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Study Title: Evaluating the impact and cost-effectiveness of Zindagi Mehfooz, a suite of digital health interventions, to improve the coverage, timeliness, and completeness of immunisation services in Pakistan

I. Background and Rationale:

In the last two decades, digital health interventions have proliferated rapidly and are currently being used by frontline health workers (FLHWs) in a range of settings to support service delivery, including decision-support, workflow planning, and data capture [1]. Limited, but emerging evidence suggests that digitally enabling FLHWs may help to improve the content, quality, and timeliness of health services for maternal and child health. In the context of immunisation services, direct to beneficiary services which send alerts and reminders to caregivers have additionally been shown to improve immunisation coverage and timeliness [2]. Despite their immense potential, few digital health interventions have successfully scaled, and among those that have, the pathway to ensuring long-term sustained implementation remains uncertain [1, 3].

The reasons for the paucity of available evidence on the impact of digital health interventions are multifaceted but include limited time and resources. The rapid pace with which technology can evolve is often seen in conflict with the one to three year timelines of impact evaluations. For many, preference is given to rapidly promoting scale-up and limiting the importance placed on evidence given that many digital solutions are bolstering access to public health interventions with known efficacy. However, increasingly, the absence of evidence is seen as barrier to securing long-term funding from governments and transitioning from reliance on donor support [4]. Particularly in the context of suites of digital interventions implemented across heterogenous populations of beneficiaries, health workers, and health systems, evidence on the impact of the individual parts as well as the overall program can inform understanding of what works and what may require optimization.

In Pakistan digital health interventions have been used to bolster a range of supply and demand side health interventions. Direct to beneficiary solutions have sought to improve medication compliance in patients with non-communicable diseases, and several telemedicine initiatives have sought to enable female doctors to practice remotely [5]. Among FLHWs examples of digital solutions are emerging, however, few solutions have scaled widely [5]. Zindagi Mehfooz (ZM) is the exception.

ZM is a suite of digital health interventions, centered around a mobile phone based Electronic Immunisation Registry (EIR). The ZM-EIR features an Android application that enables vaccinators to digitally enroll children into the platform using smartphones. Each child is assigned a unique identification through quick-response barcodes linked to their digital immunization records. The decision support system within the Registry guides vaccinators for routine and catch-up immunizations, and a 2-way SMS reminder feature automatically sends reminders to parents for their children's upcoming vaccine appointments. The Registry is linked to a web-based dashboard that generates immunization reports based on longitudinal immunization records and enables supervisors to access real-time performance data, including details of children who are unvaccinated or who have defaulted. Additionally, the Registry has other features, including a child registry to help identify zero dose children through a birth registry, call center to answer queries of parents/caregivers, real-time workforce tracking, and geospatial tagging of immunization events for GIS-based analysis, etc. Since its inception in 2012, ZM has scaled to all 29 districts in Sindh Province. To date,

over 3,096 vaccinators at 1,694 public and private sector immunisation clinics have used the system to enroll 3.8 million children and 1.3 million women with 31 million immunisation visits recorded.

This study, funded by Gavi, the Vaccine Alliance, aims to generate evidence on the effectiveness of ZM. Drawing from qualitative and quantitative methods, study activities will determine the impact and cost-effectiveness of ZM on immunisation coverage and timeliness as compared to the status quo prior to introduction. Additional efforts to analyse system generated data will aim to determine program reach, coverage, data quality and use. Where appropriate, we will contextualise ZM functions with available evidence and standards as in the case of Electronic Immunisation Registries (EIRs), decision-support tools, call centres- including but not limited to WHO EIR recommendations. In particular, this desk review will consider how the EIR component measures against established EIR standards.

Study Goal and Aims/
Study Goal: The overall goal of the study will be to evaluate the impact and cost effectiveness of Zindagi Mehfooz, a suite of digital health immunisation interventions, on increasing the proportion of children 12-23 months fully immunised in Sindh province through the increased availability and use of data.

Study Aim 1 (Reach). Determine barriers and facilitators to programme initiation
Objective 1.1 (Programme reach) Draw from ZM system data and programme records on vaccinator registration and training and Government records on numbers of vaccinators to determine proportion of eligible vaccinators trained by the programme and registered within ZM from 2017 to 2019 in alignment with MICS 6 from 2018-2019 and MICS 5 in 2014
Objective 1.2 (Provider use) Conduct secondary analysis of system generated data to determine what proportion of vaccinators trained to use ZM upload details for at least 1 client in Sindh
Objective 1.3 (Stakeholder perceptions) Conduct in-depth interviews with vaccinators, clients, and supervisors and other key stakeholders) to understand perceptions about the benefits of ZM and effects on immunisation service delivery (decision-support algorithm, registry, SMS alerts and reminders)

