BMC Research Notes

RESEARCH NOTE Open Access

The participation in cervical cancer screening is not altered by the Hawthorne effect among patients of doctors participating in the randomized clinical trial PaCUDAHL

Gabrielle Lisembard[1], Michaël Rochoy[2], François Quersin[1], Valérie Deken[3], Alain Duhamel[2,3], Axel Descamps[1], Christophe Berkhout[1] and Fanny Serman[1,2*]

Abstract

Objective The PaCUDAHL randomized clinical trial evaluated an HPV self-sampling device provided by the family doctor to female patients not participating in the usual opportunistic cervical screening program from 2016 to 2019. Reliable data on the Hawthorne (observer) effect (HE) in clinical trials were lacking. This nested study aimed to verify whether there was a significant difference between participating and non-participating general practitioners (GPs) in the trial, and to measure whether there was an HE in the female patients of participating GPs.

Results We carried out an analytical retrospective cohort study involving 332 GPs and their 70,983 female patients, aged 25–65, registered with the Health Insurance Fund of Flanders, using claims database for the three-year periods 2012–2015 and 2016–2019. Statistical analyses were performed using a linear generalized hierarchical mixed model with geographic level as a random effect. The patients of the 24 participating GPs did not have a cervical cancer screening rate different from that of the non-participating GPs, either before recruitment ($p = 0.24$) or during the PaCUDAHL trial period ($p = 0.15$). There were significant increases in cervical cancer screening rates over four years regardless of the group considered ($p < 0.0001$). In conclusion there was no observer effect but a significant cohort effect.

Keywords Early detection of cancer, Human Papillomavirus Viruses, Hawthorne effect, Primary health care, Uterine cervical neoplasms, Vaginal smears

*Correspondence:
Fanny Serman
fanny.serman@univ-lille.fr
[1]Department of General Medicine, School of Medicine, Lille University, Lille, France
[2]ULR 2694 – METRICS, University Hospital Lille, Lille University, Lille, France
[3]Department of Public Health, University Hospital Lille, Lille University, Lille, France

Introduction

In 2012, cervical cancer was the cause of more than 1,000 deaths per year in France, with a particularly high incidence in the Nord-Pas-de-Calais region [1, 2]. The specific mortality rate for cervical cancer had been decreasing steadily for 30 years, but this decrease has stagnated since 2000 [1, 3], with lack of screening remaining the main risk factor for cervical cancer mortality [4]. By 2020, cervical smear testing (CST) has been recommended every three years for women aged 25–65 years to detect high-grade lesions before they become carcinoma in situ. General practitioners (GPs), biologists, gynaecologists, and midwives were authorized to perform this sampling, but in France in 2012, gynaecologists performed 95% of these procedures [5, 6]. The lack of participation in pap smear test (PST) screening has largely been associated in the literature with low socioeconomic level and lack of follow-up by a gynaecologist [7–14]. In this context, the PaCUDAHL-Gé study (Participation in Cervical Cancer Screening: The Interest of a Self-Sampling HPV Device Provided by the General Practitioner) aimed to compare cervical cancer screening rates (CCSRs) among women aged 25 to 65 years who had not been previously screened for cervical cancer and who were offered (1) a self-sampling device provided by their general practitioner versus (2) the traditional cervical smear suggested by their physician [15]. The study investigators were 24 general practitioners who were randomized into two groups. The observer effect (or Hawthorne effect - HE) is defined as the awareness of being observed or assessed, which creates beliefs about the researcher's expectations (due to conformity and social desirability) and leads to change in behaviour aligned to these expectations [16, 17]. As the PaCUDAHL trial was open-label, HE raised the question of whether there was additional motivation for patients to participate in screening because their GP was involved in a clinical trial. This nested study of PaCUDAHL, registered by a protocol amendment in April 2020, aimed to compare CCSRs in health insurance reimbursement databases for patients of physicians participating (or not) in the PaCUDAHL trial before and during the trial (periods 2012–2015 and 2016–2019).

