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Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis

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Abstract

Background: Cardiovascular disease continues to be among the leading causes of morbidity and mortality among men and women globally. However, research suggests that women are significantly underrepresented in cardiac rehabilitation (CR), programmes which are shown to reduce recurrent cardiac events and related premature death. However, sex differences in referral rates have not been systematically and quantitatively reviewed. Hence, the objective of the study was to assess whether a significant sex difference exists.

Methods: We searched Scopus, MEDLINE, CINAHL, PsycINFO, PubMed, and The Cochrane Library databases for studies reporting CR referral rates in women and men published between July 2000 and July 2011. Titles and abstracts were screened, and the selected full-text articles were independently screened based on predefined inclusion/exclusion criteria. Included articles were assessed for quality using STROBE.

Results: Of 623 screened articles, 19 observational studies reporting data for 241,613 participants (80,505 women) met the inclusion criteria. In the pooled analysis, women (39.6%) were significantly less likely to be referred to CR compared to men (49.4%; odds ratio 0.68, 95% confidence interval 0.62–0.74). Heterogeneity was considered significant ($I^2 = 90\%$). There was no change in significant findings when subgroup analyses were conducted, examining fee for service vs. no fee, high-quality studies vs. others, or studies pooled by different study methodologies.

Conclusions: CR referral remains low for all patients, but is significantly lower for women than men. Evidence-based interventions to increase referral for all patients, including women, need to be instituted. It is time to ensure broader implementation of these strategies.

Keywords

Access, cardiac rehabilitation, referral, women

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Introduction

Cardiovascular disease continues to be among the leading causes of morbidity and mortality among men and women globally.[1,2] Women who suffer an acute coronary event are more likely than their male counterparts to incur morbidity and mortality within the first year of recovery, and have lower physical functioning.[1,3] For these reasons, secondary prevention is key, particularly among women.

Outpatient cardiac rehabilitation (OCR; i.e. phase II) programmes offer structured exercise, education, interdisciplinary support, counselling, and risk reduction to promote secondary prevention.[4] OCR participation is associated with an overall reduction in recurrent cardiac events and related premature death,[5,6] improved survival, functional status, and

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psychosocial wellbeing.[7] Despite this abundance of empirical evidence, Class I, Level A guideline recommendations,[3,8–10] and most-recently the development of policy positions promoting OCR referral with corresponding performance measures,[11,12] OCR is greatly underutilized.[13] Moreover, a treatment–risk paradox is observed, such that while women may be in greater need of the secondary prevention offered through OCR, historically many research studies show they are significantly less likely to access it.[14–17]

The reasons for the underuse of OCR are multifactorial;[18–21] however, OCR referral is one of the sole necessary requirements for access. Moreover, recent emerging evidence suggests that OCR referral itself is related to significantly lower mortality.[4] It has been demonstrated for over a decade at least[21–23] that women are significantly less likely to be referred to OCR than men. This is despite the fact that there are now evidence-based systematic referral strategies demonstrated to result in greater OCR use,[24–26] and performance indicators for OCR referral to promote equitable high quality care. However, to our knowledge, rates of OCR referral among women and men have not been systematically reviewed and quantified, nor has it been investigated whether with the existence of these strategies that sex bias in OCR referral persists in the current era. Therefore, the aim of this study was to review studies published in the last 10 years that have examined differences in OCR referral rates of men and women and assess whether a sex difference still exists.

Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement and recommendations were used to guide the methodology of this meta-analysis (http://www.prisma-statement.org/).[27]

Criteria for considering studies

Articles were included in the review if the following criteria were met: (i) a primary observational study (i.e. cross-sectional, prospective, or retrospective) or an interventional study (i.e. randomized or non-randomized trials); ii) examined the rate of women and men referred to community-based, phase II OCR programmes; (iii) published in English; (iv) full-length manuscript published in a peer-reviewed journal; and (v) rates of referral were reported for men and women separately and/or if an inferential test was undertaken to examine sex differences in OCR referral. Numerators and denominators for the rates were required to be reported in the publication. The numerator provided the number of study participants that were referred to OCR. The denominator had to provide the complete sample of study participants that were eligible for OCR. If this data was unavailable in the publication, the study was included if the information was provided directly from the author following request.

Meta-analyses, systematic reviews, qualitative studies, published letters, comments, editorials, case series and case reports, non-empirical, and non-peer reviewed publications (e.g. dissertations) were excluded. Additionally, published articles were excluded if they were a double cohort (and presented identical OCR referral data). A flow chart based on the PRISMA guidelines depicting study selection is presented in Figure 1.

Search methods for identification of studies

Comprehensive literature searches of Scopus, MEDLINE, CINAHL, PsycINFO, PubMed, and The Cochrane Library databases were conducted for peer-reviewed articles published from July 2000 to July 2011 with support from staff librarians. PubMed 'related article' links were used as a compliment to the other databases and were searched to identify further articles meeting inclusion criteria. Reference lists of key studies and reviews were also searched.

Subject heading search terms used were 'heart diseases', 'coronary disease', 'rehabilitation centers', 'referral and consultation', and 'health services accessibility'. Some keywords used in the search included 'cardiac rehabilitation' 'access', 'patient referral', and 'participation'. The Medline search strategy (Figure 2) shows that 'participation' key words were used in order to ensure no referral articles were inadvertently excluded.

