Evaluating the impact of chatbots on flu and COVID-19 vaccination in Tucumán

PICOS Statement

What is the problem?	Despite overwhelming medical evidence on the protection offered by second, third and fourth COVID-19 vaccine doses, uptake of these doses remain low despite available supply. Similarly, despite evidence on the protection offered by the influenza (flu) vaccine, vaccine uptake remains low despite available supply. There is particularly high risk for people living with risk factors ¹ and people older than 65.
Population: Who are the participants?	Adult citizens in the province of Tucumán in Argentina who are eligible for a next dose of the COVID-19 vaccine and/or the government-subsidized flu vaccine with an active Whatsapp phone number.
Comments	People without phone numbers in administrative databases will be excluded from our sample given phone-based message delivery.
Intervention: What are we doing?	 Participants will be sent interactive and personalized Whatsapp chatbot messages informing them they are eligible for the next dose, sharing practical information on where and when to get vaccinated, providing planning prompts and enabling them to set their own reminders to get their next dose of the COVID-19 vaccine on a convenient date. The three treatment arms are described below: T1. Chatbot: Implementation Intentions: Participants are given the opportunity to interact with a Whatsapp chatbot that: Sends them a personalized Whatsapp message reminding them to get their next COVID-19 and/or flu vaccine Prompts them to plan a day and time to receive their vaccine(s) Reminds them a day before their selected vaccination day T2. Chatbot: Reduce Frictions (Health Center Locator): Participants are given the opportunity to interact with a Whatsapp chatbot that includes T1 functionalities and: Helps them locate a health center where they can receive their vaccine(s) Reminds them a day before their selected vaccination day, including Google Maps link to get from their current location to the selected health center. T3. Chatbot: Messenger Effect (Video: Popular Personality): Participants are given the opportunity to interact with a Whatsapp chatbot that includes T2 functionalities and: Sends a video featuring the popular band La Mosca from Argentina, to complement the Whatsapp messages.
Comments	

¹ The risk groups eligible for the flu vaccine include people from 2 years to 64 years of age who have conditions such as respiratory and heart diseases, diabetics, congenital or acquired immunodeficiencies, oncohematological patients and transplant recipients, people with chronic renal failure on dialysis, severe developmental delay in children under 18 years of age, genetic syndromes, neuromuscular diseases with respiratory compromise and severe congenital malformations, cohabitants of premature infants, among others. https://www.argentina.gob.ar/salud/vacunas/novedadantigripal

Comparison:	We will conduct a randomized controlled trial (RCT) using a simple randomization with a treatment assignment using individuals' pseudo-ID (created based on DNIs <i>–Documento nacional de identidad</i> or National Identity Document–). Participants will be randomized to one of the 3 treatment arms described above or the control group.			
	The control group will be: C. Pure control: Participants are not sent any of the messages or interventions in arms T1-T3.			
Comments	For the primary analysis, we will make a unique comparison between the control group and the pooled sample including T1, T2 and T3. For the secondary analysis, we will apply two comparisons: (1) comparing T1 and T2, and (2) T2 and T3. This is described in detail in the Analytical Strategy section. (See <u>09 / Statistical Approach</u>)			
Outcome(s):	Primary outcome: 'Next dose' COVID-19 or flu vaccination rate (binary – did the individual receive at least one of the vaccines for which they are eligible? – yes/no) within four weeks of the initial message being sent to them (or the hypothetical initial message send date for control group members based on randomization. See <u>here</u> for more details.)			
	 Exploratory outcomes: Click-through from initial 'push' message to subsequent chatbot messages (in chatbot treatment arms); 'Next dose' COVID-19 or flu vaccination rate within four weeks (as described in primary outcome) across pre-defined age brackets (sub-group analysis) 'Next dose' COVID-19 or flu vaccination rate within four weeks (as described in primary outcome) across risk factor status (sub-group analysis) 'Next dose' COVID-19 vaccination rate within four weeks (as described in primary outcome) across risk factor status (sub-group analysis) 'Next dose' COVID-19 vaccination rate within four weeks (as described in primary outcome) across vaccine dose eligibility (sub-group analysis) Flu vaccination rate within four weeks (as described in primary outcome) across vaccine dose eligibility (sub-group analysis) 			
Comments	Some research participants may not be able to receive a 'next dose' vaccination due to a recent COVID-19 infection. Given the lack of timely and identifying data on COVID-19 infection, we practically cannot exclude these individuals from being included in the trial. If and when individuals disclose to the chatbot a recent COVID-19 infection, they will still be included in the analysis so as not to introduce selection bias. For the same reason, we will include in the analysis treatment group participants for whom a message cannot be successfully delivered, by imputing a hypothetical message delivery date based on their assigned batch.			
Setting:	Tucumán province in Argentina (remote delivery)			
Comments				

Contents

Administration	1
PICOS Statement	2
Background and Intervention	4
01 / Purpose	4
02 / Approach & Challenge	4
03 / Intervention Design	4
Evaluation Design	5
04 / Study Design	5
05 / Research Question	5
06 / Assignment	5
07 / Sample & Setting	6
Analytical Strategy	8
08 / Outcomes	8
09 / Statistical Approach	8
10 / Power	10
Implementation	11
11 / Trial Procedure	11
12 / Implementation Risks	11
13 / Ethical Considerations	12
14 / Data Requirements	13

Background and Intervention

01 / Purpose

This project aims to increase immunization behaviors amongst the adult population from Tucuman who are eligible for influenza vaccines and COVID-19 booster doses.

This project builds off a previous successful development and evaluation of a Whatsapp chatbot promoting COVID-19 vaccination behavior in the province of Chaco, Argentina. The Chaco chatbot was assessed through an RCT and found to cause an increase in actual vaccination greater than 3x compared to not receiving a message and almost 2x compared to receiving a static message.

Social Impact: Increased COVID-19 and Influenza vaccination greatly reduces the risk of death or hospitalization from COVID-19/Influenca and improves health outcomes across society.

02 / Approach & Challenge

We are focused on vaccination behaviors, as measured by the vaccinations database from Tucuman. To promote vaccination behaviors, we are addressing barriers related to low risk perception, intention-action gaps, and lack of information. These barriers are summarized at a high level below.

This study is guided by the <u>Health Belief Model</u> – as it relates to people's motivations to seek vaccination to avoid disease – and on Noel Brewer's vaccination uptake model below.



Figure 1. Health Belief Model

Source: The BeSD expert working group. Based on: Brewer NT, Chapman GB, Rothman AJ, Leask J, and Kempe A (2017). Increasing vaccination: Putting psychological science into action. Psychological Science for the Public Interest. 18(3): 149-207

Identified barriers:

Our desk-based research and fieldwork identified behavioural barriers specific to the local context.

- Perceived low risk from Covid. In focus groups and interviews with residents and healthcare workers, we identified very low perception of risk as a key barrier to vaccination. In early 2022 case numbers fell to very low levels in Argentina, overall vaccination rates were high and restrictions ended; according to interviewees this contributed to a feeling that the pandemic was ending and getting first or additional vaccinations wasn't necessary.
- Lack of any reminder service. Currently, residents do not receive personalized communication or reminders from the local government or health services with information about when they are eligible for their next dose or prompting them to complete their set of vaccinations.
- **Confusion over how and when to get the vaccine**. After the main mass-vaccination drive ended, pop-up and vaccination-only sites were closed down, and vaccination became available primarily in hospitals and health clinics.

How our intervention addresses the barriers identified:

- Lack of any reminder service: First, the chatbot provides personalised information to let users know which dose they are now eligible for, based on the dates of the doses of their previous vaccinations. Second, whilst the core chatbot messages themselves act as a prompt to get vaccinated, the chatbot also allows users to set their own reminder for a convenient date that they want to get the vaccine. This helps deal with an inattention barrier (i.e., getting vaccinated slips your mind). There is strong evidence demonstrating the use of mobile message reminders to increase uptake of vaccines, including the influenza vaccine and COVID-19 vaccine. A Cochrane review of 55 studies found that SMS messages increase relative uptake by 29% on average. In addition, the reminder we are using gives the user the agency to set a reminder for the day before a date that is convenient for them.
- Low visibility of vaccination centers: The chatbot enables users to find their nearest vaccination center(s). To do this, the chatbot has a location function where users can share their current location (either by "dropping a pin" in WhatsApp, or typing their home postcode), after which the chatbot will provide a list of their nearest center(s), how far away they are, and directions for how to get there (in a later reminder message). This addresses the friction cost of having to go to an outdated government website and find the information yourself, and removes the risk that the information will be incorrect. The chatbot also provides opening hours for each centre.By combining a reminder service with an information service about locations of vaccine centers, the chatbot addresses the fact that residents may not otherwise know where to get vaccination and receive no prompts from their environment.

