

Cancer Screening Invitations in the Developing World

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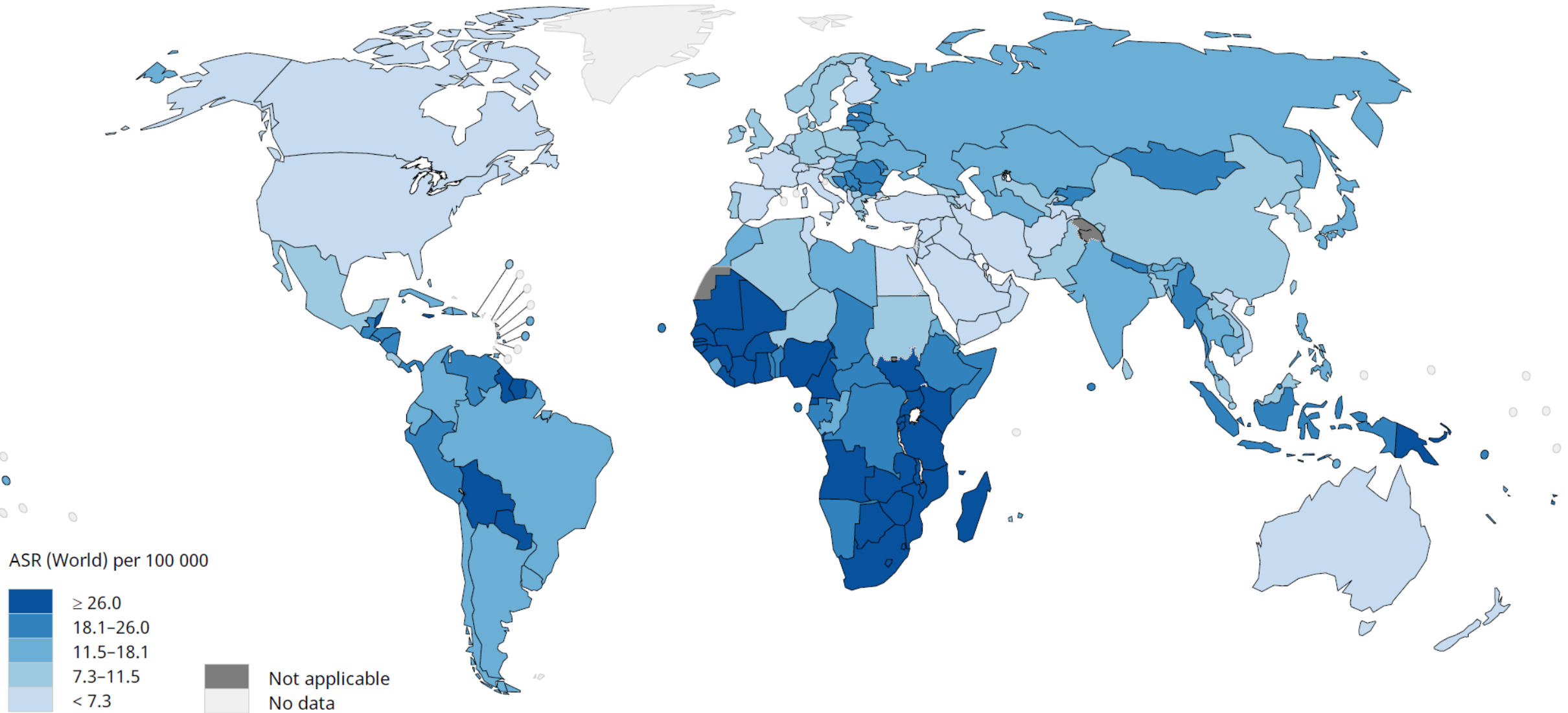
The project in a Nutshell

- Collaboration between
 - Armenia National SDG Innovation Lab (joint initiative of UN and the Government of the Republic of Armenia, supported by the UNDP)
 - Ministry of Health of the Republic of Armenia
 - Academia: Armenak Antinyan, Marco Bertoni and Luca Corazzini
- Policy problem to be solved
 - Increase the uptake of a cervical cancer screening program that runs in the Republic of Armenia
- Scientific contribution
 - To the best of our knowledge, the first RCT in the developing world that studies the impact of invitation letters and reminders on (cervical) cancer screening uptake.