Study Aim 2 (Registry coverage). Determine proportion of children amongst those eligible at a population level contained within the ZM registry
Objective 2.1 Model estimated number of children eligible for vaccination in study area over time using census data by district based on the ZM implementation period per district from 2017 to 2019 in alignment with MICS 6 from 2018-2019 and MICS 5 in 2014
Objective 2.2 Draw from ZM system generated data to determine the number of unique children contained within ZM vaccination registry
Objective 2.3 Conduct in-depth interviews and observations with vaccinators, clients, and supervisors (and other key stakeholders) to understand their views on differences in registry coverage observed and effects on uptake of immunisation services

Study Aim 3 (Data quality, use). Determine the availability, use, and quality of ZM data across key stakeholder groups
Objective 3.1 Conduct secondary analyses of system generated data, reports and dashboards to determine frequency of ZM data use by supervisors, managers, and Government staff at all levels.
Objective 3.2. Conduct secondary analyses of system generated data to determine data accuracy, completeness, and timeliness of entry by clinic, and provider characteristics.
Objective 3.3 Conduct in-depth interviews with key stakeholders at the district and provincial levels as well as ZM staff to understand differences in newly available data (disaggregated gender data, geographical data, GIS analysis, vaccinator monitoring data) and data use patterns, perceptions on link between data use and immunisation coverage, completion, and timeliness.
Objective 3.4 Conduct direct observations of immunisation services to understand the broader context within which implementation is occurring and to identify barriers to data entry and use.

Study Aim 4 (Impact): To determine whether ZM usage (dose response high use, moderate use, and low use) in 27 districts of Sindh province is associated with significant differences in the proportion and timeliness of children 12-23 months fully immunised (BCG, DTP3, IPV/OPV3, Measles1) from 2014 to 2019.

Objective 4.1 Compare the proportion of children 12-23 months whose caregivers report receiving (both reported and from card) BCG, DTP3, IPV/OPV3, and Measles1 immunisation in MICS-6 2018-19 to those who reportedly received BCG, DTP3, IPV-1/OPV3, Measles1 in MICS-5 2014 (full immunization).

Objective 4.2 Compare the proportion of children 12-23 months who did not receive DPT 1 between MICS-6 2018-19 and MICS-5 2014 (zero dose vaccination).

Objective 4.3 Compare the proportion of children 12-23 months whose caregivers report receiving on time (from vaccination card) BCG, DTP3, IPV/OPV3, and Measles1 immunisation in MICS-6 2018-2019 to those who reportedly received BCG, DTP3, IPV-1/OPV3, Measles1 in MICS-5 2014 (timeliness).

Study Aim 5 (Impact). To determine whether ZM implementation in 27 districts of Sindh province is associated with significant differences in the proportion of children 12-23 months in the poorest and poorer socioeconomic strata (and other dimensions of equity) fully immunised (BCG, DTP3, IPV/OPV3, Measles1) from 2014 to 2019.

Objective 5.1 Compare the estimates of zero dose immunisation, full immunization, and timeliness of immunisations MICS- 6 2018-2019 and MICS 5 2014 across the wealth quintiles, by the child's gender, levels of mother's / father's education, and other sociodemographic characteristics.

Study Aim 6 (Impact). To determine the incremental cost effectiveness of ZM as compared to status quo in 27 districts of Sindh province from a program perspective from 2014 to 2019.

Objective 6.1 Using an ingredients approach and drawing from budget and expense summary by category for the calendar year 2019, estimate the economic costs of ZM implementation, including program development, start-up and on-going implementation.

Objective 6.2 Draw from MICS analyses to determine incremental changes in coverage for individual vaccines (BCG, DTP3, IPV/OPV3, and Measles1) for the calendar year 2019.

Objective 6.3 Use the lives saved tool to model the incremental lives saved associated with changes in immunisation outcomes for the calendar year 2019 as compared to 2014

Objective 6.4 Estimate the incremental cost per life saved and cost per Disability Adjusted Life Year Averted of ZM implementation in calendar years 2019-20 versus status quo of 2014 (pre-implementation)

Objective 6.5 Conduct probabilistic sensitivity analyses to identify key cost drivers and assess uncertainty.

