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ABSTRACT

Promoting Breast Cancer Screening Take-Ups with Zero Cost: Evidence from an Experiment on Formatting Invitation Letters in Italy*

We ran a randomized field experiment to ascertain whether a costless manipulation of the informational content (restricted or enhanced information) and the framing (gain or loss framing) of the invitation letter to the breast cancer screening program in Messina, Italy, affects the take-up rate. We show that giving enhanced loss-framed information about the risks of not having a mammography increases the take-up. This manipulation is especially effective among subjects with lower baseline take-ups – those living farther away from the screening site, residing in municipalities with low education, or with no recent screening experience – contributing to reduce socio-economic inequalities in screening. When we investigate the mechanisms behind our findings, we show that subjects exposed to our proposed manipulation are also less likely to postpone the appointment, signaling enhanced awareness about the risks related with delayed participation.

JEL Classification: C93, H51, I11, I18

Keywords: breast cancer screening, framing, information provision, randomized field experiment

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"An ounce of prevention is worth a pound of cure"

Benjamin Franklin

1. Introduction

Breast cancer is the most common neoplastic disease worldwide among women and the second most common cause of cancer mortality in developed countries (International Agency for Research on Cancer – IARC 2012). In addition, breast cancer is associated with very high costs for national health care systems. Overall, spending for breast cancer alone typically amounts to about 0.5-0.6 percent of the total health care expenditure of developed countries (Organization for Economic Co-operation and Development - OECD 2009).

Mammography screening programs at population-level are a key component of breast cancer control in many countries. The continuous implementation of these policies over the last decades mirrors the current consensus on the effectiveness of mammography screening. In a recent review of the evidence the IARC concludes that "after a careful evaluation of the balance between the benefits and adverse effects of mammographic screening […], there is a net benefit from inviting women 50 to 69 years of age to receive screening" (see Lauby-Secretan *et al.* 2015, pp. 2356-2357).[1] According to their results, this conclusion holds even after taking into account the uncertainty about the magnitude of the effects of screening on mortality (see e.g. Welch *et al*. 2016) and the recent evidence on overdiagnosis (see e.g. Bleyer *et al.* 2012),

In 2003 the European Council recommended population-based screening for women aged 50–69 years, with a target coverage rate of 75%. As of March 2014, screening programs based on EU indications were active in almost all the EU28 member states, although screening rates were still below the EU target rate in many states (Altobelli and Lattanzi 2014).The medical literature has identified the lack of knowledge about the disease and about the risks related to non-participation, as well as organizational barriers (e.g., screening invitations during working hours or the need to reach a screening center located far away), as relevant factors that may hamper participation (Altobelli and Lattanzi 2014, James *et al.* 2006).

In this study we developed a field experiment to evaluate the effectiveness of policies aimed at increasing the take-up rate for breast cancer screening at a low cost. The available empirical evidence shows that the use of invitation letters and reminders sent to women at their

[1] Evidence about the effectiveness on other age groups is instead mixed. According to Cutler (2009) and Moore *et al* (2009) these programs are also highly cost-effective.

homes increases take-up rates for breast cancer screening (Baron *et al*. 2008, Carrieri and Wuebker 2016). However, knowing which specific elements of the invitation letters affect take-up rates is very relevant for health policy makers. This would enable tailoring interventions to induce the participation of more women in the screening programs. Most notably, sending invitation letters with a different content would be at (almost) zero cost for the existing health care systems (Sunstein 2014, Purnell *et al.* 2015).

We focus on two aspects of the invitation letter that could trigger participation, namely the level of information disclosed and its framing. On the one hand, the role that information provision can play in triggering "optimal" choices has been recognized in many areas of research in the social sciences, including school choice (Hastings and Weinstein 2008, Hussain 2017, McGuigan *et al.* 2016, Ehlert *et al.* 2017), healthy eating (Wisdom *et al.*, 2010), energy efficiency (Newell and Siikamäki 2014), tax compliance (Bott *et al.*, 2017), and borrowing behavior (Bertrand and Morse 2011). On the other hand, the seminal paper of Rothman and Salovey (1997) put forward the hypothesis based on Prospect Theory (Tversky and Kahneman 1981) that gain-framed messages shall be more effective at promoting prevention behaviors (such as vaccines) and loss-framed messages at promoting detection behaviors (such as screening). This theory has been amply verified empirically (see O'Keefe and Jensen 2009).

Given these considerations, we hypothesize that invitation letters containing a loss-framed message with enhanced information about the consequences of not taking part in the program are more effective at increasing take-up rates than letters with a gain-framed content and with a restricted informational content. We test this prediction empirically by comparing the take-up rates of four different treatments – gain or loss framed messages with enhanced or restricted information – with a baseline of no information.

We ran our experiment in the Province of Messina, in Southern Italy (Sicily). The Messina Local Health Authority (LHA) has only recently implemented a population-level breast cancer screening program complying with the EU-mandated standards. The program started with a pilot in 2014, and was scaled up to reach population-level coverage by 2015, allowing all women aged 50-69 who are resident in the Province to have a free mammography every two years. Take-up rates have been low since its very beginning. Of those invited for screening, less than 15 percent of subjects took part in it. In order to improve this unsatisfactory outcome, in 2016 we teamed up with the Local Health Authority (LHA) of Messina and evaluated experimentally the set of policies described above.

Subjects involved in the Messina screening program are randomly invited to take a mammography in one of the available dates. In our experiment, we exploit this feature of the program to assign subjects to the different treatment groups. As shown in Figure 1, our manipulations affected women invited for screening during the 7^{th} to 11^{th} week of 2017 (from February 13 to March 19). We sent a different invitation letter to women invited in each week. For the rest of the year, a standard letter similar to our baseline was used. We observe a total of 6,194 subjects, evenly distributed among the five weeks of our experiment.

Our empirical analysis relies on population-level administrative data from the Messina LHA and the mail company managing the delivery of the invitation letters. Results show that the take-up rate in the group that received the letter combining the loss frame with enhanced information on the negative consequences of not taking the mammography is about 2.5 percentage points higher than in the baseline group. This is a sizeable effect, as it corresponds to 25% of the take-up rate in the baseline group (9.9%).[2] The other treatments, instead, are not effective. In addition, the data reveals that this effect is larger for subjects identified by the literature as having a higher risk of non-participation (Altobelli and Lattanzi 2014), that is, those living farther away from the screening sites, residing in municipalities with lower average education, and with no recent screening experience. Therefore, our manipulation helps in decreasing socio-economic inequalities in screening. Finally, when we investigate the mechanisms behind our findings, we show that subjects exposed to our proposed manipulation were also less likely to postpone the appointment, signaling enhanced awareness about the risks related with delayed participation.

Our contribution to the literature is threefold. First, as far as we know, no other study analyzes how the framing of the invitation letter interacts with its informational content to induce a subject to participate in a screening program. Second, two methodological aspects distinguish our contribution from most existing studies on framing and information provision effects on breast cancer screening take-up. On the one hand, while most of the literature focuses on small-scale experiments involving specific samples of individuals - such as young college students - our population-level randomized field experiment targets the whole population of

[2]Our results are robust to several specification tests. In particular, as our treatment varies by week, we provide evidence against the hypothesis that our findings could be attributed to seasonality in screening behavior or to potential confounding factors that are specific to a given treatment week. Additionally, the statistical significance of the estimated effect is confirmed even when we take into account the problem of multiple testing.

women participating in the national breast screening program in a geographical area. On the other hand, instead of relying on self-reported measures of perceived importance of screening, future screening intentions, or recall data about mammography attendance - as done by most existing studies – in our analysis our outcome variables is derived from administrative data regarding the *actual* decision of women to have a mammography. Third, by estimating heterogeneous effects we show that our proposed manipulation is especially helpful at increasing the take-up rate of groups with a higher risk of non-participation, enhancing the relevance of our results for policy makers interested at decreasing social inequalities in screening.

The paper unfolds as follows. Section 2 provides a review of the relevant literature. Section 3 presents the institutional context and Section 4 describes our experimental design. Our data and empirical methodology are presented in Sections 5 and 6, respectively. We describe our results in Section 7, followed by our conclusions.

2. Background literature

Our work broadly fits within the literature on "nudging", that has recently received considerable attention from economists and policy makers, as witnessed by the awarding of the 2017 Nobel Prize to Richard Thaler. A "nudge" can be defined as "any aspect of the choice architecture that alters people's behavior in a predictable way without forbidding any options or significantly changing their economic incentives" (Thaler and Sunstein 2008). More specifically, our research is grounded in two areas of research in behavioral economics: "information disclosure" and "gain-loss framing". In addition, it contributes to the literature on how to improve cancer screening take-up.

First, empirical evidence on the importance of information disclosure on individuals' ability to make "better" choices has been documented in many economic fields, including education (see Hastings and Weistein 2008, Hussain 2017, McGuigan *et al*. 2016, Ehlert *et al*. 2017), junk food consumption (Wisdom *et al.* 2010), borrowing money (Bertrand and Morse 2011), and energy efficiency investments (Newell and Siikamäki 2014).[3]

Second, decades of research have highlighted that individual choices are affected not only by the provision of information but also by the way such information is framed.

[3] Still, some empirical studies have shown that information overload discourages cancer prevention and detection behaviors (Jensen *et al*. 2014a).