Cervical cancer (CC)

- CC is the **fourth most frequent cancer** among women in the world, with roughly 570,000 new cases in 2018 (9.3% of all female cancers) (GLOBOCAN, 2018)
- Yearly, around 90% of deaths occur in low- and middle-income countries (LMIC)
 - Absence of organized screening programs or **low participation if a program is present** (e.g., Gakidou et al., 2008; O'Donovan et al., 2019; Sankaranarayanan, 2001).
 - In the last 40 years Sharp decline of cervical cancer incidence in high-income countries due to organized screening programs

Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages



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Data source: GLOBOCAN 2018
Graph production: IARC
(<http://gco.iarc.fr/today>)
World Health Organization

CC screening

- Luckily, **CC is one of the most preventable** among the relevant human cancers.
 - **Mono-causal genesis**: infection of the uterine cervix with human papillomavirus (HPV) needs to persist for many years to generate cancer.
- Main prevention devices (European Commission, 2015):
 - Population-based **HPV vaccination** of girls aged 12+
 - Population-based **Pap-test** screening of women aged 25-64, every 3 years
 - This has been recently substituted by the introduction of **HPV testing** every 5 years for women above 30

CC screening programs in LMICs

- Despite large benefits, **lack of infrastructures and scarce health care resources limit the possibility to implement adequate screening activities in LMICs** (Lazcano-Ponce et al, 1999; Rao 2012)
- When in place, low participation in these programs (WHO, 2002) due to:
 - **Information gaps, cultural and socio-economic barriers**
- In HICs, invitation letters and reminders stimulate participation in CC screening programs (Decker et al., 2013; Eaker et al., 2011; Radde et al., 2016; Tavasoli et al., 2016)
- Some evidence that framing of letters also matters (Bertoni et al., 2020)
- ***Lack of research on how these results extend to LMICs***

Why invitation letters and reminders may not work in LMICs?

- **Absence of insurance and low income**
 - patients frightened to detect any illness as they would find it impossible to get treated if cancer is detected - which in turn may deter attendance
- **Traditional cultural values** (even about medical exams)
- **Distrust toward the medical system** (corruption and low quality)
- Response to screening programs and various invitation strategies can be different between HIC and LMIC

What do we do?

- We worked with the **Health Ministry of Armenia and Armenia SDG Innovation Lab** to evaluate the effects of invitation letters and reminders aimed at enhancing screening participation

Armenia

- Post-communist, middle income country in transition
- Population: about 3,000,000
- GDP per capita: 4,000 USD (2017)
- Poverty: 25.7% (2017)
- CC Incidence:
Armenia= 8.4, Europe=11.2
- CC Mortality:
Armenia= 5.6, Europe=3.8