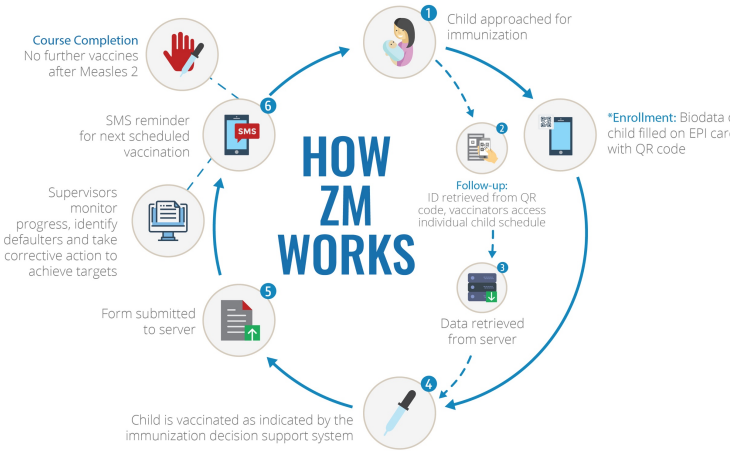
III. Methods

Program description

ZM is a digital health intervention comprised of various interventions including:

1. web-interface for data visualisation, mobile based data entry and access for vaccinators,
2. geo-spatial data for vaccination events,
3. 2-way interactive SMS reminders for parents/caregivers,
4. call centre to answer queries of parents/caregivers,
5. offline mode to work in areas of poor connectivity,
6. child registry for enrolling newborns or never-vaccinated children,
7. immunization decision support system (iDSS) to guide vaccinators on routine and catch-up immunizations,
8. defaulter reports for vaccinators,
9. gamified videos for training vaccinators,
10. AI based predictive analytics to identify children high likely to drop out.

Figure 1. Overview of ZM



The android application is used to capture data when beneficiaries arrive at primary health care facilities for immunisation services. The child's biodata, including the name, address, and date of birth are filled on the expanded program for immunisation (EPI) card and entered into the application at the time of enrolment linked to a QR code[1]. During follow-up visits, the child's ID can be retrieved by scanning the QR code, data are retrieved from the server giving the vaccinator access to individual child's vaccine schedule. The child is then vaccinated and their data on services received inputted into the ZM app which is submitted to the server. To remind caregivers of when they need to next visit the clinic, text message reminders are sent up to 3 automatic personalized SMS reminders a day before, on the day of, and six days after the scheduled immunisation date (if the child failed to show up for his appointment). A child is considered to have completed the full course of immunisations after the second dose of measles. All data inputted into the ZM app are collated on a central web-based dashboard which supervisors can use to monitor progress, identify defaulters, and take corrective action to achieve targets.

Theory of change

Figure 2 outlines the theory of change for ZM. Green boxes depict programme activities by level of the health system from beneficiaries, providers, managers, implementation support from the program, and district/ provincial level. Programme activities lead to outputs, outcomes, and ultimately impact -- depicted in varying shades of pink to red. Assumptions underpinning the movement between boxes are highlighted in yellow. Quadrants of the theory of change are shaded to link key components to (a) programme initiation, (b) coverage, (c) data quality and use, or (d) impact; each of which has associated aims and objectives.

Study design

This is a mixed methods, effectiveness study. Impact will be assessed using a pre/post study design which draws upon UNICEF's Multiple Indicator Cluster Surveys published in 2014 (MICS-5) and 2018-19 (MICS-6). Alternative study designs, including experimental or quasi-experimental designs such as a

[1] **QR Code** is a two-dimensional version of the barcode, typically made up of black and white pixel patterns

