Exploring the influence of rural residence on uptake of organized cancer screening – a systematic review of international literature

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Abstract

Lower screening uptake could impact cancer survival in rural areas. This systematic review sought studies comparing rural/urban uptake of colorectal, cervical and breast cancer screening in high income countries. Relevant studies (n=50) were identified systematically by searching Medline, EMBASE and CINAHL. Narrative synthesis found that screening uptake for all three cancers was generally lower in rural areas. In meta-analysis, colorectal cancer screening uptake (OR 0.66, 95% CI=0.50-0.87, I^2 = 85%) was significantly lower for rural dwellers than their urban counterparts. The meta-analysis found no relationship between uptake of breast cancer screening and rural versus urban residency (OR 0.93, 95% CI=0.80-1.09, I^2=86%). However, it is important to note the limitation of the significant statistical heterogeneity found which demonstrates the lack of consistency between the few studies eligible for inclusion in the meta-analyses. Cancer screening uptake is apparently lower for rural dwellers which may contribute to poorer survival. National screening programmes should consider geography in planning.

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1. Introduction

Cancer screening programmes aim to identify specific cancers at the earliest pre-symptomatic stage [1]. Colorectal, breast and cervical screening programmes have been found to reduce mortality because of the opportunity to detect precancerous lesions and preclinical cancer enabling early and potentially curative treatment leading to better cancer outcomes [2-6]. Cancer screening is currently the preserve of high income countries (as defined by the World Bank in 2019 as those with a gross national income per capita of more than US $12,535 [7]); the World Health Organization does not recommend cancer screening in low-income countries due to the lack of supporting health service infrastructure[8]. In many countries there are national screening programmes for breast cancer using x-ray mammography usually at a screening facility [9]; pap-smears for cervical cancer usually in primary care[10]; and faecal occult blood test (FOBT) or faecal immunochemical testing (FIT) for colorectal cancer screening often administered by post[11]. In the USA a colonoscopy in secondary care every 10 years after the age of 50 is a popular form of bowel cancer screening[11].

Those who do not engage with screening present with cancer more advanced in stage and have poorer outcomes. Differential screening uptake has been identified in terms of several factors including for example, income, immigration status and geography[12]. In rural areas access to cancer screening is hampered by distance to screening facilities, few available transport options for rural residents [13] and the nature of rural communities where the lack of anonymity can affect health care seeking behaviours [14].

Overall cancer outcomes between urban and rural-dwellers demonstrates inequalities, with rural-dwellers being less likely to survive [15-18], this includes for example poorer 2 year survival [15] and relative five year survival rates [16] from lung cancer and one year mortality after diagnosis with eight common cancers (colorectal, lung, breast, prostate, melanoma, oesophagogastric, cervical and ovarian) [17].A systematic review examining international survival differences between rural and urban cancer patients found that rural residents are 5% less likely to survive cancer compared to urban dwellers [18]. These survival differences have been attributed to variations in cancer treatment and follow-up care between rural and urban areas [19,20], and demographic differences [13,21,21].

Several studies suggest that the rural cancer survival disadvantage occurs because rural dwellers with cancer live further from hospitals, with consequent difficulties in accessing diagnosis and treatment facilities [23-25]. This view is supported by studies which have found that rural dwellers are more likely to be diagnosed with more advanced cancer than their urban counterparts [26-28]. There have been attempts to address this with policy initiatives such as avoiding centralization [29] and using technology and telemedicine [30,31] although practical considerations mean that health services can never completely overcome the geographical challenges to efficiently manage symptomatic rural patients [32].

Although a number of studies have assessed the effectiveness of targeted interventions to improve cancer screening uptake in rural areas [33] in general less attention has been given to the pre-symptomatic stage of cancer development and whether differential uptake of cancer screening exists which could be a component of rural cancer survival disadvantage. We suggest that it is conceivable that lower overall rural cancer screening uptake results in a lower proportion of early stage curable cancer in rural areas. If true, this could be an important factor in determining poorer rural cancer survival overall. Further, it is also possible that geography has more impact on uptake of some screening modalities compared to others. Health care insurance aside it may be less burdensome, for example, for rural dwellers to adhere to colorectal screening administered by post than to travel to a breast screening centre.

Currently, there is only one systematic review comparing breast cancer screening uptake between rural and urban areas [34]. Conducted in 2012, this global review comprising 28 studies found reduced uptake of screening mammogram by rural compared to urban-dwellers. Studies have also reported lower uptake of cervical screening [35,36] and colorectal cancer screening [37,38] in rural areas in comparison to urban areas. To our knowledge, no systematic reviews have yet explored potential geographical impacts on colorectal or cervical cancer screening uptake between rural and urban areas. We conducted a systematic review and meta-analyses of global literature examining the influence of rural residence on the uptake of colorectal, cervical and breast cancer screening in high income countries.

2. Material and methods

2.1 Evidence Acquisition: Identification of studies, data extraction and quality assessment

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [39]. The search strategy was developed with assistance from a medical librarian (MB), and the protocol was registered with Prospero (Prospero protocol registration number CRD42020166004). All searches were conducted on 20th January 2020 with each database searched from their respective date of inception until this date; Medline (from 1946); Embase (from 1946) and CINAHL (from 1981) (See Appendix Table A.1 for full search strategies of all databases). Search terms were ('mammography' or 'early detection of cancer' or 'early detection' or 'screening' or 'identification' or 'Vaginal smears' or 'pap smear' or 'smear test' or 'cervical smear' or 'occult blood' or 'Faecal immunochemical test' or 'bowel screening' or 'colonoscopy' or 'breast cancer screening' or 'bowel cancer screening' or 'cervical cancer screening') and ('rural health' or 'rural health services' or 'remote and rural health' or 'rural population' or 'rural communities') and ('suburban health' or 'urban health' or 'urban health services' or 'urban population'). Medical Subject headings (MeSH) and Embase Subject headings (Emtree) terms were used, as well as free text to widen the search where it was judged appropriate. Inclusion and exclusion criteria are shown (Table 1). There were no restrictions applied in terms of how the screening uptake data were collected. Following feedback from peer reviewers in the preparation of this paper, a second search was performed. Medline (from 1946 to 20th January 2020) was searched using the original search terms with the additional terms 'Remote', 'Remoteness' and 'Regional'.

Identified studies were collated using RefWorks and duplicates were removed. Titles were screened in RefWorks and removed if judged irrelevant. Abstracts of remaining titles were obtained and independently screened by two reviewers (LW and LI or PM). If two reviewers disagreed over inclusion; a third reviewer adjudicated. Data were extracted (by LW) into Microsoft Excel spreadsheets; one for study details and the other for primary outcomes. Data extracted included: participant criteria, study details and primary outcomes including uptake proportions and risk estimates if present and recording the most adjusted risk estimate provided. Where data were presented in graphs/images the authors were contacted for the specific figures. Where this was not possible to obtain, only the available data was recorded. Data about uptake of screening were assigned to either the rural or urban uptake column in the data extraction tables, based on the author's definition of rurality and urbanity used in each study.

A quality assessment of included studies was undertaken using the National Heart, Lung and Blood Institute's (NIH) Tool for Observational cohort and Cross-sectional Studies [40]. (Appendix Table A.2) Five of the 14 NIH tool criteria were judged to be irrelevant for the cross-sectional studies included in this review and were not assessed. For each of the nine criteria specifications were derived to describe "good", "fair" or "poor" or "not reported" cancer screening quality(Appendix Table A.3). The importance of each of the criteria was also determined and the overall study quality could then be assessed as "good", "fair" or "poor" (i.e. a composite numerical score was not created). Quality assessment was completed by two independent reviewers (LW and PM or LI). The inter-rater reliability was then assessed by calculation of a Kappa score. Poor quality did not result in the exclusion of a study from the systematic review.

2.2 Narrative synthesis

For all included studies narrative synthesis involved assessment of each individual studies' screening outcomes by percentage uptake and odds ratio. Reported percentage uptake was compared between urban and rural populations to determine whether there had been rural advantage, disadvantage or no difference. Where studies reported screening uptake data for multiple years, each year was assessed for geographical screening differences and then the overall conclusion reached based on the predominant pattern. Several studies measured screening uptake for different time intervals, e.g. measuring lifetime screening mammography uptake and mammography uptake in the last 2 years. In these instances, each individual time interval was assessed comparing the rural versus urban screening uptake. If the time intervals within one study found conflicting results i.e. lower rural uptake in one particular time interval and higher rural uptake in another this was described as a mixed outcome.

2.3 Meta-analysis

Separate meta-analyses were planned for each screening type. Studies which compared uptake of cancer screening between urban and rural populations, using a binary method of geographical classification for rural and urban areas; and used a multivariate analysis to calculate an odds ratio, adjusted for socioeconomic status were included. In each case the urban group was the reference group, with odds ratios converted if presented with a rural referent. Where standard errors were not reported, these were calculated from the odds ratios and 95% confidence intervals (CI) reported. Review Manager 5.3 was used to conduct the meta-analyses and produce forest plots. The inverse variance method was used. To assess the heterogeneity of included studies, the *I*-squared (I^2) figure was calculated. A random effects model was used to calculate the overall pooled estimates.

