REVIEW

Efficacy of Patient Letter Reminders on Cervical Cancer Screening

A Meta-analysis

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OBJECTIVE: To perform a meta-analysis on existing randomized controlled trials to investigate the efficacy of patient letter reminders on increasing cervical cancer screening using Pap smears.

METHODS: A search was conducted for all relevant published and unpublished studies between the years 1966 and 2000. Eligibility criteria included randomized controlled studies that examined populations due for Pap smear screening. The intervention studied was in the form of a reminder letter. The Mantel-Haenszel method was used to measure the summary effect of the intervention. A test for homogeneity using the Mantel-Haenszel method was performed.

RESULTS: Ten articles fulfilled the inclusion criteria, including one unpublished study. The test for homogeneity showed evidence of heterogeneity ($\chi^2 = 31$, 9 df, $P < .001$). An analysis for causes of heterogeneity was pursued. Division into subpopulations based on socioeconomic status resolved the heterogeneity ($\chi^2 = 5.2$, 8 df, $P = .75$). The studies evaluating those in lower socioeconomic groups had a smaller response (odds ratio [OR], 1.16; 95% confidence interval [CI], 0.99 to 1.35) than those studies using mixed populations (OR, 2.02; 95% CI, 1.79 to 2.28). The pooled odds ratio showed that patients who received the intervention were significantly more likely to return for screening than those who did not (OR, 1.64; 95% CI, 1.49 to 1.80).

CONCLUSIONS: Patient reminders in the form of mailed letters increase the rate of cervical cancer screening. Patient letter reminders have less efficacy in lower socioeconomic groups.

KEY WORDS: screening; meta-analysis; cervical cancer; Pap smear; randomized controlled trial.

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Early detection of cervical cancer through screening can lower mortality by 20%–60%.¹ Despite public health education on the benefits of screening for cervical cancer, the overall percentage of women who had a recent Pap test according to the Centers for Disease Control and Prevention's National Health Interview Survey between 1987 and 1992 remained at 67%.² Certain subpopulations have been found to lag behind the general population in cervical cancer screening rates. Those less likely to be screened include the elderly, women living in rural areas, non-English-speaking Hispanics, those below the poverty index, and women with less than a high school education.³

Interventions to improve Pap smear screening have had mixed results, with some studies finding significant improvement in screening while others only a modest benefit, if any. We are aware of only one other meta-analysis specifically dealing with patient reminders for cervical cancer screening.⁴ This meta-analysis, which pooled 6 studies, found that women had a higher likelihood of obtaining a Pap smear if they received reminders. But there was marked heterogeneity in the pooled studies so that the significance of the results was unclear. The authors did not pursue an examination for sources of heterogeneity. We found 2 additional meta-analyses of letter reminder interventions. A meta-analysis on reminders promoting mammography found an improvement in mammography completion rates using a letter intervention (OR, 1.48; $P < .001$).⁵ However, this study also had evidence of heterogeneity that could not be explained. A meta-analysis of computer-based reminder systems using physician and patient letters combined did not show a benefit for Pap smear screening (OR, 1.15; 95% confidence interval [CI], 0.89 to 1.49) but found improved preventive practices for vaccinations, breast cancer screening, colorectal cancer screening, and cardiovascular risk reduction.⁶

Many questions remain unanswered regarding interventions to increase the rate of screening for cervical cancer. Letter mailings are attractive because of their low cost and relatively low effort expended, but clinical utility is still not established. The heterogeneity and variable findings in previous studies suggest that these

interventions may have an efficacy that varies by population groups. This is a matter of particular concern for those populations who lag behind in screening rates. On the other hand, this heterogeneity may have resulted from differences in the intervention or methodology between studies. None of the previous studies found an explanation for heterogeneity. In this analysis, we evaluated studies assessing the efficacy of mailed patient reminder letters on the rate of Pap smear screening. In addition, we examined the causes for heterogeneity between the studies included in the meta-analysis, with particular attention to whether certain population groups are less responsive to the intervention.

METHODS

Data Collection

We performed a computerized search of the literature using MEDLINE and Cancerlit between the years 1966 and 2000. The following key words were used in order to identify all relevant articles: cervical cancer, mass screening, vaginal smear, Pap smear, Papanicolaou smear, reminder systems, reminders, letters, and randomized controlled trial. The abstracts were reviewed to further isolate pertinent articles, which were then retrieved. Each article's bibliography was reviewed to identify publications not obtained from the literature search. Inquiries were made to authors in an attempt to locate unpublished studies.