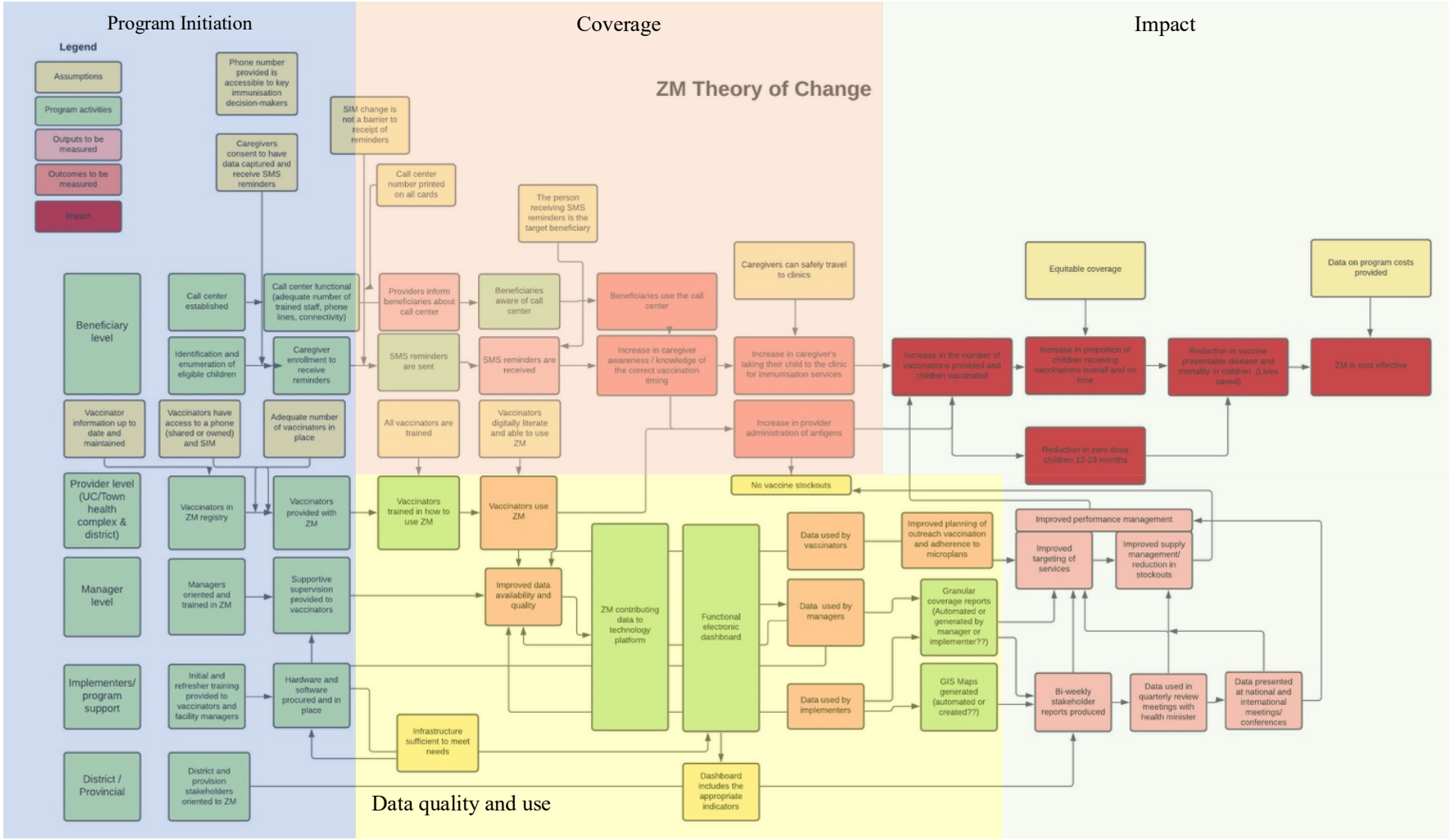
Randomized Controlled Trial (RCT), were deemed infeasible given the absence of control area. Efforts to assess impact will be complemented by qualitative research (direct observations and in-depth interviews) and secondary analyses of system generated data to assess performance and data quality and use.

Study setting

As of February 2020, ZM had scaled to 27 of 29 health districts in Sindh. (ZM was implemented in the last two districts in Sindh after February 2020.) All facilities registered in ZM will be included in the study. Secondary analyses of system generated data from 2014 to 2019 in alignment with MICS 5 and MICS 6 will be carried out across all 27 districts. Primary data collection activities will be conducted in 12 districts whose selection will be based on a combination of vaccinator performance and immunisation coverage. While metrics for assessing performance will be finalised through stakeholder consultation, it is tentatively envisioned that secondary analyses of system generated data on vaccinator ZM app use (e.g. frequency of uploads; proportion of trained vaccinators active within the last 2 weeks) will provide a foundation for stratifying vaccinators and in turn districts into categories of high and low performers. Estimates of immunisation coverage will be assessed using MICS data and thresholds for high and low performance determined in consultation with the study team. Once strata are defined, up to 12 clinics (4 urban, 8 rural) will be randomly selected based on a combination of performance indicators i.e. implementation of ZM (High users vs. low users) and immunisation coverage (High vs. low). This stratification will make use of the immunisation coverage data from the surveys (MICS and PDHS) as well as the effective usage of ZM (from system data). The hypothetical strata could be the following:

- High ZM use and high Immunisation coverage
- High ZM use and low Immunisation coverage
- Low ZM use and high Immunisation coverage
- Low ZM use and low Immunisation coverage

Figure 2. Theory of Change



Data collection

Table 1 summarises the data sources by study aim. The research is planned to be carried out in 2021-2022 depending on COVID-19 and feasibility of primary, in-person data collection. Secondary analyses of system generated data will focus on four sources of data (1) ZM registry data; (2) data on vaccinator engagement with the ZM app, including frequency and duration of use; (3) call data records of alerts and reminders; and (4) stakeholder engagement with dashboards. Access to these data will be facilitated by the IRD team.