Individuals can be sensitive to whether an alternative is framed in terms of its associated costs (*loss* frame) or benefits (*gain* frame) (Tversky and Kahneman 1981). To account for this shift of preferences, Prospect Theory proposes that people take more risks when they evaluate options in terms of associated costs, whilst they are more risk adverse when the same options are described in terms of associated benefits.[4]

Extending the logic of Prospect Theory to the domain of health persuasion, Rothman and Salovey (1997) (also see Rothman *et al*. 2006) contend that different levels of risk or uncertainty are involved in different health behaviors. They make a primary distinction between prevention and detection behaviors: "A behavior can prevent the onset of a health problem (e.g., condoms can prevent the spread of sexually transmitted diseases), [or] it can detect the development of a health problem (e.g., mammography can detect a potentially cancerous tumor)." Prevention behaviors are perceived as relatively non-risky since they help in maintaining good health (a *gain*), but on the other hand, detection behaviors serve to identify illnesses (a *loss*) and therefore they are perceived as relatively risky. On the basis of this difference, gain-framed messages are hypothesized to be more effective at promoting prevention behaviors and loss-framed messages at promoting detection behaviors.

Several studies have provided evidence in favor of this hypothesis. Gain-framed messages have been shown to help in increasing the prevention behaviors such as walking and exercising (Latimer *et al*. 2008, Northoff and Carstensen 2014, Mikels *et al*. 2016. O'Keefe and Jensen 2007 provide a meta-analytic review). However, loss-framed messages appear to be more effective than gain-framed ones in advocating breast cancer detection behaviors (see O'Keefe and Jensen 2009 for a meta-analytic review). For instance, in a seminal paper on the topic, Meyerowitz and Chaiken (1987) show that – among 90 female college students – those exposed to loss-framed messages were more motivated to perform breast self-examinations

[4]For example, if people have to choose between two treatment programs concerning the number of lives that will be lost, they are quite risk-takers if they are asked about avoiding a certain loss. However, if the same program is described in terms of the number of lives that will be saved, individuals are more risk-adverse. Evidence in favor of the "gain-loss" framing effect has been provided in several field of economics, for instance, with regard to consumption of private goods (Levin and Gaeth 1988), cooperation games and provision of public goods (Andreoni 1995, Rage and Telle 2004) and environmentally sustainable behaviors (Cheng 2011). Another example of nudging in health persuasion is Altmann and Traxler (2014) who show that reminders enhance dental check-up participation.

than the ones exposed to gain-framed messages. Similarly, by using a sample of 130 women aged 40+, Banks *et al*. (1995) show that exposure to loss-framed videos on breast cancer screening is more effective than exposure to gain-framed videos at enhancing self-reported mammography utilization measured 12 months after the intervention took place. Cox and Cox (2001) and Schneider *et al*. (2001) carried out analogous experiments reporting similar findings while more mixed findings are reported – among others – by Finney and Iannotti (2001), who sent differently framed reminder letters to 900 women involved in a breast cancer screening program in Indiana and Ohio.[5]

Finally, three recent papers on enhancing cancer screening take-ups are particularly close to ours in terms of the research question and the methodology adopted. First, Goldzahl et al. (2018) take into consideration a breast cancer screening program in two French departments and they test four manipulations of the invitation letter to the program: *i.* a new logo on the envelope; *ii.* patient-approved clarity in the letter's content; *iii,* a combination of the two previous treatments; *iv,* information on the number of women receiving mammograms in the recipient's area of residence. The authors find no significant effect on the take-up rate. Second, Bourmaud *et al* (2016) assessed the effect of providing a 12-page information leaflet on the take-up rate for breast cancer screening on a randomly selected sample of French women. They found a significant negative effect on the take-up rate. Third, investigating bowel cancer screening take-up in England, Wardle *et al* (2016) show that endorsement of the screening program by general practitioners on the invitation letter increased the overall take-up rate, while an enhanced reminder letter was especially effective at increasing the take-up rate of subjects residing in socio-economically deprived areas. Contrarily, the provision of information leaflets did not improve take-ups.

The manipulations designed in the aforementioned studies differ significantly from ours. By including additional information leaflets, some of them are not zero-cost. In addition, they do not consider the role played by the *interaction* of framing and information provision, which we deem to be a particular innovative contribution of this paper.

3. Institutional context

[5]Additionally, recent evidence shows that message framing effects can depend on the characteristics of the message recipient, which act as moderator variables (van't Riet *et al*. 2008, Zhao *et al*. 2012, van't Riet *et al*. 2014, Wansink and Pope 2014, van't Riet *et al*. 2016, Jensen *et al*. 2017).

3.1. Breast cancer screening programs

There is by now a consensus that early detection of breast cancer increases the effectiveness of medical treatments and reduces the risk of dying from breast cancer (Lauby-Secretan *et al.* 2015). Therefore, the design of effective screening programs that conform to internationally accepted standards plays a key role in fighting breast cancer. The current evidence is that women taking part in modern mammography screening programs have a 30% to 40% lower risk of dying for breast cancer (Paci *et al*. 2014, Weedon-Fekjaer *et al*. 2014, Coldman *et al*. 2014, Lauby-Secretan *et al*. 2015, Fang and Wang 2015). More specifically, a recent review by the IARC concludes that "Women 50 to 69 years of age who were invited to attend mammographic screening had, on average, a 23% reduction in the risk of death from breast cancer; women who attended mammographic screening had a higher reduction in risk, estimated at about 40%." (Lauby-Secretan *et al.* 2015, p.2356). This is equivalent to an average of 8 deaths prevented per 1,000 screened women.

Some studies have questioned the "mainstream" view illustrated above (see e.g. Welch *et al.* 2016). In particular, a recent strand of literature (see e.g. Bleyer *et al* 2012 and Elmore and Fletcher 2012) highlights that a higher screening rate may not only reduce mortality, but also lead to more cases of over-diagnosis, that is, to cases where "breast cancers […] would never have been diagnosed or never caused harm if women had not been screened" (Lauby-Secretan *et al*. 2015, p.2354). The available estimates of the phenomenon vary largely across studies and there is not a consensus yet on the most appropriate methodology to quantify this phenomenon (Carter *et al*. 2015; Nelson *et al*. 2016; Houssami, 2017). However, to the best of our knowledge, the estimated extent of over-diagnosis in Italy – the country of interest of this study – is low, as it ranges between 1 and 4.6 percent (see the review by Puliti *et al*. 2012), leading us to consider the phenomenon as negligible for our population of interest.[6]

The rigor of the Italian screening program is surely among the determinants of this low rate of over-diagnosis. Together with the other members of the EU, Italy has endorsed a set of recommendations aimed at guaranteeing high quality standards with implementing and administering nationwide breast cancer screening programs. In line with two specific

[6] Beckmann *et al*. (2015) and the Independent UK Panel on Breast Cancer Screening (2012) provide additional comparable international evidence. According to Duffy and Parmar (2013), estimates of higher over-diagnosis rates shall be mostly attributed to a short follow-up period and lack of adjustment for lead time (that is, the time between the detection of a disease under the screening program and its usual clinical presentation).

resolutions of the European Parliament (European Parliament, 2003, 2006) breast cancer screening programs should in fact satisfy four main requirements:

i) Breast cancer screening must be offered as a public health program to women aged between 50 and 69, encouraging them to have a mammography every two years;[7]

ii) The invitation letter sent to targeted women must provide information about the aims of the screening program, the screening interval, the potential benefits of breast screening, possible monetary charges to the participant, how to change the appointment, obtain the medical report and interpret results;

iii) Mammographies conforming to accepted protocols and clinical standards must be carried out by qualified radiologists using modern dedicated X-ray equipment and appropriate image receptors;[8]

iv) In order to increase the precision of breast screening tests and limit the risk of false positive/negative results, medical reports must be based on a double reading procedure in which two radiologists independently carry out their assessments.[9]

Finally, two additional institutional details about Italy, the country of interest of this study, are worth mentioning. First, in case of cancer detection the Italian public health system pays almost all direct costs related to cancer treatment. This feature makes the offer of a free and pre-booked mammography very attractive from a financial perspective. Second, in this country Local Health Authorities are responsible for the implementation of the national breast cancer screening program. This includes the administration of the screening program, the invitation of targeted women, the organization of training activities for radiologists and medical staff involved in the program, and the periodic evaluation of the results of the screening program.

[7] The specific age range targeted by the screening programs is motivated by the fact that, as empirically observed, risk of breast cancer increases with age, with a cumulative incidence among women in Europe and North America of about 2.7% by age 55, 5.0% by age 65, and 7.7% by age 75 (Key *et al.*, 2001). Lauby-Secretan *et al.* 2015 also highlight that the evidence on the effectiveness of breast cancer screening on other age ranges is mixed. According to estimates based on data between 2008 and 2013 (see Italian Association for Medical Oncology - AIOM 2017), the probability of breast cancer in Italy is 2.4% up to 49 years (1 out of 42 women), 5.5% between 50 and 69 years (1 out of 18 women), and 4.7% between 70 and 84 years (1 out of 21 women).

[8] In order to ascertain his/her qualification, a radiologist is required to evaluate a minimum of 500 screening cases per year and participate in specific training programs.

[9] Using observational data for the Austrian region of Tyrol, where double reading is not performed, Buchberger *et al.* 2018 show that sensitivity of screening increases for the average women if mammographies are combined with ultrasound scans.

In spite of this de-centralized organization, the need to comply with the EU guidelines assures that the quality of the screening service provided is the same irrespectively of the characteristics of each local health care center which offers the service. .

3.2. The national breast cancer screening program in the Province of Messina

We ran our field experiment in the Province of Messina, located in the north-east of Sicily. The Province of Messina includes 107 municipalities with a resident population of 636,653 individuals (306,911 males and 329,742 females, ISTAT, 2017), distributed over a geographical area of about 3,247 km^2. Starting with a pilot study in 2014 and reaching population-level coverage in 2015, the Messina LHA has implemented the national breast cancer screening program by inviting all women aged 50-69 living in the Province to have a free mammography every two years. The female population aged between 50 and 69, actively targeted by the screening program, comprises 92,048 individuals.