3. Results

3.1 Evidence synthesis: Characteristics of included studies

The two searches over three databases yielded 853 titles (Figure 1). The initial search yielded 47 included studies and the further search in May 2021 resulted in a total of 50 studies. Characteristics of the 50 included studies are shown in Appendix Table A.4 [35-38, 41-86]. Many studies measured uptake for more than one cancer type: colorectal screening uptake (n=17 studies), screening mammography uptake (n=32 studies) and cervical cancer screening uptake (n=18 studies). The sample size of the included studies ranged from 178 to 8,617,498 participants. Five studies did not clearly report the sample size [38,66,69,74,83], 17 studies included 10,000 to 100,000 participants [45,48,49,37,51,52,57,58,62,63,65,70,71,76,77,81,84]. Eleven studies included over 100,000 patients [46,47,35,50,60,67,78,79,80,82,85].

Studies obtained data about cancer screening uptake from either self-report surveys using telephone, postal or face-to-face questionnaires (n=32 studies) or from population databases (n=17) (See Table A.4). One study used physician recordings of FOBT screening returns [51]. The most common survey used was the USA Behavioural Risk Factor Surveillance telephone Survey (BRFSS, n=12). Population databases are datasets where the information for people who are eligible for screening in that private or national programme are kept, information about whether the individuals were invited and subsequently attended screening is also present. Examples of population databases included ‘The Scottish Breast Cancer Screening Programme Information System’ and ‘The United Healthcare and Commercial Healthcare Claims data’.

The included studies were conducted in 12 countries. The majority of studies (n=25) were conducted in the USA [41,42,43,45,47,48,49,35,37,50,52,53,56,58,59,60,36,68,38,69,74,75,77,82,86]. Six studies were from Canada [44,46,64,66,79,81] and seven studies from Australia [55,62,63,80,83,84,85]. Three studies were from the UK [62,65,67], and two studies from Korea [61,72] and two from France [70,76]. There was one study from each of Israel [51], Japan [57], the Netherlands [71], Spain [73], Austria [54] and Croatia [78]. One study, accounted for above, presented uptake data from the UK and from Australia [62].

For breast cancer screening involving mammography; 19 studies included women in a certain age group [42,44,68,46,54,58,62,63,64,65,66,69,70,72,76,78,79,81,86], for example: women aged 50–69 (n = 5). One study gathered data from American Indian or Alaskan native women over 40 years [77]. Twelve studies included women older than a certain age [43,48,35,50,52,59,60,36,61,74,82,85], e.g. two studies included women over 50 years.

For cervical cancer screening 10 studies used an age limit as part of their target population [68,45,46,67,69,71,72,73,83,86], these limits varied between studies. Four studies included women over 18 [48,35,50,36], one study included women under 45 [75], another included women under 40 [57] and one study included women over 24 [59].

For colorectal cancer screening of all modality types six studies included men and women 50 years and/or older [55,47,49,77,85,37]. One study included only veterans over 50 years [53]. Only one study exploring colorectal screening included just women aged 50 or above [36]. Three studies included men and women aged 50 to 75 years [41,56,38]. Three studies looked at men and women above a specific age (over 40 years old and over 65 years old) [51,52,57]. One study included men and women aged 55 or 65 years [84]. One study included men and women aged 50-70 [68] and one study included men and women turning 50,55 or 60 years old [80].

3.2 Geographical (rural-urban) classification methods

The most common method of rural-urban classification, used by 14 studies, was a unique author identified classification method (See Table 2 for rural-urban classification method used). Eight studies used the Rural-Urban Continuum Codes, developed by the USA Department of Agriculture.

3.3 Quality assessment

Nineteen studies were given a poor-poor quality rating, 19 studies were given a fair-fair rating, nine studies were given a good-good rating, two studies were given a fair-poor rating and one study was given a good-poor rating (see Appendix Table A.5). Raters agreed on 47/50 studies, $\kappa=0.90$ indicating strong agreement [87]. Overall most studies were of fair to poor quality (n=40), due to: the use of self-reported surveys as data sources; ambiguous measures of rurality; no adjustment for key potential confounding variables; unclear descriptions of target populations and missing response rate information among eligible participants. Good quality studies reported cancer screening uptake using population databases with complete population coverage. Better quality studies also adjusted the reported estimates for likely confounding variables such as socioeconomic status and age.

3.4 Narrative synthesis

Table 3 shows a summary of outcomes with respect to place of residence for the three cancers screened. For colorectal cancer screening 12/17 studies reported a higher urban than rural uptake in all of their measured screening modalities and intervals [41,47,49,51,52,53,57,36,38,77,68,80].All of these studies were USA-based , except one conducted in Japan [57] and one conducted in Australia [80]. Four studies reported a higher rural uptake of colorectal screening[51, 55,84,85] ,three of which were conducted in Australia and one from Israel.

One USA study reported a mixed picture [56]; FOBT uptake in the last one year was higher in rural areas, whereas colonoscopy uptake in the last 10 years was higher in urban areas. Hughes *et al.* [56] also measured screening according to two different criteria: (1) whether the individual had a sigmoidoscopy in the last 5 years with a FOBT in the last 3 years, which had higher rural uptake, and (2) having had a FOBT in the last year or a sigmoidoscopy in the last 5 years with a FOBT in the last 3 years or a colonoscopy in the last 10 years or that their colorectal screening was considered 'up-to-date' which had a high uptake in urban locations.

More than half (20/32) of the studies , found a higher urban screening mammography uptake compared to rural uptake[43,44,35,48,50,52,54,58,60,36,61,66,69,70,74,77,79,82,86,68]. Most of these studies were conducted in the USA (14/20), three in Canada, and one study each in Austria, Korea and France.

Ten studies found that rural areas had a higher uptake of mammography[42,46,62,63,64,72,76,78,81,85].Three studies came from Canada, two studies came from Australia. One study each came from: the USA, Korea, Croatia and France. One study included both Australia and Scotland.

One USA study found mixed results in mammography uptake with different screening intervals [59]. Lifetime mammography was higher in the 'farm' group but mammography uptake in the last two years was higher in the urban group. One UK study found no urban-rural differences for uptake of mammography [65].

Eleven (of 18) studies found a higher urban uptake of cervical screening [43,45,46,48,50,36,69,73,75,86,68].Most of these studies were conducted in the USA (n=9), one in Canada and Spain. Five studies conducted in Japan, the UK, the Netherlands, Korea and Australia found a higher rural uptake of cervical screening [57,67,71,72,83]. Two USA studies, found mixed results in terms of different screening intervals, resulting in either a higher rural or urban uptake for cervical screening [35,59].

3.5 Meta-analyses

Two meta-analyses were conducted for mammography uptake and colorectal screening. There was no meta-analysis undertaken for cervical screening as only one cervical study used a binary rural-urban classification method.

3.5.1 Breast cancer screening

Five studies were included in the meta-analysis (See Appendix Table A.6 for included studies details). One study provided two separate odds ratios for uptake in Scotland and Australia [62]. The Forest plot (Figure 2) shows that 4/5 five studies found rural residents' uptake of screening mammography was lower than their urban counterparts, although not all of the odds ratios were statistically significant and overall the meta-analysis demonstrated no statistically significant findings in regards to a lower rural breast screening uptake (overall pooled odds ratio 0.93, 95% CI 0.80-1.09). Heterogeneity was high (I^2 = 86%) indicating differences between the included studies.

3.5.2 Colorectal cancer screening

Each of the four studies included in the meta-analysis found that people living in rural areas were significantly less likely to uptake colorectal cancer screening that those in urban areas (Figure 3). The heterogeneity between studies was 85%. (See Appendix Table A.7 for included studies details). The pooled odds ratio was 0.66 (95% CI 0.50 - 0.87) indicating that the rural population was significantly less likely to participate in colorectal cancer screening than the urban population.

4. Discussion

4.1 Main findings

The narrative analysis demonstrates the same pattern for all three cancer screening types of decreased screening uptake in rural compared with urban residents. The meta-analysis for colorectal screening also showed this pattern of lower rural screening uptake. Considering the different modalities of screening such as colorectal screening via post and facility-based screening, it is clear that travel burden is not the only important determinant of uptake.

