCG, bOPV, PCV and DTP were most affected by stock-outs. The national shortage of BCG in 2014 and 2015 as a result of manufacturing problems affecting the global BCG supply [13] could not have been responsible for these stock-outs, because the children surveyed in this study were born in 2016 and 2017. However, there was a global shortage of the specific DTP-containing vaccine used in the public sector in 2016 and 2017 [14], which may explain why stock-outs accounted for relatively high proportions of all missed doses of DTP at 6, 10 and 14 weeks, and 18 months of age. South Africa had not experienced any other national vaccine shortages from 2016 to 2019, thus the stock-outs reported in this study for BCG, OPV and PCV were caused by a lack of effective vaccine management at provincial, district or facility level. Thus, further investigation at all levels is required, as the reasons for vaccine stock-outs may differ per province, and may include issues related to funding, cold chain capacity, procurement and distribution practices or a combination of these [15].

Reasons related to lack of access ("clinic not open after working hours", "no clinic nearby", "health facility closed on day of visit" and "vaccinator not on duty") accounted for 24.5 % of all HFO-related reasons. While the reason "having no one to take child to the clinic" has been categorised as a personal obstacle in this study, this could possibly also be related to clinics not being open after working hours, since this reason implies that the caregiver is not available to take the child to the clinic during working hours. Reasons related to lack of access have been reported by all South African studies investigating reasons for missed vaccinations [5–10], thus these findings were unsurprising. The NDoH

recognised this challenge when introducing the national vaccination programme against coronavirus disease 2019 (COVID-19), and thus made COVID-19 vaccination widely available through private health establishments, occupational health sites, temporary outreach sites and community pharmacies, many of which offered vaccination services on weekends [16,17]. Thus community pharmacies and pharmacist vaccinators played an important role in expanding access to COVID-19 vaccines [18].

The reason "Information not given by clinic" accounted for 17.1 % of all HFO-related reasons in this study. While this reason affected all vaccines scheduled from 6 weeks to 18 months, DTP3, MCV1, PCV3, MCV2 and DTP4 (respectively given at 14 weeks, and 6, 9, 12 and 18 months) were most affected. Apart from DTP3, these vaccines were scheduled much later in the first year of life, and Table 4 shows that the bigger the gap in time between the vaccines, the larger the proportion of caregivers who were "not informed". Thus, it may be possible that some caregivers forgot that they had been informed. However, many children whose caregivers said they were not informed about these missed doses, had received vaccines scheduled at older ages. Most strikingly, 66 % of children whose caregivers were not informed that their child had missed DTP3, had received vaccines scheduled at older ages, with 50 % receiving DTP4. These findings imply that vaccinators do not always check the RtHB to prevent missed vaccination opportunities (MVOs), or the concept of catch-up vaccination is poorly understood and implemented. On the other hand, it is possible that not being able to administer MeasBio® at the same time as other vaccines, may have complicated catch-up vaccination to the extent that vaccination coverage has been compromised. Because of the high risk for severe outcomes from measles, when a child who has missed or is eligible for MCV1 or MCV2 is brought to the clinic, MCV must always be prioritised above any other vaccine that the child might have missed or is scheduled for that visit. As a result, the scheduled vaccine would have had to be postponed, as it couldn't be given simultaneously with MCV. The results from this study suggest that if scheduled vaccinations had to be postponed, this information was not always communicated to caregivers, resulting in children missing these vaccinations. Also, our findings suggest that caregivers were not always informed by clinic staff to return for further routine doses after their infants had received their vaccinations scheduled at 14 weeks of age.

Reasons related to vaccine hesitancy accounted for only 2.5 % of children, a finding that is supported by all South African studies reporting on infant immunisation coverage and reasons related to missed vaccinations [5–10]. However, despite widespread positive media coverage of the launch of the national survey and intensive community mobilisation activities at national, provincial and local levels, field workers were unfortunately unable to access some gated communities and security complexes [3]. It is precisely these communities who, because of their relatively high incomes, have greater access to vaccination misinformation on the internet and social media platforms, compared to the vast majority of South Africans [5]. Also, one of the many negative impacts of the COVID-19 dis- and misinformation infodemic that accompanied the pandemic, is that this has undermined public confidence in vaccines routinely administered to infants and children in many countries, including South Africa [19,20]. It is thus possible that had this national survey been undertaken during or after the COVID-19 pandemic, higher levels of vaccine hesitancy may have been found.