03 / Intervention Design

The intervention is a vaccine messaging chatbot that will be sent to adult citizens in the province of Tucumán in Argentina who are eligible for the next dose of the COVID-19 vaccine and/or the government-subsidized flu vaccine with an active Whatsapp phone number.

Once the intervention is launched, equal numbers of initial messages will be pushed daily across all experimental arms for 12 days². The order in which participants are sent messages will be prespecified during the random assignment process. (This process is described in more detail in the <u>Implementation section</u>.)

In Table 1 below, we describe the control condition and the 3 treatment arms. To see the full messaging flow for all arms, see <u>Appendix II</u>.

CONDITION	DESCRIPTION				
C. Control	Participants are not sent any message				
	Note: Following the trial period, if any messages are found to be effective at encouraging vaccination, these individuals would be sent the most effective message.				
T1. Chatbot: Implementation intentions	 Participants are sent a Whatsapp chatbot that Send them a personalized Whatsapp message reminding them to get their next COVID-19 and/or flu vaccine. See <u>Personalization of Messages</u> section for more details. Prompts them to plan a day and time to receive their vaccine(s) Reminds them a day before their selected vaccination day 				
T2. Chatbot: Reduce Frictions (Health Center Locator):	 Participants are sent a Whatsapp chatbot that includes all T1 functionalities AND Helps them locate a health center where they can receive their vaccine(s) Reminds them a day before their selected vaccination day, including Google Maps link to get from their current location to the selected health center. 				
T3. Chatbot: Messenger Effect (Popular Personality)	 Participants are sent a Whatsapp chatbot that includes all T2 functionalities AND Sends a video by the popular band La Mosca from Argentina, to complement the Whatsapp messages. 				

Figure 2 below visually represents the information in the table above for a research participant who is only eligible for the next dose of the COVID-19 vaccine. The content of the flow will vary slightly depending on vaccine eligibility and health risk factors / age.

² The timeline is subject to WhatsApp approvals.

Figure 2. Structure of intervention design for research participant eligible for the next dose of the COVID-19 vaccine



Personalization of messages

All treatment arms will be pushed a personalized message. For the chatbot treatment arms (T1-T3), this will be the start of their conversation with the chatbot. This message serves to inform the recipient of the purpose / functionality of the chatbot, notify the recipient of their vaccine eligibility, and motivate the recipient to get the vaccine. In Figure 3 below, we identify the ways in which this message is personalized to the individual and tailored based on vaccine eligibility and risk level / age.

Figure 3. Design choices for personalization and tailoring of initial message

The image below shows the first message for an individual assigned to T3. Personalized Message who is eligible for the government-subsidized flu vaccine because they are older than 65.



Across treatment arms, the personalized message that participants are first sent will be tailored based on the vaccine(s) that they are eligible to receive and risk level / age. Table 2 below illustrates the sub-groups that will be sent initial messages tailored to their eligibility.

Table 2. Sub-groups based on vaccine eligibility and population characteristics tomessage personalization

		Population Characteristic						
		Low-risk Risk Factors ³		65+				
Vaccine	COVID-19	Intro message A						
engionity	Flu	N/A (Low-risk & <65 years ineligible for gov't subsidized flu vaccine)	Intro message B	Intro message C				
	COVID-19 & flu	N/A (Low-risk & <65 years ineligible for gov't subsidized flu vaccine)	Intro message D	Intro message E				

The content of the personalized message will vary only slightly across eligibility subgroups. Box 1 illustrates practically how personalized messages are distinct across eligibility subgroups.

Box 1. Example of Personalized Message Distinction

Consider the following hypothetical research participants:

- Raul (T1) eligible for the flu vaccine
- Maria (T2) eligible for COVID
- Paula (T3) eligible for COVID and flu vaccine

³ The risk groups eligible for the flu vaccine include people from 2 years to 64 years of age who have conditions such as respiratory and heart diseases, diabetics, congenital or acquired immunodeficiencies, oncohematological patients and transplant recipients, people with chronic renal failure on dialysis, severe developmental delay in children under 18 years of age, genetic syndromes, neuromuscular diseases with respiratory compromise and severe congenital malformations, cohabitants of premature infants, among others. https://www.argentina.gob.ar/salud/vacunas/novedadantigripal

The personalized message that Raul is sent will be slightly different from the message that Maria or Paula are sent because of differences in their **eligibility**. The personalized message that Maria is sent is also slightly different from what Paula or Raul are sent because of the differences in their eligibility.

See <u>Appendix I</u> to see the specific content of the personalized messages.

Evaluation Design

04 / Study Design

This is a 4-arm individual-level randomized controlled trial (RCT) to test:

- whether sending a vaccination messaging chatbot in Tucumán, Argentina, can increase vaccine uptake amongst adults who have not completed their full COVID-19 vaccination schedule (i.e., not received a second, third, fourth, etc. dose of the vaccine) and/or have not received their annual flu vaccine; and
- 2. the effect of specific chatbot functionalities in achieving this outcome.

05 / Research Questions

To investigate whether chatbot functionalities designed to make the process of getting a COVID-19 vaccination easier, reducing forgetfulness, closing the intention-action gap, and/or boosting motivation can improve COVID-19 and flu vaccination rates.

There are several research questions for this trial:

- **Primary research question:** Does sending a vaccination messaging chatbot increase COVID-19 and flu vaccine uptake over a 4-week period amongst mobile-connected residents of Tucumán?
- Secondary research question: To what extent does sending a message with specific chatbot functionalities enhance any effect on increasing COVID-19 and flu vaccine uptake?
 - Robustness check (exploratory): To what extent does receiving a message with specific chatbot functionalities enhance any effect of increasing COVID-19 and flu vaccine uptake

• Exploratory research questions:

- Is there evidence that the effect of the chatbot and specific chatbot functionalities appear to vary across age groups, by vaccine eligibility (COVID-19 vs. flu), or by whether individuals are judged to be in a high-risk group?
- What is the overall clickthrough rate on the chatbots, and is there evidence that clickthrough rates vary across chatbots with different sets of functionalities?
- <u>Via post-trial qualitative research with a random subset of participants:</u> What were users' perceptions of the personalized message, the chatbot in general, and specific functionalities? How–if at all–did the message / chatbot affect

individuals' decision to get vaccinated? What was the vaccination experience like for individuals?

• **Insight:** If the results of the trial are positive, the Ministry of Health of Tucuman will consider permanently integrating the chatbot flows into their program of vaccination campaigns, pushing vaccination reminders to residents at timely vaccination moments (e.g., start of flu season or when a resident is due for a booster). If we find evidence that certain versions of the chatbot work best for certain subgroups, the Ministry of Health of Tucuman could segment their outreach strategy and deliver the best-performing chatbot for each group.

Null or negative trial results will provide valuable information for government decision-makers to assess the efficiency and efficacy of vaccination communication approaches. If the results of the trial are null, the Ministry of Health of Tucuman could consider integrating a simplified version of the chatbot flow that simply provides information about the vaccine without pushing reminders to reduce monetary costs.

If the results of the trial are negative, the Ministry of Health of Tucuman may conduct additional research to understand what aspects of the intervention were making individuals more reluctant to get vaccinated and avoid such risks in future initiatives.

06 / Assignment

METHOD:	The sample will be split using simple randomization with a treatment assignment using individuals' pseudo-ID. We will use a random number seed to ensure the randomisation is replicable.
STRUCTURE:	Simple
ARMS:	4
UNIT OF ASSIGNMENT:	Individuals (Patient identification number) ⁴
UNIT OF MEASURE:	Individuals

- Linking assignment to outcome: We will merge the outcome data from the vaccination database of Tucuman using the patient identification number variable, which is included in all phone number databases we will use to build our sample and conduct randomization.
- Internal Validity:
 - <u>Excludability</u>: Because the messages / chatbots are fully automated, the only difference in the experience of the participants across experimental arms

⁴ Each individual has a unique patient identification number. This ID doesn't provide any sensitive information from the individual.

should be the differences in the planned chatbot messages. In addition, outcome data for participants across experimental arms will be recorded identically through standard administrative processes.