4.2 Context with other literature

The importance of accounting for socioeconomic status when assessing differences in cancer screening uptake in different geographical areas has been recently confirmed by the independent review of adult screening programmes in England, where socioeconomic status accounted for much of the difference in cancer screening uptake at area (local authority or clinical commissioning group) level [88]. Our findings also accord with the systematic review of Leung *et al* [34] , in which mammography uptake was compared in rural and urban areas. Leung *et al* [34] included data from studies using categorical rural-urban measures and used the most rural and most urban figures in their meta-analysis. They found rural residents had a significantly lower uptake for receiving lifetime mammography screening and of mammography screening being up-to-date. As in our review, Leung *et al* [34] found a high proportion of USA studies (16/28). Taken with our findings this suggests a lack of research exploring rural-urban cancer screening uptake differences in other countries. Together Leung *et al* [34] and the current review add to current understanding of rural cancer outcomes. As previously noted, research has found that rural cancer patients are more likely to be diagnosed with more advanced disease [27] than their urban counterparts. Later stage diagnosis has been found to significantly affect mortality for colorectal, breast and cervical cancers [89]. Since cancer screening supports diagnosis of cancer prior to symptoms becoming apparent [8], as a precancerous lesion or preclinical cancer, the systematic review evidence about screening supports the notion that differential uptake of cancer screening by rural and urban residents is a candidate mechanism for geographical cancer inequality.

4.3 Strengths and limitations

A major strength of this review is it's international focus, including studies from a large range of high income countries. Thus differing scales of rurality and urbanity, from the American, Australian and European continent are included. Additionally a range of healthcare systems, with differing funding models which might promote or hinder screening behaviour, are included, which enables a broader scope of understanding the rural cancer screening uptake behaviour

A key review strength is that we have, for the first time, attempted to combine the most comparable studies, with respect to classifying geography and controlling for socioeconomic status, in meta-analyses. This is the best evidence yet of a universal trend to lower rural cancer screening uptake. This is the first systematic review to consider differential rural versus urban cancer screening uptake across the three cancers (cervical, breast and colorectal) most commonly screened for in national screening programmes worldwide. This is important since the findings suggest that rural cancer screening uptake is lower across the world and across the three mains screening programmes. In some respects this is surprising since rural geography potentially could have been less of an impediment to participating in postal screening for colorectal cancer, than endoscopy or the other two programmes in which travel to a healthcare facility is required.

A further strength is that the review considers a range of screening modalities. For example, it appears that rural uptake of endoscopic colorectal cancer screening is consistently low across relevant studies compared to breast screening by mammography where there appears to be some international variation in rural uptake. This could result from a general requirement to perform invasive endoscopic investigations in hospitals, with associated travel and other indirect costs whereas it is often possible to undertake breast cancer screening using mobile mammography units which travel to rural areas for concentrated timed episodes of community-based breast cancer screening [90]. However, there is a lack of research measuring mobile mammography uptake in the USA. Brooks *et al* [91] emphasise lack of data about which patients use mobile mammography units in the USA. Similarly, it would be important to understand whether rurality differentially impacts endoscopic colorectal cancer screening more than postal screening in areas where both methods of screening are employed..

Our systematic review was focused on published research and we did not search any grey literature. A limitation is that we did not assess publication bias. However, formal assessment of publication bias using funnel plots would have been inappropriate as both meta-analyses conducted contained less than 10 studies each and involved observational studies [100,101].

The review is limited by the relatively high proportion of included studies conducted in the USA and Canada, systems where screening uptake will be strongly influenced by individuals' coverage by private insurance or medical programmes. Countries, such as Scotland and Australia, where screening is often offered free at the point of use are relatively underrepresented. It is likely, therefore, that socioeconomic factors will have a varying confounding effect upon the influence of rural geography on screening uptake across the included studies. In the USA, for example, more rural-dwellers aged under 65 are uninsured [92]. Moreover, the USA possesses indigenous and native populations that more often reside in rural areas [93]. Research has found that these groups have lower cancer screening uptake and poorer access to health services as well as lower socioeconomic status [13,94].

Limitations of our approach include that meta-analysis could not be performed for cervical screening and the significant heterogeneity (I^2 values greater than 80%) obtained in the meta-analyses for breast and colorectal cancer screening. This suggests between-study differences and thus a cautious approach is needed when interpreting the pooled estimates [102,103]. Considering the differences between the studies in terms of their population demographics and measurement of uptake criteria the heterogeneity might have been expected. That said despite known differences between studies in their methodology and in the organisation of cancer screening the direction of the effect for the statistically significant bowel screening meta-analysis and the narrative analysis for all cancer screening types were the same.

Another limitation results from heterogeneity across studies in how rurality and urbanity have been defined and classified. Only nine studies reported a binary rural-urban classification with adjustment for socioeconomic status and so were sufficiently comparable to be included in a meta-analysis. Different studies employ different classifications based on factors such as geographical area, population density, distance from services, or other economic factors[95-97]. The classifications employed by researchers will likely capture the geographical factors they perceive most important in their own countries and analyses. Viewed in this way different, but nationally relevant classifications, may partly mitigate differing concepts and scales of residential geography across continents such that rurality has meaning within the study's own setting [98,99], tending to equalize differences due to healthcare systems, demographics, geographical size and topography [13]. The fact that, overall, the majority of the results suggest poorer rural cancer screening uptake speaks to a global trend, at least in the developed world.

5. Conclusions

Throughout the world rural populations appear to tend toward lower uptake of screening for breast, cervical and colorectal cancer. The effect seems to be universal, but there may be a gradient, with rural uptake poorest for hospital-based screening. The results partly suggest that less disparity in urban/rural uptake when travel burden, to engage in screening, can be reduced by e.g. mobile mammography units. Ease of use of testing and patient acceptability may also offer avenue for improving uptake in rural areas, where healthcare contact may be limited and so screening education and support more difficult to access. FIT is an example of a simpler form of postal screening in comparison to FOBT, for colorectal screening, however its recent implementation e.g. in the UK means that uptake data is limited. Further research can explore these issues.

Geographical cancer outcome inequality appears to be a definite phenomenon and is likely multi-factorial. In this regard, poorer uptake of cancer screening by rural populations should be viewed as one likely and real underlying mechanism. Policy efforts should focus on reducing the burden for rural dwellers to engage in national cancer screening programmes. In order to do so, should mean that developers of screening programmes incorporate consideration of coverage area geography into service plans.

In future, geographical influences on cancer screening uptake should receive greater attention from researchers in countries other than the USA, and consideration should be given to internationally collaborative research where data collection and analyses can be planned in advance to minimise or account for different health systems, demographics and scales of geography.

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Table 1. Inclusion and exclusion criteria for studies to be included in the systematic review.

Inclusion	Exclusion
Cross-sectional and cohort studies	Study types other than cross-sectional or cohort
Screening uptake data provided for both rural and urban areas	Only rural or only urban areas assessed
Studies of cervical, colorectal or breast cancer screening	Studies only including screening for cancers not cervical, colorectal or breast.
Participants are over 18 years of age	Participants under 18 years of age
The participants are eligible for the specific modality of screening in the context of their programme or country	Study includes participants who are not eligible for screening
High income countries	Countries with low and middle incomes
English language papers	Non-English language papers
Data included in a peer reviewed publication	Unpublished data

Table 2. Rural-urban classification method used by the fifty included studies.

Classification used	Studies using this classification
Unique study –specific author defined method	Rochat et al, 1976 [75]; Eliakim et al, 1988 [51]; Ikeda et al, 1989 [57]; Bryant et al, 1992 [44]; Palm et al, 1993 [71]; Rettig et al, 1994 [74]; Séguret et al, 1995 [76]; McGahan et al, 2001 [67]; Gobl et al, 2011 [54]; Park et al, 2011 [72]; Cobigo et al., 2013 [46]; Lee et al, 2015 [61]; Goodwin et al, 2019 [55]; Sun et al, 2018 [80]
Rural-Urban continuum codes, developed by the US Department of Agriculture	Coughlin et al, 2004 [49]; Coughlin et al, 2002 [35]; Kakefuda et al, 2006 [59]; Coughlin et al, 2008 [48]; Brown et al, 2009 [43]; Khan et al, 2010 [60]; Bhanegaonkar et al, 2012 [42]; Moss et al, 2019 [68]
US Census Metropolitan Statistical Area zip code classification	Zhang et al, 2000 [86]; Fisher et al, 2007 [53]; Ojinnaka et al, 2015 [38]; Tran et al, 2019 [82]
Accessibility /Remoteness Index of Australia plus	Ward et al, 2011 [84]; Leung et al, 2014 [63]; Weber et al, 2014 [85]; Leung et al, 2015 [62]
Federal Information Processing Standards	Doescher et al, 2009 [50]; Cole et al, 2012 [47]
Rural-urban Commuting Area codes	Fan et al, 2012 [52]; Anderson et al, 2013 [41]; Caldwell et al, 2016 [45]; Davis et al, 2017 [37]
Frontier and Remote classification	Hughes et al, 2015 [56]
California medical service study area classification	Jackson et al, 2009 [58]
Urban Influence Codes	Larson et al, 2006 [36]
Scottish 8-fold urban rural classification	Leung et al, 2015 [62]
UK Office for National Statistics Urban Rural Classification	Maheswaran et al, 2006 [65]
Census Metropolitan Area and Census Agglomeration Influenced Zones classification system	McDonald et al, 2010 [66]
Zip code based rural-urban designation system used by the Centres for Medicare and Medicaid service	Orwat et al, 2017 [69]
French National Institute for Statistics and Economic studies environmental classification: Merged islets for statistical information	Ouédraogo et al, 2014 [70]
Municipality size	Puig-Tintoré et al, 2008 [73]
2000 US Census definition	Schumacher et al, 2008 [77]
Croatian Rural Development Strategy 2008-2013 classification	Stamenić et al, 2011 [78]
First level rural-urban classification created based on statistics Canada classification	St-Jacques et al, 2013 [79]
Postal code conversion using information at census enumeration area level	Tatla et al, 2003 [81]
Regional subdivisions developed by the Commonwealth Department of Primary Industries and Energy and the Department of Health Services and Health in Australia	Wain et al, 2001 [83]
Distance from Mammography facility	Mah et al, 1997 [64]