In-depth interviews will be conducted with stakeholders, including caregivers, vaccinators, supervisors, district and provincial managers. Among caregivers, in-depth interviews will focus on their perceptions of ZM as part of the immunisation service delivery experience as well as their experiences with SMS reminders and the call centre. Among vaccinators, in-depth interview guides will include domains on (1) perceptions of ZM including call centre, registry, decision-support algorithm, and alerts and reminders; (2) factors underpinning differences in ZM coverage/ uptake; and (3) barriers and facilitators to data quality and use, including understanding differences in ZM coverage observed. Among supervisors, in-depth interview guides will include the experiences, perceived benefits and challenges of ZM on vaccinator supervision with a targeted focus on supervisor dashboard and reports and the contribution of ZM within the overall EPI programme. Where appropriate interviewers will probe on domains related to (1) perceptions of ZM including call centre, registry, decision-support algorithm, and alerts and reminders; (2) factors underpinning differences in ZM coverage/ uptake; and (3) barriers and facilitators to data quality and use, including understanding differences in ZM coverage observed. Among district and provincial managers, in-depth interviews will include domains on (1) perceptions of ZM and role within the EPI Programme; and (2) data quality and use.

Direct observations of vaccinations will be conducted as part of facility visits and occur over a one day window per facility and aim to facilitate improved understanding of the health systems context, and barriers/ facilitators to ZM app use, SMS registration, and call centre uptake. Data collection activities will entail the capture of detailed minute by minute activities of vaccinators with a specific focus on their use of ZM as part of their immunisation service delivery activities.

The economic costs of ZM will be estimated from a programme perspective for a 5-year analytic time horizon (2017-2019). Programme costs are defined as the costs associated with start-up and ongoing implementation. These will be captured using an ingredients approach based on programme activities, drawing from ZM EIR financial data related to start-up and implementation. Incremental changes in coverage will additionally be used in the lives saved tool (LiST) to model the incremental lives saved attributed to ZM.

Table 1. Summary of data sources and needs by study aim

Study aims		Data source	Data needs
1	ZM Initiation: barriers and facilitators	In-depth interviews with vaccinators, clients, and supervisors	Understand perceptions related to how clients, vaccinators, and supervisors perceive the benefits of ZM and how this effects immunisation coverage, completion, timeliness and equity
		System generated data: Provider profile, app use	Provider uploads
		Program records on training	Proportion of eligible vaccinators trained by the programme
		Government records on number and profile of health facility staff, including vaccinators	Number of vaccinators, number of overall facility staff

2	Registry coverage	Census data	Model estimated number of children eligible for vaccination in study area over time using census data
		System generated data: ZM registry	Determine the number of children contained within ZM vaccination registry
		In-depth interviews with vaccinators, clients, and supervisors	List of providers / clinics and ZM registry coverage; sampling will be stratified by low/ mid/ high coverage sites
3	Data quality, use	System generated data: ZM registry, reports and dashboards	Determine frequency of ZM data use by supervisors, managers, and Government staff at all levels
		System generated data: ZM registry	Determine data accuracy, completeness, and timeliness of entry by clinic, and provider characteristics
		In-depth interviews with key stakeholders: Union Council, district and provincial levels, ZM staff	Differences in data use patterns, perceptions on link between data use and immunization coverage, completion, and timeliness.
		Direct observations of immunization services	Understand the broader context within which implementation is occurring and to identify barriers to data entry and use
4	Impact on immunisation	MICS-5 2014 and MICS-6 2018-2019	Compare the proportion of children 12-23 months who were fully immunised in MICS-6 vs.MICS-5 Compare the proportion of children 12-23 months who did not receive DPT 1 (zero dose) in MICS-6 vs.MICS-5 Timeliness of full immunisations in MICS-6 vs.MICS-5
5	Equity	MICS-5 2014 and MICS-6 2018-2019	Compare the estimates of zero dose immunisation, full immunization, and timeliness of immunisations between the two surveys across the wealth quintiles, by the child's gender, levels of mother's / father's education, and other sociodemographic characteristics.
6	Cost effectiveness analysis	ZM EIR financial data	Programme costs associated with start-up and implementation of ZM from 2017-2019
		Lives Saved Tool	Model the incremental lives saved associated with changes in immunisation outcomes for the calendar year 2019 as compared to 2014

Sampling

Primary research will focus principally on in-depth interviews in health facilities and associated district health offices with direct observation to document the immunisation service delivery environment and how ZM is used by vaccinators as part of the immunisation service delivery process. Table 2 summarises the sampling by target respondent.