- <u>Blinding and Masking</u>: Although participants will be aware of the motivational message they have been exposed to, and whether they have been exposed to the chatbot, prior to outcome data collection, we do not expect many to be aware that they are in a trial where different participants are exposed to different conditions. Participants' treatment assignment will also not be known to those involved in recording the outcome data.
- Spillovers:
 - Because participants will access the chatbot exclusively through an initial (push) message initiated by the bot, we can strictly control who is sent the intervention and thus minimize the main risk of contamination. Only mobile numbers associated with members of the treatment groups will be able to interact with the corresponding arms.
 - Whilst more than one individual can share the same phone number, we do not believe this poses a major spillover risk for this study. It is possible that individuals in the treatment group know individuals in the control group and show them the chatbot service or share screenshots, but we believe this risk is low. In theory, we could reduce this risk by excluding individuals who live in the same household, but in practice, we will be unable to identify individuals who live in the same household. Importantly, this contamination would likely increase vaccination levels in the Control group, which would bias our estimated treatment effects towards zero, meaning that any effect we do estimate may be considered a lower bound for the true effect of the treatment.

• <u>Attrition:</u>

- We are using an administrative dataset on COVID-19 vaccinations for our outcome measure. Any attrition in this context would result from being unable to match randomized individuals to the vaccination dataset due to reasons other than them not taking up a vaccination within the outcome window.⁵ Individuals may become ineligible to receive a Covid or flu vaccine in Argentina, for example if they get a vaccination in another country, move from Argentina, etc. Our vaccination data set will not be able to tell us this information However, we will not have access to this information in the vaccination dataset, and will mark the individuals as not having received a vaccination. This form of attrition will not reduce the sample size in analysis but could instead slightly bias the primary outcome towards 0. We do not expect any bias to differ systematically between trial arms.
- <u>Compliance</u>

⁵ Note that we are unable to distinguish between cases where the individual did not take up a vaccination - and hence do not appear in the vaccination dataset - and cases where the individual did take up a vaccination but this is either missing from the dataset or cannot be matched back to the randomization dataset due to errors in the DNI variable used for merging datasets.

We can't validate phone numbers ahead of randomization. For this reason, we expect there will be a high percentage of phone numbers that do not have a valid WhatsApp number. Even though they won't receive a message, we will still include them in the analysis.

07 / Sample & Setting

• Sample characteristics:

- \circ $\,$ To define the sample, we will use a combination of 2 datasets:
 - For vaccination data: MoH of Tucuman vaccinations database
 - For phone numbers: administrative health data from Tucumán
- We will exclude all observations that do not meet all of the following inclusion criteria:
 - Is 18 years of age or older;
 - Is a resident of the provinces of Tucumán;
 - Is eligible to receive their next COVID-19 dose⁶ (i.e., 2nd, 3rd, 4th, etc. dose of the COVID-19 vaccination) OR a government-subsidized flu vaccine⁷;
 - Mobile number is valid after following the cleaning steps specified in the <u>Appendix IV</u>.
- Our dataset comprises a total sample of 486,339 observations (i.e., phone numbers in Tucumán in administrative databases provided by provincial Ministries of Health). After exclusions, our sample comprises about 419,251 mobile numbers.
- **Reaching your sample:** We defined our sample using a combination of two datasets (a detailed explanation of this process is described in Appendix IV):
 - MoHT created the telephone database and reviewed it to exclude any duplicates or numbers that appear to be fake. After this process, they queried their vaccination database to identify individuals who meet the vaccine eligibility inclusion criteria defined above and who are at least 18 years old. They merged both datasets and shared the result of this with BIT.
 - 2. BIT exhaustively cleaned the data shared by MoHT: removing duplicates, phone numbers that don't seem correct based on length, and checking a list of exclusions (check Box 3 in Appendix IV).
 - 3. BIT created a random seed to perform randomisation and created a variable indicating treatment assignment. Additionally, based on the random seed, BIT created a treatment order for message batching.

⁶ See Box 2 in Appendix IV for COVID-19 eligibility

⁷ See Box 1 in Appendix IV for flu eligibility

- **Bias in representation:** Our sample will be fairly representative of mobile-connected Argentinian adults who are eligible for a follow-up dose of the COVID-19 vaccine and/or government-subsidized flu vaccine. We list limitations to generalizability below:
 - Because of the inclusion requirement that individuals have an active Whatsapp account, the estimated impact on COVID-19 or flu vaccination *may not generalize to digitally disconnected populations (due to limited access to internet or internet-enabled devices).*
 - Because we are targeting follow-up COVID-19 vaccine doses, the estimated impact on COVID-19 vaccination may not generalize to groups with high reluctance to get vaccinated against COVID-19 (i.e., those who have not had a first dose of the vaccine).
 - Because eligibility for the government-subsidized flu vaccine is conditional on age (65+) or health risk factors, the estimated impact on flu vaccination *may not generalize to younger Argentinians without health risk factors*.
 - Because phone numbers in our databases were provided voluntarily by users willing to receive digital services from governments, the estimated impact on vaccine uptake may not be generalizable to citizens with lower levels of trust in government or with lower levels of awareness and interest in government services.

SAMPLE SIZE	419,251
SAMPLE / ARM:	The sample will be split using simple randomization with a treatment assignment using individuals' pseudo-ID.
	Control: ~104,564 participants
	T1. Chatbot: Implementation Intentions: ~104,564 participants
	T2. Chatbot: Reduce Frictions (Health Center Locator): ~104,563
	participants
	T3. Chatbot: Messenger Effect (Video: Popular Personality):
	~104,564 participants

Analytical Strategy

08 / Outcomes

For outcome measures related to vaccination rates, we measure this over a four week period from when an individual's initial message was sent or hypothetically sent (for the control group) based on randomization. (For more details on the message sending schedule, see <u>here</u>.) We measure vaccination rate over a four week period for the following reasons:

1. To increase comparability of results from the first phase of the project to the current phase;

- 2. To allow enough time to schedule reminders and get the vaccine, considering the practical challenges of getting a vaccine within a shorter period of time (e.g., work constraints, child care, transportation logistics);
- 3. Intuitively, we believe that the effects of the intervention will have faded out by 4 weeks and analysis of the first phase found that of the individuals assigned to the chatbot who established a reminder, the majority set a date within 2 weeks of receiving the initial message.

For the outcome, there are some points we are taking into consideration:

- Some research participants may not be able to receive a 'next dose' vaccination due to a recent COVID-19 infection. Given the lack of timely and identifying data on COVID-19 infection, we practically cannot exclude these individuals from being included in the trial. If and when individuals disclose to the chatbot a recent COVID-19 infection, they will still be included in the analysis so as not to introduce selection bias.
- Additionally, to also avoid selection bias, we will include in the analysis treatment group participants for whom a message cannot be successfully delivered, by imputing the attempted delivery date.
- If there are some people who are randomized, but for whom there is no record of any message sent attempts, we will also impute their delivery date based on their position in the randomisation list. This would occur only in the event that our SMS delivery partner, Botmaker, makes a mistake during implementation.
- For people for whom there are unsuccessful message attempts before successful message delivery, we will use the actual message delivery when constructing the outcome measure.

Primary measure: 'Next dose' COVID-19 or flu vaccination rate

- **Point of collection:** Four weeks after the initial message is sent⁸ (or the hypothetical initial message send date for control group members based on randomization.)
- **Type**: Binary Did the individual receive at least one of the vaccines for which they are eligible?
- Note: We will also conduct subgroup analyses based on age and risk factor

Exploratory measure: Flu vaccination rate (sub-group analysis of flu vaccine eligible participants)

- **Point of collection:** Four weeks after the initial message is sent (or the hypothetical initial message send date for control group members based on randomization).
- **Type**: Binary Did the individual receive the next dose of the flu vaccine for which they are eligible?

Exploratory measure: 'Next dose' COVID-19 vaccination rate (sub-group analysis of COVID-19 vaccine eligible participants)

⁸ In the case of messages that fail to be sent after repeated attempts, we will use the last date in which an unsuccessful attempt was made.