Our study has certain limitations. First, the possible underrepresentation of children from a relatively wealthy segment of South African society (i.e. those living in gated communities and security complexes) was a limitation of this study, that possibly resulted in an underestimation of vaccine hesitancy. Because caregivers living in these communities have greater access to the internet and social media, an online survey advertised via a social media platform is likely to yield a greater proportion of vaccine hesitancy-related reasons for missed vaccinations. This is because people who use the internet and social media have a high likelihood of encountering vaccine mis- and disinformation, and are thus more likely to be vaccine hesitant [21]. Furthermore, this argument is supported by findings from two South African surveys on HPV vaccine uptake by age-eligible girls [11,12]. The first was a national online survey advertised on Facebook, of caregivers of girls attending private schools [11], while the second was a paper-based self-administered survey of caregivers of girls attending public schools in a district of Gauteng Province [12]. Globally, studies investigating HPV vaccine confidence have found much higher levels of vaccine hesitancy towards HPV vaccines than towards early childhood vaccines [22], as did these two South African studies [11,12]. However, the study using an online survey reported that 61.4 % of caregivers of unvaccinated girls provided vaccine hesitancy-related reasons for not being vaccinated [11], compared to only 49.2 % of caregivers of unvaccinated girls in the study using the paper-based survey [12]. While data on internet access was not collected in either study, clearly 100 % of participants in the online survey had internet access, which may explain the higher levels of vaccine hesitancy reported in that study.

Second, the plan to collect voice recordings of the reasons for missed vaccinations given by caregivers was shelved, due to insufficient funds being available for the survey [3]. Thus, another limitation of this study is that, instead of capturing verbatim reasons given by caregivers, the field workers interpreted these reasons according to their understanding, and then captured their interpretations electronically in a text box truncated at 50 characters, including spaces. There is thus the possibility of interviewer bias in capturing the free text reasons for missed doses.

However, these limitations did not affect the validity of the finding that HFOs are major barriers to achieving high levels of vaccination coverage in South Africa. First, although vaccine stock-outs were not verified by conducting a survey in health facilities, the finding on vaccine stock-outs was based on data collected from RtHBs, thus was not subject to misinterpretation by field workers. Second, three of the four reasons related to lack of access were among the original codes that field workers could select from, with the only interpreted free text that was captured being for the reason "clinic not open after working hours", which is unlikely to be subject to misinterpretation. Third, the finding that many children who had missed vaccinations were not caught up despite having received later vaccinations, was also based on data collected from RtHBs. Thus this study has provided compelling evidence that supports previous findings, and while the data stratified at district level have not been reported here, these data have been shared with the NDoH, thus allowing for targeted interventions to build capacity at district level. Reducing HFOs is not easy to achieve, and requires stakeholders to implement interventions at national, provincial and district levels, under the leadership of the NDoH.

5. Conclusions, current interventions and recommendations

The results of this large, representative national survey confirm that the majority of missed vaccinations in South Africa are caused by HFOs, as previously reported by several smaller surveys conducted over the past two decades [5–10]. In this study, vaccine stock-outs accounted for more than half of all HFO-related reasons, while other important HFOs included lack of access to vaccination services; and information about missed vaccinations not being shared with caregivers coupled with MVOs, with children not being caught up at subsequent visits. In contrast, vaccine demand was relatively high, with reasons related to vaccine hesitancy, forgetting, lack of motivation and lack of information being in the minority.