Methods

This was a retrospective cohort study using the claims database of the Health Insurance Fund (HIF) of Flanders for the three-year periods 2012–2015 and 2016–2019. The research questions were: (1) whether there was a significant difference between physicians enrolled in PaCUDAHL and other physicians in the research area before their recruitment, either in their sociodemographic characteristics or in the CCSR of their patients (period 2012–2015); (2) whether the CCSRs changed after recruitment due to the HE (period 2016–2019).

Population

The database provided by the HIF listed 402 general practitioners practising in the area as of January 30, 2015. Doctors who had fewer than 100 women as referring general practitioners, those who refused to answer the telephone survey on PST practice, retired doctors, or those who left the practice by December 31, 2019, were excluded (see Fig. 1).

Of the 332 included physicians, 24 were recruited between January and December 2015 from 4 random lists stratified by gender and PST practice to serve as study centres in the PaCUDAHL study and were designated as the "participating group". The remaining 308 physicians in the area were referred to as the "non-participating group". The variables of interest provided by the HIF were the physician's name, gender, address, the size of their total and female patient base, and the CCSRs of these eligible patients over the two time periods. Other variables included the doctor's PST achievement (2015 telephone survey [18]), the deprivation rate of their neighbourhood [19, 20], the urban or rural area of their neighbourhood, and the density of gynaecologists around their practice [21]. Cervical cancer screening uptake was assessed by the number of women who had at least one PST cytology or PST procedure reimbursed during the relevant time periods.

Statistical methods

In the descriptive analysis, continuous quantitative variables are expressed as mean ± standard deviation (SD) or median [interquartile range (IQR)]; categorical variables are expressed as frequencies and percentages. In this study, there were two hierarchical levels for the data: the individual GP level (participating role of the GP and cervical cancer screening participation rate among the GP's listed eligible female patients) nested within the geographic level. The associations of CCSR between GP groups and between time periods of interest were analysed using a linear generalized hierarchical mixed model with geographic level as a random effect. This statistical model considers the hierarchical structure of the data. There was no adjustment for GP characteristics or socioeconomic level, as no difference was found between GP groups. All statistical tests were two-tailed and performed at the 0.05 level. Data were analysed using SAS software® version 9.4 (SAS Institute, Cary, NC).

Ethics

PaCUDAHL-Gé was promoted by the University Hospital of Lille and financed by the French Ministry of Health (PREPS: LIC-14-14-0615). Approval was obtained from the French Agency for the Safety of Health Products (ANSM: 2015-A01331-48) and the Ethics Committee (CPP Nord-Ouest III: 2015-23). The amendment for the