- **Point of collection:** Four weeks after the initial message is sent (or the hypothetical initial message send date for control group members based on randomization.)
- **Type**: Binary Did the individual receive the next dose of the flu vaccine for which they are eligible?

Exploratory measure: Click-through to chatbot messages (in chatbot treatment arms)

- Point of collection: Ongoing throughout chatbot session following initial push message⁹
- **Type**: Discrete, level reached in message flow
- **Rationale:** Descriptively analyze how far in the chatbot flow users progress for each arm

09 / Statistical Approach

Primary Analysis: Chatbots on 'Next dose' COVID-19 or Flu Vaccination Rate

For the Primary Analysis, we will conduct 1 comparison between the control group and a pooled sample including T1, T2 and T3. Table 3 below describes the comparison to be made.

Table 3: Primary comparison on 'Next dose' COVID-19 or Flu Vaccination Rate

	T1	T2	Т3	What is the effect on 'next dose' COVID-19 or flu vaccinations rates of
Control	Hypothesis 1		1	Being sent a WhatsApp chatbot compared to not being sent any message

Secondary analysis: Effect of chatbot functionalities on 'Next dose' COVID-19 or Flu Vaccination rate.

For the Secondary Analysis, we will conduct 2 comparisons and one robustness check. Table 4 below describes the comparisons to be made.

Table 4: Secondary comparison on 'Next dose' COVID-19 or Flu Vaccination Rate

	T1	Т2	Т3	What is the effect on 'next dose' COVID-19 or flu vaccinations rates of
T1		H2		Being sent a chatbot that includes a health center locator in the T2 chatbot?
T2			H3	Being sent a chatbot that includes a video featuring the popular band La Mosca from Argentina in the T3 chatbot?

Robustness check:

⁹ After the chatbot pushes the initial message, a user has 24 hours from the last message sent (either by the chatbot or the user) to continue interacting with the chatbot within our experimental flow.

We will employ a 'Treatment on the Treated' approach to investigate the extent to which receiving a message with specific chatbot functionalities enhances the effect of increasing COVID-19 and flu vaccine uptake. Table 5 describes the comparisons to be made:

	-			
	T1	Т2	Т3	What is the effect on 'next dose' COVID-19 or flu vaccinations rates of
T1		H4		Receiving a chatbot that includes a health center locator in the T2 chatbot?
T2			H5	Receiving a chatbot that includes a video featuring the popular band La Mosca from Argentina in the T3 chatbot?

Table 5:	Robustness	check on	the secondary	/ analy	vsis

Hypotheses and models

- Hypotheses: We are aiming to reject the following hypotheses that the difference between COVID-19 or flu vaccination rate over a 4-week period is statistically indistinguishable among...
 - Primary analysis:
 - H1: Participants who are sent a WhatsApp chatbot (T1-T2-T3) compared to those who are assigned to not receive any message
 - Secondary analysis:
 - H2: Participants who are sent a basic Whatsapp chatbot (T1) compared to those who are sent the same chatbot with an additional health center locator functionality (T2)
 - H3: Participants who are sent the T2 Whatsapp chatbot compared to those who are sent the same chatbot with an additional motivational video message featuring a popular figure (T3)
 - Robustness check:
 - H4: Participants who receive a basic Whatsapp chatbot (T1) compared to those who receive the same chatbot with an additional health center locator functionality (T2)
 - H5: Participants who receive the T2 Whatsapp chatbot compared to those who receive the same chatbot with an additional motivational video message featuring a popular figure (T3)
- For the primary analysis:
 - Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.18 percentage points taking into consideration a sample with 5% of attrition.
 - Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the Chatbot intervention on the binary primary outcome of vaccination rate. Random assignment of individuals to receive the Chatbot

allows us to identify the effects. Our primary analysis will use the following covariate-adjusted regression. We will include all complete cases and make a missing-at-random assumption:

$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 1_i + \beta_2 T 2_i + \beta_3 T 3_i + X_i' \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

And,

- Y_i is a binary indicator of whether the individual receives a vaccination within 4 weeks of the assigned data for the sending of the initial message (COVID-19 or flu) (1 if they do, 0 if not);
- \circ p_i is the probability that the individual receives a vaccination;
- For s = 1-3, Ts_i is a set of dummy variables indicating whether individual i is

assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);

- \circ X, is a vector of pre-treatment covariates
 - Woman (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu vaccine only eligible (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)
- For the secondary analysis:
 - Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.24 percentage points taking into consideration a sample with 5% of attrition.
 - Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the chatbot functionalities on the binary primary outcome of vaccination rate. Random assignment of individuals to receive the Chatbot allows us to identify the effects. Our primary analysis will use the following covariate-adjusted regression. We will include all complete cases and make a missing-at-random assumption.
 - We will apply two equations for each hypothesis:

(1)
$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 1_i + \beta_2 T 2_i + X_i' \gamma$

(2)
$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 2_i + \beta_2 T 3_i + X_i' \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

and,

- Y_i is a binary indicator of whether the individual receives a vaccination within 4 weeks of the assigned data for the sending of the initial message (COVID-19 or flu) (1 if they do, 0 if not);
- \circ p_i is the probability that the individual receives a vaccination;
- For s = 1-3, Ts_i is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- \circ X, is a vector of pre-treatment covariates
 - Woman (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu vaccine only eligible (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)
- Multiple Comparison Adjustments: We are interested in multiple comparisons across arms to understand the effect of specific functionalities of the chatbot. We are therefore making a total of 2 comparisons: (H2: β 3= β 2), (H3: β 4= β 3) and so we will use the Benjamini-Hochberg Procedure for multiple comparison adjusted p-values.
- For the robustness check:
 - Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.24 percentage points taking into consideration a sample with 5% of attrition.
 - Model: We will use a logistic regression to estimate the Treatment on the Treated (ToT) effect of the chatbot functionalities on the binary primary outcome of vaccination rate. Our robustness check will use the following covariate-adjusted regression. We will include only individuals who receive the chatbot.
 - We will apply two equations for each hypothesis:

(H4)
$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T I_i + \beta_2 T 2_i + X_i' \gamma$

(H5)
$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 2_i + \beta_2 T 3_i + X_i' \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

- Y_i is a binary indicator of whether the individual receives a vaccination within 4 weeks of the assigned data for the sending of the initial message (COVID-19 or flu) (1 if they do, 0 if not);
- $\circ p_i$ is the probability that the individual receives a vaccination;
- For s = 1-3, Ts_i is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- \circ X, is a vector of pre-treatment covariates
 - Woman (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu vaccine only eligible (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)
- Multiple Comparison Adjustments: We are interested in multiple comparisons across arms to understand the effect of specific functionalities of the chatbot. We are therefore making a total of 2 comparisons: (H4: β 3= β 2), (H5: β 4= β 3) and so we will use the Benjamini-Hochberg Procedure for multiple comparison adjusted p-values.

Exploratory Analysis: Chatbots and Personalized Message on 'Next dose' COVID-19 or Flu Vaccination Rate (Sub-Group Analysis: Age)

- Hypothesis: We are aiming to reject the hypothesis that the difference between COVID-19 or flu vaccination rate over a 4-week period for age sub-groups among participants assigned to the treatment arms compared to participants assigned to the control is statistically indistinguishable from zero. Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.35 percentage points for individuals aged 18-29; 0.26 percentage points for those aged 30-49; 0.38 percentage points for those aged 50-64 years old; and 0.39 for those aged 65 and above. These calculations take into consideration a sample with 5% of attrition.
- Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the Chatbot intervention on the binary primary outcome of vaccination rate. Random assignment of individuals who are sent the Chatbot allows us to identify the effects. Our analysis will use the following covariate-adjusted regression. We will include all complete cases and make a missing-at-random assumption. For age categories 18-29, 30-49, and 50-64, 65+, we will separately run the following regression:

$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 1_i + \beta_2 T 2_i + \beta_3 T 3_i + X_i \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

and,

- *Y_i* is a binary indicator of whether the individual receives a vaccination within 4 weeks of the assigned data for the sending of the initial message (COVID-19 or flu) (1 if they do, 0 if not);
- *p*_i is the probability that the individual receives a vaccination;
- For s = 1 3, *Ts_i* is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- X_i is a vector of pre-treatment covariates
 - Sex (binary)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu vaccine only eligible (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)