Table 2. Sample size by activity and respondent type [N=~90 key informants]

Study population	Description	Inclusion	Exclusion	In-depth interviews
Caregivers of children <2 yrs	Individuals who come into facilities to have their children vaccinated	• >=18 yrs of age • Consent to participate • Consecutive sampling with an purposive sampling effort to include equal numbers of male and female caregivers	• <18 yrs •	2 per facility N=24 caregivers
Vaccinators	Individuals who have been trained to use ZM as part of immunisation service delivery activities	• Where possible equal numbers of male and female vaccinators	• Does not consent	N=36 vaccinators
Supervisors	Supervisors of vaccinators who are working in selected facilities	• Where possible equal numbers of male and female supervisors	• Does not consent	N= 12 supervisors
District level EPI Managers/ personnel	District managers in selected districts responsible for the EPI programme and EPI-related data management and use	• Where possible equal numbers of male and female managers	• Does not consent	N=10 district EPI managers
Provincial EPI and/ or Data focal person	Provincial leadership responsible for EPI Programme and/or EPI-related data use	• Where possible both male and female Provincial representatives	• Does not consent	N= 3 Provincial representatives
ZM implementation and data teams	ZM leadership and staff familiar with start-up and implementation of ZM and use of ZM data	• Where possible both male and female ZM leadership and implementers	• Does not consent	N= 5 ZM reps managers, implementers, trainers, data team reps

Recruitment

For each component of the study, the human subjects are employed by Government of Sindh and/or IRD or are caregivers of children brought in for immunisation and enrolled within the ZM system. They will be associated with districts and facilities prioritized through the quantitative analysis process segmented as follows. The target will be 1 district per category with 3 facilities per district for an

estimate of 12 facilities and 3 vaccinators per facility and their associated supervisors and district health managers.

- High ZM use and high Immunisation coverage
- High ZM use and low Immunisation coverage
- Low ZM use and high Immunisation coverage
- Low ZM use and low Immunisation coverage

District EPI teams in prioritised districts will be approached to obtain consent to engage with facilities, vaccinators, clients, supervisors, and those who use ZM data in their areas as part of the study.

A trained Gallup team of enumerators will reach out to selected facilities and/or district office to coordinate research activities providing information related to the overall purpose of the study, anonymity of the respondents, time commitment, and how the information obtained will be used and shared. Afterwards, each facility and/or district office will be asked to give time for a formal meeting in which a letter from the relevant authority will also be shown and time for interviewing or accompaniment as well as rules for engagement would be finalized with the respondents.

The survey team will include a provincial coordinator, local supervisor, and interviewers. Supervisors and data collectors will both be roughly equally male and female, acknowledging that the majority may be male due to low proportion of female vaccinators and supervisors. The research team will be at least undergraduate educated and able to speak Sindhi and Urdu language as this is the language most comfortable across the survey intended area. Most of the researchers would have over 5 years experience in doing this sort of research and will be thoroughly trained prior to data collection.

Table 3. Recruitment strategy for qualitative research

Study population	Recruitment strategy
Caregivers of children <2 yrs	Caregivers will be invited to participate in an exit interview after they have come for vaccination services in selected facilities.
Vaccinators	Selected facilities will be invited to participate through an introduction by IRD and a letter from the Provincial EPI Programme and the associated District EPI Manager. Vaccinators in those facilities will be invited to participate in the study.
Supervisors	Supervisors associated with the selected facilities and vaccinators will be invited to participate through an introduction by IRD and letter from the Provincial EPI Programme and the associated District EPI Manager.
District	Selected districts will be approached through an introduction by the IRD team and a letter from the Provincial EPI leadership.
Provincial	The research team will work with IRD to identify the most appropriate Provincial-level EPI Programme and/or Data representatives for in-depth interviews.
Program	The research team will work with IRD to identify the most appropriate leadership and management team members for in-depth interviews.

Data analysis

Qualitative analyses

Initial analyses of in-depth interviews will occur through daily debriefings which are embedded into the schedule for data collection. Debriefings will yield preliminary findings which will be in turn, presented during a Workshop with the full research and implementation team. Debriefings will be carried out using a framework, in google sheets wherein the rows consist of the domains explored in the IDIs and the consent scripts. Each respondent will be assigned a row in the spreadsheet and notes from the interview will be used to fill out the cell related to each respondent's statements for each question/domain in the interview. This will enable daily examination of response trends, themes, and areas where revision to the interview guides are required. Audio recordings will be transcribed and translated into English. A Codebook will be developed to code the transcripts in preparation for analysis in Nvivo. The first ten interview transcripts will be coded by two separate qualitative analysts for consistency and to clarify and updates needed to the Codebook. The analysis will be conducted using Grounded Theory in Nvivo. The results will be synthesized and summarized with illustrative quotes alongside relevant study aim quantitative analyses.

