



Short Communication

Efficacy of self-sampling in promoting participation to cervical cancer screening also in subsequent round

Annarosa Del Mistro ^{a,*}, Helena Frayle ^a, Antonio Ferro ^{b,1}, Gianpiero Fantin ^c, Emma Altobelli ^{d,e}, Paolo Giorgi Rossi ^{f,g}^a Immunologia Diagnostica Molecolare Oncologica, Istituto Oncologico Veneto IOV-IRCCS, Via Gattamelata, 64, 35128 Padova, Italy^b Dipartimento di Prevenzione, Azienda ULSS 17, Este-Monselice, 35042 Este, PD, Italy^c Dipartimento Materno-Infantile, Azienda ULSS 7, Pieve di Soligo-Conegliano, Via Brigata Bisogno, 4, 31053 Conegliano, TV, Italy^d Department of Life, Health and Environmental Sciences, University of L'Aquila, 67100 L'Aquila, Italy^e Epidemiology and Biostatistics Unit, ASL 4 Teramo, Italy^f Servizio Interaziendale di Epidemiologia, Azienda Unità Sanitaria Locale, Via Amendola, 2, 42122 Reggio Emilia, Italy^g IRCCS-Arcispedale S. Maria Nuova, 42122 Reggio Emilia, Italy

ARTICLE INFO

Article history:

Received 12 August 2016

Received in revised form 22 November 2016

Accepted 19 December 2016

Available online 23 December 2016

Keywords:

Self-sampling

Cervical cancer

Screening

Participation

HPV test

ABSTRACT

Offering self-sampling devices improves participation of under-screened women. We evaluated participation in routine screening following the self-sampling intervention in two organized population-based screening programmes located in North-East Italy.

Data on participation at 3-years-interval after a randomized clinical trial assessing the response to two strategies offering self-samplers (sent at home or offered free at local pharmacy) with a control action (sending reminders for a cervical specimen taken at the clinic) in 30–64 yr-old women non-respondent to the regular call-recall invitation were analyzed.

Up to April 2016, 2300 women out of the 2995 recruited in the trial in 2011 were re-invited to perform a screening test at clinic; overall, 698 women adhered. Participation was similar in the three arms (29–32%), and highest (47–68%) among those who participated in the previous round. Over the two rounds, 44.6%, 32.3% and 30.3% women had at least one test in the self-sampling at home, self-sampling at pharmacy and test at the clinic arms, respectively.

Our data indicate that the beneficial effect of offering self-sampling devices to nonparticipating women is maintained over time. Self-samplers are useful to increase overall coverage; their sporadic use does not seem to increase the proportion of women regularly repeating the test.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The efficacy of cervical cancer screening on reducing cervical cancer incidence and mortality depends upon several factors, including participation of the target population. Most tumours occur in women never- or under-screened (Zucchetto et al., 2013), and coverage to the call-recall strategy in use by population-based organized programmes in Europe is at best 80% (Elfstrom et al., 2015). Improvement in cervical cancer screening participation of never- and under-screened women by

the use of home-based self-sampling devices has been demonstrated by several randomized controlled trials (RCTs), as summarized in a recent systematic review and meta-analysis (Verdoodt et al., 2015).

Cervical cancer is causally linked to persistent infection by high-risk human papillomavirus types (hrHPV); there is now substantial evidence that hrHPV testing is more effective than cytology as primary screening test (Arbyn et al., 2012; Ronco et al., 2014), and its implementation is occurring in several countries, including Italy. Since self-sampled specimens are adequate for hrHPV testing but not for cytology (Snijders et al., 2013; Arbyn et al., 2014; Arbyn and Castle, 2015), self-sampling could consequently be implemented as well.

If the efficacy in increasing screening uptake has been now assessed in several contexts, it is not known if there is an effect in women's long term habits about cervical cancer screening. Our aim was to evaluate participation in routine screening following the self-sampling intervention of women involved in a RCT on self-sampling in the previous round.

* Corresponding author.

E-mail addresses: annarosa.delmistro@ioveneto.it (A. Del Mistro), helena.frayle@ioveneto.it (H. Frayle), amito.af@libero.it (A. Ferro), gianpiero.fantin@ulss7.it (G. Fantin), emma.altobelli@cc.univaq.it (E. Altobelli), paolo.giorgirossi@ausl.re.it (P. Giorgi Rossi).

¹ Present address: Direttore Sanitario, Azienda ULSS 22 Bussolengo (VR), Italy.