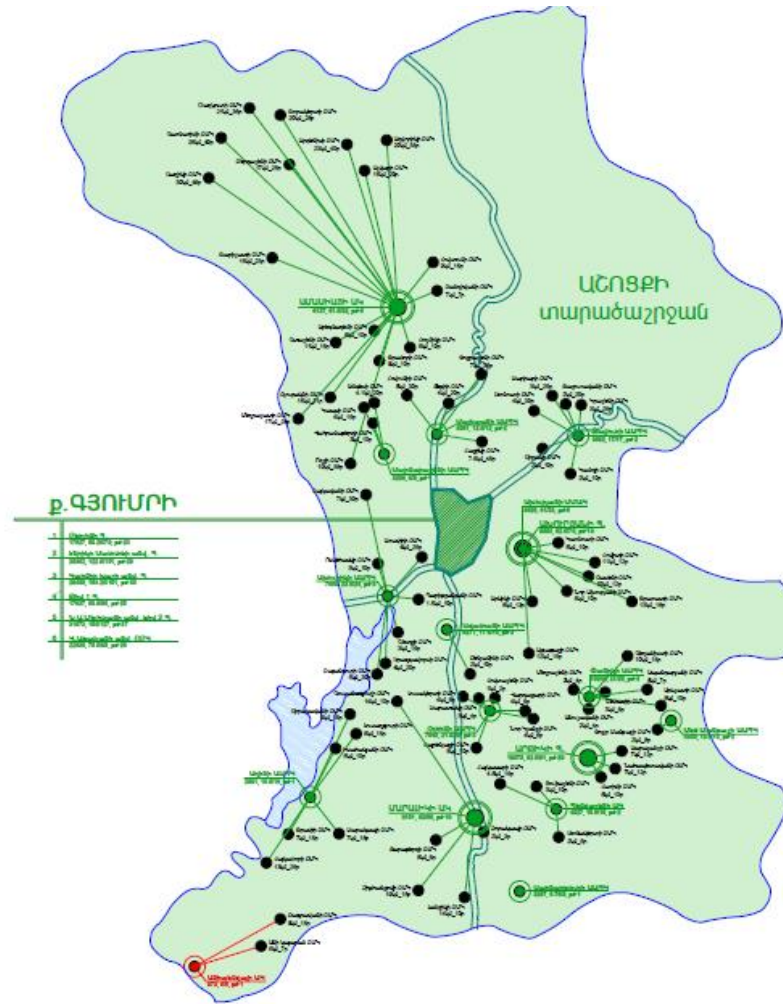


CC screening and treatment in Armenia

- Screening

- **Up to 2014: opportunistic screening not through PAP testing** (pay out of pocket if you want to do it)
- **Since 2015:** "Disease Prevention and Control Project in Armenia" project funded by the World Bank (2015-2020).
- **One free screening slot for each woman aged 30-60 every three years.**
- **No invitation system.** Mostly advertised using classical advocacy tools as TV and radio programmes, leaflets in supermarkets and the like.
- As of Feb 19, participation was not satisfactory for the Government

The region of interest



-44% of the population below the poverty line (the highest poverty rate in Armenia)

-Population 251,941 (2011 Census)

-Urban: 146,908 (58.3%)

-Rural: 105,033 (41.7%)

Experimental design

- We manipulate
 - Presence of a letter
 - Presence of a reminder on top of the letter (Altmann & Traxler, 2017, Calzolari & Nardotto, 2016)
 - The frame of the invitation letters and reminders (Positive framing; Negative Framing; Concerned for others framing) (Rothman and Salovey, 1997; Bertoni et al 2019; Du, Li, Lu & Lu, 2019)
- 8 treatments (different invitations) + 1 control (no invitation)

The letter frames

- **Neutral (slightly positive invitation):**

- Please note that scientific studies demonstrate that participating in cervical cancer screening programs can have relevant positive effects on the treatment of an early diagnosed disease.

- **Negative Framing:**

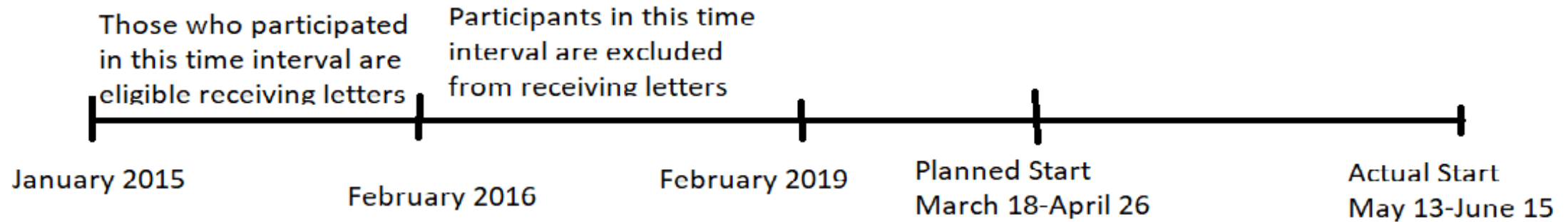
- Please note that scientific studies demonstrate that not participating in cervical cancer screening programs can have relevant negative effects on the treatment of a lately diagnosed disease: it increases the mortality rate, implies more extensive surgeries, less effective treatments, with lower chances of recovery.

- **Concern for Others:**

- Your family members, relatives and friends expect you to live a long and healthy life with them. Detecting and curing a potential cancer at early stages can help you fulfil their expectations. Go to the screening for your loved ones!

Assignment to treatment

- Shirak target population: about 36,000 eligible women aged 30-60 who have not attended the program as of Feb 2019 (or attended in 2015/2016)