Table 3. Overall rural-urban outcomes for the three cancer screening forms.*

Colorectal screening (n=17 studies)	Cervical screening (n=18 studies)	Breast screening (n=32 studies)
Higher urban uptake (n=12)	Higher urban uptake (n=11)	Higher urban uptake (n=20)
Anderson et al, 2013 [41]; Cole et al, 2012 [47]; Coughlin et al, 2004 [49]; Davis et al, 2017 [37]; Fan et al, 2012 [52]; Fisher et al, 2007 [53]; Ikeda et al, 1989 [57]; Larson et al, 2006 [36]; Moss et al, 2019 [68]; Ojinnaka et al, 2015 [38]; Schumacher et al, 2008 [77]; Sun et al, 2018 [80].	Brown et al, 2009 [43]; Caldwell et al, 2016 [45]; Cobigo et al, 2013 [46]; Coughlin et al, 2008 [48]; Doescher et al, 2009 [50]; Larson et al, 2006 [36]; Moss et al, 2019 [68]; Orwat et al, 2017 [69]; Puig-Tintoré et al, 2008 [73]; Rochat et al, 1976 [75]; Zhang et al, 2000 [86].	Brown et al, 2009 [43]; Bryant et al, 1992 [44]; Coughlin et al, 2008 [48]; Coughlin et al, 2002 [35]; Doescher et al, 2009 [50]; Fan et al, 2012 [52]; Gobl et al, 2011 [54]; Jackson et al, 2009 [58]; Khan et al, 2010 [60]; Larson et al, 2006 [36]; Lee et al, 2015 [61]; McDonald et al, 2010 [66]; Moss et al, 2019 [68]; Orwat et al, 2017 [69]; Ouédraogo et al, 2014 [70]; Rettig et al, 1994 [74]; Schumacher et al, 2008 [77]; St-Jacques et al, 2013 [79]; Tran et al, 2019 [82]; Zhang et al, 2000 [86].
Higher rural uptake (n=4)	Higher rural uptake (n=5)	Higher rural uptake (n=10)
Eliakim et al, 1988 [51]; Goodwin et al, 2019 [55]; Ward et al, 2011 [84]; Weber et al, 2014 [85].	Ikeda et al, 1989 [57]; McGahan et al, 2001 [67]; Palm et al, 1993 [71]; Park et al, 2011 [72]; Wain et al, 2001 [83].	Bhanegaonkar et al, 2012 [42]; Cobigo *et al.*, 2013 [46]; Leung et al, 2014 [63]; Leung et al, 2015 [62]; Mah et al, 1997 [64]; Park et al, 2011 [72]; Stamenić et al, 2011 [78]; Séguret et al, 1995 [76]; Tatla et al, 2003 [81]; Weber et al, 2014 [85].
Mixed results (n=1)	Mixed results (n=2)	Mixed results (n=1)
Hughes et al, 2015 [56].	Kakefuda et al, 2006 [59]; Coughlin et al, 2002 [35].	Kakefuda et al, 2006 [59];
		Rural and urban uptake equal (n=1)
		Maheswaran et al, 2006 [65].

* Outcomes based on percentage uptake and odds ratios found in the studies. Mixed results due to different outcomes in either screening modality for the cancer type or for screening interval measured.

Figure 1. PRISMA diagram demonstrating search yield and final papers included in the systematic review.

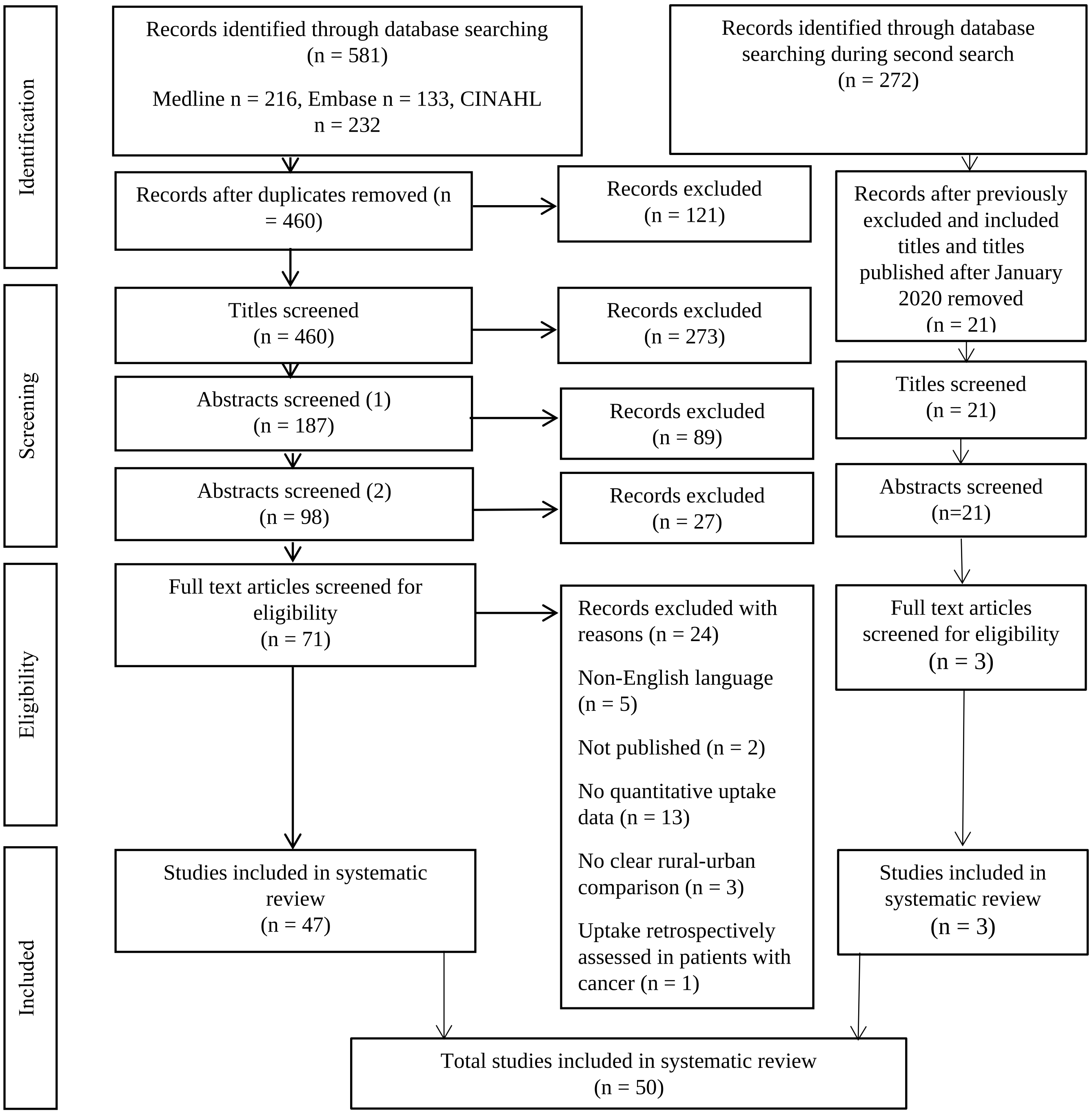
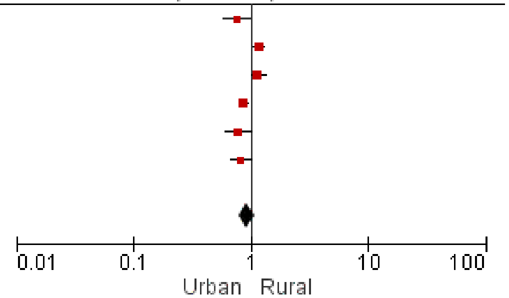