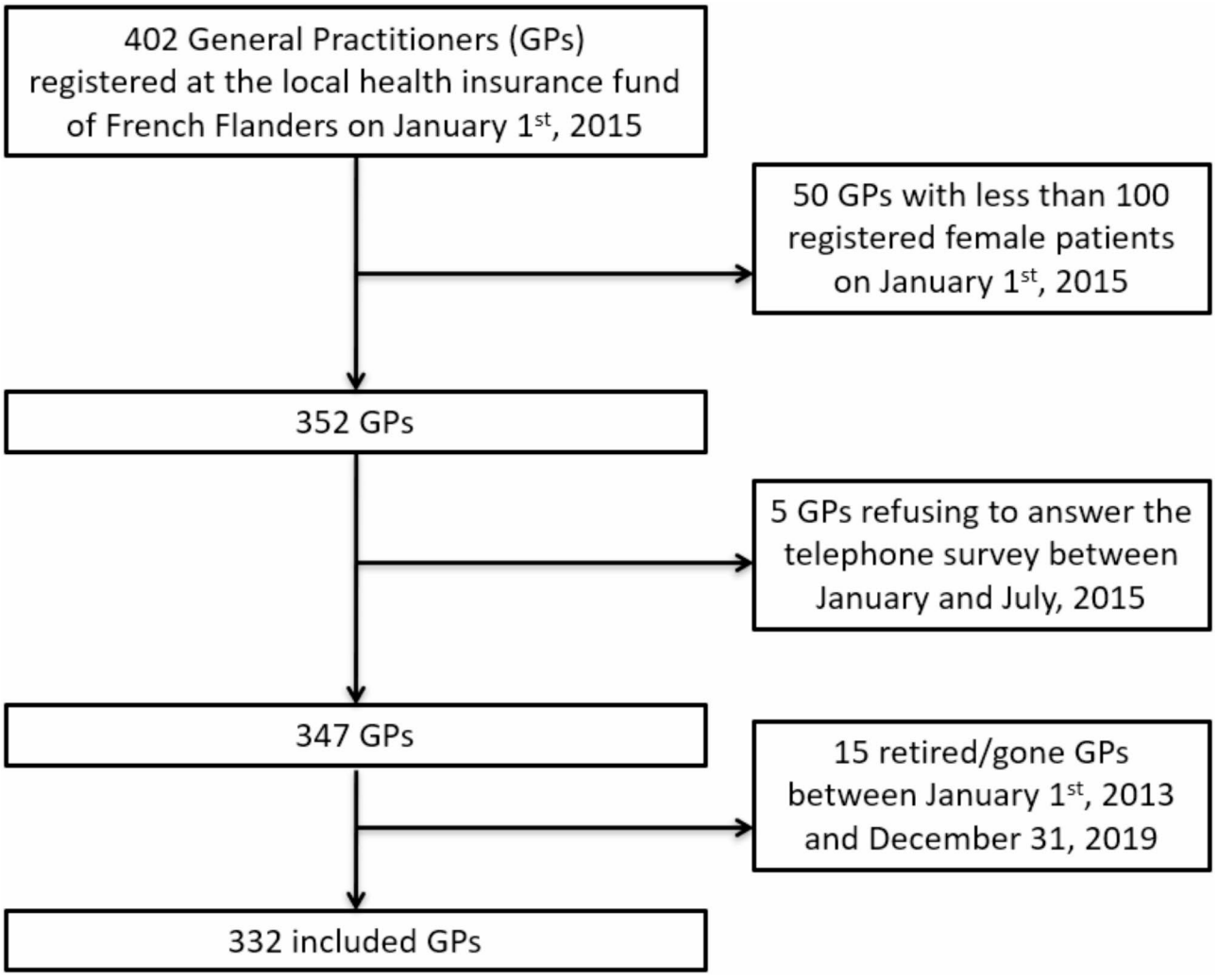

Fig. 1 Study flow chart. GP general practitioner

current study was approved by the ANSM on 12/12/2019 and by the Ethics Committee on 04/20/2019. The protocol is available on ClinicalTrials.gov (NCT02749110). Participating GPs gave their informed oral consent to the use of their data registered in the health insurance claim database when they were called for the telephone survey. No individual patient data were used in this article. None of the authors have any financial competing interests.

Results

The total number of patients at the end of 2015 for the 332 included referring GPs was 232,176, of which 70,983 were women aged 25 to 65. Of these GPs, 52.7% achieved PSTs themselves. There was no difference between the 24 GPs recruited to the PaCUDAHL study and the others in terms of socio-demographic characteristics, PST performance and area deprivation. Table 1 shows all these characteristics for both groups.

The mean CCSR in patients of the 332 doctors was 43.5 (± 8.7)% at the end of 2015. There was no baseline CCSR difference between groups ($p = 0.24$), with a mean of 44.9 (± 9.0)% in the participating group *versus* 43.4 (± 8.7)% in the non-participating group, with a computed difference of 2.03 [95% CI -1.35 to 5.42].

Table 2 Summarizes the mean CCSR in the two groups of Doctors before and during the PaCUDAHL trial time interval

The mean CCSR in patients of the 332 physicians was 43.5 (± 8.7)% at the end of 2015. There was no difference in baseline CCSR between the groups ($p = 0.24$), with a mean of 44.9 (± 9.0)% in the participating group versus 43.4 (± 8.7)% in the non-participating group, for a calculated difference of 2.03 [95% CI -1.35 to 5.42]. Table 2 summarizes the mean CCSR in the two physician groups before and during the PaCUDAHL study period.