A study was eligible for consideration for this analysis if the population consisted of patients considered by the study authors to be due for Pap smear screening. Studies were included regardless of which Pap smear screening interval guideline they followed. Eligibility criteria then included randomized controlled studies of a patient intervention in the form of a letter, with no other intervention in combination. Studies involving repeat or follow-up letters for nonresponders were included in the analysis. The control groups received no intervention. There were no restrictions on country of origin or language. The studies meeting all these eligibility criteria were retained for analysis.

Analysis

We extracted data from eligible articles to allow comparison of the number of women screened by Pap tests in intervention and control groups. In the studies evaluating other interventions such as phone calls and physician reminders, only data regarding patient letters was extracted. Two authors independently extracted the data. Odds ratios for number of women screened were calculated for individual studies. Using a fixed effect model with the Mantel-Haenszel method, the data was analyzed to assess the summary effect of the intervention. A test for homogeneity using the Mantel-Haenszel method was also performed to test the hypothesis that all of the studies

were measuring the same effect. We then performed an analysis of possible causes of heterogeneity.

RESULTS

The initial search of the literature located 421 articles. On review of abstracts, 24 articles that dealt with the primary question of this study were retained. Four additional articles that were not isolated by the literature search were obtained by bibliography review. Of these 28 studies, 15 were randomized controlled trials. Three articles were excluded because they evaluated combinations of interventions and did not examine letter reminders separately.⁷⁻⁹ Three papers were not analyzed because the study population was not restricted to those due for Pap smear screening.¹⁰⁻¹² Inquiries for any unpublished studies on the subject were made of authors whose names were obtained from the literature review. Of those returned, one unpublished study fulfilled the inclusion criteria and was included (Kvale et al., unpublished data, October, 1999).

Ten articles were retained for analysis. The studies originated from 4 countries and several different practice settings. As shown in Table 1, most of the studies identified eligible patients through medical records. One study used a central cytology registry to match patients with the computerized records of a group practice.¹³ Another study used a mailed survey to identify subjects.¹⁴ This technique raised some concern that the survey itself could have alerted patients to the need for cancer screening. One study looked at the use of personalized letters versus standard letters.¹⁵ For our analysis we combined these two letter reminder groups. Two studies included recommendations for other screening tests such as mammography in their letter intervention.^{15,16} Pritchard et al. also included an informational brochure.¹⁷ Two studies sent a second reminder letter to nonresponders.^{13,18} Several articles specifically excluded patients who had undergone a hysterectomy.^{13,14,17,19}

The unpublished study by Kvale et al. differed in several respects from the other studies (Kvale et al., unpublished data, October, 1999). This population-based study of Medicaid recipients included a significant percentage of disabled patients. The patients were identified and followed by reviewing Medicaid claims data. The letters were written and signed by the study authors who were not otherwise associated with the insurance group or health care of the patients.

Although in all studies the eligible populations were those considered by the authors due for a Pap smear, studies varied greatly in what they considered to be an appropriate screening interval for cervical cancer. The intervals varied from between 1 and 5 years with one study recommending different screening intervals for different age groups.¹⁵

Data were not available for comparison of subgroups between each study. Several studies examined different variables associated with Pap smear screening as a result of the letter intervention. Two studies found an association between younger age and higher Pap smear screening rates

Table 1. Characteristics of Studies

Author	Country	Year	Age Range	Screening Interval	Setting	Follow-up	Outcome Measure
Binstock	USA	1997	25–49	3 y	HMO [†] , Southern California	1 y	Pap test by laboratory records
Bowman	Australia	1995	18–70	3 y	Community population by random survey	6 mo	Pap test by self report
Buehler	Canada	1997	18–69	3 y	FP [‡] clinics, New Foundland	6 mo	Pap test by Provincial cytology registry
Burack	USA	1997	18–40	1 y	HMO [†] , inner city minority	1 y	Pap test by computer entry
Hogg	Canada	1998	unknown	<age 35: 1 y ages 35–39: 3 y >age 60: 5 y	Medical center, rural community	6 mo	Pap test by computer entry
Kvale	USA	1999	18–71	3 y	Medicaid (non-HMO [†]), Wisconsin	6 mo	Pap test by billing records
McDowell	Canada	1989	18–35	1 y	FP [‡] center, Ottawa	1 y	Pap test by computer entry
Pierce	UK*	1989	35–62	5 y	Group practice, London	1 y	Pap test as assessed by practitioner
Pritchard	Australia	1995	36–69	2 y	University practice, Lockridge	1 y	Pap test recorded by practitioner
Somkin	USA	1997	20–74	3 y	HMO [†] , Oakland, California	6 mo	Pap test by computer entry

*United Kingdom.