2. Methods

In late 2011 we conducted a RCT on the use of self-sampling to increase participation within organized screening programmes in six Local Health Authorities (LHA) in Italy (Giorgi Rossi et al., 2015). Women aged 30–64 years not respondent to regular invitation were randomly allocated to one of three arms: (B1) re-call standard invitation to perform testing at the clinic (control group); (B2) home-mailed self-sampling device or (B3) self-sampling device picked-up at an area pharmacy (intervention groups). The women who received the self-sampler at home showed higher response rates (ranging from 14.6 to 33.6%) than the other two groups (B1: 3.5–22.9%; B3: 4.5–15.8%), with an estimated impact on the overall test coverage of +4.3% compared with +2.2% for standard reminder. Heterogeneity between centres was high.

Two of the participating centres (Este and Pieve di Soligo) are located in the Veneto region; the average response rates in the B1, B2 and B3 arms of the women residing in this area were 17.85%, 31.77% and 13.64%, respectively. Taking advantage of the use of a unique centralised software for managing all three cancer screenings within the whole region, we investigated how the women involved in the self-sampling trial are responding to the regular invitation at the subsequent cervical screening round, three years later. We present relative risk (RR) of participating and relative 95% Confidence Interval (95%CI) estimated with binomial exact distribution. We also calculated the “user loyalty” effect, i.e. how much the probability to participate in the second round is increased in women that participated in the previous round compared to those who did not participate in previous round. We present the following comparisons:

First round participation: B2 (self-sampler at home) vs B1 (control); B3 (self-sampler at pharmacy) vs B1.

Second round participation: B2 vs B1; B3 vs B1.

Second round “user loyalty” effect: within each arm (B1, B2 and B3), women participating in the first round vs those not participating in the first round.

At least one test in the two rounds: B2 vs B1; B3 vs B1.

3. Results

Overall, 2995 (997 B1; 1001 B2; 997 B3) women were recruited in the two centres in 2011, obtaining results in line with the whole trial:

better results for self-sampler at home than for standard reminder (RR 1.86; 95% confidence interval (CI) 1.58–2.18), while there was no statistical difference (RR 0.84; 95%CI 0.69–1.02) in the participation with self-sampler at the pharmacy. Up to the end of April 2016, after excluding those who migrated or exited the screening target age, 2300 women were re-invited (776 B1; 746 B2; 778 B3) for the subsequent screening round with a standard invitation letter to perform a screening test at the clinic. One of the two centres (Este) has been using hrHPV testing since April 2009 (Zorzi et al., 2013; Del Mistro et al., 2014), while for the other centre (Pieve di Soligo) in the first round the standard test was cytology, and since June 2015 the programme adopted hrHPV testing according to Italian recommendations (Ronco et al., 2012); therefore, the control arm in the second round mostly had a different test than in the first round.

Overall, the participation was similar in the three arms (30% B1; 32% B2; 29% B3) (Fig. 1). On the other hand, participation was higher among the women who participated in the previous round than in those who did not (68% B1; 47% B2; 48% B3) (Table 1), i.e., women who had participated to the trial demonstrated an increased “user loyalty” to the screening programme; very strong in the arm with clinic sampling (B1), where participation was 3.3 times higher in previously responders than in non-responders (95% CI 2.74–3.99), less strong but still evident among those who previously received the self-sampling at home (RR 2.09; 95% CI 1.70–2.56), and among those invited to pick up self-sampling at the pharmacy (RR 1.86; 95% CI 1.47–2.34) (Table 1).

The positive effect was observed only for the comparison: self-sampler sent at home vs control, with 44.6% of women covered, compared to the 30.3% in the control arm (RR 1.54; 95% CI 1.37–1.73). For the comparison self-sampler at pharmacy vs control there was almost no difference neither at the first round nor over the 2 rounds: total women covered in pharmacy arm 33% (RR 1.06; 95% CI 0.93–1.21).