The Province is divided into eight public health districts, and five health care centers (hospitals and clinics) offer the screening program, all satisfying the main quality and procedural requirements imposed by the European guidelines described in the previous section.[10] Figure 2 shows the boundaries of the eight health districts in the Province of Messina and the geographical localization of the five health care centers involved in the national breast cancer screening program. The LHA collects the time slots that the health care centers can devote to the screening program, guaranteeing that there are enough slots to cover the entire targeted population in the district for each year.

In spite of the financial and organizational effort of the LHA of Messina, as well as of the high quality of the health care centers, the participation rate in the breast cancer screening program in the Province of Messina has been very low. Of all the invited women, only 14.7%, and 13.3% had a mammography within the national breast cancer screening program in 2015 and in 2016, respectively. In Italy, the average participation rate to the national breast cancer screening program among women aged 50-69 in the period 2013-2016 was 53% (Italian National Health Institute - ISS 2017), with northern regions being the best performers and

[10] The eight districts are: the city of Messina, Taormina, Milazzo, Lipari, Barcellona Pozzo di Gotto, Patti, Mistretta, Sant’Agata Militello. The Ospedale “San Vincenzo” in Taormina, the Poliambulatorio in Messina, and the Ospedale “Barone Romeo” in Patti serve the population in the corresponding districts; the Presidio Ospedaliero in Sant’Agata Militello serves the districts of Sant’Agata Militello and Mistretta; the Presidio Ospedaliero “G. Fogliani” in Milazzo serves the districts of Milazzo, Barcellona Pozzo di Gotto and Lipari.

southern regions being associated with the lowest coverage (the highest and lowest average take-up rates are respectively recorded in the Province of Trento – 77% – and in Campania – 21%. The coverage in the Province of Messina is also well below the regional average for Sicily for the same period, equal to 44%). Hence, we purposively focus our attention on an area with a very low participation rate, where the need and margins to improve take up rates are higher.

4. The experimental design and procedures

4.1. The invitation letters

In designing our experiment, we actively collaborated with the screening unit to modify the wording of the invitation letter, while always satisfying the main requirements imposed by the European guidelines described in the previous section. The baseline version of the invitation letter includes two pages, and we provide an example of this, as used in our experiment, in the Appendix. On the first page, after briefly introducing the national breast cancer screening program as offered in Messina, the invitee finds all the information about the date, time and venue of the mammography, as well as other useful information to attend the mammography and, if needed, to change the date and time of the appointment. The first page also carries the letterhead and the address of the LHA of Messina, as well as other information about the institutions in charge of implementing the program in question. The second page contains a short description of the aims of the national screening program, as well as the usual form required by the Italian law for the processing of personal data. The patient must sign and hand in this form when attending the mammography.

Our baseline invitation letter contains no information on the consequences of screening. We used this during the first week of our experiment. Over the following four weeks, we employed a 2x2 design and manipulated the invitation letter by changing the brief introduction and description of the national breast cancer screening program offered for Messina along two dimensions:

i) The *framing*: either *gain-framed*, by pointing out the potential benefits of participating in the national breast cancer screening program, or *loss-framed*, by emphasizing the potential negative consequences of not taking the mammography;

ii) Including *enhanced* or *restricted information* about the potential benefits (negative consequences) of participating/not participating in the national breast cancer screening program;

The paragraphs of the invitation letters that have been manipulated in our design are reported in Table 1. It is worth noting that the information provided in the "Enhanced" treatments contains general statements on the potential advantages/disadvantages of participating/not participating in the national breast cancer screening program which do not require any specific medical knowledge to be understood.

4.2. Procedures

Each participant was randomly assigned by the LHA computer system to one of the time slots made available by the health care center serving her district of residence. Then, the screening unit gave the lists with names, tax codes and addresses to a professional private mail company. This mail company sent these invitation letters to the targeted women three weeks before the assigned appointments, thus keeping a fixed time interval between the invitation dispatch and the screening date.

Our experiment focuses on the invitation letters sent to women targeted for mammography slots during working days of the five consecutive weeks, from February 13 to March 19 (weeks 7-11 of 2017). Feasibility constraints imposed by the mail company prevented us from carrying out a person-by-person or day-by-day randomization. Instead, each week was associated with a specific version of the invitation letter, with all invitations in the same week receiving the same letter format. As discussed above, Figure 1 shows the order in which the five versions of the invitation letters were sent to targeted women, together with the weeks of the corresponding mammographies. This order was decided by the authors in accordance with the LHA before women were actually randomized to slots. Only one letter was sent to each women, and there were no deviations between the assigned and actual letter type delivered.

5. The Data

Our data came from two administrative sources. From the administrative archives of Messina's LHA we obtained: the date of birth, whether the woman had undergone a mammography scan in the public health system between January 2014 and June 2016 (as a consequence of previous screening invitations in the 2014 pilot or in the population-level program started in 2015, or due to a GP prescription), whether she had already been invited to have a mammography in the LHA screening program in previous years (either in the 2014 pilot or in the population-level program started in 2015), the allotted health care center and the actual screening take-up after the invitation – our outcome. This only monitors program participation, that is, screening in the allotted slot or in a different one after re-scheduling. We will distinguish between these two when we study the mechanisms behind program participation. Instead, we do not have information on screening carried out at private health care centers or at public health care centers on the basis of a GP prescriptions.

We used the unique national tax number (*codice fiscale*) to merge this piece of information with the administrative archive of the mail company that managed the delivery of the invitation letters. This archive contains information on the date of the invitation (and hence on the treatment status), home address and whether the letter was sent by regular or express mail. Although the latter was the default option, some remote areas of the Province of Messina were not covered by express mail services. In those instances, regular mail was the only feasible option.[11] We also used home and health care center addresses to compute home-hospital travel time.[12] In total, we used data about 6,194 women.[13]

We report the allocation of subjects in our sample among the various treatment groups in Table 2, and show descriptive statistics for the other variables used in the analysis in Table 3. Table 2 shows that by design the sample is evenly distributed across the five treatment groups. Table 3 reveals that, on average, only a small fraction of subjects (10.4 %) actually chose to take part in the screening program. Similarly, only 13.6% of subjects had previously undergone a mammography in the public health system between January 2014 and June 2016, when we started to engage with the LHA. This is in spite of the fact that, given the population-level coverage of the LHA's screening program, about 95% of all subjects in our sample had already been invited to the screening in previous years. The other 5% is likely to have being excluded either because they were too young to be invited before or because they had recently moved from other LHAs. The average year of birth is 1958 (so the average age is 59), about 85% of

[11] As shown in Table 4 below, the distribution of delivery by express mail is balanced across treatment groups. Additionally, data on actual letter delivery is not available.

[12] We compute travel time by car under standard traffic conditions by using the *georoute* routine for STATA.

[13] This corresponds to 95% of the full population involved in the screening program during the experimental weeks. For the remaining group (347 observations), either we cannot merge the two data sources because of reporting errors in the individual identifier (77 observations), or there are missing data in the variables used in the analysis (207 observations). Since the distribution of travel time has a long right tail, we also drop outliers in terms of travel time (the top 1% – 63 observations). Results are unaltered if we do include these observations. Subjects with missing data and travel time outliers are evenly distributed across treatment groups (the p-value of a test for joint equality of prevalence among treatments is 0.54).

the subjects received the invitation letter via express mail, and the average home-hospital travel time is about 27 minutes. The distribution of travel time – reported in Appendix Figure A1 – is skewed to the left, with a long right tail including people living in remote rural areas of the Province or on the Aeolian Islands. The median travel time is much lower than the mean (almost 7 minutes lower). Therefore, all analyses that involve travel time as the outcome focus on the median instead of the mean, as the former is less sensitive than the latter to the presence of outliers. Finally, the largest fraction of women in our sample was invited to have their mammography at health care center 5.[14]

6. Empirical Methodology

We use the following regression model:

$$Screened_i = \alpha + \beta_1 RestrictedGain_i + \beta_2 RestrictedLoss_i + \qquad (1)$$

$$+\beta_3 EnhancedGain_i + \beta_4 EnhancedLoss_i + \gamma X_i + \varepsilon_i$$

where the index *i* stands for the individual, and the outcome is a dummy variable equal to 1 if the subject takes part in the screening program, and to 0 otherwise. We regress this variable on a constant, a set of four dummy variables for belonging to each treatment group and the covariates in vector *X*, that include: a dummy equal to 1 if the subject received an invitation to have a mammography within the LHA's screening program between January 2014 and June 2016 and to 0 otherwise; a dummy equal to 1 if the woman had a mammography in the public health system between January 2014 and June 2016 and to 0 otherwise; year of birth fixed effects; a dummy equal to 1 for letter delivery via express mail and to 0 for regular mail; fixed effects for the health care center where the subject is invited to have the mammography; home-hospital travel time.

In Equation (1), the constant identifies the mean outcome (screening prevalence) for the baseline group. Given randomization, the coefficient β_j, $j=1, \ldots, 4$, associated to each of the treatment indicators identifies the average treatment effect on screening prevalence of each manipulation with respect to the baseline.

[14] Health care center names have been anonymized for confidentiality reasons. Health care center 1 is the omitted category in all analyses. It is worth remembering that women are invited to take the screening in the hospital of the district of residence, and that all hospitals follow the same scanning protocol.