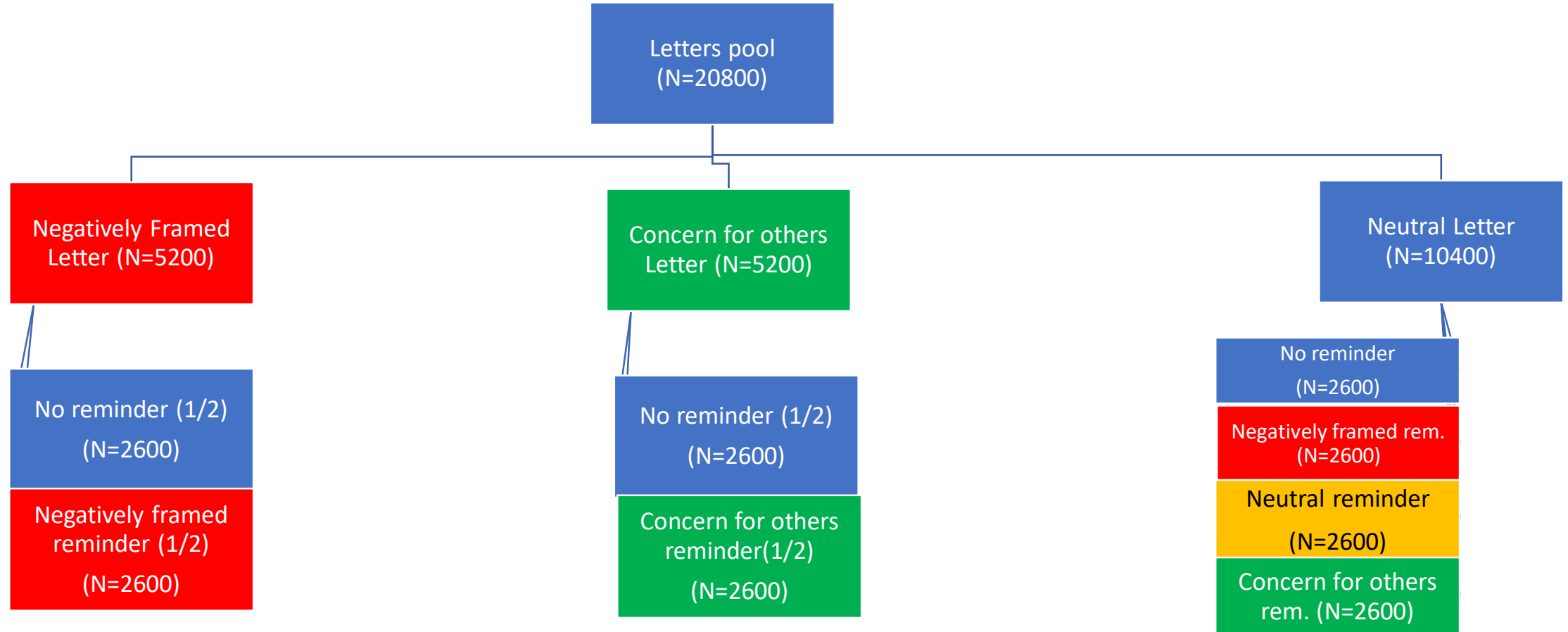


- 20,800 people receiving letters
 - Letters received 3 weeks before the scheduled week
 - Reminders received 1 week before the scheduled week
- Those individuals who did not receive letters are kept as the «control group»

Randomization

- We opted for **individual-level randomization, stratified by GP**
- Select a share of patients per GP in letter sample equal to share of patient per GP in the population
- Each letter type was equally represented within GP
- Day of letter delivery also independently and individually randomized