Exploratory Analysis: Chatbots and Personalized Message on 'Next dose' COVID-19 or Flu Vaccination Rate (Sub-Group Analysis: Risk Factors)

- Hypothesis: We are aiming to reject the hypothesis that the difference between COVID-19 or flu vaccination rate over a 4-week period for risk factor sub-groups among participants assigned to the treatment arms compared to participants assigned to the control is statistically indistinguishable from zero. Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.50 percentage points for the group with a risk factor and 0.17 for those who don't have a risk factor, taking into consideration a sample with 5% of attrition.
- Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the Chatbot intervention on the binary primary outcome of vaccination rate. Random assignment of individuals who are sent the Chatbot allows us to identify the effects. Our analysis will use the following covariate-adjusted regression. We will include all complete cases and make a missing-at-random assumption. For individuals with risk factors and those without, we will run the following regression:

$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 1_i + \beta_2 T 2_i + \beta_3 T 3_i + X_i' \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

- *Y_i* is a binary indicator of whether the individual receives a vaccination within 4 weeks of the assigned data for the sending of the initial message (COVID-19 or flu) (1 if they do, 0 if not);
- *p_i* is the probability that the individual receives a vaccination;
- For s = 1 3, *Ts_i* is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- *RF_i* = a dummy variable indicating whether individual i has health risk factors (1 if they do, 0 if not);
- X is a vector of pre-treatment covariates
 - Sex (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Flu vaccine only eligible (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)

Exploratory Analysis: Chatbots and Personalized Message on COVID-19 ONLY Vaccination Rate (Sub-Group Analysis: Eligible for COVID-19 Vaccine)

- Hypotheses: We are aiming to reject the hypothesis that the difference between COVID-19 vaccination rate over a 4-week period for the comparisons specified for the primary analysis is statistically indistinguishable from zero. Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.26 percentage points taking into consideration a sample with 5% of attrition.
- Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the Chatbot intervention on the binary primary outcome of vaccination rate. Random assignment of individuals who are sent the Chatbot allows us to identify the effects. Our analysis will use the following covariate-adjusted regression estimated on the sub-group that is eligible for a COVID-19 vaccination. We will include all complete cases and make a missing-at-random assumption:

$$Y_i \sim bernoulli(p_i)$$
; $logit(p_i) = \beta_0 + \beta_1 T 1_i + \beta_2 T 2_i + \beta_3 T 3_i + X_i' \gamma$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

- Y_i is a binary indicator of whether the individual receives a COVID-19 vaccination within 4 weeks of the assigned data for the sending of the initial message (1 if they do, 0 if not);
- *p_i* is the probability that the individual receives a vaccination;
- For s = 1 3, Ts_i is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- X is a vector of pre-treatment covariates
 - Sex (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)

Exploratory Analysis: Chatbots and Personalized Message on Flu Vaccination ONLY Rate (Sub-Group Analysis: Eligible for Flu Vaccine)

- Hypotheses: We are aiming to reject the hypothesis that the difference between Flu vaccination rate over a 4-week period for the comparisons specified for the primary analysis is statistically indistinguishable from zero. Using a two-tailed hypothesis test, we have an 80% likelihood of detecting a difference if the baseline is 3% and the true effect is greater than or equal to 0.23 percentage points taking into consideration a sample with 5% of attrition.
- Model: We will use a logistic regression to estimate the Intention-To-Treat (ITT) effect of the Chatbot intervention on the binary primary outcome of vaccination rate. Random assignment of individuals who are sent the Chatbot allows us to identify the effects. Our analysis will use the following covariate-adjusted regression estimated on the sub-group that is eligible for the flu vaccination. We will include all complete cases and make a missing-at-random assumption:

$$Y_i \sim bernoulli(p_i); \ logit(p_i) = \beta_0 + \beta_1 T \mathbf{1}_i + \beta_2 T \mathbf{2}_i + \beta_3 T \mathbf{3}_i + X_i' \gamma$$

where the function *logit* is defined as the log-odds ratio

$$logit(p) = log(\frac{p}{1-p})$$

- *Y_i* is a binary indicator of whether the individual receives a flu vaccination within 4 weeks of the assigned data for the sending of the initial message (1 if they do, 0 if not);
- *p_i* is the probability that the individual receives a vaccination;

- For s = 1 3, Ts_i is a set of dummy variables indicating whether individual i is assigned to the corresponding treatment arm (T1-T3) (1 if they are, 0 if not);
- X, is a vector of pre-treatment covariates
 - Sex (binary)
 - Age (categorical: 18-29, 30-49, 50-64, 65+)
 - Province (categorical)
 - Health risk factor (binary)
 - Flu & COVID-19 vaccine eligible (binary)
 - Length of time since previous dose (discrete: days)
 - Date of initial intervention text message (categorical)

Racial Equity Analysis

Given data availability constraints, we may not be able to disaggregate data by race.

10 / Power

Table 4: Power Calculations

Alpha			5% (Bonferroni multiple comparison adjusted)		
		80%			
Baseline	Drimony analysia	Secondamy			
3.0%	(4 arms and 1 comparison)	analysis (4 arms and 2 comparisons)	(accounting for 5% attrition, rounded)	мы рр.	
~	~		398,288	0.18	
~		~	398,288	0.24	

Notes: pp = percentage points; MDD = minimum detectable difference

Implementation

11 / Trial Procedure

The MoH of Tucuman will establish its own WhatsApp Business account linked to Botmaker, the meta partner who is responsible for the chatbot programming. Botmaker will integrate the experimental chatbot flows into this account in such a way that participants can only access the experimental chatbot flow to which they have been assigned.

Intervention Pilot

We will pilot the intervention for a week to conduct implementation checks. During this week we will send the chatbot according to the schedule in the following table. The control group

will not actually receive a message, but we include numbers in this table of hypothetical messages that would be sent. On the first day, we will push 1000 initial messages.

All phone numbers included in the pilot will be identified in our dataset with an indicator of their inclusion in the pilot. They will be included in the analysis once the implementation for the rest of the sample is completed. After the pilot messages have been sent, we will pause implementation for the remainder of the week to analyze and communicate the outcomes of the pilot with MoH of Tucumán.

Table 6. Pilot Messaging Schedule

Pilot Week 1					
	Day 1	Day 2			
Control (Hypothetical)	Tucuman: 250	Data Analysis. Identify needs for implementations and			
T1. Chatbot: Implementation Intentions	Tucuman: 250	take relevant actions.			
T2. Chatbot: Reduce Frictions (Health Center Locator)	Tucuman: 250				
T3. Chatbot: Messenger Effect (Video)	Tucuman: 250				
Total	1000				

Intervention Post-Pilot

Upon initiating implementation again, we will send a sufficient number of messages per day based on the approved messages allowed to send by WhatsApp. The following timeline is subject to WhatsApp approvals.

Group	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
A2	285	250	220	190	2,700	2,400	2,100	21,000	21,000	21,000	18,000	15,419
A3	285	250	220	190	2,700	2,400	2,100	21,000	21,000	21,000	18,000	15,418
A4	285	250	220	190	2,700	2,400	2,100	21,000	21,000	21,000	18,000	15,419
Reminders (save 15% of space)	128	113	99	86	1,215	1,080	945	9,450	9,450	9,450	8,100	6,938
Reminders from days before	0	128	241	340	425	1,640	2,720	3,665	13,115	22,565	32,015	40,115
Total to send	983	991	1,000	995	9,740	9,920	9,965	76,115	85,565	95,015	94,115	93,310
Max. N° messages allowed	1,000	1,000	1,000	1,000	10,000	10,000	10,000	100,000	100,000	100,000	100,000	100,000

Additional notes on randomization and implementation strategy:

- BIT will randomize the dataset using a random seed to assign the sample to experimental arms and to order individuals in 12 batches within each experimental arm. We will create a batch variable from 1 to 12. BIT will split the data in smaller datasets based on the number of the batch and eligibility. Each day, BIT will send messages according to the number of the batch. Botmaker will record when the bot attempts to send a message and when each message is delivered. For example, on Day 1 of the trial, they will only send initial messages to individuals assigned to batch 1 and on Day 2, batch 2. The control group will be logged by their hypothetical assignment. For example, individuals from batch 1 of the control group will be recorded as Day 1.
- Batches are designed to be balanced across the arms to ensure that we do not send

significantly more messages to one trial arm than another.