In Table 4 we provide evidence in favor of successful randomization by reporting the mean (median for travel time) by treatment group of each of the covariates listed in Table 3. The stars reported in the Table indicate significant differences between the mean (median for travel time) of a given covariate for each treatment group with respect to the control group. In addition, the last column reports the p-value of a joint test of equality in means (medians for travel time) among treatments. Overall, the distribution of covariates is comparable among treatments, suggesting that randomization worked well. This is confirmed by the absence of many statistically significant differences between the control group and the other ones and by the p-values reported in the last column, that are always above 0.1.[15]

The evidence regarding balancing presented in Table 4 suggests that the inclusion of covariates in vector *X* shall not affect the estimation of the treatment effects of each manipulation, but may still be useful to increase precision. We verify this by estimating Equation (1) both with and without controls.

Since we are analyzing a binary dependent variable, we estimate Equation (1) using both a logit model and a linear probability model (i.e. using OLS).[16] We always estimate standard errors that are robust to the presence of heteroscedasticity.

7. Results

7.1. Main results

Table 5 reports average marginal effects on screening prevalence of each treatment with respect to the baseline. We estimate Equation (1) with logit (Columns 1 and 2) and linear probability (Columns 3 and 4) models, with (Columns 2 and 4) and without (Columns 1 and 3) the inclusion of the covariates in vector *X*. As a benchmark, in the last line of the table we also report the mean outcome in the baseline group.

The main result is that receiving a letter with enhanced information content that is loss-framed to highlight the risks related to the decision of not taking part in the screening program

[15] We also estimated a multinomial logit model for predicting treatment group on the basis of the covariates in vector *X*. The pseudo R-squared of the model is equal to 0.0012 and the correlation between actual and predicted treatment status is also close to zero, reinforcing the evidence on balancing shown in Table 4.

[16] The linear probability model that does not include covariates in vector *X* delivers simple estimates of mean-comparisons of the outcome among the various treatments.

increases participation with respect to the control group by 2.3 to 2.8 percentage points, depending on the specification. Compared to the prevalence of screening in the baseline group – equal to 9.9 percentage points – this effect is equivalent to a 23 to 28% increase, a very pronounced one.[17] On the other hand, none of the other manipulations deliver significant effects.[18] Finally, as expected, the inclusion of covariates and the choice of different estimation methods do not alter estimation outcomes in a relevant way.

7.2. Threats to identification

Our experiment compares the outcomes of five treatment groups to which subjects were randomly allocated. However, for feasibility reasons, each group received an invitation to take the screening in a different week: the 7th to 11th weeks of the year. Although these are five consecutive weeks, thus concentrated in a relatively narrow time interval, it could still be that the observed differences in screening rates among treatment groups are due to seasonality in screening behavior, that would have been present even if all subjects had received the same letter.

To provide evidence against this hypothesis, we consider subjects invited to take a mammography in the Messina LHA program in 2015 and 2016.[19] Even in this years, subjects were randomly assigned to invitation dates. However, while in 2017 we sent different letters to subjects invited in different weeks, in 2015 and 2016 all subjects received the same invitation letter, comparable to our baseline invitation letter. Therefore, a significantly higher take-up rate during the 11th week of 2015 or 2016 would suggest that the treatment effect estimated for 2017 could be attributable to seasonality. Table 6 compares the estimates of Equation (1) obtained from logit models without controls for the weeks 7th to 11th of 2015, 2016 and 2017, and shows that no significant pattern can be detected in years before 2017, when our

[17] For the logit specifications, we can also express these estimated effects in terms of odds-ratios, as commonly done in epidemiology. When we do so, we get an effect of 1.318 and 1.316 for the models without and with covariates, respectively, suggesting that subjects exposed to the "enhanced-loss" manipulation are close to 32 percent more likely to participate in the program than subjects in the control group.

[18] In Appendix Table A1 we report the estimated differential effects between the "Enhanced - Loss" manipulation and all of the other ones, and show that the former leads to significantly higher screening rates compared with any of the latter.

[19] There is no data available before 2014, as the screening program started in that year. We omit 2014 as only a pilot study was implemented in that year.

manipulations were not active. This evidence supports a causal interpretation of our main results for 2017.[20]

Although we had verified ex-ante that our experimental period included no special festivities or public holiday, the presence of confounding factors that are specific to a given treatment week and can affect take-up rates is an additional concern for identification. For instance, every October the major breast cancer charities organize the "Breast cancer awareness month", and advertise participation to breast cancer screening programs. Had we selected a treatment week in the month of October, this initiative would have confounded identification of our treatment effects.

In Figure 3 we provide indirect evidence that it is unlikely that subjects invited to take a mammography in different weeks were exposed to different concurring campaigns or policies concerning breast cancer screening. We report the results of Google trend searches (see D'Amuri and Marcucci 2017) for the keywords "breast cancer" and "mammography" (*tumore alla mammella* and *mammografia*) for the whole Sicily (no finer geographic disaggregation is possible) for the period between the dispatch of the first invitation letters – three weeks before the first treatment week – and the last treatment week. If there was any concurring campaign active in a specific week but not in the others, then we would expect to find different trends in Google searches among weeks. Still, Figure 3 shows that there is no clear different search pattern by week, dispelling this concern.[21] Appendix Figure A2 provides additional supporting evidence by showing that Google searches for "flu", "cold", "physician", and "doctor" (*influenza*, *raffreddore*, *medico*, and *dottore*) in Sicily are also stable over the study period.

We have also investigated two additional potential week-specific confounding factors. First, we are worried that week-specific weather shocks could have affected the take-up.

[20] Covariates are not available in the data for years before 2017. Results using linear probability models are fully comparable and available from the authors. Estimated effects for 2015 are in some cases associated with large standard errors. This is due to the low number of mammography slots made available by the health care centers in those weeks. We have also tried to estimate a difference-in-differences model, after stacking the data and using as pre-treatment period years 2015 and 2016. We still get an effect of the "enhanced – loss" manipulation that is equal to 2.4 percentage points, but it becomes far from significant ($p>0.1$). This is not surprising given the absence of effects in the pre-treatment years and the loss of precision generated by the difference-in-differences model.

[21] Search trends for these keyword for the whole Italy, and even the whole World, are also rather homogeneous over these weeks (results are available from the authors).

Appendix Table A2 reports balancing tests like the ones shown in Table 4 for the millimeters of the rainfall per day and the average temperature in Celsius degrees in the municipality of the assigned health care center in the day when the woman was invited to take the mammography. Data are provided by the *Osservatorio Acque Regione Siciliana*, and are collected by weather stations placed in the municipalities of interest. On the one hand, rain and cold could decrease the opportunity cost of leisure, increasing the likelihood of screening. On the other hand, they could cause travel difficulties, decreasing participation.[22] Results for rainfall show that the incidence of rain is close to zero in all weeks but the one when we implemented the "Enhanced – positive" manipulation. Although the difference across weeks is significant, its magnitude is small. Similarly, average daily temperature was mildly higher in the "Restricted - loss" week. Even in this case – although significant – the magnitude of the differences is small. In addition, as shown in Appendix Table A3, all of our estimated effects are wholly unaltered by the inclusion of rainfall and average temperature among the controls, and the estimated coefficients for rainfall and temperature are close to zero and not statistically significant (see Appendix Table A3). This result dispels the concern that weather differences between weeks could have significantly affected take-up rates.

Second, a strike organized on March 8th 2017 – a date that falls during the "Enhanced – positive" manipulation week – could also have affected take-up. First, aggregate data from the Ministry of Public Administration[23] for the whole of Italy show that participation in the strike was modest (25 percent of the interested workforce) and mostly concentrated in the school sector. Second, if the strike affected participation in the breast cancer screening program – either because women were involved in the protests or because they were unable to reach the hospital as a consequence of the strike – we would expect to see a sharp drop in participation during that specific day of that week. Yet in Appendix Table A4 we show that the estimated differences in participation across the days of the week interested by the strike are not significant ($p = 0.36$), weakening this concern. In fact, even if we assumed that the take-up rate for the 8th of March was as high as the highest take-up rate during the week (11.7%, for the 9th of March), the weekly take-up rate would change only marginally, from 10.3% to at 11.1%. Hence, the difference with the take-up rate of the baseline group would be equal to 1.2

[22]This might be especially true for the 342 subjects residing in the Aeolian Islands. Still, both the magnitude and the significance of our results is unaltered when we drop these subjects (results are available from the authors).

[23]http://www.funzionepubblica.gov.it/sites/funzionepubblica.gov.it/files/8_marzo_dati_adesione.pdf

percentage points. Given a standard error of the estimated effect of 1.2 percentage points, this difference is still below the minimum effect that we can significantly detect.

A final threat to identification in our setup could be the presence of spillover effects. In fact, it could be that women receiving different letters interact with each other and discuss about the differences in the content of the letters. If this was the case, then we would be estimating a lower bound of the true treatment effects. A possible solution to avoid this threat could have been to use the local area or town as a unit of randomization, but the mail company prevented us from doing this for feasibility reasons. Still, we believe that the likelihood of interactions is rather low, because of the relatively small scale of our intervention. In fact, out of a target population of the program of close to 90,000 women, only 6,000 were invited to take the mammography in the experimental weeks. Hence, each different type of letter was received by less than 1.5 percent of the population of interest, dampening this concern.

7.3. Multiple hypothesis testing

Our empirical analysis compares the effectiveness of four different manipulations with respect to a baseline. Let the familywise error rate (FWER) be the probability of rejecting at least one true null hypothesis, that is, of making at least one type I error. If a single test is performed at the 5% level of confidence and the null hypothesis being tested is true, we expect a 5% chance of incorrectly rejecting it. If N independent tests are simultaneously carried out and all corresponding null hypotheses are true, the probability of at least one incorrect rejection is $1\text{-}0.95^N$. In our case, since $N=4$, this probability is equal to 18.5%, well above the assumed 5%. This probability will be equal to 34.4% if we assume a 10% level of confidence.