4. Discussion

We analyzed the participation rates at the subsequent (three years later) routine screening round of women previously involved in a randomized clinical trial on the use of self-sampling to increase compliance of non-responders. Overall, some 30% women participated (with no differences between the three RCT arms), and cumulatively 30–45% of them had at least one test over the two rounds. The observed higher participation of women randomized to the control arm is consistent with previous studies (Giorgi Rossi et al., 2012)

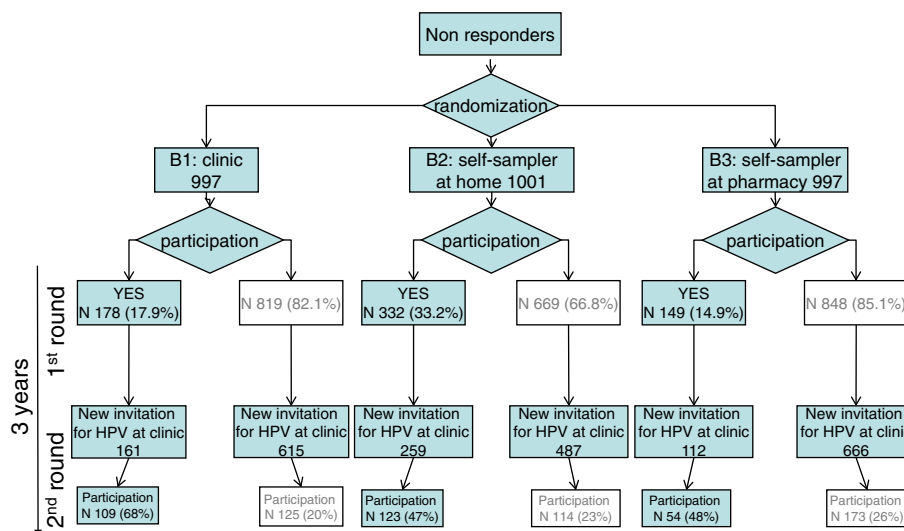


Fig. 1. Flow chart of the study conducted in two organized population-based screening programmes located in North-East Italy; self-sampling trial round (1st round) and subsequent round (2nd) after three years, by original study arms and by participation. N = number of women.

Table 1

Participation rates of women involved in the self-sampling RCT (first round), compared to participation at the subsequent round (second; 3-yr interval, all women invited at clinic), by original RCT arm. Probability to participate (RR) was highest among women receiving self-sampler at home at first round, and among previously adherent women at second round.

Arm (N randomized)	First round		Second round						At least one test in 1st or 2nd round RR (95%CI)
	Respondent N (%)	RR (95%CI)	Previously participants		Previously non-participants		“User loyalty” effect RR (95%CI)		
			Invited at clinic N	Respondent N (%)	Invited at clinic N	Respondent N (%)			
B1: clinic (997)	178 (17.9)	Comparator	161	109 (68)	615	126 (20)	3.30 (2.74–3.99)	Comparator	Comparator
B2: self-sampler at home (1001)	332 (33.2)	1.86 (1.58–2.18)	259	123 (47)	487	114 (23)	2.09 (1.70–2.56)	1.05 (0.90–1.22)	1.54 (1.37–1.73)
B3: self-sampler at pharmacy (997)	149 (14.9)	0.84 (0.69–1.02)	112	54 (48)	666	173 (26)	1.86 (1.47–2.34)	0.96 (0.83–1.22)	1.06 (0.93–1.21)

N = number of women.

RR (95%CI) = Relative Risk (95% Confidence Interval).

and is a measure of the women's “user loyalty” to the screening programme. On the other hand, a lower effect in women invited in the self-sampling arms was expected since they did not have any contact with screening clinics in the first round, and during the second round were invited for a sample at the clinic. Actually, the higher participation in the self-sampling at home did not change the attitude to participate and in the second round, when a standard call-recall strategy was proposed, the participation was the same of the control arm, suggesting that the observed “user loyalty” effect in self-sampler arms is merely a self-selection of the women based on their propensity to participate.

Organized screening has proven to be an effective mean to reduce cervical cancer incidence and mortality in most industrialized countries (Arbyn et al., 2011). Coverage and participation of the target population are crucial elements of this preventive strategy, and increasing screening coverage is still a priority. Offering self-sampling devices to non-participating women is a promising option since it actually increases participation (Verdoodt et al., 2015).

Self-collected samples are adequate for performing hrHPV testing by clinically validated assays (Snijders et al., 2013; Arbyn et al., 2014; Arbyn and Castle, 2015), but not for cytological analyses. Therefore, it can be efficiently introduced only in programmes already using hrHPV testing as primary screening test; to this regard, since cervical screening implementation by hrHPV testing is taking place or planned in several countries (i.e. in Italy it is expected to be complete by 2018; in The Netherlands it will be introduced in 2017), this will not constitute a drawback.