Study selection

Citations from all databases were reviewed by two of the authors (TJFC, SG) and were rejected if the reviewer was able to determine from the title or abstract that the paper did not examine OCR referral. Original articles of relevant abstracts were obtained. Duplicate cohorts were identified if the recruitment site and dates, and the number of study participants were identical between papers. In this case, the publication reporting the most relevant and higher-quality evidence in relation to the objectives herein was included in the review.

The selected full-text articles were independently screened by two authors (TJFC, SG) based on predefined inclusion/exclusion criteria determined by the systematic review working group and guided by PRISMA.[27] Discrepancies were resolved by discussion and consensus.

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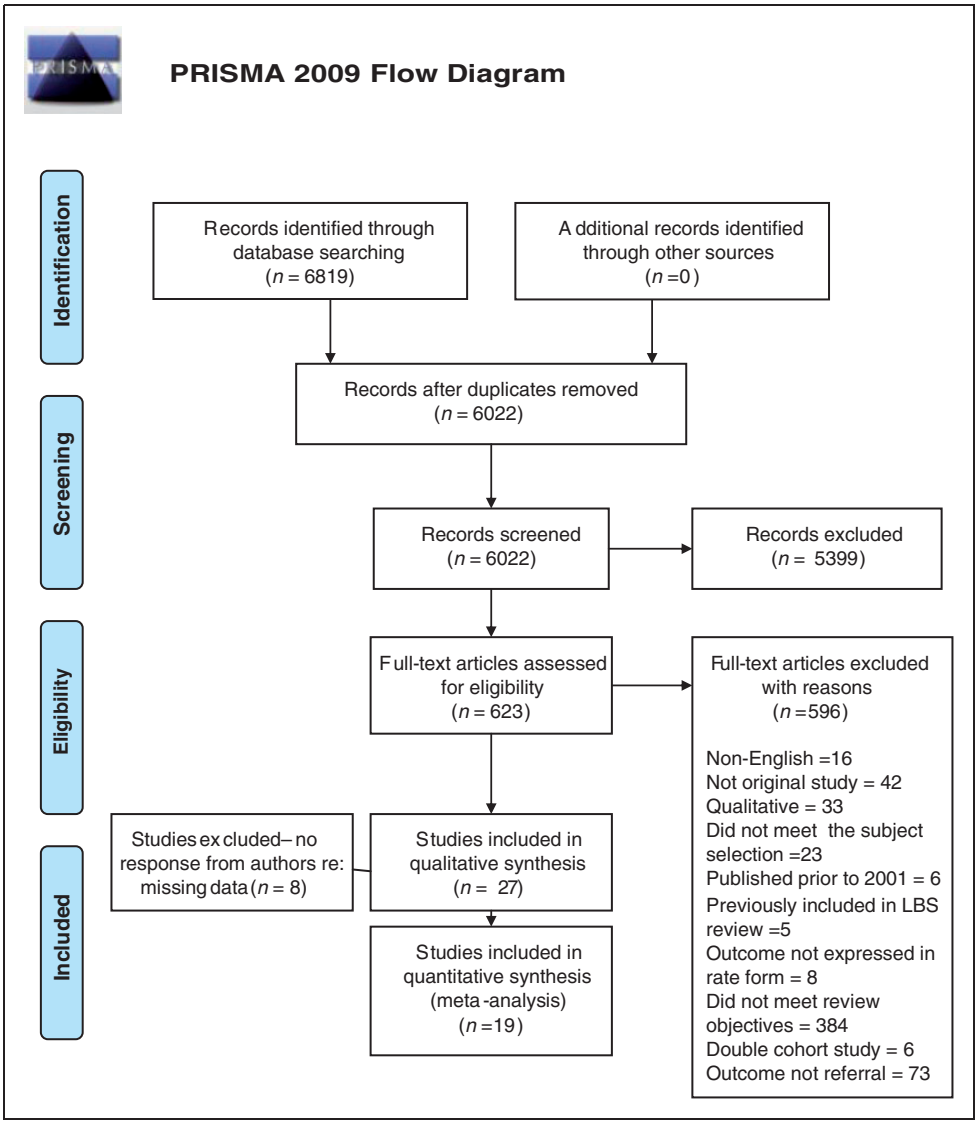

Figure 1. PRISMA flow chart.

Data extraction process and quality assessment

Data were independently extracted from studies meeting inclusion criteria by the second author (SG) and verified by the senior author (LBS). Discrepancies were resolved by the principal investigator (TJFC). The data extraction form was developed, and piloted before use. Most centrally, it included the numerator for number of patients referred and the denominator. Each study was evaluated for quality based on the objectives of this review. Quality ratings were achieved according to the criteria from the US Preventive Services Task Force,[28] which outlines specific rating criteria for good-, fair-, and poor-quality rankings. Two authors completed separate ratings, and disagreements were resolved by third author ranking.

Data synthesis and analysis

Data were analysed using SPSS version 20.0[29] and quantitatively analysed by Review Manager Analysis software version 5.0.[30] A random-effects model was used to compute odds ratios (OR). To determine the impact of heterogeneity on the meta-analysis, I^2 statistics were used. An I^2 score $\leq$40% was considered unimportant heterogeneity.[31] The combined results were examined using the random-effects model, as some heterogeneity in the methodology of the studies was inevitable. Egger's regression intercept of funnel plot asymmetry was computed to test the presence of publication bias.