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 581)
Medline n = 216, Embase n = 133, CINAHL n = 232
Records identified through database searching during second search (n = 272)
Records after duplicates removed (n = 460)
Records excluded (n = 121)
Records after previously excluded and included titles and titles published after January 2020 removed (n = 21)
Titles screened (n = 460)
Records excluded (n = 273)
Titles screened (n = 21)
Abstracts screened (1) (n = 187)
Records excluded (n = 89)
Abstracts screened (2) (n = 98)
Records excluded (n = 27)
Abstracts screened (n=21)
Full text articles screened for eligibility (n = 71)
Records excluded with reasons (n = 24)
Non-English language (n = 5)
Not published (n = 2)
No quantitative uptake data (n = 13)
No clear rural-urban comparison (n = 3)
Uptake retrospectively assessed in patients with cancer (n = 1)
Full text articles screened for eligibility (n = 3)
Studies included in systematic review (n = 47)
Studies included in systematic review (n = 3)
Total studies included in systematic review (n = 50)

Figure 2. Forest plot of mammography screening uptake comparing rural and urban dwellers.*

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Brown 2009	-0.27	0.14	13.0%	0.76 [0.58, 1.00]	
Leung 2015	0.16	0.05	19.6%	1.17 [1.06, 1.29]	
Leung b 2015	0.14	0.07	18.3%	1.15 [1.00, 1.32]	
Ouedraogo 2014	-0.14	0.04	20.2%	0.87 [0.80, 0.94]	
Schumacher 2008	-0.25	0.13	13.7%	0.78 [0.60, 1.00]	
Zhang 2000	-0.19	0.11	15.2%	0.83 [0.67, 1.03]	
Total (95% CI)			**100.0%**	**0.93 [0.80, 1.09]**	

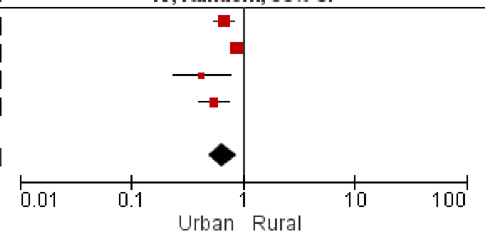
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 35.81$, df = 5 ($P < 0.00001$); $I^2 = 86\%$
Test for overall effect: Z = 0.86 (P = 0.39)



*Leung 2015 represents the Scottish uptake figure, Leung b 2015 represents the Australian uptake figure.

Figure 3. Forest plot of colorectal screening uptake comparing rural and urban dwellers.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Anderson 2013	-0.4	0.103	28.9%	0.67 [0.55, 0.82]	
Davis 2017	-0.128	0.028	33.5%	0.88 [0.83, 0.93]	
Hughes 2015	-0.844	0.304	13.5%	0.43 [0.24, 0.78]	
Schumacher 2008	-0.598	0.158	24.1%	0.55 [0.40, 0.75]	
Total (95% CI)			**100.0%**	**0.66 [0.50, 0.87]**	



Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 19.45$, df = 3 (P = 0.0002); $I^2 = 85\%$
Test for overall effect: Z = 2.89 (P = 0.004)

Appendix A

Table A.1. Search strategies for the three databases.

	Embase search (N = 133 titles)	**Medline search (N = 216)**	**CINAHL search (N = 232)**
1.	Exp mammography	Exp mammography	Screening or early detection or identification
2.	Early cancer diagnosis	'Early detection of Cancer'	Rural population or rural areas or rural communities
3.	Vagina smear	Vaginal smears	Urban population
4.	Exp uterine cervix cytology	Smear test. tw.	1 AND 2 AND 3
5.	Exp Papanicolaou test	Pap smear. tw.	
6.	Occult blood	Cervical smear$.tw.	
7.	F?ecal immunochemical test.tw.	Occult blood	
8.	Bowel screening .tw.	F?ecal immunochemical test. tw.	
9.	Colonoscopy	Bowel screening. tw.	
10.	(breast adj4 cancer adj4 screening) .mp.	Colonoscopy	
11.	(bowel adj4 cancer adj4 screening) .mp.	(breast adj4 cancer adj4 screening).mp.	
12.	(cervical adj4 cancer adj4 screen-ing) .mp.	(bowel adj4 cancer adj4 screening).mp.	
13.	Rural health care or rural health	(cervical adj4 cancer adj4 screening).mp.	
14.	Rural population	Rural health	
15.	(remote adj6 rural adj6 health) .tw.	Rural health services	
16.	Urban health or urban population	(remote adj6 rural adj6 health).tw.	
17.	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12	Rural population	
18.	13 OR 14 OR 15	Urban health	
19.	16 AND 17 AND 18	Suburban health	
20.		Urban health services	
21.		Urban population	
22.		1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13	
23.		14 OR 15 OR 16 OR 17	
24.		18 OR 19 OR 20 OR 21	
25.		22 AND 23 AND 24	

Table A.2. National Heart, Lung and Blood Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies [ref]

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

*CD=cannot determine; NA=not applicable; NR=not reported

Table A.3. National Heart, Lung and Blood Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies as applied to the systematic review.

	Quality		
Criteria	Good	Fair	Poor
1. Was the research question or objective in this paper clearly stated?	Required: clear aim stated and objectives	Required: Aim/objectives stated May be exploratory study of population, needs to state this	No clear research question or objective
2. Was the study population clearly specified and defined?	Required: - Age - Gender - Country	Required: - Age - Gender - Country	Population is vague or measured after data collection
3. Was the participation rate of eligible persons at least 50%?	Required: - For a database - For the population sent surveys/invites	Required	Below 50% or unclear
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?	Required	Required	Inclusion and exclusion not clear Data collected at grossly different time points and aggregated Subjects recruitment not clear or not the same
5. Was a sample size justification, power description, or variance and effect estimates provided?	Confidence intervals and odds ratios present	Confidence intervals or odds ratios present	No confidence intervals or odds ratios
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Cross-sectional so not required		

Table A.3. National Heart, Lung and Blood Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies as applied to the systematic review, continued.

	Quality		
Criteria	Good	Fair	Poor
7. Was the time frame sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Cross-sectional so not required		
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Will have rural-urban measure measuring different levels	May have	Only has rural and urban uptake
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Required: - Need rural-urban measure - Rural-urban measure is valid (previous use and method based on applicable measurement)	Required: - Need rural-urban measure - Rural-urban measure is applicable to all areas of that country/region	If no measure of rural-urban stated or explained (cannot then conclude rural versus urban and this means little) Rural-urban method is subjective (e.g. one village is rural measure and city is urban) Reasoning for rural-urban designation not present
10. Was the exposure(s) assessed more than once over time?	Not relevant for cross- sectional studies		
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Required: - Screening uptake measured objectively based on attendance	Required: - Screening uptake measured objectively	Screening uptake may be measured through self-report survey or questionnaires given by an interviewer

Table A.3. National Heart, Lung and Blood Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies as applied to the systematic review, continued.

	Quality		
Criteria	Good	Fair	Poor
12. Were the outcome assessors blinded to the exposure status of participants?	Not stated in any study Criteria not used		
13. Was loss to follow-up after baseline 20% or less?	Not relevant for cross-sectional studies		
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Required: - Adjustment for both socio-economic status and age	Required: - Adjustment for socio-economic status	No adjustment

Table A.4. Characteristics of included studies that compared rural and urban cancer screening uptake

First author, year	Population size and country	Data source	Cancer(s) screened for	Variables adjusted for	Rural % uptake	Urban % uptake
Anderson *et al.*, 2013 [41]	4,260 USA	Utah Behaviour Risk Factor Surveillance Survey	Colorectal	Age, education, Gender, health insurance, income, marital status, personal health provider, race	FOBT received in last year, Sigmoidoscopy in last 5 years or colonoscopy in last 10 years: 56.8%	FOBT received in last year, Sigmoidoscopy in last 5 years or colonoscopy in last 10 years: 68.3%
Bhanegaonkar *et al.*, 2012 [42]	8,243 USA	West Virginia Medicaid's Free-for-service programme	Breast	None reported.	Screened in last 1 year: 1999: 26.8% 2000:30.1% 2001:30.5% 2002:29.5% 2003:29.8% 2004:27.9% 2005:28.0% 2006:27.9% 2007:29.7% 2008: 27.9%	Screened in last 1 year: Metropolitan /nonmetropolitan urban 1999: 21.2%/20.4% 2000:26.2%/24.2% 2001:24.7%/24.3%

					Screened in last 2 years: 1999-2000:45.2% 2001-2002: 46.4% 2003-2004: 46.0% 2005-2006:44.7% 2007-2008:45.7%	2002:25.1%/24.9% 2003:23.7%/23.5% 2004:23.8%/22.9% 2005:25.2%/22.8% 2006:26.2%/23.4% 2007:24.9%/22.4% 2008: 23.2%/21.1% Screened in last 2 years: Metropolitan /nonmetropolitan: 1999-2000:40.4%/38.0% 2001-2002: 39.2%/39.1% 2003-2004: 38.1%/37.2% 2005-2006:40.4%/37.2% 2007-2008:37.9%/34.4%