List, Shaikh and Xu (2016) have devised a bootstrap-based methodology for testing multiple null hypotheses simultaneously in experimental settings with multiple treatments. This procedure asymptotically controls the FWER and, by incorporating information about dependence ignored in classical multiple testing procedures (Bonferroni and Holm 1979), it has a greater ability to detect truly false null hypotheses.

To verify that the significance of the estimated effect of the “enhanced – loss” manipulation is confirmed even when we account for multiple testing, we apply the List, Shaikh and Xu (2016) method to our data. Focusing on unconditional take-up rate comparisons across treatments and using 1,000 bootstrap iterations we obtain a p-value of 0.082, confirming the statistical significance of our main empirical result, at least at the 10 percent level of confidence.[24]

7.4. Heterogeneous effects

According to the medical literature there are inequalities in screening take-up along several socio-economic dimensions. For instance, those living father away from the screening site are less likely to attend screening programs (Altobelli and Lattanzi 2014), and so are the less educated.[25] Additionally, there is persistence in screening (Vyas 2014), so that it is unlikely that women who did not take part in the program in the past will suddenly begin to participate. To understand whether our proposed manipulation can help to decrease such healthcare disparities, we estimate heterogeneous effects along these three dimensions.[26]As we only estimate a non-zero average effect for the "Enhanced-Loss" manipulation, in this section we only report heterogeneous effects for subjects exposed to this manipulation with respect to the baseline group. Other results are available from the authors. As a matter of fact, for no other manipulation we estimate heterogeneous treatment effects that are significantly different from zero at the standard level of confidence.

Panel A of Table 7 reports the effect of the "Enhanced-Loss" manipulation obtained from split-sample estimation of Equation (1) between those who have travel times below and above the sample median (close to 20 minutes), using logit models with and without covariates.[27]The "Enhanced Loss" effect is larger and only statistically significant for the latter group (3.5 vs. 0.8 percentage points in the model with covariates).Unsurprisingly, given that the screening prevalence in the baseline group is smaller among those living farther away from the hospital, the differential effect is even starker in percentage terms (40 percent vs. 7.3 percent in the model with covariates). To test for the significance of the difference between the effects in the two subsamples, we jointly estimate the models using seemingly unrelated estimation. We reject that the two effects are equal with a p-value of 0.08 and 0.09 for the models without and with controls. It appears that for subjects living farther away from the screening site, the manipulation significantly increases the perceived risks of negative outcomes related to non-

[24] When we apply the Bonferroni and Holm (1979) procedure we obtain p = 0.096.

[25] For instance, Palència *et al.* (2010) estimate that in Italy the prevalence of breast cancer screening is 25% higher among women with tertiary education than among women with primary or lower education.

[26] We have also estimated differential effects by age, but detected no relevant pattern.

[27] Results using linear probability models are fully comparable and available from the authors.

participation, enough to compensate for the higher travel time and hence trigger participation. As screening centers are located in urban areas, subjects residing farther away from the screening sites come from remote areas and may have lower education, a relevant determinant of screening take-up (Palència *et al.* 2010). If this was the case, our heterogeneous effects by distance could instead be capturing heterogeneities by education of subjects. Although we do not have data on the education of subject in our study, we can still measure the share of inhabitants with at least a high school degree in the municipality of residence of each subject in our sample, using data from the Italian 2011 Population Census. The last two columns of Panel A in Table 7 show that our results on heterogeneous effects by distance hold even when we include this variable (as well as population density by municipality) among the controls, dispelling this concern.[28]

Next, in Panel B of Table 7 we report heterogeneous effects between subjects residing in municipalities with a percentage of high school graduates above and below the median in the sample (45%). Results show that the effect of the “Enhanced-Loss” manipulation is only significant for the latter group (3.7 vs. -0.1 percentage points in the models with covariates, with the difference in the effects being statistically different from zero with a p-value of 0.06). Therefore, enhanced salience of the losses related to non-participation is more effective at raising the attendance of the low educated. Although in our sample the take-up rate in the two groups in the baseline week is very similar (9.8% vs. 10%), this change in the invitation letter could contribute to decrease the inequality in screening by education detected by others in the literature (see e.g. Palència *et al.* 2010).

Finally, in Panel C of Table 7 we distinguish between women who had a mammography in the public health system between January 2014 and June 2016 and the others, and show that the “Enhanced-Loss” manipulation only exerts a significant positive effect on women who did not undertake a mammography in the past two years (2.8 vs. 0.7 percentage points in the model with covariates, the difference in the effect is statistically different from zero with a p-value of 0.04). As women with no recent screening experience have a substantially lower propensity to participate in the baseline week (5.9% vs. 37%), our manipulation is especially effective at enhancing take-up among a group that has a high risk of non-participation. For the non-screened group, in fact, the effect is equal to close of 50% of the take-up in the baseline week.

[28] The effect of the “enhanced-loss” manipulation in the full sample is unaltered by the inclusion of these covariates.

7.5. Mechanisms

What are the mechanisms behind our results? A plausible explanation of the estimated effect is that providing negatively framed information on the consequences of the choice enhances salience of the letter and increases the perceived importance of participating in the screening program (akin to a psychological "unpacking" effect, see Van Boven and Epley 2003 and Angelini *et al*. 2017). Without survey evidence on the effects of our manipulation on subjects' perception of breast cancer risk and screening effectiveness, as well as on its association with participation, we can only provide indirect evidence on this mechanism.

Subjects in our experiment had the possibility to contact the LHA and reschedule the appointment if the proposed date did not fit their schedule, and about one third of subjects who participated in the program did so. In all but 17 cases, they requested to postpone the appointment. We believe that showing up at the prescribed date instead of postponing the appointment can be considered as a proxy of perceived importance of the program and of the risks related with delayed participation. We therefore provide indirect evidence on our proposed mechanism by testing whether, on top of being more likely to participate, subjects who received the "enhanced – loss" letter were less likely to postpone the appointment conditional on participation.

Let T be a treatment dummy, let D be participation in the program and P postponement of the appointment. We are interested in studying the effect of T on Pr(P|D). By the definition of conditional probability, we have that $\Pr(P|D) = \Pr(P, D) / \Pr(D)$. Therefore,

$$\frac{dPr(P|D)}{dT} = \frac{1}{\Pr(D)}\left[\frac{dPr(P,D)}{dT} - \frac{dPr(D)}{dT}\Pr(P|D)\right]$$

The right hand side is identified because we observe in the data $Pr(P|D), Pr(P, D)$ and $Pr(D)$, and can estimate the effects of T on $Pr(P, D)$ and $Pr(D)$ using simple regressions. We estimate these equations jointly to allow for correlation among the estimates of the two effects, and do inference using the delta method. For this analysis we use linear probability models to facilitate the computation of marginal effects. Table 8 reports the treatment effects for the "enhanced-loss" manipulation from models with and without covariates.[29] It shows that this treatment

[29] The effects of the other manipulations are not shown for brevity but available from the authors. We detect a negative effect on Pr(P|D) also for the "restricted - loss" and the "enhanced - gain" manipulation, but of a much smaller size than the effect of the "enhanced – loss" manipulation (between one third and one half, depending on

decreases the probability of postponement conditional on participation by about 30 percentage points, or 58% with respect to the probability of postponement conditional on participation in the baseline group, equal to 52 percentage points. This result suggests that our manipulation was especially effective at enhancing the perceived importance of screening and of the risks related with delayed participation.

8. Discussion and conclusion

In this study, we ran a population-level randomized field experiment on about 6,000 women involved in the national breast cancer screening program of the Province of Messina in Sicily - Italy. We investigated whether a cost-free manipulation of the framing (gain vs loss) and informational content (restricted or enhanced information) of the program invitation letter increases take-up rates.

In line with our theoretical predictions, we find that the treatment containing loss framed messages with enhanced information about the negative consequences of declining a mammography significantly increases the take-up rate of close to 25% with respect to the take-up rate in the control group. The other treatments (restricted gain-framed information, restricted loss-framed information, enhanced gain-framed information) are instead ineffective.

To appreciate the potential effects of our manipulation on survival rates, we carried out some "back of the envelope" calculations.[30] Assuming that screening prevents the death of 8 out of 1,000 screened women, as estimated by Lauby-Secretan *et al*.(2015), by increasing the take-up rate from 10 to 12.5%, our manipulation would save 10 instead of 8 lives out of 10,000 invited women, increasing the survival rate by 25% at zero cost. Given that the target population for the Province of Messina program is nearly 90,000 women, we estimate that switching to the “enhanced-loss” letter would prevent the deaths of 18 more women as compared to the current situation.

All things considered, we believe that our study has great relevance not only for economists and other social scientists interested in understanding the behavioral motives that guide investment in health promoting behaviors, but also, and especially, for policy makers keen to design cost-effective screening programs.

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the specification – the differences against the "enhanced - loss" manipulation are significant with p<0.05). Estimation of the effect of the “enhanced-loss” manipulation on P for the subsample with D=1 also delivers a negative effect of 25 percentage points (p<0.01), but this is biased by the “conditional-on-positive” issue discussed by Angrist and Pischke, 2008.

[30] For confidentiality reasons we cannot have access to data on cancer detection or mortality.

To begin with, the conclusions of our experiment could help to improve the design of the invitation letters for national breast cancer screening programs in order to increase take-up rates at zero cost. For instance, the “European guidelines for quality assurance in breast cancer screening and diagnosis", published by the European Commission in 2006, on p.390 advise health policy-makers that the invitations to the screening program should be *“positively framed (e.g. 9 out of 10 recalled women are found to be normal rather than 1 out of 10 recalled women will have cancer)”*. Our experimental findings from the Province of Messina, an area with a very low take-up rate, do not lend empirical support to this advice. To ensure that the highest possible take-up rate is achieved, our findings would call for an update of the guidelines, at least for programs implemented in comparable areas with very low take-up rates, where the need to intervene and improve participation is more pressing.