Potential causes of heterogeneity were explored by performing sensitivity and subgroup analyses to

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Identifies *heart disease and other cardiac conditions*

1 Cardiovascular Diseases/
2 Cardiovascular Disease*.ti,ab.
3 Exp Heart Diseases/
4 Cardiac Rehab*.ti,ab.
5 Heart Disease*.ti,ab.
6 Arteriosclerosis/ or atherosclerosis/ or coronary artery disease/
7 Coronary Disease/
8 Myocardial revascularization/ or angioplasty, balloon, coronary/ or coronary artery bypass, off-pump/
9 (Myocardial infarction or Acute coronary syndrome).ti,ab.
10 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

Identifies *Rehabilitation & Secondary Prevention*

11 Rehabilitation.fs
12 Rehabilitation/
13 Aftercare/
14 Progressive Patient Care/
15 Rehabilitation Centers/ or rehabilitation centre*.ti,ab.
16 (cardiac adj4 rehab).ti,ab.
17 Recovery of Function/
18 Convalescence/
19 Comprehensive health care/
20 Ambulatory Care / or Outpatients/
21 Cardiac Care Facilities/
22 Patient Education as topic/
23 Secondary prevention/ or secondary prevention.ti,ab.
24 Exp excerise/
25 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25

Identifies Access Referral & Enrollment/Participation

26 Health Services/
27 Utilization.fs
28 Health Services Accessibility/
29 Delivery of Health Care/
30 Referral and consulation/ or Gatekeeping/
31 (Referral or access or enroll*).ti,ab.
32 Exp Patient Acceptance of Health Care/
33 Attitude to Health/
34 Patient Dropouts/
35 Patient Compliance/
36 (patient adj3 complian*),ti,ab.
37 (program*adj3 utili*).ti,ab.
38 (program*adj3 access*).ti,ab.
39 (program*adj3 adher*).ti,ab.
40 Patient Participation/
41 Refusal to participate/
42 (program*adj3 attend*).ti,ab.
43 (enroll?ment adj3 (program* or patient*)).ti.ab.
44 Healthcare Disparities/
45 Health Behavior/ or Health Behaviour.ti.ab.
46 Health Knowledge, Attitudes, Practice/
47 Treatment Refusal/
48 26 / - 48
49 10 and 25 and 48
50 Limit to humans
51 Limit 57 to yr="2000 -Current"
52 Limit 58 to 'all adult (19 plus years)"

Figure 2. Cardiac Medline search strategy.

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examine difference in outcome based on the following: (1) study quality; (2) data source for referral (i.e. registry and/or medical chart, self report, and medical records (i.e. requiring patients to consent for participation); (3) fee for OCR vs. no fee (i.e. universal health care system); (4) assessment of eligibility to participate in OCR (i.e. beyond cardiac diagnosis only) vs. inclusion of all patients with a cardiac diagnosis; and (5) single-site studies vs. multiple site studies.

Results

Figure 1 displays the results of the search and application of inclusion/exclusion criteria. Over 6500 titles were retrieved from the electronic and manual search sources. Of these, 623 full papers were identified for possible inclusion in this meta-analysis. Reasons for study exclusion are also outlined in Figure 1. Referral as measured by the proportion of men and women referred to OCR was available for 19 manuscripts, which reported information on a total of 80,505 women and 161,108 men.

Characteristics of included studies

The overview and quality rating of included studies are shown in Table 1. Nine (47.4%) studies were rated as good,[22,23,32–38] eight (42.1%) studies were rated as fair,[24,39–45] and two (10.5%) were rated poor quality.[46,47]

The 19 included studies were observational in design and reported on data collected between 1995 and 2008. The majority of studies were conducted in the USA ($n=7$),[22,24,38,41,43,46,47] four in Canada,[33,34,42,45] three in Australia,[23,36,44] two in England,[35,37] one in Ireland,[41] one in France,[39] and one in New Zealand.[32] Fifteen (78.9%) were multisite studies. In four (21%) studies, observation of referral rates was made in the context of a quality improvement initiative or systematic referral strategy.[24,34,43,47]

A total of 241,613 study subjects were included in the meta-analysis. One study accounted for 60.3% of the total participants.[22] In the majority of studies, patients were recruited for the study in-hospital prior to discharge ($n=8$; 42.1%), while six studies (31.6%) used registry or administrative data only for analyses. In three studies (15.8%), participants were recruited from outpatient cardiology or primary care clinics, one study (5.3%) used registry data and medical charts, and one (5.3%) used registry and OCR programme data. Nine (47.4%) of the included studies enrolled patients with multiple eligible cardiac diagnoses or procedures,[32,34–36,38,43,44,45,47] three (15.8%) studies included coronary artery disease patients,[23,24,33] three (15.8%) studies included acute coronary syndrome (ACS) patients only,[37,39,42] two (10.5%) included myocardial infarction (MI) patients,[40,41] one (5.3%) included percutaneous coronary intervention (PCI) patients only,[22] and one (5.3%) study included PCI or coronary artery bypass graft patients.[45] Of the nine (47.4%) studies that reported the mean age of the study sample, ages ranged from 60.6 to 69.0 years. Among the 19 included studies, women accounted for one-third of the overall study participants (range 22.9–46.9%).