Sample allocation and treatments



The RCT was implemented in Shirak province between May-July, 2019

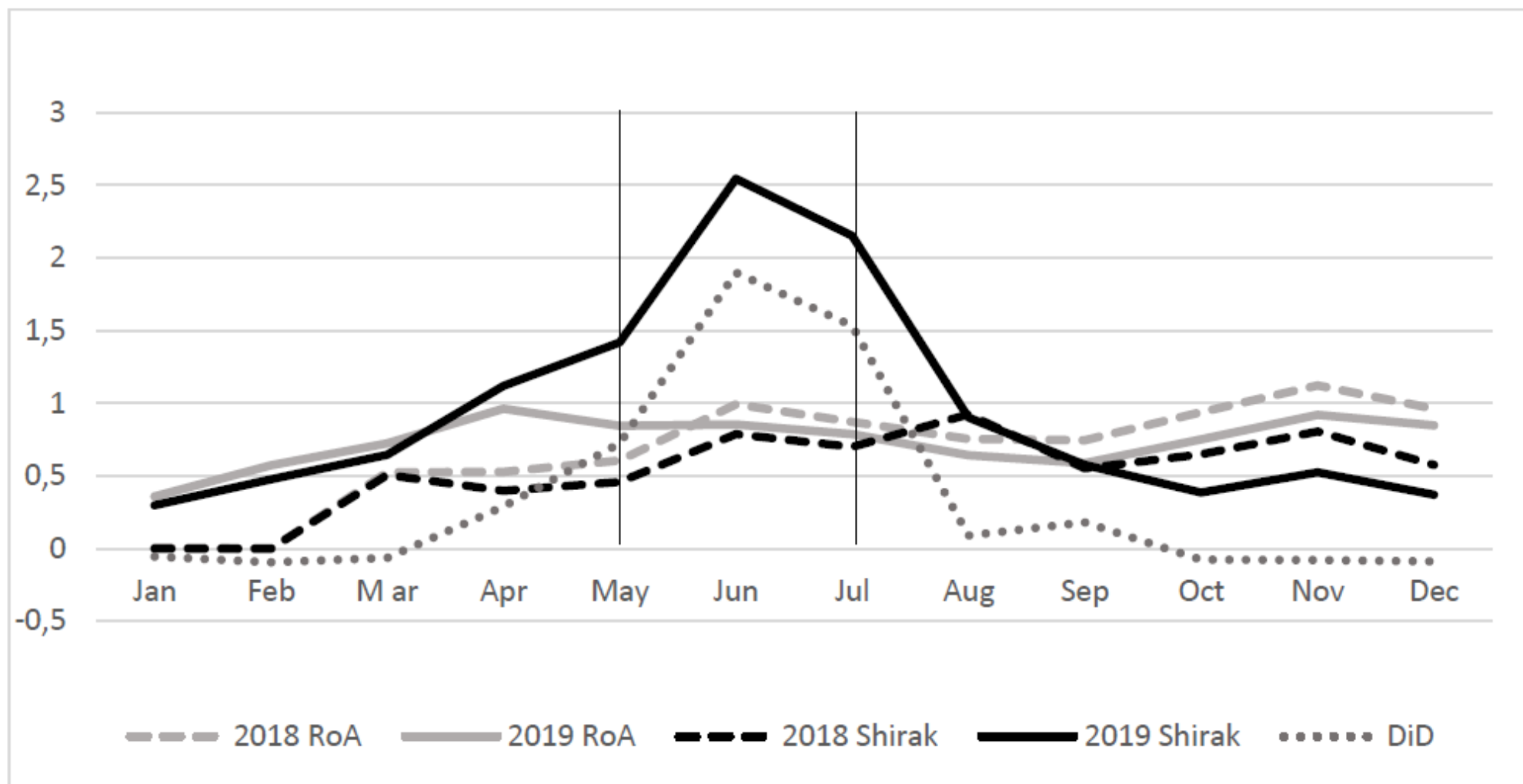
Implementation



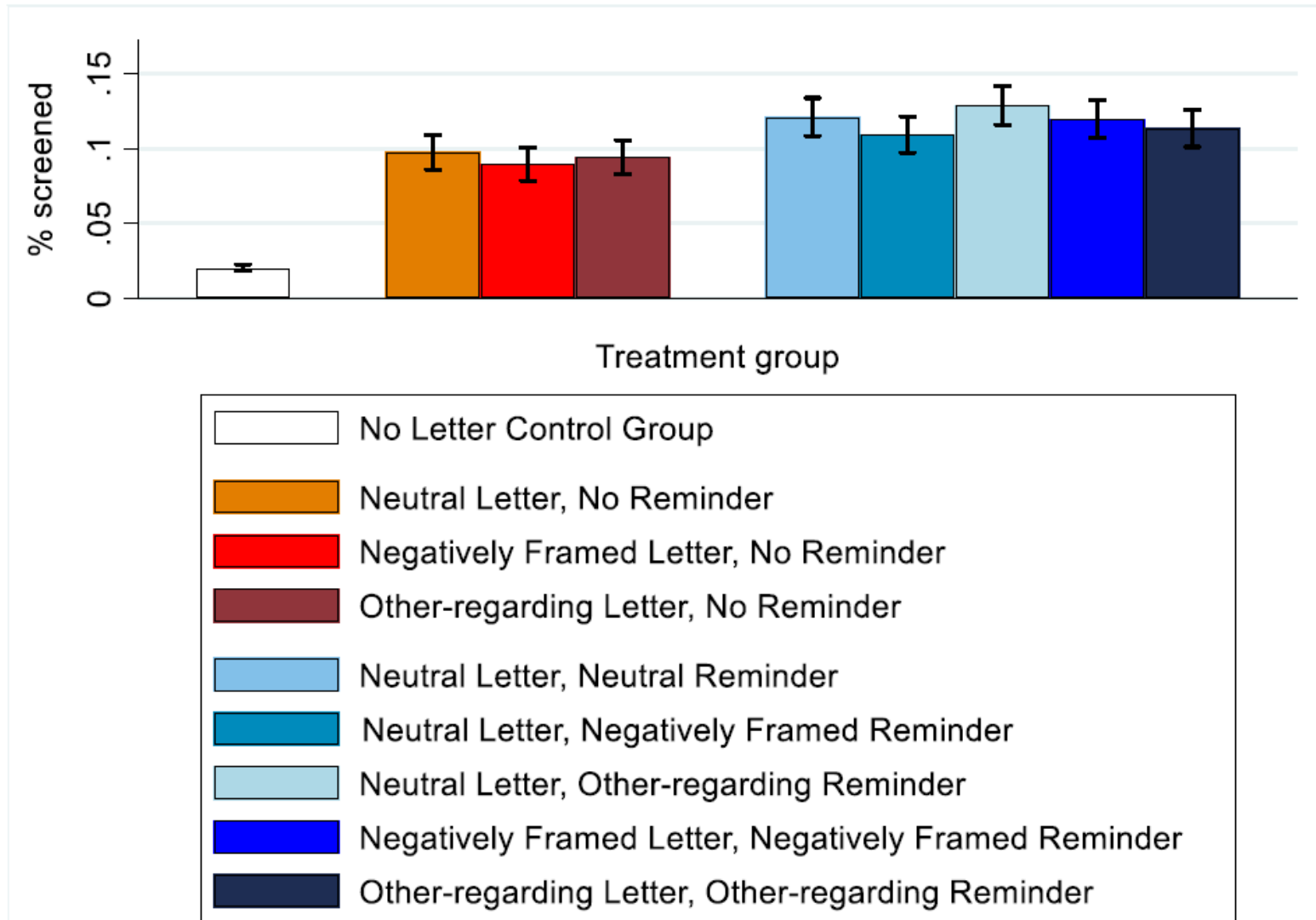
Data

- Internal records of the hospitals
- Background data (date of birth, place of residence, GP id)
- Take-up:
 - For the time being: we measure take-up until 19 July 2019

Prima facie evidence: regional data



Screening Participation by Treatment Group



Econometric specification

$$Screened_{ij} = \alpha_j + \sum_{t=1}^8 \beta_t * (Group_{ij} = t) + \varepsilon_{ij}$$

- i is subject, j is physician, t is treatment
- Given individual level randomization, non need to cluster by GP (but it makes no difference)
- Inclusion of covariates makes no difference either
- **Potential issue: letter not delivered (wrong address, person not at home, ...)**
 - We gathered mail company data on this
- We use treatment assignment as an instrument for reception.
- Given one-side non-compliance only, IV identifies the ATE (Bloom result)

Table 1. The effects of different invitation types on take-up

Dependent variable	(1) Screening participation ITT - treatment dispatched	(2) Screening participation ITT - treatment dispatched	(3) Screening participation TOT - treatment received
Parameter estimated	OLS	OLS	TOLS
Estimation method	OLS	OLS	TOLS