[†]Health maintenance organization.

[‡]Family practice.

(Kvale et al., unpublished data, October, 1999),¹⁴ but other studies could not find such an association.^{13,16,17,19} A single study examining rural versus urban populations could not find any relationship to Pap smear completion rates.¹³ No study examined Hispanic populations or response rate by educational status. None of the studies specifically involved an elderly population (age > 65) in its intervention although one study did look at the 60 to 69 age group and did not find a significant difference in response.¹⁷ The study by Pierce et al. noted a large proportion of the study population was of lower socioeconomic status, but a test for association by socioeconomic status was not performed.¹⁹ Two studies were solely targeted at a specific low socioeconomic group, those in Medicaid-eligible populations (Kvale et al., unpublished data, October, 1999).²⁰ One study was conducted in a rural population.¹⁵

All of the selected studies included data reflecting the number of Pap smears performed in the intervention and the control group, allowing calculation of odds ratios (Table 2). A pooled odds ratio and confidence interval were calculated. As shown in Figure 1, patients receiving reminder letters were found to be significantly more likely to undergo cancer screening compared to those under routine care (OR, 1.64; CI, 1.49 to 1.80).

Test for Homogeneity

The test for homogeneity performed on the main effect among the trials yielded a χ^2 value of 31 with 9 degrees of freedom ($P < .001$) indicating heterogeneity. Possible sources of heterogeneity were investigated. We examined

factors related to the intervention: number of letters sent (single or repeated), screening interval chosen (yearly vs greater than yearly), and length of follow-up (6 months or less vs greater than 6 months). Hogg et al. used variable screening intervals dependent on age and was excluded for the screening interval analysis.¹⁵ The setting in which the intervention was conducted was then investigated: type of practice (HMO vs other), country (USA vs other), year study conducted (earlier than 1998 vs after), rural setting (vs urban and mixed), and socioeconomic status (low vs other). Only one study was conducted in a rural setting so that lone study¹⁵ was compared to all others. When socioeconomic status was stratified, the studies performed in Medicaid eligible populations (Kvale et al., unpublished data, October, 1999)²⁰ were compared to the other studies, which were conducted in populations of mixed socioeconomic

Table 2. Summary of Data from Studies

Study	N		Obtained Pap Smear	
	Cases	Controls	Cases, %	Controls, %
Binstock	1,526	1,526	26	16
Bowman	178	155	37	25
Buehler	178	208	11	6
Burack	964	964	29	28
Hogg	212	120	8	4
Kvale	5,564	5,538	3	2
McDowell	111	437	68	8
Pierce	140	134	32	15
Pritchard	206	185	26	17
Somkin	1,188	1,188	19	9

FIGURE 1. Odds of randomized controlled trials individually and combined.

status. None of the potential causes investigated resolved the heterogeneity except socioeconomic status. When the studies were divided according to socioeconomic status, the hypothesis of homogeneity was accepted (Table 3). This suggests that the cause for the heterogeneity may be the variation in socioeconomic status among the studies.

Sensitivity Analysis

In the presence of significant heterogeneity, we tested the stability of our conclusions using more conservative assumptions to calculate effect size. Using a random effects model, we recalculated our results. When the Dersimonian and Laird method was applied, the summary effect combining all ten studies continued to be significant (Table 3). The results of stratification according to socioeconomic status using a random effects model were markedly similar to the findings from the fixed effects model. This is not unexpected because model choice should not be an issue in the absence of heterogeneity.²¹

DISCUSSION

Our meta-analysis of 10 studies on patient reminders found a benefit of mailed letters in increasing the rate of

cervical cancer screening. We also found that patient letter reminders had less efficacy in lower socioeconomic groups.