OCR referral rates

Overall OCR referral rates for each study are displayed in Table 1. Referral rates ranged from 22.2%[39] to 73.7%.[41] The overall OCR referral rate was (mean ± standard deviation) 43.4 ± 14.8%). When examining the OCR referral rates by sex, rates for men (49.4 ± 15.5%) ranged from 25.6%[39] to 81.4%.[41] The CR referral rates for women (39.6 ± 14.4%) ranged from 14.0%[39] to 66.0%.[40]

When examining women's CR referral rates by country of study origin, of the seven studies undertaken in the USA,[22,24,38,41,43,46,47] rates ranged from 18.2%[38] to 59.0%.[41] In the four studies undertaken in Canada,[33,34,42,45] rates ranged from 20.5%[42] to 50.9%.[34] In the four studies undertaken in Europe (UK, France, and Ireland),[35,37,39,40] rates ranged from 14.0% [39] to 66.0%,[40] and in the four studies undertaken in Australia,[23,36,44] or New Zealand[32] ranged from 37.0%[44] to 41.6%.[23]

Sex differences in OCR referral

Table 1 presents the results of inferential tests for sex differences in OCR referral among the 19 included studies. Overall, 11 of the 18 studies (61.1%) that included a statistical analysis of sex differences reported that women were significantly less likely to be referred than men, and seven of the 18 studies (38.9%) reported no significant sex differences. One study did not analyse sex differences.[46] Of the eight studies testing sex differences that undertook adjusted analyses, five (62.5%) reported that women were significantly less likely to be referred than men and one (25%) reported no significant sex difference.

Meta-analysis and subgroup specified analysis

The pooled analysis revealed that women were significantly less likely to be referred to OCR than men (OR 0.68, 95% confidence interval, CI, 0.62–0.74; Figure 3). Heterogeneity was considered significant ($I^2=90\%$). There was no significant publication bias, as evidenced by funnel plot asymmetry (Figure 4). Two large studies[22,24] accounted for approximately 90% of the

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Table 1. Studies evaluating OCR referral among men and women

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
Aragam et al. (2011)	Observational retrospective, 145,661 PCI patients, 49,370 women (33.9%), age 64, registry data, 2003–2008, 31 hospitals (multisite), USA	The incidence and predictors of referral to cardiac rehabilitation were assessed among consecutive patients and surviving to hospital discharge in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium registry. The 6-year cardiac rehabilitation referral rate was calculated from this registry database.	Registry	Overall sample referral: 87,706/145,661 = 60.2% Women's referral rate: 28,680/49,370 = 58.1% Men's referral rate: 59,026/96,291 = 61.3% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 0.94, 95% CI 0.92–0.96	Good
Brown et al. 2009)	Observational retrospective, 72,817 CAD patients, 23,374 women (33.2%), 64.1 years, registry data/medical charts, January 2000–September 2007, 156 hospitals (multisite), USA	To determine factors independently associated with OCR referral, which are currently not well described at a national level using the AHA's Get With The Guidelines programme.	Registry	Overall sample referral: 40,974/72,817 = 56.3% Women's referral rate: 12,620/23,374 = 54.0% Men's referral rate: 28,354/49,443 = 57.3% OCR referral differences between men and women: Yes (women were less likely to be referred)	Fair

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				Analysis: $p < 0.0001$ (unadjusted)	
Cottin et al. (2004)	Observational retrospective, 1394 ACS patients, 399 women (29.0%), hospital (predischarge), January 1998–June 1998, 77 hospitals (multisite), France	To specify the characteristics of patients referred to OCR. Eligible patients were surveyed with the French nationwide PREVENIR survey. Patients were assessed both at the acute stage and at 6 months via a survey in public or private French CCUs. All French regions were involved. Data on rehabilitation practice were collected during the 6-month follow-up period.	General practitioner medical records, self report & hospital medical records	Overall sample referral: 310/1394 = 22.2% Women's referral rate: 56/399 = 14.0% Men's referral rate: 254/995 = 25.6% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 0.6, 95% CI 0.44–0.87	Fair
Cupples et al. (2010)	Observational (OCRoss sectional), 332 MI patients, 97 women (29.2%), outpatient cardiology or primary care clinics, May 2005–February 2007, 38 hospitals (multisite), Ireland	To determine, within primary care, how many patients are invited to and attend OCR after MI. Patients were identified from primary care records 12–16 weeks after a confirmed diagnosis of MI and were posted questionnaires.	Outpatient GP records & self-report	Overall sample referral: 235/332 = 70.8% Women's referral rate: 64/97 = 66% Men's referral rate: 171/235 = 72.8%	Fair