Table 1 Descriptive results of participating and non-participating groups before the trial

		Non-participating GPs	Participating GPs	*p*
		n **= 308**	***n*** **= 24**	
gender of the doctor, **n (%)**	Male	241 (78.2)	18 (75.0)	0.71
performance of PST by the doctor, n(%)	Yes	163 (52.9)	12 (50.0)	0.78
doctors registered patients, n	mean (± SD)	697 (± 295)	733 (± 219)	0.45
	median (IQR)	666 (490 to 851)	679 (615 to 841)	
doctors registered female patients, n	mean (± SD)	374 (± 160)	383 (± 112)	0.72
	median (IQR)	351 (261 to 449)	360 (319 to 440)	
Density of gynaecologists				
< 5 km	median (IQR)	5 (0 to 13)	2.5 (0 to 10.5)	0.98
< 20 km		7 (0 to 20)	5.5 (0 to 14)	0.42
European Deprivation Index of office's location, n(%)	median (IQR)	1.8 (-0.6–3.6)	2.1 (-0.5–4.9)	0.30
	mean (± SD)	2.2 (± 3.7)	2.2 (± 3.7)	
	values range	[-4.3–13.7]	[-3.3–15.6]	
distribution of doctor's office location, n(%)	1st quintile	19 (6.2)	1 (4.2)	0.92
(among the national	2nd	19 (6.2)	1 (4.2)	
quintiles of the European	3rd	58 (18.8)	6 (25.0)	
Deprivation Index)	4th	63 (20.4)	4 (16.7)	
	5th (most deprived)	149 (48.4)	12 (50.0)	
doctor office's location,	rural area	106 (34.4)	9 (37.5)	0.76
n (%)	urban area	202 (65.6)	15 (62.5)	

(GP general practitioner, PST Pap smear Test, IQR interquartile range, SD standard deviation, *p* value is calculated with chi-squared test for categorial variables and Student test for continuous ones)

Table 2 Comparative results of pap smears participation between periods and groups

Variable	2012–2015 CCSR [++] (before trial)	2016–2019 CCSR [++] (during trial)	Estimated difference (95% CI)[+]	*p*-value
participating (24 GPs)	44.88 ± 9.03	48.85 ± 9.95	3.97 (2.09 to 5.84)	< 0,0001
non-participating (308 GPs)	43.42 ± 8.66	47.43 ± 8.69	4.01 (3.49 to 4.54)	

[+] Regression estimated difference from linear mixed model with 95% confidence interval

[++] Mean ± standard deviation

P effect participation = 0.13

P effect period = < 0.000

CCSR cervical cancer screening rate 1

Discussion

The CCSR in patients of the 24 referring physicians recruited to the PaCUDAHL study did not differ from those of the non-recruited physicians, either at baseline ($p = 0.24$) or during the PaCUDAHL study period ($p = 0.15$). The key results of this nested study are very robust as they are based on almost all practicing GPs in a large area. Therefore, no HE was detected in this study. However, there was a cohort effect in both groups with a significant increase in CCSRs between 2012 and 2015 and 2016–2019. This strengthens the internal validity of the PaCUDAHL trial findings. Absence of difference before trial was expected due to the randomization of recruited GPs. Absence of HE indicates that the observed screening outcomes were not artificially inflated by GPs awareness of participation.

In France, cervical cancer screening has been part of the public health objectives reimbursed to GPs since 2011 and organized by sending invitation letters to relevant patients in France since 2018. These measures reflect a global increase in the national promotion of this screening, with a significant effect in this cohort. For clinical practice, these findings emphasize the effectiveness of broader public health initiatives such as invitation letters in improving cervical cancer screening uptake. Therefore, clinicians should continue to leverage both organized screening strategies and GPs interventions. Future research could identify which components of ongoing public health interventions (invitation letters, reimbursement changes, national campaigns) are most influential in increasing cervical cancer screening participation. Additionally, given the regional limitations noted, future studies should investigate the generalizability of these results beyond Northern France. In 2024, a clinical trial was funded in Ile-de-France to evaluate whether direct intervention by a GP to contact unscreened women would improve CCSR [22].

The HE could be present during any doctor-patient encounter, especially when enrolled in a clinical trial. Researchers have not yet reached agreement on the existence of HE, and there is considerable inconsistency in the description and definition of the phenomenon [17, 23]. This effect did not appear to be significant in this study, probably because the increase in CCSR with individual invitation letters to patients at the national level induced a similar, stronger effect in both groups [24]. Further clarity on the definition and measurement of the HE in healthcare interventions could guide future trial methodologies, ensuring accurate interpretation of behaviour change mechanisms.