Brown *et al.*, 2009 [43]	1,922 USA	Tennessee Behavioural Risk Factor Surveillance Survey	Breast and cervi-cal	Age, education, employment, health factors, household number, income, insurance status, marital status	Screened breast in last 2 years: 71.3% Cervical screening in last 3 years: 73.4%	Screened breast in last 2 years: 78.3% Cervical screening in last 3 years: 81.5%
Bryant *et al.*, 1992 [44]	1,273 Canada	The Alberta Knowledge, Attitude and behaviour study	Breast	Age, Education, Employment, income, marital status	Lifetime screening: 37.0% Screened in the last year: 14.5% Screened in last 2 years: 20.3%	Lifetime screening: 63.0% Screened in the last year: 31.7% Screened in last 2 years: 41.8%

Caldwell *et al.*, 2016 [45]	49,839 USA	Medical Expenditure Panel Survey (2005-2010) an American community survey (2005-2009) and Area health resource file	Cervical	Age, Area health supply context, chronic conditions, deprivation, education, employment, Insurance and expenses, location, marital status, race, self-reported health, sex, survey year	Screened in last 3 years: 81.3%	Screened in last 3 years: 87.3%
Cobigo *et al.*, 2013 [46]	1,458,739 Canada	Institute for Clinical Evaluative Sciences	Breast and Cervical	None reported.	Breast screening in last 2 years: 60.2%	Breast screening in last 2 years: 59.6%

					Cervical screening in last 3 years: 65.6%	Cervical screening in last 3 years: 66.4%
Cole *et al.*, 2012 [47]	1998: 1,134,885 2005: 301,812 USA	Behavioural Risk Factor Surveillance Survey	Colorectal	Age, education, employment status, gender, general health, income, marital status race	FOBT in last year, sig-moidoscopy/colonoscopy in last 5 years: 48.1%	FOBT in last year, sig-moidoscopy/colonoscopy in last 5 years: 54.0%
Coughlin *et al.*, 2008 [48]	Breast: 91,492 Cer-vical: 97,820 USA	Behavioural Risk factor Surveillance Survey and Area re-source file	Breast and Cervi-cal	Age, education, health insurance. household number, income, marital status, race,	Breast screening in last 2 years: 70.6% Cervical screening in the last 3 years:83.3%	Breast screening in last 2 years: Suburban:75.4% Metropolitan:77.6% Cervical screening in the last 3 years: Suburban: 89.0%

						Metropolitan:86.1%
Coughlin *et al.*, 2004 [49]	Men: 23,565 Women:37, 847 USA	Behavioural Risk Factor Surveillance Survey	Colorectal	Age, general health status, health insurance coverage, residence in health professional shortage area, Hispanic ethnicity, marital status, education, physician visit race, sex,	FOBT in the past 1 year: 16.2% Sigmoidoscopy/colonoscopy in last 5 years: 28.2%	FOBT in the past 1 year: Suburban: 19.3% Metropolitan: 22.0% Sigmoidoscopy/colonoscopy in last 5 years: Suburban: 31.5% Metropolitan: 35.2%

Coughlin *et al.*, 2002 [35]	Breast: 108,326 Cervical: 131,813 USA	Behavioural Risk Factor Surveillance Survey	Breast and Cervical	Age, area, education, household number, marital status, race, self-reported health, smoking status, Year of survey	Breast screening in lifetime: 81.5% Breast screening in the last 2 years: 66.7% Cervical screening in lifetime: 94.5% Cervical screening in last 3 years: 81.3%	Breast screening in lifetime: Suburban: 84.4% Metropolitan: 87.3% Breast screening in the last 2 years: Suburban: 92.3% Metropolitan: 75.4% Cervical screening in lifetime: Suburban: 77.1% Metropolitan: 93.9% Cervical screening in last 3 years: Suburban: 89.0% Metropolitan: 84.5%

Davis *et al.*, 2017 [37]	64,711 USA	Oregon's Health services division and All Prayer All claims database (Oregon Health authority) and Area health resource file	Colorectal	Data year, distance to the nearest endoscopy facility, history of accessing primary care. insurance, race, Sex,	*Having received colorectal screening during 4 year study period: [REF]	*Having received colorectal screening during 4 year study period: 1.14 (CI 1.07 – 1.21)
Doescher *et al.*, 2009 [50]	409,675 USA	Behavioural Risk Factor Surveillance Survey	Breast and Cervical	Age, Census region, education, employment status, having a health insurance plan. income,	Breast screening in the last 2 years: Adjacent to metropolitan: 73.4% Remote micropolitan: 73.7% Remote non-core: 71.1%	Breast screening in the last 2 years: 75.4% Cervical screening in last 3 years: 86.0%

				race/ethnicity, self-reported health, sex,	Cervical screening in last 3 years: Adjacent to metropolitan: 85.4% Remote micropolitan: 85.2% Remote non-core: 84.9%	
Eliakim *et al.*, 1988 [51]	20,251 Israel	Physician's records of sending and receiving FOBT kits	Colorectal	None reported.	FOBT: 59.0%	FOBT: Urban upper middle class: 16.7% Urban lower socioeconomic status: 10.2%
Fan *et al.*, 2012 [52]	Breast:6,359 Colorectal:11,850 USA	2005 Medicare Current Beneficiary Survey and	Breast and Colorectal	Age, education, income, insurance, marriage status,	FOBT in last 2 years: Large rural: 23.4% Small rural: 17.9% Isolated rural: 21.0%	FOBT in last 2 years: 27.4% Sigmoidoscopy/colonoscopy in the last 5 years: 48.8%

		Areas re-source file		race/ethnicity, self-reported health, comorbidities. sex,	Sigmoidoscopy/colonoscopy in the last 5 years: Large rural: 44.6% Small rural: 42.6% Isolated rural: 35.4% FOBT in last year or sigmoidoscopy/colonoscopy in last 5 years: Large rural: 50.2% Small rural: 47.5% Isolated rural: 42.7% Breast screening in last 1 year: Large rural: 51.8% Small rural: 45.2% Isolated rural: 44.0%	FOBT in last year or sigmoidoscopy/colonoscopy in last 5 years: 55.0% Breast screening in last 1 year: 53.0%

Fisher *et al.*, 2007 [53]	500 USA	Durham VA medical centre lab database	Colorectal	Age, gender, post office box, prior FOBT, race	*FOBT returned in 9 month period: 0.80 (CI 0.50- 1.10)	* FOBT returned in 9 month period: [REF]
Gobl *et al.*, 2011 [54]	309 Austria	Questionnaire	Breast	Age, educational status, emotional status. marital status, self-reported health, smoking behaviour,	*Breast screening in the last 5 years: [REF]	*Breast screening in the last 5 years: 1.27 (CI 0.54-3.04)
Goodwin *et al.*, 2019 [55]	371 Australia	Self-report survey. Online and in-person recruitment	Colorectal	Age	Whether they had returned a completed FOBT kit: 69%	Whether they had returned a completed FOBT kit: Metropolitan: 64% Regional: 66%

Hughes *et al.*, 2015 [56]	393 USA	Postal questionnaire	Colorectal	Age, asked about colorectal screening last check up, education, personal doctor, polyps removed previously. time since last check up	FOBT in last year: 12.4% Colonoscopy in last 10 years: 71.9% Sigmoidoscopy in last 5 years and FOBT in last 3 years: 14.9% FOBT in last year or sigmoidoscopy in last 5 years and FOBT in last 3 years or colonoscopy in last 10 years or colorectal screening 'up-to-date': 74.4%	FOBT in last year: 7.5% Colonoscopy in last 10 years: 87.5% Sigmoidoscopy in last 5 years or FOBT in last 3 years: 14.3% FOBT in last year or sigmoidoscopy in last 5 years and FOBT in last 3 years or colonoscopy in last 10 years or colorectal screening 'up-to-date': 88.1%

Ikeda *et al.*, 1989 [57]	40,213 Japan	Self-completion questionnaire	Colorectal and cervical	None reported.	Colorectal screening in last year: 33.9% Cervical screening in last year: 31.0%	Colorectal screening in last year: Town: 41.4% City: 38.2% Cervical screening in last year: Town: 25.0% City: 27.0%
Jackson *et al.*, 2009 [58]	33,938 USA	California Health Interview Survey	Breast	Education, income, mammography facility location, Median home values, white collar workers	Breast screening in last 2 years: 73.9%	Breast screening in last 2 years: 77.9%

Kakefuda *et al.*, 2006 [59]	Total:1,255 Cervical: 947 Over 40 Breast: 788 USA	Behavioural Risk Factor and Surveillance Survey and Colorado Farm Family Health and Hazard survey	Breast and Cervical	None reported.	Breast screening in lifetime: Non metropolitan: 79.0% Farm: 84.8% Breast screening in last 2 years: Non-metropolitan: 62.0% Farm: 73.7% Cervical screening in lifetime: Non-metropolitan: 96.2% Farm: 99.6% Cervical screening in last year: Non-metropolitan: 61.2%	Breast screening in lifetime: 84.1% Breast screening in last 2 years: 73.9% Cervical screening in lifetime: 97.7% Cervical screening in last year: 67.1%