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				OCR referral differences between men and women: No Analysis: OR 1.38, 95% CI 0.8–2.3	
Doolan-Noble et al. (2004)	Observational retrospective, 2001 PCI, CABG, ACS, HF patients, 840 women (41.9%), registry and OCR programmes, February 2002, 38 hospitals (multisite), New Zealand	Conducted an audit of 38 OCR programmes. OCR staff initiated an audit form on receipt of each referral to their programme. Completed forms were then returned to the National Heart Foundation for data entry and analysis. A data set was provided by the New Zealand Health Information Service (NZHIS) that included all patients with a hospital stay.	Registry & OCR programmes	(1) Including unmatched patients ($n = 912$ referred): Overall sample referral: 912/2001 = 45.6% Women's referral rate: 320/840 = 38.1% Men's referral rate: 592/1157 = 51.1% (2) Not including unmatched patients ($n = 766$ referred): Overall sample referral: 611/1696 = 36.0% Women's referral rate: 211/731 = 28.8% Men's referral rate: 400/965 = 41.4% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 0.72, 95% CI 0.57–0.91	Good

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
Dunlay et al. (2009)	Observational prospective, 179 MI patients, 61 women (34.1%), 64.8 years, hospital (predischarge), June 2004–May 2006, 1 hospital (single site), USA	Patient were prospectively recruited to participate in the study and provided with a self-report survey prior to hospital discharge.	Medical records & self-report	Overall sample referral: 132/179 = 73.7% Women's referral rate: 36/61 = 59.0% Men's referral rate: 96/118 = 81.4% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: $p = 0.001$ (unadjusted)	Fair
Grace et al. (2008)	Observational prospective, 1268 CAD patients, 358 women (28.2%), 67.3 years, outpatient cardiology clinics, 2004–2006, 97 hospitals (multisite), Canada	A multilevel design of outpatients nested within cardiologists' practices. CAD patients were identified retrospectively from outpatient cardiology practices and sent a request in the post to participate in the study. Participants completed a baseline survey and at 9-months post reOCRuitment. After 9 months, OCR referral was self-reported and thereafter verified at 40 OCR centres.	Self-report & OCR programmes	Overall sample referral: 550/1268 = 43.4% Women's referral rate: 144/358 = 40.2% Men's referral rate: 406/910 = 44.6% OCR referral differences between men and women: No Analysis: χ^2 2.02, $p = 0.17$	Good

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
Grace et al. (2007)	Observational prospective, 506 PCI, CABG, ACS, HF patients, 116 women (22.9%), 60.6 years, hospital (predischarge), September 2003–August 2004, 2 hospitals (multisite), Canada	In-patients were recruited from either Site 1: which automatically refers eligible patients via a computerized prompt or Site 2: usual referral strategy at physician's discretion. OCR referral was discerned in a mailed survey 9 months post-recruitment.	OCR records & self-report	Overall sample referral:262/506 = 51.8% Women's referral rate: 59/116 = 50.9% Men's referral rate: 203/390 = 52.1% OCR referral differences between men and women: No Analysis: χ^2 3.53, $p = 0.17$	Good
Grace et al. (2005)	Observational prospective, 529 ACS patients, 171 women (32.3%), 62.9 years, hospital (predischarge), 12 hospitals (multisite), Canada	ACS patients recruited from CCU and surveyed at 6 months and 1-year post hospitalization. Reported information about OCR referral.	Self-report	Overall sample referral: 149/529 = 28.2% Women's referral rate: 35/171 = 20.5% Men's referral rate: 114/358 = 31.8% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: χ^2 7.07, $p = 0.008$	Fair
Harrison et al. (2005)	Observational cross-sectional), 236 angina, ACS, PCI, CABG, concomitant HF, CAD patients, 74 women (31.4%), 67.3 years, registry data,	Survey of patients eligible for OCR to investigate uptake of services. Effects of individual and geographic factors on utilization were explored. Survey sent to eligible patients from the HES	Self-report	Overall sample referral: 140/236 = 59.3%	Good

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
	January 2000–December 2001, multisite, England	database (which included all residents of the locality eligible for entry into a OCR programme). Participants were asked if they had been invited to attend a OCR programme.		Women's referral rate: 31/74 = 41.9% Men's referral rate: 109/162 = 67.3% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: χ^2 12.54, $p < 0.001$	
Heid et al. (2004)	Observational OCRoss sectional, 202 ACS, CAD, stable angina, chest pain patients, 84 women (41.6%), 64.6 years, hospital (predischarge), June 2001–December 2001, 1 hospital (single site), USA	To compare referral rates between men and women who were admitted to an urban community hospital for a cardiac event. Data were abstracted from a random selection of eligible patient charts at an urban community hospital.	Medical records	Overall sample referral: 87/202 = 43.1% Women's referral rate: 35/84 = 41.7% Men's referral rate: 52/118 = 44.1% OCR referral differences between men and women: No Analysis: χ^2 0.115, $p = 0.73$	Fair
Johnson et al. (2010)	Observational OCRoss-sectional, 4596 angina, ACS, PCI, CABG, concomitant HF, CAD, patients, 1761 women (38.3%), registry data, January 2002–August 2007, multisite, Australia	This study identified participants from the Hunter New England Heart and Stroke Register Database. Eligible individuals were sent a questionnaire in the post to examine OCR referral patterns.	Self-report	Overall sample referral: 2256/4596 = 49.1%	Good