Limitations

Backward selection is a data-driven procedure that may fail to identify the best subset of variables associated with CCSRs and introduce bias in the estimation of coefficients. The CCSRs included only women who had a Pap smear cytology reimbursed by the health insurance, while PSTs performed in hospitals or mother and child welfare centres were not included (we calculated this underestimation in our population to be 4.5%). Only 75% of women aged 25–65 years are included in the primary health insurance database (24% of the population are insured by other organizations and 1% have no health insurance), and it is unclear how these included women compare with women nationally. The CCSR in this study cannot be generalized nationally due to the low uptake of cervical cancer screening in Northern France, which, as in the UK, is associated with lower education and income levels [25].

Abbreviations

95% CI	95% confidence interval
ANSM	French agency for the safety of health products (agence nationale de la Sécurité des Médicaments)
CPP	Ethics committee (Comité de Protection des Personnes)
CCSR	Cervical cancer screening rate
GP	General practitioner
IQR	Interquartile range
HIF	Health insurance fund
HPV	Device provided by the general practitioner
HPV	Human papillomavirus
PaCUDAHL-Gé Trial	Participation in cervical cancer screening: the interest of a self-sampling
PST	Pap smear test
SD	Standard deviation

Acknowledgements

The authors wish to acknowledge the whole PaCUDAHL-Gé research group.

Author contributions

GL and FS managed this nested study. CB designed the PaCUDAHL-Gé protocol. MR, ADe and FQ managed and coordinated the necessary preliminary studies including the telephone survey. GL and FS wrote the manuscript. VD and ADu analysed the dataset. All authors reviewed the manuscript.

Funding

This study is a nested study to the PaCUDAHL-Gé trial. PaCUDAHL was promoted by the University Hospital of Lille and funded by the French Ministry of Health (PREPS: LIC-14-14-0615). In this article, the grant has only been of use for analysis costs.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study is a preliminary study to the PaCUDAHL trial. Agreement was gathered from the French Agency for the Safety of Health Products (ANSM: nr. 2015-A01331-48) and the Ethics Committee of Caen (CPP Nord-Ouest III: nr. 2015-23). The participation of GPs was voluntary. Participating GPs gave their informed oral consent to the use of their data registered in the claim database when they were called to declare whether they were performing pap-smears or not. No individual patient data were used in this article.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 14 April 2024 / Accepted: 13 March 2025
Published online: 24 March 2025

References

1. Binder-Foucard F, Belot A, Delafosse P, Remontet L, Woronoff A, Bossard N. Estimation Nationale de l'incidence et de La Mortalité par cancer En France Entre 1980 et 2012. Partie 1 – Tumeurs solides. Saint-Maurice (Fra). Inst Veille Sanit. 2013. https://www.santepubliquefrance.fr/content/download/144413/2127823?version=1
2. Dépistage. et prévention du cancer du col de l'utérus. Actualisation du référentiel de pratiques de l'examen périodique de santé (EPS). HAS. 2013.
3. Duport N, Heard I, Barré S, Woronoff AS. Focus. Le cancer du col de l'utérus: état des connaissances en 2014. Bull Epidémiol Hebd. 2014;(13–14–15):220–221. https://beh.santepubliquefrance.fr/beh/2014/13-14-15/2014_13-14-15_1.html
4. Collège National des Gynécologues et Obstétriciens, Marès P, Body G, PHILIPPE H-J, Daraï E, Luton D. Gynécologie obstétrique. Elsevier Masson; 2015.
5. Grillo F, Vallée J, Chauvin P. Inequalities in cervical cancer screening for women with or without a regular consulting in primary care for gynaecological health, in Paris, France. Prev Med. 2012;54:259–65.
6. Duport N, Serra D, Goulard H, Bloch J. [Which factors influence screening practices for female cancer in France?]. Rev Epidemiol Sante Publique. 2008;56:303–13.
7. Limmer K, LoBiondo-Wood G, Dains J. Predictors of cervical cancer screening adherence in the united States: a systematic review. J Adv Pract Oncol. 2014;5:31–41.
8. Seidel D, Becker N, Rohrmann S, Nimptsch K, Linseisen J. Socio-demographic characteristics of participation in the opportunistic German cervical cancer screening programme: results from the EPIC-Heidelberg cohort. J Cancer Res Clin Oncol. 2009;135:533–41.
9. Nelson W, Moser RP, Gaffey A, Waldron W. Adherence to cervical cancer screening guidelines for US women aged 25–64: data from the 2005 health information National trends survey (HINTS). J Womens Health. 2009;18:1759–68.
10. Barre S, Massetti M, Leleu H, Catajar N, de Bels FBulletin Epidémiologique Hebdomadaire, 2017;2–3:39–47. https://www.santepubliquefrance.fr/content/download/182959/2308501?version=1
11. Kim M-H, Song Y-M, Kim B-K, Park S-M, Ko GP. Trends in cervical cancer mortality by socioeconomic status in Korean women between 1998 and 2009. Korean J Fam Med. 2013;34:258.