In conclusion, our data indicate that response is higher (Round 1 and Round 1 + 2) in the group receiving self-samplers at home than in the group who received a reminder for a sample at the clinic. On the contrary, the invitation for collecting the self-sampler at pharmacy had no effect. The increase in overall participation in the self-sampling at home arm is completely due to the increase in first round, while in the second round, when all the women were re-invited with a standard call-recall strategy, participation was similar, although higher in previously participating than non-participating women (“user loyalty” effect). Therefore, self-sampling can be useful to increase overall coverage, but, if used once in a life-time, does not seem to increase the proportion of women regularly repeating the test.

Conflict of interest statement

The authors have no conflict of interest to disclose.

Acknowledgments

The authors wish to thank Luca Paccagnella (Regione Veneto) for data extraction, and all the health professionals involved in the organized cervical cancer screening programmes.

The self-sampling randomized clinical trial is registered at www.clinicaltrials.gov: NCT01647724.

The study has been funded by the Agenzia Sanitaria Regionale Abruzzo on behalf of the Italian Ministry of Health ex l. 138 2004, grant of the 2009 edition.

References

- Arbyn, M., Castle, P.E., 2015. Offering self-sampling kits for HPV testing to reach women who do not attend in the regular cervical cancer screening program. *Cancer Epidemiol. Biomark. Prev.* 24:2015. <http://dx.doi.org/10.1158/1055-9965.EPI-14-1417> (Published online first February).
- Arbyn, M., Castellsagué, X., de Sanjosé, S., et al., 2011. Worldwide burden of cervical cancer in 2008. *Ann. Oncol.* 22, 2675–2686.
- Arbyn, M., Ronco, G., Anttila, A., et al., 2012. Evidence regarding human papillomavirus testing in secondary prevention of cervical cancer. *Vaccine* 30S, F88–F99.
- Arbyn, M., Verdoodt, F., Snijders, P.J.F., et al., 2014. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. *Lancet Oncol.* 15, 172–183.
- Del Mistro, A., Frayle, H., Ferro, A., et al., 2014. Cervical cancer screening by high risk HPV testing in routine practice: results at one year recall of high risk HPV-positive and cytology-negative women. *J. Med. Screen.* 21, 30–37.
- Elfstrom, K.M., Arnheim-Dahlstrom, L., von Karsa, L., Dillner, J., 2015. Cervical cancer screening in Europe: quality assurance and organisation of programmes. *Eur J Cancer* 51, 950–968.
- Giorgi Rossi, P., Camilloni, L., Cogo, C., et al., 2012. Health technology assessment report: methods to increase participation in cancer screening programmes. *Epidemiol. Prev.* 36 (1 Suppl. 1), 1–104.
- Giorgi Rossi, P., Fortunato, C., Barbarino, P., et al., 2015. Self-sampling to increase participation in cervical cancer screening: an RCT comparing home mailing, distribution in pharmacies, and recall letter. *Br. J. Cancer* 112, 667–675.
- Ronco, S., Accetta, G., Angeloni, C., et al., 2012. HTA report: Ricerca del DNA di papillomavirus umano (HPV) come test primario per lo screening dei precursori del cancro del collo uterino. *Epidemiol. Prev.* 36 (3/4 Suppl. 1), e1–e72.
- Ronco, G., Dillner, J., Elfström, K.M., et al., 2014. Efficacy of HPV-based screening for preventing invasive cervical cancer: follow-up of European randomised controlled trials. *Lancet* 383, 524–532.
- Snijders, P.J., Verhoef, V.M., Arbyn, M., et al., 2013. High-risk HPV testing on self-sampled versus clinician-collected specimens: a review on the clinical accuracy and impact on population attendance in cervical cancer screening. *Int. J. Cancer* 132, 2223–2236.
- Verdoodt, F., Jentschke, V.F., Hillemanns, P., Racey, C.S., Snijders, P.J.F., Arbyn, M., 2015. Reaching women who do not participate in the regular cervical cancer screening programme by offering self-sampling kits: a systematic review and meta-analysis of randomized trials. *Eur. J. Cancer* 51, 2375–2385.
- Zorzi, M., Del Mistro, A., Farruggio, A., et al., 2013. Use of high-risk human papillomavirus DNA test as primary test in a cervical cancer screening programme: a population-based cohort study. *BJOG* 120, 1260–1267.
- Zucchetto, A., Ronco, G., Giorgi Rossi, P., et al., 2013. Screening patterns within organized programs and survival of Italian women with invasive cervical cancer. *Prev. Med.* 57, 220–226.