In addition, the effect of our proposed manipulation is stronger for subjects identified by the literature as being at higher risk of non-participation, such as those living farther away from the screening sites, the low educated and those with no recent screening experience. Therefore, our costless manipulation has proven to be effective at reducing socio-economic inequality in screening, a key objective of many health policy makers.

Finally, we have provided evidence that subjects receiving the “enhanced information – loss framing” letter were not only more likely to get screened, but also less likely to postpone the appointment conditional on screening, suggesting that our manipulation enhanced the perceived importance of screening and of the risks related with delayed participation.

Needless to say, our analysis could be extended in several directions, for instance by examining a different reference population (e.g. by focusing on an area with a higher baseline take-up rate), by studying long-term effects on take-up at subsequent waves of the screening program as well as on health outcomes, and by combining different treatments.

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Tables

Table 1. Manipulations of the invitation letter content: information and framing

	INFORMATION INCLUDED	INFORMATION EXCLUDED
GAIN FRAMING	Treatment "Enhanced - Gain" On page 1: *"Scientific studies demonstrate that participating in breast cancer screening programs can have relevant positive effects on the treatment of an early diagnosed disease: it reduces the mortality rate, allows for less extensive surgeries, more effective treatments, with higher chances of recovery."* On page 2: "*Scientific evidence demonstrates that an early diagnosis of this cancer can have relevant positive effects on the treatment of the disease. In particular, it has been documented that an early diagnosis of this cancer reduces the mortality rate, allows for less extensive surgeries, more effective treatments, with higher chances of recovery."*	Treatment "Restricted - Gain" On page 1: *"Scientific studies demonstrate that participating in breast cancer screening programs can have relevant positive effects on the treatment of an early diagnosed disease."* On page 2: "*Scientific evidence demonstrates that an early diagnosis of this cancer can have relevant positive effects on the treatment of the disease."*
LOSS FRAMING	Treatment "Enhanced - Loss" On page 1: *"Scientific studies demonstrate that not participating in breast 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."* On page 2: "*Scientific evidence demonstrates that a late diagnosis of this cancer can have relevant negative effects on the treatment of the disease. In particular, it has been documented that a late diagnosis of this cancer increases the mortality rate, implies more extensive surgeries, less effective treatments, with lower chances of recovery."*	Treatment "Restricted – Loss" On page 1: *"Scientific studies demonstrate that not participating in breast cancer screening programs can have relevant negative effects on the treatment of a lately diagnosed disease."* On page 2: "*Scientific evidence demonstrates that a late diagnosis of this cancer can have relevant negative effects on the treatment of the disease."*

Table 2. Allocation of the sample among treatment groups.

Treatment Group	(1) Observations	(2) Percent
Baseline	1,237	19.97%
Restricted - Gain	1,238	19.99%
Restricted - Loss	1,245	20.10%
Enhanced - Gain	1,238	19.99%
Enhanced - Loss	1,236	19.95%
Total	6,194	100%

Table 3. Descriptive statistics.

Variable	(1) Mean	(2) Std. dev.
Outcome:		
Screened	0.104	0.305
Covariates:		
Screened Jan14 - Jun16	0.136	0.343
Invited to screen in previous years	0.922	0.268
Year of birth	1958.1	6.232
Express mail	0.848	0.359
Home-hospital travel time (minutes)	27.76	28.66
Health care center 1	0.093	0.291
Health care center 2	0.309	0.462
Health care center 3	0.120	0.325
Health care center 4	0.132	0.338
Health care center 5	0.345	0.476

Notes: the table reports descriptive statistics for the outcome and covariates used in the analysis. Health care center names have been anonymized for confidentiality reasons. Number of observations: 6,194.

Table 4. Balancing tests.

	(1) Baseline	(2) Restricted Gain	(3) Restricted Loss	(4) Enhanced Gain	(5) Enhanced Loss	(6) Joint equality (p-value)
Screened Jan14 - Jun16	0.131	0.128	0.137	0.143	0.142	0.71
Invited to screen in previous years	0.928	0.922	0.925	0.921	0.916	0.86
Year of birth	1958.3	1958.2	1957.9	1958.0	1958.2	0.48
Express mail	0.866	0.855	0.841	0.836**	0.844	0.58
Home-hospital travel time (median)	19.95	19.64	21.38*	20.80	20.63	0.38
Health care center 1	0.096	0.092	0.092	0.092	0.095	0.99
Health care center 2	0.301	0.307	0.311	0.317	0.309	0.96
Health care center 3	0.122	0.120	0.120	0.118	0.121	0.99
Health care center 4	0.133	0.133	0.128	0.131	0.133	0.98
Health care center 5	0.347	0.347	0.349	0.342	0.341	0.97

Notes: the table reports the mean (median for travel time) of each variable by treatment group. Stars indicate significant differences in mean (median for travel time) of a given covariate between each treatment group and the control group. Column (6) reports the p-value test for joint equality in means (medians for travel time) among treatments. Health care center names have been anonymized for confidentiality reasons. Number of observations: 6,194. *** p<0.01, ** p<0.05, * p<0.1.

Table 5. Main results: the effects of framing and enhancing information on the probability of screening.

	(1) Logit	(2) Logit	(3) Linear Probability Model	(4) Linear Probability Model
Restricted - Gain	-0.009	-0.009	-0.008	-0.007
	(0.013)	(0.012)	(0.012)	(0.011)
Restricted - Loss	-0.001	-0.001	-0.001	-0.002
	(0.012)	(0.012)	(0.012)	(0.012)
Enhanced - Gain	0.004	0.001	0.004	0.001
	(0.012)	(0.012)	(0.012)	(0.012)
Enhanced - Loss	0.026**	0.023**	0.028**	0.025**
	(0.012)	(0.011)	(0.013)	(0.012)
Covariates	No	Yes	No	Yes
Mean outcome – Baseline group	0.099	0.099	0.099	0.099

Notes: the table reports the average causal effects of each treatment on the probability of screening. Columns (1) and (2) report average marginal effects from logit models, while Column (3) and (4) report those obtained with linear probability models. The covariates included in Columns (2) and (4) are listed in Table 3. The mean outcome for the baseline group is reported in the last line as a benchmark. Number of observations: 6,194. Standard errors robust to the presence of heteroscedasticity reported in parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Table 6. Robustness: testing for seasonality.

	(1) 2015	(2) 2016	(3) 2017
Year Week 8 / Restricted - Gain	-0.028	0.002	-0.009
	(0.021)	(0.014)	(0.013)
Year Week 9 / Restricted - Loss	-0.003	0.015	-0.001
	(0.027)	(0.013)	(0.012)
Year Week 10 / Enhanced - Gain	-0.028	-0.005	0.004
	(0.022)	(0.014)	(0.012)
Year Week 11 / Enhanced - Loss	0.004	0.002	0.026**
	(0.021)	(0.013)	(0.012)
Observations	3,484	6,094	6,194

Notes: the table reports the average marginal effects on screening rates by week in 2015, 2016 and 2017. The baseline is Year Week 7. Logit models without covariates. Standard errors robust to the presence of heteroscedasticity reported in parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Table 7. Heterogeneous effects of framing and enhancing information on take-up probabilities.

	(1)	(2)	(3)	(4)	(5)	(6)
Panel A. By home-hospital travel time	Above median	Below median	Above median	Below median	Above median	Below median
Enhanced - Loss	0.035**	0.018	0.035**	0.008	0.033**	0.006
	(0.018)	(0.016)	(0.017)	(0.015)	(0.017)	(0.016)
Observations	3,094	3,100	3,094	3,100	3,094	3,100
Mean outcome – Baseline group	0.088	0.110	0.088	0.110	0.088	0.110
Panel B. By % with at least high school by municipality	Above median	Below median	Above median	Below median	Above median	Below median
Enhanced - Loss	-0.001	0.044***	-0.001	0.037**	-0.001	0.037**
	(0.017)	(0.017)	(0.017)	(0.016)	(0.017)	(0.016)
Observations	2,705	3,489	2,705	3,489	2,705	3,489
Mean outcome – Baseline group	0.098	0.100	0.098	0.100	0.098	0.100
Panel C. By screening experience in the Jan 14-Jun 16 period	Screened	Not Screened	Screened	Not Screened	Screened	Not Screened
Enhanced - Loss	0.001	0.027**	0.007	0.028**	-0.004	0.026**
	(0.049)	(0.011)	(0.049)	(0.011)	(0.050)	(0.011)
Observations	843	5,351	842	5,351	842	5,351
Mean outcome – Baseline group	0.370	0.05	0.370	0.059	0.370	0.0590
Covariates	No	No	Individual	Individual	Individual and municipality	Individual and municipality

Notes: the table reports the average marginal effects of each treatment on the probability of screening, estimated with logit models. The estimation sample is reported at the top of each panel and column. The covariates included in Columns (3) and (4) are listed in Table 3. Models in Column (5) and (6) include as additional covariates population density and the share of residents with at least high school in each subjects' municipality of residence from the 2011 Italian Population Census. The mean outcome for the baseline group is reported in the last line as a benchmark. Standard errors robust to the presence of heteroscedasticity reported in parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Table 8. Effects of the "enhanced – loss" manipulation on the probability of postponing the appointment conditional on participation

	(1) Linear probability model	(2) Linear probability model
Enhanced - Loss	-0.323***	-0.319***
	(0.068)	(0.068)
Observations	6,194	6,194
Covariates	No	Yes

Notes: the table reports the average marginal effects of each treatment on the probability of postponing the appointment conditional on screening, estimated with linear probability models. The detailed estimation methodology is reported in the text. The covariates included in Columns (2) are listed in Table 3. Standard errors robust to the presence of heteroscedasticity reported in parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Figure 1. Timing of dispatch of the five invitation letter formats

Randomly assigned week of invitation	Week 7: 13/2 – 19/2	Week 8: 20/2 – 26/2	Week 9: 27/2 – 5/3	Week 10: 6/3 – 12/3	Week 11: 13/3 – 19/3
Format of the letter	Baseline	Restricted Info – Gain Frame	Restricted Info – Loss Frame	Enhanced Info – Gain Frame	Enhanced Info – Loss Frame

Notes: "Info" stands for information

Figure 2. Geographic location of the health care centers involved in the screening program in the Province of Messina.