- If a participant from the treatment group reaches out to our WhatsApp number before they are scheduled to be included in the trial, they will receive a default message with information to contact *Hospital Público Virtual* service from the Ministry of Health of Tucumán. If any of the citizens contact the WhatsApp business account and are eligible and part of one of the treatments, they will later receive the treatment group chatbot message at a later date when they are scheduled to be included in the trial.
- Given the rolling design of this trial, where participants receive the intervention on consecutive dates during the trial period, we have to divide the pure control group into a "pure control group for each day" to ensure the timing of the 4 week outcome window is similarly distributed between treatment and control. To tie our hands, before trial launch and during randomization we will randomly assign a batch for each individual in the control group. If they are part of the batch 1, we'll assume a delivery date as the same date when 'Day 1' was delivered for the treatment groups. The purpose of this strategy is to ensure that the pure control group is observed over the same time periods (in the rolling design) as the other five arms.

12 / Implementation Risks

Implementation checks and mitigation strategies:

Add, delete, or amend the concerns listed below as appropriate:

RISK	WHO WILL CHECK?	HOW WILL THEY CHECK?
Correct assignment, i.e., did participants receive the intervention in line with their group allocation?	BIT	Include a project team member's phone number in each arm for the entirety of the trial.
Proportion of inaccurate contact numbers for participants higher than estimated	BIT	Only include participants for which we have a unique mobile number to mitigate this risk.
Did participants receive (or were exposed to) the intervention as & when intended?	BIT	Every 2 days, check that messages sent align with message send date assignment.
Did participants see or experience the intervention as intended?	BIT	During pilot and trial, check that chatbot flows are working according to participant assignment
Health center locator unintentionally directs participants to closed health centers or health centers far from their location	BIT	Collect data during post-trial qualitative study

13 / Ethical Considerations

We adhere to the ethical principles as described in <u>the Belmont Report</u> and the <u>Tri-Policy</u> <u>Council Statement</u>. The key principles are: respect for persons, beneficence, and justice. This trial protocol will be reviewed by an independent research board prior to its implementation.

LEVEL OF RISK:	Minimal risk
JUSTIFICATION:	Standard research methods; Recipients are non-vulnerable adults; Anonymous data; Impacts estimated from VCF1 were positive

- **Consent:** We determined that not obtaining informed consent was justifiable for the following reasons: (1) The study does not involve any level of coercion, (2) vaccination services are not conditional on participation in the intervention, (3) vaccination data is already collected by the Ministry of Health of Tucuman, (4) the individuals included in the study voluntarily provided their phone numbers by interacting with other digital services from the province government, and (5) individuals randomly assigned to the chatbot arms are asked at the beginning of the interaction if they wish to continue interacting with the chatbot.
- Selection of participants: We exclude children under 18 years old to better answer our research question given that children's vaccination behaviors are likely to be affected by the beliefs and behaviors of their parents / guardians. It is possible that persons of diminished autonomy (e.g., cognitive impairment) or vulnerable groups (e.g., pregnant persons) are included in this trial. However, we believe that their inclusion in the research is important given the individual and collective benefits of vaccination, especially for pregnant persons.
- Sharing of research benefits: Treatment participants will receive reminders and/or tools intended to increase vaccine uptake. If the intervention is effective, treatment participants would have reduced their risk of infection and/or severe illness from COVID-19 and flu infections which may also have second-order benefits for people around treatment participants. Furthermore, if found to be effective, control group participants will receive the most effective version of the intervention so that they could also benefit from the research.

Risks & Monitoring

ETHICAL RISK	LEVEL OF RISK Rate from 1-5 how serious the risk is and how likely it is to occur	MITIGATION
Intervention may backfire and lead to worse outcomes	1	This risk has been minimized by developing the messages based on the evidence available from related research, as well as input from experts at BIT and consultations with the Government of Argentina's Unidad de Ciencias del Comportamiento y Políticas Pública. This research also

builds on the first phase of the project which had positive impacts on vaccination rates.
To further mitigate this risk, we have conducted a focus group with local residents of Argentina in which they tested a version of the BI-informed chatbot message flow in their own mobile phones.

14 / Data Requirements

Data sources:

1. <u>Tucuman vaccinations database</u>

PURPOSE:	Outcome measures (COVID-19 & flu vaccine(s) received including date, dose number, brand), participant IDs (DNI), and covariates (e.g., sex, age, health risk factor)
OWNER:	Ministerio de Salud de Tucumán & Unidad de Ciencias del Comportamiento y Políticas Públicas
REQUEST:	Data will be requested by BIT to the Unidad de Ciencias del Comportamiento y Políticas Públicas, who will share the data including the patient number ID as a unique identifier of citizens. Data will be shared in CSV or XLSX format using encrypted data transfer software.
ACCURACY / RELIABILITY:	We believe this data is accurate and reliable. The vaccination dataset from Tucuman province provides information to NOMIVAC, which is a computerized management model that maintains a nominalized registry that centralizes vaccination records associated with specific individuals and provides updated, consistent and reliable data. This is the most up to date information. See <u>page</u> for more information.
HISTORICAL:	No historical pull of data for sample population. (We have worked with NOMIVAC data during the first phase of this project.)
PII / CONSENT:	These data won't contain personally identifiable information. A data sharing agreement has been signed between BIT and the government of Argentina's Unidad de las Ciencias del Comportamiento y Políticas Públicas for the purpose of sharing these data.
COUNTRY:	<u>Collected</u> : Argentina <u>Stored</u> : USA

2. Phone numbers from Tucumán

|--|

OWNER:	Gobierno Provincial de Tucumán & Unidad de Ciencias del Comportamiento y Políticas Públicas
REQUEST:	Data will be requested by BIT to the Unidad de Ciencias del Comportamiento y Políticas Públicas, who will request the data from the administrative healthcare dataset of Tucuman. The Ministry of Health of Tucumán will merge the phone number with the patient identification number. Then they will share it to BIT in CSV or XLSX format using encrypted data transfer software.
ACCURACY / RELIABILITY:	Potential accuracy/reliability concerns (due to incorrect phone numbers or no longer active phone numbers) will be mitigated in the steps taken to clean the data. See Appendix IV.
HISTORICAL:	No historical pull of data.
PII / CONSENT:	These data will contain personally identifiable information in the form of individuals' phone numbers. A data sharing agreement has been signed between BIT and the government of Argentina's Unidad de las Ciencias del Comportamiento y Políticas Públicas for the purpose of sharing these data.
COUNTRY:	<u>Collected</u> : Argentina <u>Stored</u> : USA

3. Treatment assignment

PURPOSE:	Merge participant phone numbers (source 2) with participant health records (source 1) using the patient identification number, and generate random treatment assignment
OWNER:	BIT
REQUEST:	This data source will be created by BIT using data sources 1-2 as inputs.
ACCURACY / RELIABILITY:	No concerns about accuracy/reliability of these data.
HISTORICAL:	No historical pull of data.
PII / CONSENT:	These data will contain personally identifiable information in the form of individuals' phone numbers. A data sharing agreement has been signed between BIT and the government of Argentina's Unidad de las Ciencias del Comportamiento y Políticas Públicas for the purpose of sharing these data.
COUNTRY:	<u>Collected</u> : Argentina <u>Stored</u> : USA

Variable construction:

VARIABLE	TYPE	COLLECTION POINT	SOURCE	MEASUREMENT
Vaccination	Dependent	4 weeks after receiving first push message	Tucuman vaccination data.	Binary - Y/N; individual level
Treatment	Independent	Baseline		
Phone number				

Data Management:

• **Security and storage:** We only have access to an anonymized ID called patient ID. Data will be stored in project folders with access restricted to the project team only. Data will not be transmitted to third parties, except where this is appropriate under the conditions of appropriate data sharing agreements.