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				Women's referral rate: 669/1761 = 38.0% Men's referral rate: 1587/2835 = 56.0% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 0.62, 95% CI 0.53–0.74	
Johnson et al. (2004)	Observational retrospective, 1202 angina, ACS, PCI, CABG, concomitant HF, CAD, patients, 410 women (34.1%), registry data, March 1998–February 1999, 22 hospitals (multisite), Australia	To examine referral patterns among eligible cardiac patients. Participants were identified by the Hunter Area Heart and Stroke Registry and a self-report survey was sent to eligible participants.	Medical Records & self-report	Overall sample referral: 493/1202 = 41.0% Women's referral rate: 153/410 = 37.0% Men's referral rate: 340/792 = 42.9% OCR referral differences between men and women: No Analysis: AOR 1.24, 95% CI 0.89–1.71	Fair
Labresh et al. (2004)	Observational prospective, 1738 PCI, CABG, ACS, HF patients, 798 women (45.9%), hospital (predischarge), July 2000–June 2001, 24 hospitals (multisite), USA	Hospitals participated in the GWTG programme for at least 1 year. Outcome measurements of the quality improvement intervention were taken at the beginning of the programme (baseline), at 4–6 months and finally at 10–12 months.	Medical Records	Baseline (preintervention): Overall sample referral: 577/1738 = 33.2%	Poor

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				Women's referral rate: 239/798 = 30.0% Men's referral rate: 338/940 = 36.0% OCR referral differences between men and women: Not analysed	
Norris et al. (2004)	Observational OCRoss-sectional, 5081 PCI, CABG patients, 1180 women (30.2%), registry data, January 1995–December 2000, multisite, Canada	Women who underwent revascularization were selected from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease registry. OCR referral was obtained for all eligible women in the registry for the selected and reported for study dates.	Registry	Overall sample referral: 1470/5081 = 28.9%	Fair
				Women's referral rate: 283/1180 = 24.0% Men's referral rate: 1187/3901 = 30.4% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 1.19, 95% CI 1.01–1.40	
Raine et al. (2002)	Observational prospective, 719 ACS patients, 337 women (46.9%), hospital (predischarge), April 1995–November 1996, 94 hospitals (multisite), England	A prospective national survey of several indicators among acute cardiac admissions. A random sample of hospitals were asked to report data on a subsample of patients admitted for ACS.	Medical records	Overall sample referral: 274/719 = 38.1%	Good
				Women's referral rate: 107/337 = 31.8% Men's referral rate: 167/382 = 43.7%	

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				OCR referral differences between men and women: Yes (women were less likely to be referred)	
				Analysis: $p = 0.002$ (unadjusted)	
Roblin et al. (2004)	Observational prospective, 578 ACS, CABG, PCI patients, 148 women (25.6%), outpatient cardiology or primary care clinics, January 1997–December 1999, 1 hospital (single site), USA	Examined referral to OCR among post-hospital cardiac patients that had at least 1 outpatient cardiology visit. Computerized hospital discharge records were used to identify eligible participants. Data were abstracted from the onsite medical charts for OCR referral verification.	Medical records	Overall sample referral: 141/578 = 24.4%	Good
				Women's referral rate: 27/148 = 18.2%	
				Men's referral rate: 114/430 = 26.5%	
				OCR referral differences between men and women: No	
				Analysis: AOR 0.66, 95% CI 0.40–1.06	
Stewart Williams (2009)	Observational retrospective, 2375 CAD patients, 872 women (36.7%), 69.0 years, registry data, July 1996–December 2000, multisite, Australia	Secondary analysis of which eligible patients were identified from a registry that connect both hospital and OCR data. Information on OCR referral was examined. The aim of this paper is to show how non-linear decomposition methods can be used to explain the disOCRiminatory effects of inequalities in access to care.	Registry & OCR programmes	Overall sample referral: 1170/2375 = 49.3%	Good
				Women's referral rate: 363/872 = 41.6%	

(continued)

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Table 1. Continued.

Publication	Study design and location	Methods	Source of outcome measure	Results	QA grade
				Men's referral rate: 807/1503 = 53.7% OCR referral differences between men and women: Yes (women were less likely to be referred) Analysis: AOR 0.60, 95% CI 0.39–0.92	
Stiller et al. (2004)	Observational prospective, 203 MI, PCI, CABG, angina patients, 55 women (27.1%), hospital (predischarge), 1 hospital (single site), USA	Patients were recruited from a metropolitan medical centre if they were eligible for OCR. Participants completed a survey 3-weeks post hospital discharge that asked about OCR referral.	Medical records & self-report	Overall sample referral: 114/203 = 56.2% Women's referral rate: 26/55 = 48.1% Men's referral rate: 88/148 = 59.5% OCR referral differences between men and women: No Analysis: $\chi^2 = 2.02$, $p = 0.151$	Poor

ACC, American College of Cardiology; ACS, acute coronary syndrome; AOR, adjusted odds ratio; CABG, coronary artery bypass graft; CAD, coronary artery disease; CCU, coronary care unit; CI, confidence interval; GWTG, Get With The Guidelines; MI, myocardial infarction; N/A, not applicable; OCR, outpatient cardiac rehabilitation; OR, odds ratio; PCI, percutaneous coronary intervention; QA, quality assessment.