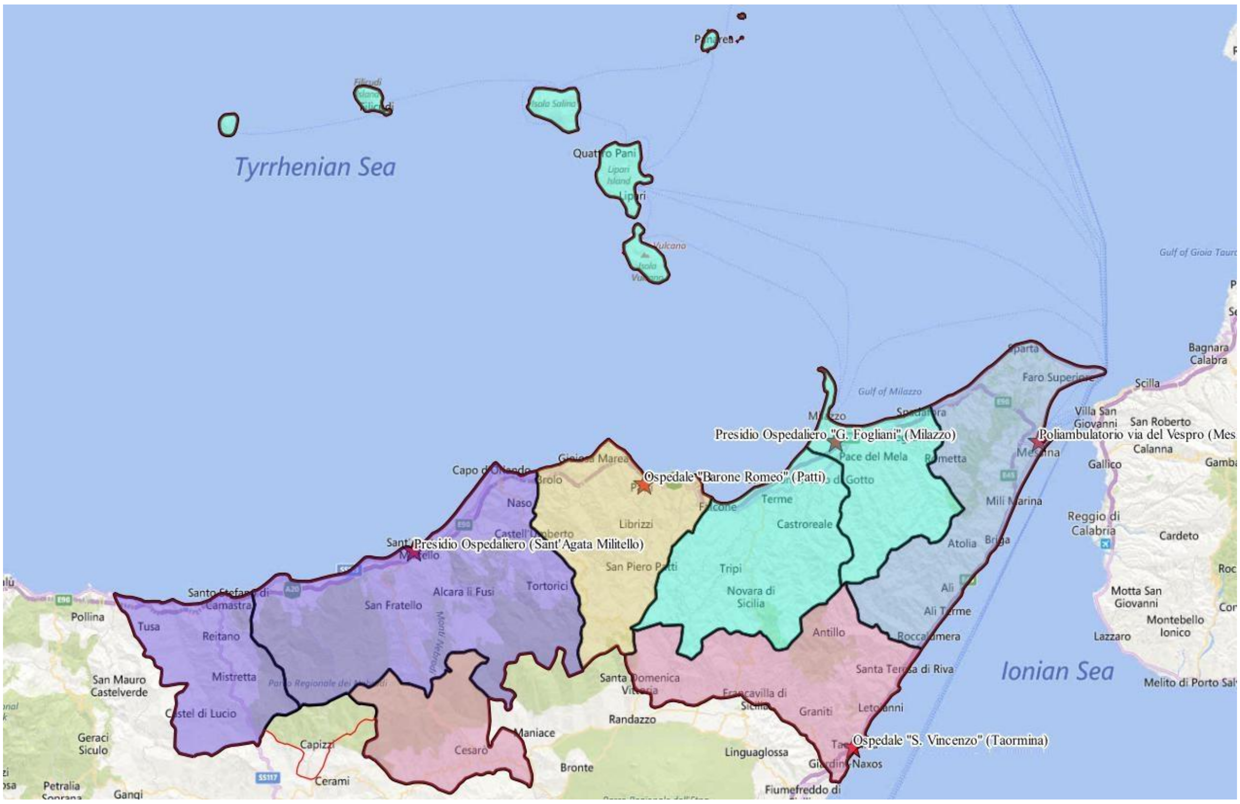
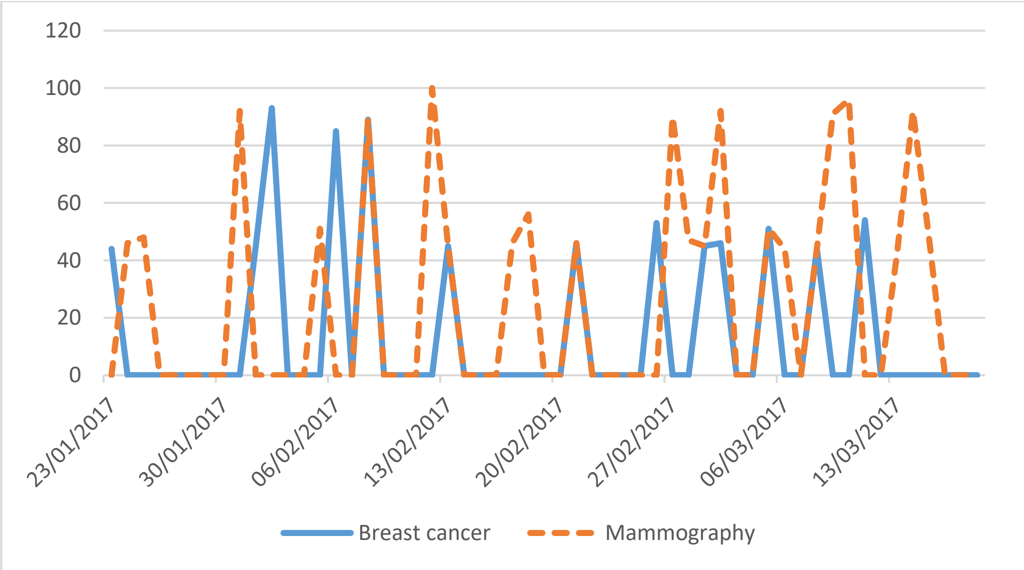


Figure 3. Google trend searches for "breast cancer" and "mammography" in Sicily over the experimental period



Notes: Numbers represent search interest relative to the highest point on the chart. A value of 100 is the peak popularity for the term. A value of 50 means that the term is half as popular. Likewise, a score of zero means the term was less than 1% as popular as the peak.

Appendix– For Online Publication

1. Additional Tables and Figures

Table A1. Differential effects on the probability of screening between the "Enhanced - Loss" and the other treatments. Absolute differences, p-values in brackets.

Enhanced - Loss vs. …	(1) Logit	(2) Logit	(3) Linear Probability Model	(4) Linear Probability Model
Restricted - Gain	0.034***	0.032***	0.036***	0.032***
Restricted - Loss	0.026**	0.024**	0.028**	0.026**
Enhanced - Gain	0.022*	0.022*	0.024*	0.024*
Covariates	No	Yes	No	Yes

Notes: the table reports the difference in average causal effects of the Enhanced – Loss manipulation with respect to each of the other treatments. As in Table 5 in the Main Text, Columns (1) and (2) report average marginal effects from logit models, while Column (3) and (4) report those obtained with linear probability models. The covariates included in Columns (2) and (4) are listed in Table 3. Number of observations: 6,194. Standard errors robust to the presence of heteroscedasticity are not reported. *** p<0.01, ** p<0.05, * p<0.1

Table A2. Balancing tests for rainfall and average daily temperature

	(1) Baseline	(2) Restricted Gain	(3) Restricted Loss	(4) Enhanced Gain	(5) Enhanced Loss	(6) Joint equality (p-value)
Rainfall (mm/day)	0.000	0.397***	0.213***	5.283***	0.133***	0.000
Average daily temperature (Celsius Degrees)	12.764	12.895*	14.135***	13.532***	12.923*	0.000

Notes: the table reports the mean by treatment group of rainfall (mm/day) in the municipality where the health care center each woman had to take the mammography at is located, in the day when she was invited to take the mammography. Stars indicate significant differences in mean (median for travel time) of a given covariate between each treatment group and the control group. Column (6) reports the p-value test for joint equality in means among treatments. Number of observations: 6,194. *** p<0.01, ** p<0.05, * p<0.1

Table A3. Main results including rainfall and average daily temperature among the controls

	(1) Logit	(2) Linear Probability Model
Restricted - Gain	-0.009	-0.008
	(0.012)	(0.011)
Restricted - Loss	-0.003	-0.003
	(0.013)	(0.012)
Enhanced - Gain	0.001	0.000
	(0.014)	(0.013)
Enhanced - Loss	0.023**	0.024**
	(0.011)	(0.012)
Rainfall (mm/day)	-0.000	0.000
	(0.001)	(0.001)
Average Daily Temperature (Celsius Degrees)	0.001	0.001
	(0.003)	(0.003)
Other covariates	Yes	Yes
Mean outcome – Baseline group	0.099	0.099

Notes: the table reports the average causal effects of each treatment on the probability of screening. Column (1) reports average marginal effects from a logit model, while Column (2) reports those obtained with a linear probability models. The other covariates included are listed in Table 3. The mean outcome for the baseline group is reported in the last line as a benchmark. Number of observations: 6,194. Standard errors robust to the presence of heteroscedasticity reported in parenthesis. *** p<0.01, ** p<0.05, * p<0.1

Table A4. Differences in daily take-up rates during the week of the 8th March strike

	(1) Monday 6-3-2017	(2) Tuesday 7-3-2017	(3) Wednesday 8-3-2017	(4) Thursday 9-3-2017	(5) Friday 10-3-2017	(6) Saturday 10-3-2017	(7) Joint equality (p-value)
Take-up	0.083	0.115	0.074	0.118	0.123	0.088	0.36
N. Obs.	192	296	230	272	203	45	

Notes: the table reports the daily take-up rates in the week of the 8th March strike. Column (7) reports the p-value test for joint equality in take-up rates among treatments. Number of observations: 1,238.