					Farm: 63.2%	
Khan *et al.*, 2010 [60]	237,499 USA	Behavioural Risk Factor Surveillance Survey and Area re-source file	Breast	Age, education, gender, income, physician supply.	Breast screening in last 2 years: 72.0%	Breast screening in last 2 years: 77.0%
Larson *et al.*, 2006 [36]	9,358 USA	Medical Ex-penditure Panel Survey and Area re-source file	Breast, Cervical and Colorectal	Age, education, health context infor-mation of area, health status, household income, hysterectomy, insurance, race/ethnicity, region.	FOBT in last 2 years: 21.4% Breast screening in last year: 46.0% Breast screening in the last 2 years: 61.7%	FOBT in last 2 years: Large metropolitan: 32.7% Small metropolitan: 34.1% Adjacent to metropoli-tan:27.9% Breast screening in last year: Large metropolitan: 55.7% Small metropolitan: 56.2%

					Cervical screening in the last year: 51.3% Cervical screening in the last 2 years: 69.4%	Adjacent to metropolitan:50.4% Breast screening in the last 2 years: Large metropolitan: 72.8% Small metropolitan: 71.7% Adjacent to metropolitan:68.0% Cervical screening in the last year: Large metropolitan: 59.3% Small metropolitan: 62.8% Adjacent to metropolitan:60.8%

						Cervical screening in the last 2 years: Large metropolitan: 75.6% Small metropolitan: 77.6% Adjacent to metropoli-tan:74.0%
Lee *et al.*, 2015 [61]	178 Korea	Structured questionnaire	Breast	None reported.	Breast screening 'regu-larly screened': 22.9%	Breast screening 'regularly screened': 49.6%
Leung *et al.*, 2015 [62]	Scotland: 27,416 Australia: 9,890	Scottish Breast Screening Programme information system (2008-2010) and Austral-	Breast	Age, degree of depriva-tion.	Breast screening in last 2 years: Scotland: 76.0% Australia: 84.0%	Breast screening in last 2 years: Scotland: 74.0% Australia: 83.0%

		ian longitudinal study on women's health 1946-51 cohort in 2010 survey				
Leung *et al.*, 2014 [63]	11,200 Australia	Australian longitudinal study of women's health - uses mailed questionnaire self-report	Breast	body mass index, country of birth, depression. Ease of obtaining mammogram, education, financial status, marital status, pressure for time,	Breast screening in lifetime: 2001: 91.0% 2004:95.0% 2007:97.0% 2010:97.0% Breast screening in the last 2 years: 2001: 80.0% 2004:85.0% 2007:84.0% 2010:87.0%	Breast screening in lifetime: 2001:Urban:90.0% Inner regional: 90.0% Outer regional: 91.0% 2004:Urban:95.0% Inner regional: 95.0% Outer regional:95 % 2007: Urban:95.0% Inner regional: 96.0% Outer regional:96.0%

						2010: Urban:96.0% Inner regional: 96.0% Outer regional:96.0 % Breast screening in the last 2 years: 2001:Urban:77.0% Inner regional:77.0% Outer regional:79.0% 2004: Urban:81.0% Inner regional:82.0% Outer regional:81.0% 2007: Urban:83.0% Inner regional:85.0% Outer regional:84.0% 2010: Urban:83.0% Inner regional:84.0% Outer regional:84.0%

Mah *et al.*, 1997 [64]	1,231 Canada	Telephone survey	Breast	Health beliefs and attitudes, Location,	Breast screening in the last 2 years: 18.0%	Breast screening in the last 2 years: 39.0%
Maheswa-ran *et al.*, 2006 [65]	34,868 UK	National Health Ser-vice screen-ing pro-gramme da-tabase	Breast	Distance, location of mammo-gram facility. Socioeconomic sta-tus, urban-rural	Breast screening in the last 3 years: 79.0%	Breast screening in the last 3 years: Intermediate: 78.0% Mainly urban: 78.0%
McDonald J *et al.*, 2010 [66]	Unclear number Canada	Canadian Community Health Sur-vey	Breast	age, education, ethnicity, immigration status, income, language. marital status,	*Breast screening in life-time: No MIZ: 0.65 (p = 0.02) * Breast screening in the last 2 years: No MIZ: 0.7 (p = 0.02)	*Breast screening in lifetime: CMA: [REF] Tract CA: 0.92 (p = 0.20) Non-tract CA: 0.92 (p = 0.14) Strong zone:0.94 (p = 0.37) Moderate zone:0.9 (p = 0.09) Weak zone: 0.91 (p = 0.13)

				province of residence, Survey year,		* Breast screening in the last 2 years: CMA: [REF] Tract CA: 0.85 (p = 0.002) Non-tract CA: 0.96 (p = 0.42) Strong zone:0.85 (p = 0.003) Moderate zone:0.85 (p = 0.001) Weak zone: 0.95 (p = 0.38)
McGahan *et al.*, 2001 [67]	8,617,498 eligible UK	Annual Health Authority Returns	Cervical	None reported.	Cervical screening in the last 3 years: 69.7% Cervical screening in last 5 years: 86.2%	Cervical screening in the last 3 years: Urban outside London: 67.9% Urban London: 65.5% City outside London: 64.4% City London: 58.0%

						Cervical screening in last 5 years: Urban outside London: 85.5% Urban London: 80.7% City outside London: 80.8% City London: 72.7%
Moss *et al.*, 2019 [68]	1776 USA	National Trends Survey and American Community survey.	Colorectal Cervical Breast	College education, marital status, self-reported health status, race/ethnicity, racial segregation	If ever had Colorectal screening in lifetime: 65.8% If ever had Cervical screening in lifetime: 95.1% If ever had Breast screening in lifetime: 91.5%	If ever had Colorectal screening in lifetime: 69.5% If ever had Cervical screening in lifetime: 95.7% If ever had Breast screening in lifetime: 96.1%

Ojinnaka *et al.*, 2015 [38]	Unclear number USA	Behavioural Risk Factor Surveillance Survey	Colorectal	Adjusts for BRFSS design.	FOBT in lifetime: 31.7% Lifetime Colonoscopy or sigmoidoscopy: 62.2% Any colorectal screening undertaken: 68.6%	FOBT in lifetime: City centre of Metropolitan statistical area: 37.6% Out of city centre of metro-politan statistical area: 33.0% Suburban county: 20.6% Lifetime Colonoscopy or sig-moidoscopy: City centre of Metropolitan statistical area: 65.9% Out of city centre of metro-politan statistical area: 68.0% Suburban county: 57.3% Any colorectal screening un-dertaken:

						City centre of Metropolitan statistical area: 73.2% Out of city centre of metropolitan statistical area: 72.8% Suburban county: 61.8%
Orwat *et al.*, 2017 [69]	Unclear number USA	UnitedHealthcare commercial healthcare claims data	Breast and Cervical	None reported.	Breast screening in the last 2 years: 2008: 72.0% 2011: 72.5% Cervical screening in last 3 years: 2008: 76.2% 2011: 74.6%	Breast screening in the last 2 years: 2008: 76.6% 2011: 77.6% Cervical screening in last 3 years: 2008: 84.3% 2011: 83.0%
Ouédraogo *et al.*, 2014 [70]	13,565 France	Merged islets for statistical information	Breast	Age, deprivation, insurance,	Breast screening in the last year: 48.7%	Breast screening in the last year: 54.2%

		and the thirteen French departments		nearest screening facility, Residence.		
Palm *et al.*, 1993 [71]	10,387 The Netherlands	Nationwide screening programme database	Cervical	Variables measured not utilised in results obtained.	Cervical screening in the last year: 57.9%	Cervical screening in the last year: 54.8%
Park *et al.*, 2011 [72]	4,139 Korea	Korea National Cancer Screening Survey	Breast and Cervical	Age, education, household income, insurance. marital status, residence	Breast screening in lifetime: 59.5% Cervical screening in lifetime: 75.9%	Breast screening in lifetime: Metropolitan: 54.9% Urban: 55.6% Cervical screening in lifetime: Metropolitan: 75.8% Urban: 75.0%

Puig-Tintoré *et al.*, 2008 [73]	5,789 Spain	Postal questionnaire	Cervical	Age, municipality size. Regions, socioeconomic level,	Cervical screening in lifetime: 77.8% Cervical screening in the last 3 years: 66.0%	Cervical screening in lifetime: 5-30,000 people: 85.2% 30-200,000: 85.1% >200,000 : 86.9% Metropolis: 91.4% Cervical screening in the last 3 years: 5-30,000 people: 74.2% 30-200,000: 74.2% >200,000: 75.2% Metropolis: 83.8%
Rettig *et al.*, 1994 [74]	Unclear number USA	Nebraska Behavioural Risk Factor Surveillance Survey	Breast	Age, race.	Breast screening in the last year: 29.0%	Breast screening in the last year: 40.0%