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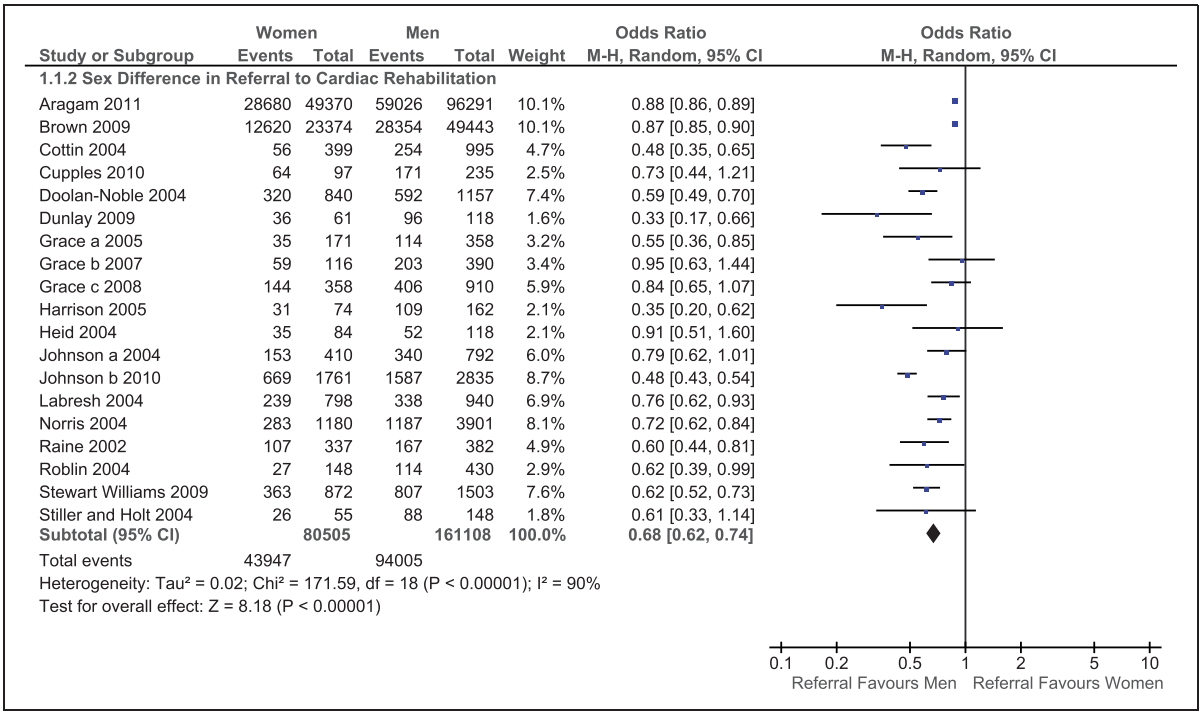

Figure 3. Pooled analysis of studies.

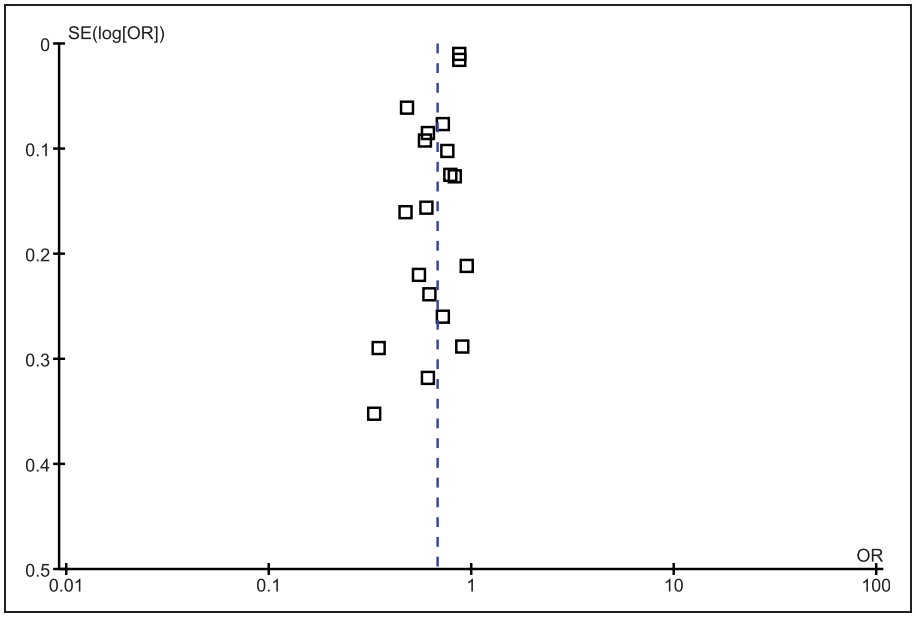

Figure 4. Funnel plot indicating no significant publication bias.

total number of patients included in the analysis; however, when the meta-analysis was re-analysed excluding these two studies, the odds ratio remained statistically significant (from 0.68 to 0.63) thus, still favouring a sex bias.