Figure A1. Kernel estimate of home-hospital travel time density

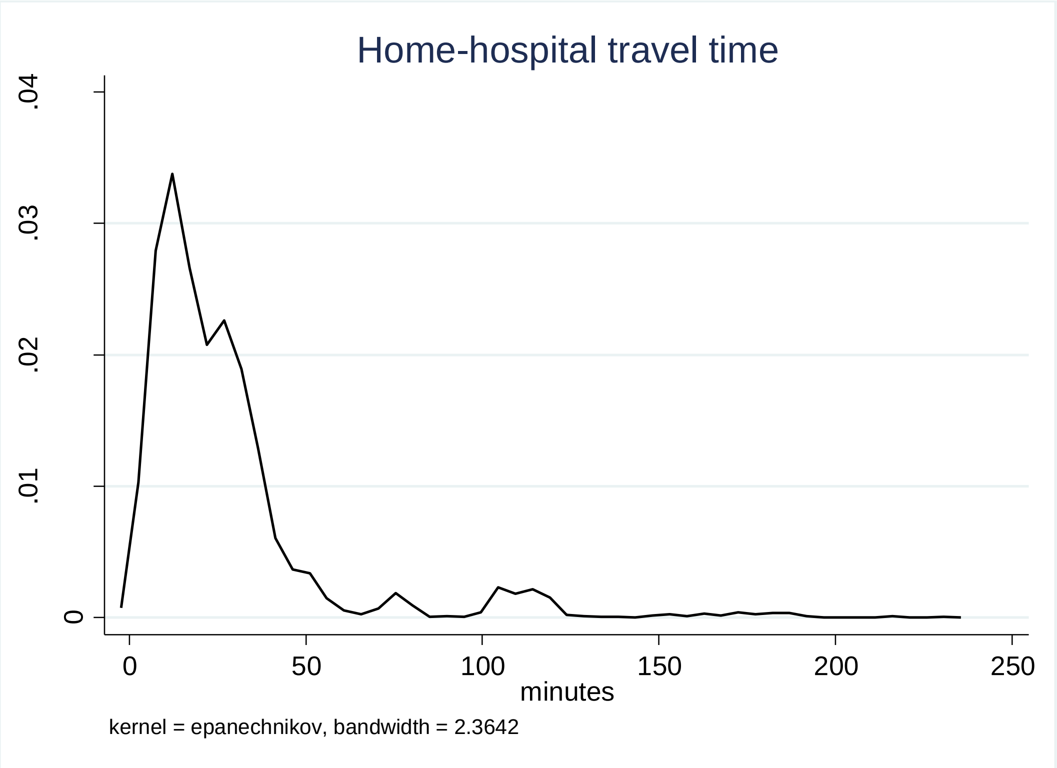
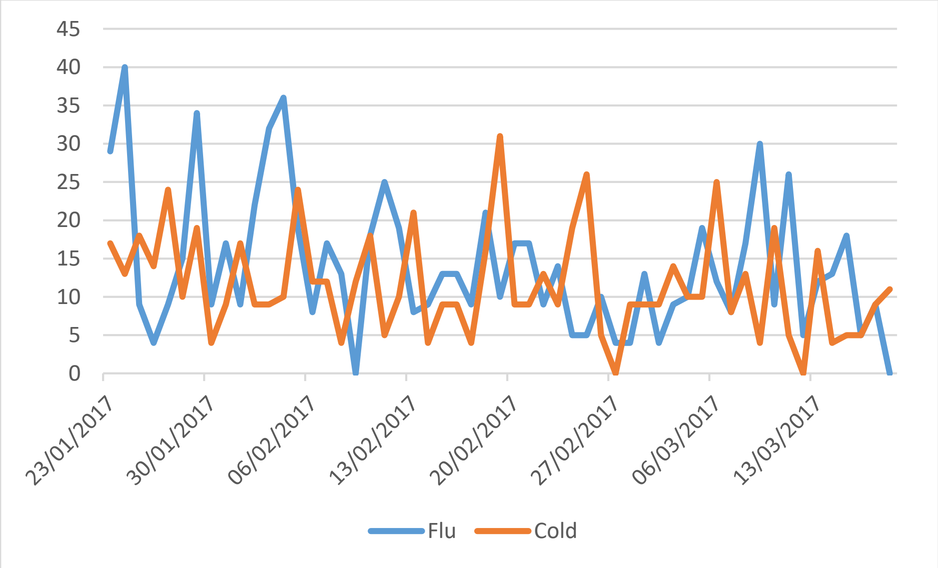
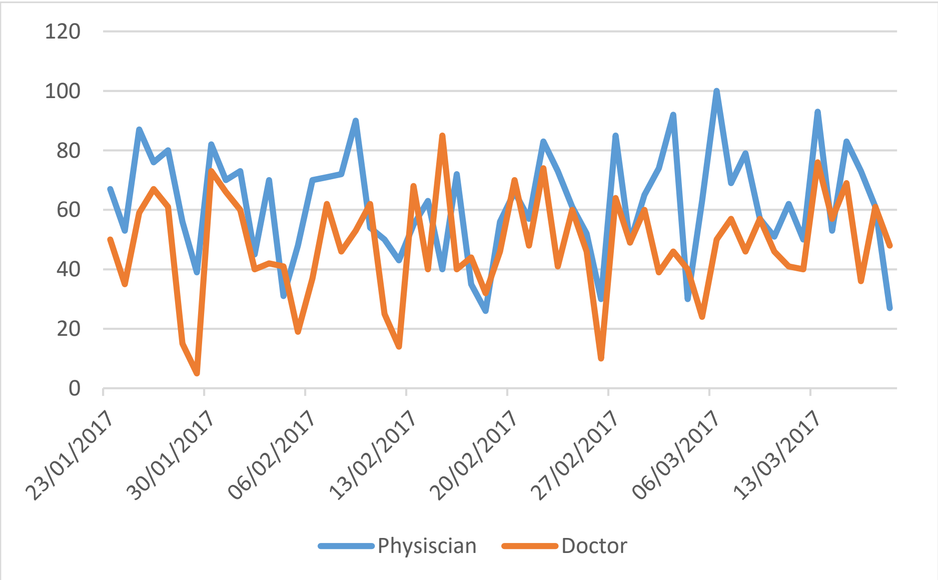


Figure A2. Google trend searches for "flu", "cold" (Panel A), "physician" and "doctor" (Panel B) in Sicily over the experimental period

Panel A



Panel B



Notes: Numbers represent search interest relative to the highest point on the chart. A value of 100 is the peak popularity for the term. A value of 50 means that the term is half as popular. Likewise, a score of zero means the term was less than 1% as popular as the peak.

2. The invitation letter format

[The invitation letters were originally written in Italian. The following letter refers to the "enhanced information – loss framing" treatment.]

[PAGE 1]

Azienda Sanitaria Provinciale
Prevention Department

Address: XXXX
Tel. XXXX

LOCAL RADIOLOGY UNIT

Director: Dr. XXXX

Senology unit: Dr. XXXX

Address: XXXX

Dear Madam,

this Azienda Sanitaria Provinciale (ASP), in collaboration with your general practitioner, is promoting a breast cancer prevention campaign, inviting all women between 50 and 69 to have a mammography.

Scientific studies demonstrate that not participating in breast 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.

For this reason, we have booked an appointment for you to have the mammography at the following address and date:

Address: XXXX

Date and Time: XXXX

The mammography is free and you do not need a medical prescription. You only need to show your tax code, your identity card and the present letter to the radiologist.

Please, call the following telephone number XXXX from Monday to Friday, from 09.00 to 13.00 if:

- you have already had a mammography in the last 12 months;
- you want to modify date and/or time of the appointment;
- you had a breast surgery.

In case you previously had a mammography, please bring the results with you.

Please read carefully the information reported in the back of the present letter, under the law dated 28th of March, 2001, n.145.

Sincerely yours,

Your General Practitioner,
Dr. XXXX

The Direction of the Local Radiology Unit
Dr. XXXX

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In industrialized western countries, due to its incidence, breast cancer represents a concerning social disease. Italian estimates show that every year more than 31,000 women are diagnosed with breast cancer (data from the Italian Association for Cancer Registries).

Scientific evidence demonstrates that a late diagnosis of this cancer can have relevant negative effects on the treatment of the disease. In particular, it has been documented that a late diagnosis of this cancer increases the mortality rate, implies more extensive surgeries, less effective treatments, with lower chances of recovery.

For this reason, in the last 20 years, great attention has been paid to early diagnosis through the promotion of high quality national screening programs by targeting all women between 50 and 69(who represent the age category with higher risk of breast cancer).

The early diagnosis activities involve an integrated approach of different services in senology and will be implemented in collaboration with a network of oncological and epidemiological institutions. This collaboration guarantees monitoring and valuable assistance in case of breast cancer diagnosis.

DO NOT MISS THIS OPPORTUNITY!!!

The responsible of the Breast Cancer Screening Program

Dr. XXXX

CONSENT TO THE PROCESSING OF PERSONAL DATA (Legislative Decree 196/03)

In accordance with the Legislative Decree 196/03, ASP, responsible of the processing of personal data, informs you that your personal and sensitive data will be exclusively used for conducting the screening activities, for research purposes and for ordinary administration, and will be processed by authorized staff, under the limitations of the current law and in accordance with minimal security requirements. At any time, you can contact the secretary of the screening unit to obtain information on how your personal data will be processed as well as on the adopted security procedures adopted by ASP.

DATE______________________________

SIGNATURE_____________________________