Impact analysis: MICS

The key indicators of programme impact are coverage of antigens, full immunisation, timely immunisation and zero dose (coverage of DPT1 in children 6 weeks – 23 months) . Estimate for each indicator will be compared for MICS 2014 and MICS 2018-19. Program impact will be the difference in estimates before intervention (MICS 2014 data) and after intervention (MICS 2020 data). Sub-group analysis for heterogeneity of impact will be assessed by stratifying on gender, division, area, mother's education, wealth index quintile. Equity of impact will be assessed across the wealth quintiles and educational levels using standard measures like Relative concentration index and Slope Index of Inequality. Estimates of impact will also be estimated at the district level and regressed upon measures of program implementation strength calculated based on process indicators.

Coverage

Coverage will be assessed in the context of the ZM app's registry and aim to determine the proportion of children amongst those eligible at a population level contained with the ZM registry. Census data will be used to model the estimated number of children eligible for vaccination in study area over time. System generated data on the number of children who have biodata entered into the ZM app will serve as an estimate of the number of children reached by vaccinators and the program. Elsewhere analyses have already been conducted on the SMS component of ZM and hence will not be repeated here. Data used for the analyses will be aligned with the data used by Sindh EPI and applied to the ZM system for target setting.

Data use, quality

To assess data quality and use we will conduct secondary analyses of system generated data on the ZM registry, reports, and dashboards. Details on the characteristics of vaccinators (age, gender, duration of time as provider, education) and other key stakeholders will be provided by IRD, merged with system generated data, and the data file anonymized before granting access to the local evaluation team. Data quality analyses will aim to assess the accuracy, completeness, and timeliness of data entered into the ZM app by providers. Providers will be stratified into high/mid/low data quality and high/mid/low data use categories. Determinants of high data quality and high data use will be assessed by provider characteristics and clinic. Among district and provincial stakeholders, data on the digital footprint of engagement with dashboards will be used to assess high/mid/low data use categories.

Program initiation

Program reach will be defined in terms of the proportion of eligible vaccinators trained by the programme and calculated based on programme records on vaccinator training and Government records on numbers of vaccinators. To explore user engagement, we will estimate the proportion of vaccinators trained to use ZM

who upload details for at least 1 client in Sindh. Additional thresholds for engagement may be determined based on available system generated data.

Cost-effectiveness analysis

An ingredients approach will be used to identify the costs associated with key project activities over the life of the program. Costs will be categorized into capital (costs with a life expectancy of >1 year) and recurrent costs, with the former annualized over the lifetime of the project or life span of the item as appropriate and discounted at 3%. Start-up phase costs will be viewed as one-time activities and similarly annualized over the lifetime of the project. While the full economic costs will be used to generate estimates of cost-effectiveness, we will separately generate and present an estimate of the costs associated with those activities which will be necessary to support ongoing implementation by the government following the transition of the program. Incremental changes in vaccination coverage will be inputted in the Lives Saved Tool and used to estimate lives saved as a result of ZM implementation.

Costs will be adjusted to 2019 USD dollars using consumer price indices and a foreign exchange rate obtained from oanda.com for 2019. Parameter costs and effects will be adjusted to the projected sample population for each of the 5 years of implementation. Incremental costs will be divided by incremental health effects to generate a deterministic estimate of the incremental cost-effectiveness ratio (ICER), expressed as a cost per life saved. To test for uncertainty, one-way and probabilistic sensitivity analyses will be conducted. The latter will be performed in Microsoft Excel using a Monte Carlo simulation with 1000 iterations per analysis. The resulting mean point estimate will be obtained by dividing mean costs by mean effects. The 95% CI for the ICER will be presented based on percentiles. A cost-effectiveness plane and cost-effectiveness acceptability curve will be used to calculate the probability that the intervention would be cost-effective for each of the several standard thresholds of cost-effectiveness. Cost-effectiveness will ultimately be ultimately determined according to thresholds set forth by the Commission for Macroeconomics and Health and World Health Organization.

VI. Data Custody, Management, Security, and Confidentiality Protections:

The Principal Investigator is responsible for Data Protection and Use throughout the life of the study. A data management and security plan will be developed at inception for all primary qualitative data collected. This data management and security plan will ensure adherence to data security protocols including the password protection and anonymisation of data. Primary data collected through the qualitative field research will be stored for three years after study completion. For secondary analyses of system generated data, the project team will similarly only work with anonymised data provided by IRD and ensure adherence to IRD's existing data protection and security protocols. Analysis of ZM system data will be conducted at a designated terminal within the IRD office in Karachi. No personal identifying information will be collected or used during the course of the study. Additional complementary analyses and the cost-effectiveness analyses will be conducted offsite.