One of the strengths of our analysis is that we were able to stratify the studies according to socioeconomic status. More specifically, Medicaid eligible populations from the United States were separated from the populations involved in all other studies. Lower socioeconomic groups have been shown to have lower rates of screening: 57% nationally in 1992.³ Our study demonstrates that this population may also be more resistant to letter reminders for cervical cancer screening. Because we were not able to include low socioeconomic groups from other countries and settings (such as Native American Indian reservations), these findings may not extend to other underserved populations. Several barriers to screening have been cited in underserved, low-income populations that may minimize the effect of the reminder. These barriers include other life priorities, financial restrictions, and deficits in knowledge about cancer prevention and early detection.²² It should be noted that in the study by Burack et al., the Pap smears were provided free of charge.²⁰ Alternative interventions need to be examined to determine the optimal approach to improving cervical cancer screening in this population. Other approaches have been utilized in low socioeconomic groups, usually involving multifaceted programs that are costly in time and resources.²³⁻²⁵

There was diversity in study populations included, which makes the results more generalizable. Several countries were represented, a wide variety of age ranges were included, and the studies varied in socioeconomic groups and type of physician practice. It is somewhat surprising that even with differences in health care systems in various countries, the effect of letter reminders appears to be consistent.

Despite the different populations represented, several groups were not examined in the studies included, particularly among those known to have lower rates of Pap smear screening. Little information is available about the efficacy of reminders for Pap smear screening in Hispanics, the elderly, and the less educated. The lone study conducted in a rural population did not have significantly different results from the other studies. The use of Pap smear screening in the elderly is controversial. The U.S. Preventive Services Task Force has suggested ending screening at age 65 if previous smears have

Table 3. Summary of Pooled Results

Studies	Studies, <i>n</i>	OR (95% CI)	Test for Homogeneity		Sensitivity Analysis OR (95% CI)
			M-H χ^2	<i>P</i> Value	
All studies	10	1.64 (1.49 to 1.80)	31, <i>df</i> = 9	<.001	1.73 (1.56 to 1.93)
Subgroup analysis					
Low SES*	2	1.16 (0.99 to 1.35)	5.2, <i>df</i> = 8	.75	1.17 (0.99 to 1.37)
Mixed SES	8	2.02 (1.79 to 2.28)			2.00 (1.74 to 2.31)

* Socioeconomic status.

† Random-effects analysis using Dersimonian and Laird method.

consistently been normal.¹ Regardless, there is still a need to evaluate possible methods to resolve the disparity in Pap smear rates in these populations.

The association between letter reminders and other variables in Pap smear completion remains unclear. Individual studies have shown a relationship between higher Pap smear completion rate and those who are married, employed, or premenopausal.¹⁴ While the efficacy of letter reminders in the elderly has not been specifically examined, comparisons between those younger than age 40 and those older have shown mixed results (Kvale et al., unpublished data, October, 1999).^{14,16,17,19} Interestingly, Kvale found a lower rate of screening in disabled women who received the intervention in their population of Medicaid eligible women (OR, 0.63; 95% CI, 0.49 to 0.82) (Kvale et al., unpublished data, October, 1999). Surveys have reported that women with disabilities are less likely to receive regular pelvic exams.²⁶ Possible causes might include transportation, competing health concerns, or other barriers.

There are other questions raised regarding interventions for Pap smear screening. How do other interventions compare to letter reminders? Which combination of interventions is the most efficacious? Also, the question of cost effectiveness could not be addressed. Binstock et al. evaluated the cost of the letter reminder intervention in their southern California HMO population, estimating the cost per additional Pap smear at \$4.76 when the number of tests performed increased 10% compared to controls.²⁷

Our results support the findings of the previous meta-analysis on letter reminders for Pap smear screening.⁴ Similar to our study, Pirkis et al. found that letter reminders were efficacious. However, we were able to resolve the heterogeneity through stratification by socioeconomic status. Likewise, the meta-analysis on mammography also found improvement in screening rates,⁵ but the meta-analysis of physician and patient reminders did not show a benefit.⁶ It is possible that physician and patient reminders are not comparable enough to be combined in an analysis. Differences in methodology and interventions between the trials as well as differences in the study population could result in different findings. The study did examine sources of heterogeneity from study design differences. The only factor that could have contributed to heterogeneity was a trend toward larger effect size in studies using historical control groups. Population subgroups were not stratified in this study.

A limitation of our analysis may be publication bias, referring to the increased likelihood of publication of studies showing positive results. Although the search for unpublished studies was extensive and we believe that we have included all pertinent studies, the presence of publication bias is still possible as only one unpublished study was obtained.

In summary, the use of patient reminders in the form of mailed letters increases the rate of cervical cancer screening. Among the studies evaluated in this analysis,

letter reminders had less efficacy in women from lower socioeconomic groups. This could constitute a large number of women who are at risk for cervical cancer. Future research attempting to resolve disparities among different socioeconomic groups in cervical cancer screening should target factors contributing to poor adherence.

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