<u>Letter only invitations</u>		0.073*** (0.004)	0.118*** (0.006)
Neutral Letter, No Reminder	0.077*** (0.006)		
Negatively Framed Letter, No Reminder	0.069*** (0.006)		
Other-regarding Letter, No Reminder	0.074*** (0.006)		
<u>Letter and reminder invitations</u>		0.098*** (0.003)	0.181*** (0.006)
Neutral Letter, Neutral Reminder	0.100*** (0.007)		
Neutral Letter, Negatively Framed Reminder	0.089*** (0.006)		
Neutral Letter, Other-regarding Reminder	0.108*** (0.007)		
Negatively Framed Letter, Other-regarding Reminder	0.099*** (0.007)		
Other-regarding Letter, Other-regarding Reminder	0.093*** (0.006)		
P-value of an F-test for joint equality of all treatment effects	<0.01	<0.01	<0.01
P-value of an F-test for joint equality of all “letter only” treatment effects	0.62		
P-value of an F-test for joint equality of all “letter and reminder” treatment effects	0.24		
Mean Outcome, No Letter Control Group		0.021	

Conclusions

- To the best of our knowledge the first RCT that studies the impact of invitation letters and reminders on (cervical) cancer screening participation in the developing world.
- We find huge impact of invitations letters on cancer screening participation in LMICs.
- An invitation letter is particularly effective if followed by a reminder.
- Framing of the letters does not seem to matter.