Rochat *et al.*, 1976 [75]	6,752 USA	National Fertility Survey	Cervical	None reported.	Cervical screening in the last year: 58.5%	Cervical screening in the last year: Cities: 69.9% Suburbs: 72.2% Towns: 67.2%
Séguret *et al.*, 1995 [76]	52,617 France	Herault Breast Screening Programme database	Breast	None reported.	Breast screening in last 2 years: 52.0%	Breast screening in last 2 years: 48.5%
Schumacher *et al.*, 2008 [77]	Cervical:6,435 Breast:3,293 Colorectal:2,779 USA	Open recruitment interview	Breast and Colorectal	Age, education, income, language, location, marital status, medical history	Colonoscopy in the last 5 years: 17.9% Breast screening in the last 2 years: 51.7%	Colonoscopy in the last 5 years: 50.4% Breast screening in the last 2 years:71.4%

Stamenić *et al.*, 2011 [78]	264,517 offered Croatia	Public Health Institutes shared database	Breast	None reported.	Breast screening in last 2 years: 60.6%	Breast screening in last 2 years: 58.5%
St-Jacques *et al.*, 2013 [79]	833,856 Canada	Quebec Breast cancer Screening Programme database	Breast	Age, deprivation. distance to mammography facility,	Breast screening in last 2 years: 55.4%	Breast screening in last 2 years: Montreal Islands:40.9% Montreal suburbs:52.2% Middle size cities:57.6% Small cities:56.8%
Sun *et al.*, 2018 [80]	1855201 Australia	National bowel cancer screening programme data from Department of Health	Colorectal	Age, Culuturally and Linguistically diverse status, indigenous Australian status, and socio-economic status	Returned a completed FOBT kit: Remote: 27.9% Very Remote: 25%	Returned a completed FOBT kit: Major cities: 33.4% Inner Regional: 36.5% Outer Regional: 33.7%

Tatla *et al.*, 2003 [81]	57,902 Canada	Ontario Breast Screening Programme members database	Breast	Age, initial mammography result, language, location, previous mammography history, referral by health professional, Socioeconomic status	Breast screening in last 3 years: 80.3%	Breast screening in last 3 years: 75.5%
Tran *et al.*, 2019 [82]	482,360 USA	Behavioural Risk Factor Surveillance Survey and Breast and	Breast	Age, race, education, health care coverage, household income,	Breast screening in lifetime: 93.2% Breast screening in last 2 years: 21.6%	Breast screening in lifetime: MSA Centre:95.1% Out of MSA but in CC:95.0% Suburban county of MSA: 94.2% MSA with no CC:96.1%

		Cervical cancer screening module - Random digit dialling		Location, marital status, personal doctor or health care provider.		Breast screening in last 2 years: MSA Centre:75.6% Out of MSA but in CC: 17.3% Suburban county of MSA: 18.9% MSA with no CC:14.2%
Wain *et al.*, 2001 [83]	Unclear number Australia	Cervical screening registry database	Cervical	Age. indigenous population, non-English speaking background, region, Socioeconomic status,	*Cervical screening in 2 years: Large rural centre: 1.14 (CI 1.04- 1.26) Small rural centre:1.03 (CI 0.95- 1.12) Other rural:0.73 (CI 0.68- 0.79) Other remote:0.64 (0.51- 0.90)	*Cervical screening in 2 years: Capital:[REF] Other metropolitan centre:0.96 (CI 0.90-1.02)

Ward *et al.*, 2011 [84]	74,782 (invited) Australia	National Bowel cancer Screening Programme register	Colorectal	Deprivation, location. Sex	FOBT kit returned within 18 month study period: Rural: 48.6% Remote: 46.0%	FOBT kit returned within 18 month study period: 45.6%
Weber *et al.*, 2014 [85]	232,056 Australia	Self-administered questionnaire	Breast and Colorectal	Age, education, family history of cancer, hormone replacement therapy status, income, insurance, relationship status, employment status, sampling process	FOBT completed in last 2 years: 22.3% Breast screening in last 2 years: 70.1%	FOBT completed in last 2 years: 18.0% Breast screening in last 2 years: 65.9%

Zhang *et al.*,2000 [86]	Pap smear:8,970 Mammography:2,729 USA	National Health Interview survey	Breast and Cervical	Education, income, insurance. Region	Breast screening in the last 2 years: 61.0% Cervical screening in the last 3 years: 79.0%	Breast screening in the last 2 years: 68.0% Cervical screening in the last 3 years: 82.0%

*Odds ratios presented where uptake % not available.

CA, census agglomeration. CC, City centre. CI, confidence interval. FOBT, Faecal occult blood test. MIZ, Metropolitan influence zone. MSA, Metropolitan statistical area.

Table A.5. Outcome of quality assessment by two raters.

First author	Rating A	Rating B
Anderson A.E. [41]	Fair	Fair
Bhanegaonkar,Abhijeet; [42]	Good	Good
Brown,Kathleen C. [43]	Poor	Poor
Bryant,H. [44]	Poor	Poor
Caldwell,Julia T. [45]	Poor	Poor
Cobigo,V. [46]	Good	Poor
Cole,Allison M. [47]	Fair	Fair
Coughlin,S.S.2008 [48]	Poor	Poor
Coughlin,Steven S. 2004 [49]	Fair	Fair
Coughlin,Steven S. 2002 [35]	Fair	Fair
Davis M.M. [37]	Fair	Fair
Doescher,Mark P. [50]	Fair	Fair
Eliakim,R. [51]	Poor	Poor
Fan,L [52]	Poor	Poor
Fisher D.A. [53]	Fair	Fair
Gobl,Christian S. [54]	Poor	Poor
Goodwin, [55]	Fair	Fair
Hughes A.G. [56]	Poor	Poor
Ikeda,M. [57]	Poor	Poor
Jackson,Monica C. [58]	Poor	Poor
Kakefuda,I. [59]	Fair	Fair
Khan,Nasreen [60]	Fair	Fair
Larson,Sharon [36]	Fair	Fair
Lee,Chang Hyun [61]	Poor	Poor
Leung J.[62]	Fair	Fair
Leung,Janni [63]	Poor -	Poor
Mah,Z.[64]	Poor	Poor
Maheswaran,Ravi [65]	Good	Good
McDonald J.T. [66]	Fair	Fair
McGahan,C E. [67]	Poor	Poor
Moss [68]	Fair	Fair
Ojinnaka C.O. [38]	Fair	Fair
Orwat,John [69]	Good	Good
Ouedraogo,Samiratou [70]	Good	Good
Palm B.T.H.M. [71]	Poor	Poor
Park,Mi Jin [72]	Poor	Poor
Puig-Tintore,Luis M. [73]	Fair	Fair
Rettig B. [74]	Poor	Poor
Rochat, RW. [75]	Poor	Poor
Schumacher M.C. [76]	Poor	Fair
Séguret, F [77]	Poor	Poor
Stamenić,Valerija; [78]	Fair	Poor
St-Jacques, Sylvie [79]	Good	Good
Sun [80]	Good	Good
Tatla,R K. [81]	Good	Good
Tran,Lam [82]	Fair//poor	Fair
Wain G. [83]	Good	Good
Ward,Paul R. [84]	Good	Good
Weber,Marianne F. [85]	Fair	Fair
Zhang,P. [86]	Fair	Fair

Table A.6. Summary of studies included in the meta-analysis for mammography screening

Study	Location	Outcome for uptake	Data source
Brown *et al.*, 2009 [43]	USA	Higher urban uptake	Tennessee Behavioural risk factor surveillance survey
Leung *et al.*, 2015 [62]	Scotland	Rural uptake higher	Scottish Breast Screening Programme information system (2008-2010)
Leung *et al.*, 2015 b [62]	Australia	Rural uptake higher	Australian longitudinal study on women's health 1946-51 cohort in 2010 survey
Ouedraogo *et al.*, 2014 [70]	France	Higher urban uptake	Merged islets for statistical information and the thirteen French departments
Schumacher *et al.*, 2008 [77]	USA	Higher urban uptake	Open recruitment interview
Zhang *et al.*, 2000 [86]	USA	Higher urban uptake	National Health Inter-view survey

Table A.7. Summary of studies included in the meta-analysis for Colorectal cancer screening

Study	Location	Outcome for uptake	Data source
Anderson *et al.*, 2013 [41]	USA	Higher urban uptake	Utah Behavioural Risk factor surveillance survey
Davis *et al.*, 2017 [37]	USA	Higher urban uptake	Oregon's Health services division and All Prayer All claims database (Oregon Health authority) and Area health resource file
Hughes *et al.*, 2015 [56]	USA	Higher urban uptake	Postal questionnaire
Schumacher *et al.*, 2008 [77]	USA	Higher urban uptake	Open recruitment interview