12. Martín-López R, Hernández-Barrera V, de Andres AL, Carrasco-Garrido P, de Miguel AG, Jimenez-Garcia R. Trend in cervical cancer screening in Spain (2003–2009) and predictors of adherence. Eur J Cancer Prev Off J Eur Cancer Prev Organ ECP. 2012;21:82–8.
13. Sicsic J, Franc C. Obstacles to the uptake of breast, cervical, and colorectal cancer screenings: what remains to be achieved by French National programmes? BMC Health Serv Res. 2014;14:465.
14. Menvielle G, Richard J-B, Ringa V, Dray-Spira R, Beck F. To what extent is women's economic situation associated with cancer screening uptake when nationwide screening exists? A study of breast and cervical cancer screening in France in 2010. Cancer Causes Control CCC. 2014;25:977–83.
15. Berkhout C. Participation in Screening for Cervical Cancer: Interest of a Self-sampling Device Provided by the General Practitioner - ClinicalTrials.gov. 2016. https://clinicaltrials.gov/ct2/show/study/NCT02749110. Accessed 5 Apr 2017.
16. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. J Clin Epidemiol. 2014;67:267–77.
17. Berkhout C, Berbra O, Favre J, Collins C, Calafiore M, Peremans L, et al. Defining and evaluating the Hawthorne effect in primary care, a systematic review and meta-analysis. Front Med. 2022;9:1033486.
18. Rochoy M, Raginel T, Favre J, Soueres E, Messaadi N, Deken V, et al. Factors associated with the achievement of cervical smears by general practitioners. BMC Res Notes. 2017;10:723.
19. Serman F, Favre J, Deken V, Guittet L, Collins C, Rochoy M, et al. The association between cervical cancer screening participation and the deprivation index of the location of the family Doctor's office. PLoS ONE. 2020;15:e0232814.
20. Guillaume E, Pornet C, Dejardin O, Launay L, Lillini R, Vercelli M, et al. Development of a cross-cultural deprivation index in five European countries. J Epidemiol Community Health. 2016;70:493–9.
21. Quersin F, Serman F, Favre J, Rochoy M, Descamps A, Gers E et al. Participation rate in cervical cancer screening in general practice related to the proximity of gynecology care facilities: A 3 year follow-up cohort study. Front Public Health. 2022;10.
22. Centre Hospitalier Intercommunal Creteil. Intervention with general practitioners to improve women's participation in cervical cancer screening (INDIGO) - ID NCT06527456. Clinical trial registration. clinicaltrials.gov NCT06527456; 2025.
23. Sedgwick P, Greenwood N. Understanding the Hawthorne effect. BMJ. 2015;351:h4672.
24. Musa J, Achenbach CJ, O'Dwyer LC, Evans CT, McHugh M, Hou L, et al. Effect of cervical cancer education and provider recommendation for screening on screening rates: A systematic review and meta-analysis. PLoS ONE. 2017;12:e0183924.
25. Choi S, Ismail A, Pappas-Gogos G, Boussios S. HPV and cervical cancer: A review of epidemiology and screening uptake in the UK. Pathog Basel Switz. 2023;12:298.

Publisher's note