Appendices

Appendix I: Personalized Messages Across Treatment Arms

	COVID-19	COVID-19 & Flu (Risk Factors)	COVID-19 & Flu (65+)	Flu (Risk Factors)	Flu (65+)
T1. Chatbot: Implementation Intentions	Hola, {{NOMBRE}} 👋	Hola, {{NOMBRE}} 👋	Hola, {{NOMBRE}} 👋	Hola, {{NOMBRE}} 👋	Hola, {{NOMBRE}} 👋
	Este es un mensaje del Ministerio de Salud de Tucumán. Te escribimos para avisarte que, según nuestros registros:	Este es un mensaje del Ministerio de Salud de Tucumán. Te escribimos para avisarte que, según nuestros registros:	Este es un mensaje del Ministerio de Salud de Tucumán. Te escribimos para avisarte que, según nuestros registros:	Este es un mensaje del Ministerio de Salud de Tucumán. Te escribimos para avisarte que, según nuestros registros:	Este es un mensaje del Ministerio de Salud de Tucumán. Te escribimos para avisarte que, según nuestros registros:
	Tu última aplicación de la vacuna contra COVID-19 fue el: \${{FECHA_VACUNACION (dd/mm/yyyy)}}.	Tu última aplicación de la vacuna contra COVID-19 fue el: \${{FECHA_VACUNACION (dd/mm/yyyy)}}.	Tu última aplicación de la vacuna contra COVID-19 fue el: \${{FECHA_VACUNACION (dd/mm/yyyy)}}.	Como tenés factores de riesgo (o una orden médica), *te toca tu vacuna anual contra la gripe.*	77 Como sos mayor de 65 años, *te toca tu vacuna anual contra la gripe.*
	Por eso, "jya te toca tu proxima dosis!" Podés recibirla en cualquier centro de salud y en los hospitales públicos del país de "forma gratuita " ¡Lay una vacuna	 Por eso, *jya te toca tu proxima dosis!* Como tenés factores de riesgo (o una orden médica), también *te toca tu vacuna anual contra la grine * 	 Por eso, "¡ya te toca tu proxima dosis!" Como sos mayor de 65 años, también *te toca tu vacuna anual contra la gripe.* 	Podés recibirla en cualquier centro de salud y los hospitales públicos del país *de forma gratuita.* ¡Hay una vacuna reservada para voc. po te la pierdael	Podes recibiria en cualquier centro de salud y los hospitales públicos del país *de forma gratuita.* ¡Hay una vacuna reservada para vos, no te la pierdas!
	reservada para vos, no te la pierdas!	Podés recibirlas en cualquier centro de	Podés recibirlas en cualquier centro de salud y los hospitales públicos del país *de forma gratuita * ¡Hay una yaguna reconada	Podemos ayudarte a conocer cuándo y	Podemos ayudarte a conocer cuándo y dónde conseguir tu próxima vacuna.
	dónde conseguir tu próxima vacuna. *¿Querés que continuemos?*	forma gratuita.* ¡Hay una vacuna reservada para vos, no te la pierdas!	para vos, no te la pierdas!	*¿Querés que continuemos?*	Este es un canal oficial del Ministerio de
	Este es un canal oficial del Ministerio de Salud de Tucumán.	Podemos ayudarte a conocer cuándo y dónde conseguir tus próximas vacunas. *¿Querés que continuemos?*	Podemos ayudarte a conocer cuando y dónde conseguir tus próximas vacunas. *¿Querés que continuemos?*	Este es un canal oficial del Ministerio de Salud de Tucumán.	Salud de Lucuman.
		Este es un canal oficial del Ministerio de Salud de Tucumán.	Este es un canal oficial del Ministerio de Salud de Tucumán.		
T2. Chatbot: Reduce Frictions (Health Center					
Locator)	Same as T2	Same as T2	Same as T2	Same as T2	Same as T2
T3. Chatbot: Messenger Effect (Video: Popular					
Personality)	Same as T2	Same as T2	Same as T2	Same as T2	Same as T2

Appendix II. Message Flows for Treatment Arms

To see the message flows for all treatment arms, see document here.

Appendix III. Video script for T4 – Artist: La Mosca

"[Looking directly at the camera in close-up] We have a vaccine for you [points to the camera] at your nearest public health center."

[If you are over 65 years old or have any risk factors, you can get the flu vaccine for free.]

In this chat [points downwards, as if indicating the next message in the chat], we help you decide where and when to get your vaccine.

[pause] Your vaccine is waiting for you... don't miss it!"

The two versions of the video (one for participants only eligible for the Covid-19 vaccine, and one for participants eligible for both vaccines) can be found <u>here</u>.

Appendix IV. Detailed	Sample Definition	& Implementation Plan

Stage	Description	Data source	Responsability
1	Consolidation of WhatsApp number database and identification of individuals who meet basic eligibility criteria for government-subsidized flu vaccines and COVID-19 vaccines.	Tucumán Health Services Tucuman administrative vaccination data	MoHT
2	Verification of Stage 1 database to eliminate duplicates and false numbers.	Stage 1 data	BIT
3	Perform final exclusions, and include chatbot-related variables.	Stage 2 data	BIT
4	Randomly assign treatments.	Stage 3 Data	BIT
5	Implement trial and conduct implementation checks.		BIT

Stage 1: Consolidation of WhatsApp number database and identification of individuals who meet basic eligibility criteria for government-subsidized flu vaccines and COVID-19 vaccines

- 1. MoHT will create a telephone number database, including health personnel for whom cell phone numbers are available. The database will include the following columns:
 - a. phone number(s)¹⁰ (string) [telefono]
 - b. Pseudo ID¹¹ (string) [idpaciente]
- 2. MoHT will carry out a simple procedure to eliminate duplicates or numbers that appear to be false.
- 3. After this, they will consult the vaccination database to identify residents of the province of Tucumán who are:
 - a. Are at least **18 years of age** or older at the date of consultation.
 - b. Are eligible for government-subsidized flu vaccine because they are
 - i. 65 years of age or older or
 - ii. health/security personnel or
 - iii. have a documented risk factor and have not had a flu vaccination in the current year or
 - iv. Had a medical prescription to receive the flu vaccine (See Box 1 below for more details).
 - c. MoHT will include a variable called 'elegibleatg' set to TRUE if a person is eligible for flu vaccine.
 - d. MoH Tucuman will include a variable called 'dosis' that identifies whether a person is eligible for flu vaccine due to age, risk factors, health/security employment, or combination of two or three of these."
- 4. Consult the immunization database to identify eligible persons for their next dose of COVID-19 vaccine:¹²
 - a. The person is 50 years of age or older, or has risk factors and has not received a dose of COVID-19 vaccine in the past 6 months.
 - b. The person is between 18 and 49 years old and is eligible for a booster according to the time since the last dose (i.e., has not had a COVID-19 vaccine in the last 12 months). (See Box 2 below for more details).
 - c. MoH Tucuman will include a variable named 'elegiblecovid' with value TRUE if a person is eligible for the COVID-19 vaccine booster.
 - d. MoH Tucuman will include a variable called 'dosis' that identifies whether a person is eligible for the COVID-19 vaccine due to their risk factors.
- 5. The dataset should be in wide format, where each row represents a person and will include, at a minimum, the following variables:
 - a. Pseudo ID(string)
 - b. Name (string)
 - c. Phone number (numeric)

¹⁰ If a person's pseudo ID is linked to more than one phone number in the database, all phone numbers should be included in the sample.

¹¹ The pseudo ID is a way to identify citizens through the patient identifier stored by the Ministry of Health of Tucumán, this identifier is not related to any sensitive or personal information of citizens.

¹² See the most up to date recommendations on COVID-19 vaccination published by the Ministry of Health on May 3, 2023

https://www.argentina.gob.ar/noticias/salud-actualiza-las-recomendaciones-para-la-vacunacion-de-ref uerzo-contra-covid-19-y

- d. Sex (binary)
- e. Date of birth (string)
- f. Flu vaccine eligibility (binary)
- g. Reason for flu vaccine eligibility (categorical)
- h. Date of most recent flu vaccine dose received
- i. Identifier code of the health center where most recent flu vaccine dose received
- j. Address of health center where most recent flu vaccine dose received (including post code)
- k. Name of health center where most recent flu vaccine dose received
- I. COVID-19 booster eligibility(binary)
- m. Reason for COVID-19 booster eligibility (categorical)
- n. Date of most recent COVID-19 vaccine dose received
- o. Identifier code of the health center where most recent COVID-19 vaccine dose received
- p. Address of health center where most recent COVID-19 vaccine dose received (including post code)
- q. Name of health center where most recent COVID-19 vaccine dose received
- 6. MoH Tucuman shares the database with BIT.