Subgroup analyses specified a priori were conducted. When only the nine studies rated high quality were considered, the sex difference observed in the overall sample persisted (OR 0.71, 95% CI 0.57–0.88, $p < 0.00001$). Heterogeneity was still considered

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significant ($I^2 = 89\%$). There were no significant findings resulting from analysis of the data source for referral including registry (studies) and/or medical chart (OR 0.75, 95% CI 0.69–0.81; $I^2 = 86\%$) and self-report or self-report and medical records (OR 0.62, 95% CI 0.50–0.76; $I^2 = 75\%$). In addition, there was no change in significant findings resulting from an analysis of studies that required a fee for cardiac rehabilitation (OR 0.83, 95% CI 0.78–0.89, $I^2 = 69\%$) or no fee (i.e. universal health care system; OR 0.64, 95% CI 0.56–0.74; $I^2 = 73\%$) or studies that included an assessment of eligibility to participate in OCR (beyond cardiac diagnosis only: OR 0.71, 95% CI 0.57–0.89; $I^2 = 83\%$; inclusion of all patients with a cardiac diagnosis (OR 0.64, 95% CI 0.54–0.77; $I^2 = 91\%$). Furthermore, there was no change in significant findings resulting from an analysis of single-site (OR 0.64, 95% CI 0.54–0.76; $I^2 = 39\%$) vs. multiple-site studies (OR 0.69, 95% CI 0.62–0.77; $I^2 = 91\%$)

Discussion

The results of this meta-analysis reveal that over the last decade, OCR referral remains suboptimal, particularly among women. OCR referral rates for women were 39.6% on average. Among the studies that examined sex disparities in OCR referral and including those using adjusted analyses, women were significantly less likely to be referred than men. Our pooled analysis revealed that overall men were almost 1.5-times more likely to be referred to an OCR programme than women. Furthermore, recent OCR enrolment benchmarks set by Canadian[11] and UK[4] panel experts of 70% and 85%, respectively, may not be attainable if referral rates for women remain so low.

Despite the proven benefits of OCR,[7] only an average of 34% of patients are referred, and 20% ultimately enrol.[13] Historically, it has been demonstrated that women are significantly less likely to be referred to OCR than men.[17] This is contrary to clinical practice guidelines which recommend OCR as the standard of care for secondary prevention for both men and women.[3,8–10] The reasons for the gap in evidence and resulting care are complex; however, arguably the chief explanatory factors are referral failure and lack of provider encouragement.[17,18] Although reviews have been published which examined referral to OCR among all eligible cardiac patients, and women specifically;[14–17,48,49] this is the first meta-analysis to demonstrate that the sex bias is also evident on a population-wide basis.[22–24,45] This sex difference has been observed consistently over the 10 years prior to this meta-analysis[17] and persists to date across many countries.

While there has been much growth in the body of literature over the past decade, the gender disparity in OCR referral remains a significant challenge to be upheld. There is compelling evidence to suggest that: (1) OCR referral itself may be related to lower mortality;[21] (2) systematic referral strategies significantly increase OCR referral and enrolment among women specifically;[50] and (3) approximately half of the sex difference in referral can be attributed to true discrimination.[23]

How can OCR referral rates improve?

A recent Canadian-based policy position paper[11] further reinforced that systematic referral strategies can significantly increase OCR referral and utilization. Strategies to improve referral and enrollment rates have been examined[25] and advocated. Referral strategies such as automatic referral[25,26] and interventions such as nursing- or peer-led interventions[19] can significantly improve access to OCR. Physician endorsement of OCR through a discussion with eligible patients may further increase the likelihood of successful referral and subsequent participation of women in OCR programmes.[15,50]

Unfortunately, there were no randomized studies to assess interventions to promote OCR referral identified through this meta-analysis. Future randomized controlled trials are necessary to determine the effectiveness of strategies designed to increase women's referral to OCR.

Limitations

Caution is warranted when interpreting these results considering the heterogeneity between studies (i.e. variations in outcome ascertainment, methodologies). The lack of reporting consistency throughout the literature has resulted in the heterogeneous reporting of outcomes between studies. For example, some studies reported outcome rates among all eligible patients discharged from hospital, while others reported only those who participated in their study without identifying the overall population eligible for referral. Data was rarely available for all eligible patients originally sampled within the studies and this may have resulted in reported outcome rates not truly representative of the population. Although we attempted to determine heterogeneity sources through subanalysis, we were unable to ascertain the impact of automatic systematic referral due to the low number of studies ($n = 1$) that utilized this strategy in referral approach.

The studies included in this meta-analysis encompass a period of two decades wherein the standards of practice have evolved and resulted in greater awareness of the associated benefits of cardiac rehabilitation. It is possible that the majority of the sex bias occurred in

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the earlier decade and this would be considered a limitation that may impact the generalizability of findings. Furthermore, one retrospective study[22] accounted for 60% of the total participants in the meta-analysis, which could be considered a limitation; however, this study accounted for only 10.1% weighting in the pooled analysis. Finally, the literature was limited to studies reported in English, which may limit the generalizability of these findings.

Conclusions

In one of the strongest endorsements to date (Class I, Level A) from the American Heart Association[8] and the Canadian Association of Cardiac Rehabilitation,[10] OCR should be mandated for all eligible women. Although there were a wide range of referral rates reported for both men and women, the majority of studies showed a consistent bias in terms of fewer female referrals. Men were approximately 1.5-times more likely to be referred to OCR. As with any such analysis, conclusions must be tempered with the quality of the data. In this case, the majority of observational studies achieved 'good' or 'fair' quality categorization. Prospective high-quality studies and national registries are essential tenets in moving forward. Our female patients deserve the best available cardiac care and this involves the eradication of any bias for referral to outpatient cardiac rehabilitation.

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