The technical contact for a Data Security plan is Mr. Manzer Ehsan (IT Manager at Gallup Pakistan).

VIII. Direct Personal and Social Benefits:

There are little to no risks to participating in the study. Appropriate precautions to limit risk of COVID-19 will be followed according to recommendations made by the Pakistan and Sindh health authorities.

Benefits: There are no direct benefits to the participant, however, there are significant benefits to society. Data from this activity will be shared with key stakeholders and policy-makers to inform improved policies and programs.

This study will evaluate the impact of a provincial digital health intervention (which can be considered for national and international expansion given the large population of Sindh) on the Expanded Programme of Immunisation (EPI). There is little evidence of similar studies in the peer-reviewed literature to inform policy or practice, especially research which includes a health economic component. Upon receipt of IRB approval, the researchers will register the study and upon completion of the study the findings will be shared with the scientific community through one peer-reviewed journal article with a summary highly synthesized presentation of findings. A comprehensive report with all study findings will also be developed and shared to inform future scale up and replication of ZM and similar EIR and mHealth interventions.

The study will provide evidence on the impact and cost-effectiveness of ZM, which will increase knowledge of the benefits of EIRs as part of a suite of digital health interventions and contribute to the evidence base related to digital health. It is expected that the study will contribute to decisions to implement EIRs and their design in future. The results will inform planning for implementation of systems supporting large-scale immunisation programmes by Gavi, the Vaccine Alliance, globally. The results of this study will be presented to the Ministry of Health of Sindh and the national Ministry of Health in Pakistan. The results will also inform decisions on investment in ZM and EIRs in Pakistan and elsewhere.

IX. Payment or Token of Appreciation:
There will be no monetary or non-monetary tokens provided to study participants in this research.

X. Study Management:

The field research will be led by PI- Sara Gilani of Gallup, Pakistan. She is leading the qualitative component and primary data collection for the study. Abacus, Pakistan under the guidance of Hashim Riaz with support from Khadijah Khan is leading the secondary data analysis for the study. To advise on the analysis of system data and MICS survey data and health economic analyses, HealthEnabled is coordinating the study under the guidance of Patricia Mechael and has engaged Dr Diwakar Mohan and Prof Amnesty LeFevre from Johns Hopkins Bloomberg School of Public Health (JHSPH) through the HealthEnabled expert network as advisors to provide guidance to Abacus for the secondary data analyses. IRD team including Dr. Mubarak Shah, Dr. Anokhi Ali Khan, Ms. Danya Arif and Dr. Subhash Chandir have been involved as part of the research design process and will be actively engaged in protocol finalization, the research implementation, including facilitating introductions, providing access to ZM system data and relevant financial data, and participating in in-depth interviews, review of preliminary results, and publications. Gavi, the Vaccine Alliance, which funds both the implementation and the evaluation will be engaged as an observer throughout the research process. To promote transparency in publication of results the following proposed authorship by institution: JHSPH for overall research design; Gallup and Abacus for research analysis and implementation; IRD for study design and implementation and HealthEnabled for research coordination. The authorship will be based on ICMJE guidelines, while author line will be mutually decided by all partners.

A. Field Research Management

Gallup, Pakistan will train enumerators in human subjects research protections with emphasis in communication skills, the survey protocol and methods including household and participant selection and replacement for face-to-face interviews, standard operating procedures including obtaining informed consent, using the electronic data collection and calling systems, research ethics, and COVID-19 prevention. Interviewers will also be trained to make referrals for people who have experienced violence and to COVID-19-related testing or care services. Moreover, interviewers and supervisors will be given classroom training using a comprehensive and detailed interview and

supervisor guide, wherein the interviewers will read the questionnaire along-with the instructions and the trainer will explain any important/sensitive issues. The PI from Gallup will be involved in the training of the researchers who will carry out the interviews and observations.

B. **Recordkeeping:**
Data will be reviewed by supervisors for internal consistency checks and preparation for analysis. Gallup will be responsible for transcription of interviews into text and producing a clean finalized dataset and supporting documentation, including cleaning program and codebook. Electronic data will be collected and stored on secure tablet computers with multiple layers of security, requiring log-in at the computer and application level. The data will be backed- up daily on external media, encrypted and stored in a secure environment. No personal identifying information will be collected.

C. **Reporting Unanticipated Problems/Adverse Events (AEs) to the IRD IRB**:
There is a small steering committee comprising of both PIs as well the Co-PIs (see above). The steering committee will review all adverse events reported from the supervisors and/or team members. An email and then a phone call would be made to IRB within 10 days of the steering committee confirmation that an adverse event has occurred.

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