Box 1. Eligibility for government-subsidized flu vaccination¹³

Argentina's Ministry of Health provides free flu vaccines to groups that face the highest risk of contracting influenza. These at-risk groups include:

- A. Adults over 65 years of age
- B. Risk groups at risk for influenza vaccination include persons aged 2 years to 64 years with certain conditions such as respiratory and cardiac diseases, diabetics, congenital or acquired immunodeficiencies (not oncohematological), oncohematological patients and transplant recipients. Cohabitants of oncohematological patients, persons with chronic renal failure on dialysis or with expectations of entering dialysis in the next six months, severe maturational delay in children under 18 years of age, chronic treatment with acetylsalicylic acid in children under 18 years of age, genetic syndromes, neuromuscular diseases with respiratory compromise and severe congenital malformations, cohabitants of premature infants under 1,500 g, among others. In order to receive the free vaccine, they must present a doctor's order (except for people with obesity).
- C. **Pregnant women.** It is recommended to receive the vaccine in the third semester of pregnancy. In case of not receiving it during pregnancy, it is recommended to receive it in the first 10 days after delivery.
- D. Boys and girls from 6 to 24 months
- E. Health personnel

In this trial, we only included group A (persons aged 65 years or older) and those documented as belonging to group B (persons with certain health conditions) who are 18

¹³ <u>https://www.argentina.gob.ar/salud/vacunas/novedadantigripal</u>

years or older, as well as group E (health care personnel). Additionally, based on the request of the Immunization Department, security personnel are included and citizens who had a medical prescription before.

Documentation of B or E group eligibility comes from previous immunization records. For example, if a person received a vaccine during a prioritized period, he or she would have had to present a physician's order or identification from health personnel to receive the vaccine. The health facility would have recorded that person's vaccination in the NOMIVAC system and also documented the reason for eligibility. This data is documented in a variable called "condition". Only one condition can be recorded (even if a person has several conditions) and the data can be from years ago.

Pregnancy can be a condition but the data query for the purposes of this project omits this condition because there is no way to know if a person is still pregnant so group C (pregnant) is excluded. In addition, we are excluding children under 18 years of age, thus excluding group D (children 6-24 months) and persons in group B under 18 years of age.

Box 2. Eligibility for Next Dose of COVID-19 Vaccine

In the <u>announcement</u> of the Ministry of Health, on May 3, 2023, the recommendations for the application of boosters against COVID-19 were updated. It is recommended that those who are within groups at high risk of developing severe forms of disease (people 50 years of age or older, people with immunocompromised and pregnant people) receive a booster dose against COVID-19 if 6 months have elapsed since the last dose applied, regardless of the number of boosters previously received.

Boosters against COVID-19 are available to people considered to be at low risk of complications, that is, under 50 years of age without comorbidities, and it is recommended that it be administered annually.

By May 2023, about 90% of the Argentinian population had received at least one COVID-19 vaccine and about 83% had completed their COVID-19 vaccine schedule.¹⁴ Therefore, if eligible for another dose of the COVID-19 vaccine, this is likely to be a booster dose.

Ordering and counting of vaccination doses:

In the vaccination data shared with BIT for the first phase of the project, occasionally an individual was described to have had a vaccination dose before they had the necessary previous dose (the labelling of which dose they received was inaccurate) or the previous dose was not recorded. Therefore we decided to use a "date approach", where we get the date of the last dose and then use this information to check if they are eligible for their next dose. The date approach works in all cases except one type of instance where we know

¹⁴ Based on MoH vaccination data accessed on May 23, 2023

^{(&}lt;u>https://www.argentina.gob.ar/coronavirus/vacuna/aplicadas</u>) and 2021 World Bank population estimates

that some data wasn't recorded. For this phase of the project, DICEI will follow the same protocol.

Stage 2: Verification of Stage 1 database to eliminate duplicates and false numbers (BIT)

- 7. BIT will be responsible for scanning for duplicates in the pseudo IDs and/or phone number.
- 8. BIT will perform the exclusions specified in Box 3 below.

Box 3. Whatsapp phone number inclusion and exclusion scenarios.

Inclusion scenarios:

- A) Include phone numbers with a length of 10 digits
- B) Include pseudo IDs that correspond to only 1 phone number.
- C) Include pseudo IDs that match 2 phone numbers (perhaps one is a work number, one is a landline, and there is another WhatsApp number).
- D) Include observations where the phone number is associated with 4 or less pseudo IDs. After receiving the merged data with the eligibility status, BIT will proceed to filter only the eligible observations and select a pseudo ID at random.

Exclusion scenarios:

- A) Delete observations with 6 or more consecutive digits repeated.
- B) Delete phone numbers with a length other than 10.
- C) Delete observations with identical pseudo IDs and phone number information.
- D) Delete observations where the phone number is associated with 5 or more pseudo IDs.

Stage 3: Perform final exclusions, and include chatbot-related variables.

- 9. BIT performs the following checks:
 - a. Check if there are citizens with a condition of "3 to 11 years old with risk factors" or "12 to 17 years old with risk factors". If they are 18 or 19 years old, change their eligibility to "18 to 59 with a risk factor", remove the rest.
 - b. Remove duplicate observations for all variables.
 - c. Remove duplicate observations for ID, phone number and eligibility.
 - d. Retain a random pseudo ID for those observations with phone numbers associated with 4 or fewer IDs.
 - e. Change COVID-19 eligibility to 0 if the citizen does not have a risk factor and their last COVID-19 vaccination was less than 12 months ago, or if they have a risk factor but their last vaccination was less than 6 months ago.
 - f. Remove observations of citizens who are ineligible for flu vaccination and COVID-19.
 - g. Remove observations of individuals under 18 years of age.
 - h. Exclude participants who received their COVID-19 or flu vaccination in 2024 they might have been eligible in the first cut of data, but then received the

vaccination while the team was preparing for launching.

- 10. After performing these exclusions, BIT will construct variables for the analysis and functionality of the chatbot.
- 11. BIT creates all variables related to the chatbot necessary for its functionality. They are listed below:
 - a. Eligibility (categorical)
 - b. Type of vaccine for which you are eligible (string)
 - c. Number of vaccines for which you are eligible (string)
 - d. Text for participants with a risk factor (string)
- 12. BIT merges the data with health center information using the REFES code as a key. The health center dataset includes the following variables:
 - a. Health center identifier code (string)
 - b. Variable indicating whether the health center offers flu or COVID-19 vaccination (binary)
 - c. Health center name (string)
 - d. Health center zip code (string)

Stage 4: Randomly assign treatments (BIT).

- 13. BIT creates a random seed to perform randomization and creates a variable indicating treatment assignment:
 - a. Control: treat == 0
 - b. T1. Chatbot: Implementation Intentions: treat == 1
 - c. T2. Chatbot: Reduce Frictions (Health Center Locator): treat == 2
 - d. T3. Chatbot: Messenger Effect (Video: Popular Personality): treat == 3
- 14. After treatment assignment, BIT creates the following variable for treatment 3:a. Assigned video (string)
- 15. Based on a random seed, BIT selects 250 observations from each treatment arm test with 50 participants per eligibility for the pilot.
- 16. To verify correct assignment, each BIT team member is included in both the pilot test and the trial itself.
- 17. Based on the random seed, BIT creates a treatment order and message batch variable by arm for each day (implementation plan of 12 days¹⁵).
- 18. BIT saves the data and creates a subset without the control group.

Stage 6: implement trial and conduct implementation checks

- 19. BIT will create a user group for each eligibility and treatment arm in the Botmaker platform.
- 20. BIT will send messages based on the message schedule described in Section 11 / Test Procedure.
- 21. BotMaker will give BIT access to download variables related to the user session, chatbot interaction history and a message log. This information will be hosted in BigQuery.
- 22. Every 5 days, BIT will verify that the messages sent match the message send date assignment (this verification is part of the implementation risk mitigation strategy).
- 23. After 7 days of implementation, the Ministry of Health of Tucuman will send BIT updated vaccination data for the individuals included in our sample. The data need

¹⁵ The timeline is subject to WhatsApp approvals.

only include the pseudo-ID and a binary variable indicating whether they have received a flu vaccine since the launch of the intervention and a binary variable indicating whether they have received a COVID-19 vaccine since the launch of the intervention (this check is part of the ethical risk mitigation strategy).

We will include the following data related to the sample definition in the final report of this project:

Number of people over 18 years of age, residents of Tucumán, and eligible	419,251
for influenza vaccine and/or COVID-19 booster.	