5.1. Current interventions

The NDoH, UNICEF South Africa and the South African Vaccination and Immunisation Centre at Sefako Makgatho Health Sciences University are currently collaborating on research investigating vaccine stock availability (VSA). This includes investigating stock-outs at health

facility-level, and identifying factors contributing to vaccine stock-outs at all levels. Data collection and analysis for this study are complete, and the results are expected to be published in the second half of 2024. This collaboration also includes advanced training in effective vaccine management (EVM), which is currently being offered to in-service frontline healthcare workers who are involved in vaccine management. The course aims to equip vaccinators and vaccine store personnel with knowledge and guidance on good EVM practices, in compliance with legislation for vaccine logistics and supply; provide trained frontline healthcare workers with the ability to assess and monitor vaccine supply chains and help improve the supply chain performance; establish high standards of performance to ensure the reliability, quality and availability of vaccines when and where they are needed; strengthen quality management practices through the use of standard operating procedures, assessments and development of quality improvement projects; provide frontline healthcare workers with job aids for point of care decision-making; and build capacity in terms of EVM training for master trainers. This is being achieved through 10 training modules, each with specific learning outcomes. The EVM training was launched on the NDoH Knowledge Hub (https://knowledgehub.health.gov.za/course/effective-vaccine-management-evm-training-frontline-healthcare-workers) on 4 July 2024, and by 1 November 2024, 2816 HCWs had enrolled and 215 had successfully completed all 10 modules of the course. Furthermore, the NDoH is implementing the "Reach Every District" (RED) strategy to ensure that all eligible children receive all scheduled EPI-SA vaccines, thereby reducing the number of zero-dose and under-immunised children.

In addition, during the pandemic the South African Pharmacy Council (SAPC) embarked on an initiative to expand the vaccinator workforce and strengthen the role of community pharmacies and pharmacist vaccinators by training more pharmacists as EPI-SA vaccinators. In collaboration with all South African higher education institutions (HEIs) training pharmacists, a generic short course on immunisation and injection techniques for pharmacists was developed [23], and currently at least five HEIs have been accredited by the SAPC to offer this course. Strengthening the role of private sector community pharmacists / pharmacies is vital for improving access to EPI-SA vaccinations, especially since their flexible opening hours make these ideal vaccination sites for caregivers who are unable to take time off from work to get their children vaccinated.

5.2. Recommendations

The South African COVID-19 vaccination programme was very successful in providing a high level of access to COVID-19 vaccination services, while ensuring effective EVM within the constraints of limited global supply [16]. Some of the innovations that were introduced during the pandemic could easily be expanded to enhance the performance of EPI-SA. For example, for the first time in South Africa, an electronic vaccination data system (EVDS) was used for the COVID-19 vaccination programme. After initial teething problems regarding appointments were solved by allowing unscheduled walk-ins, the EVDS issued SMS reminders and vaccination records for personal use and to facilitate EVM at all levels (facility, district, provincial and national) [16]. If applied to EPI-SA, an EVDS would enhance both access and EVM, which would in turn reduce vaccine stock-outs [15]. This EVDS could also be used to send SMS or WhatsApp vaccination reminders either directly, or by linking it to the NDoH's MomConnect platform, which currently sends infant and child health promotion messages to mothers who are registered on the platform (https://sidebyside.co.za/resources/momconnect-and-nurseconnect/). The EVDS should also be linked to all child support services and programmes to alert healthcare workers who could utilise community health workers to encourage vaccination among caregivers whose children are not up to date with their vaccinations.

In addition, access to COVID-19 vaccination services was vastly expanded through NDoH collaboration with the private sector. For example, vaccination services were provided at community pharmacies; workplaces; in mobile units and outdoors at taxi ranks and in parking lots (including "drive-through" sites); and importantly, over weekends [16]. Also, the public could access vaccination services at the sites nearest to them, regardless of which sector they usually utilised. While public-private partnerships that make EPI-SA vaccines available free of charge in the private sector have been established in some provinces, these partnerships need to be established throughout South Africa.

The global dis- and misinformation infodemic that accompanied the pandemic resulted in high levels of COVID-19 vaccine hesitancy that eroded public demand in many countries, including South Africa. Furthermore, in South Africa, public trust in authorities was severely eroded during the pandemic by corruption scandals and often misguided prohibitions that strengthened neoliberal arguments, while deepening poverty, social exclusion and marginalisation of the country's poorest [24]. Nevertheless, COVID-19 vaccination coverage may have been much lower had the NDoH not embarked on unprecedented communication and advocacy strategies, that resulted in mobilising 26.7 % of South African adults to be fully immunised by 31 December 2021 [16]. The NDoH was assisted by the Government Communication and Information System, which ran a "social listening" project aimed at tracking vaccine-related messages on social media platforms, in order to develop posters and messages that were shared on the official NDoH COVID-19 website and various social media platforms, dispelling false rumours and misinformation.

These demand creation interventions to increase COVID-19 vaccine coverage may also be relevant for increasing childhood vaccination coverage, despite only 2.5 % of children in our study being affected by vaccine hesitancy. We suggest this because first, we have argued that the in-person data collection methods used in the national survey may have resulted in an under-estimation of vaccine hesitancy, and second, that vaccine hesitancy towards childhood vaccines may feature more prominently in a post-COVID-19 South Africa [19,20]. Thus the "social listening" project used by the NDoH during COVID-19 should continue, because some of the COVID-19 vaccine demand creation strategies can also be used for increasing uptake of EPI-SA vaccines, perhaps by expanding the resources available for public use on the NDoH's MomConnect platform. Many caregivers who participated in the national survey were not the mothers of the children [3], thus MomConnect is not ideal for all caregivers. For example, a hotline and email address for the public to access information, together with an online portal for accessing the latest vaccination news and resources dispelling dis- and misinformation, would give access to the entire caregiver population. Also, using information provided on this portal, the public should be able to locate their closest vaccination site, and add themselves to a WhatsApp group that provides updates about outbreaks and catch-up campaigns.

While the national coverage survey has identified districts with zero-dose and under-vaccinated populations, this study has identified barriers to vaccination at district level (results not reported here but shared with the NDoH). Taken together with the VSA results, these data will help the NDoH and provinces to develop district specific plans utilising the RED strategy, e.g. district catch-up plans and short courses for capacity building. All of these courses should include training on reducing MVOs using different strategies, based on the findings of this study. For example, training on catch-up schedules emphasising that any contact with a child must be used as a vaccination opportunity will reduce MVOs directly, while EVM training will reduce MVOs through ensuring that safe, effective vaccines are always available. The EVM and RED strategy courses also include a module on supportive supervision which highlights that vaccination facilities must be visited, supervised and monitored often to ensure optimum performance and service delivery. Supportive supervision can thus help to reduce MVOs by eliminating modifiable HFOs other than vaccine stock-outs, such as information on stock-outs not being shared with caregivers and catch-up vaccinations not being administered at subsequent visits.

The effectiveness of the interventions we have recommended will

need to be evaluated by future research. For example, pre- and post-training knowledge testing is being used to measure the effectiveness of the EVM course, and should be used for any future training designed to capacitate healthcare workers involved in providing vaccination services. Furthermore, the impact of this training, and the impact of public demand creation interventions, should be measured by comparing official pre- and post-intervention vaccination coverage data. Finally, if the EVDS is expanded to include EPI-SA, this should not spell the end of population-based immunisation coverage surveys, which remain essential for identifying gaps at district and sub-district level. However, these should always capture data on reasons for missed vaccinations, and since national surveys are costly, these surveys could be confined to districts identified though the EVDS as having low EPI-SA coverage. Furthermore, it is essential that an online version of these surveys, advertised via a social media platform, should be included in addition to household surveys. This will ensure that all segments of South African society are reached, to provide a more holistic picture.

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CRediT authorship contribution statement

Natasha M. Masemola: Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Rosemary J. Burnett:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization. **Portia C. Makamba-Mutevedzi:** Writing – review & editing, Project administration, Data curation, Conceptualization. **Marione Schönfeldt:** Writing – review & editing, Visualization, Conceptualization. **Lesley J. Bamford:** Writing – review & editing, Visualization, Funding acquisition, Conceptualization. **Zeenat Ismail:** Writing – review & editing, Visualization, Validation. **Shabir A. Madhi:** Writing – review & editing, Visualization, Funding acquisition, Conceptualization. **Johanna C. Meyer:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

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Data availability

Data will be made available on request.

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