

Specialized Nursing Practice for Chronic Disease Management in the Primary Care Setting: An Evidence-Based Analysis

Health Quality Ontario

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About Health Quality Ontario

Health Quality Ontario (HQO) is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. HQO works with clinical experts, scientific collaborators and field evaluation partners to develop and publish research that evaluates the effectiveness and cost-effectiveness of health technologies and services in Ontario.

Based on the research conducted by HQO and its partners, the Ontario Health Technology Advisory Committee (OHTAC) — a standing advisory sub-committee of the HQO Board — makes recommendations about the uptake, diffusion, distribution or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders and policy-makers.

This research is published as part of Ontario Health Technology Assessment Series, which is indexed in CINAHL, EMBASE, MEDLINE, and the Centre for Reviews and Dissemination. Corresponding OHTAC recommendations and other associated reports are also published on the HQO website. Visit <http://www.hqontario.ca> for more information.

About the *Ontario Health Technology Assessment Series*

To conduct its comprehensive analyses, HQO and/or its research partners reviews the available scientific literature, making every effort to consider all relevant national and international research; collaborates with partners across relevant government branches; consults with clinical and other external experts and developers of new health technologies; and solicits any necessary supplemental information.

In addition, HQO collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social, and legal issues relating to the intervention assist in making timely and relevant decisions to optimize patient outcomes.

The public consultation process is available to individuals and organizations wishing to comment on reports and recommendations prior to publication. For more information, please visit: http://www.hqontario.ca/en/mas/ohtac_public_engage_overview.html.

Disclaimer

This report was prepared by HQO or one of its research partners for the *Ontario Health Technology Advisory Committee* and developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to HQO. It is possible that relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the HQO website for a list of all publications: http://www.hqontario.ca/en/mas/mas_ohtas_mn.html.

Abstract

Background

In response to the increasing demand for better chronic disease management and improved health care efficiency in Ontario, nursing roles have expanded in the primary health care setting.

Objectives

To determine the effectiveness of specialized nurses who have a clinical role in patient care in optimizing chronic disease management among adults in the primary health care setting.

Data Sources and Review Methods

A literature search was performed using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database. Results were limited to randomized controlled trials and systematic reviews and were divided into 2 models: Model 1 (nurse alone versus physician alone) and Model 2 (nurse and physician versus physician alone). Effectiveness was determined by comparable outcomes between groups in Model 1, or improved outcomes or efficiency in Model 2.

Results

Six studies were included. In Model 1, there were no significant differences in health resource use, disease-specific measures, quality of life, or patient satisfaction. In Model 2, there was a reduction in hospitalizations and improved management of blood pressure and lipids among patients with coronary artery disease. Among patients with diabetes, there was a reduction in hemoglobin A1c but no difference in other disease-specific measures. There was a trend toward improved process measures, including medication prescribing and clinical assessments. Results related to quality of life were inconsistent, but patient satisfaction with the nurse-physician team was improved. Overall, there were more and longer visits to the nurse, and physician workload did not change.

Limitations

There was heterogeneity across patient populations, and in the titles, roles, and scope of practice of the specialized nurses.

Conclusions

Specialized nurses with an autonomous role in patient care had comparable outcomes to physicians alone (Model 1) based on moderate quality evidence, with consistent results among a subgroup analysis of patients with diabetes based on low quality evidence. Model 2 showed an overall improvement in appropriate process measures, disease-specific measures, and patient satisfaction based on low to moderate quality evidence. There was low quality evidence that nurses working under Model 2 may reduce hospitalizations for patients with coronary artery disease. The specific role of the nurse in supplementing or substituting physician care was unclear, making it difficult to determine the impact on efficiency.

Plain Language Summary

Nurses with additional skills, training, or scope of practice may help improve the primary care of patients with chronic diseases. This review found that specialized nurses working on their own could achieve health outcomes that were similar to those of doctors. It also found that specialized nurses who worked with doctors could reduce hospital visits and improve certain patient outcomes related to diabetes, coronary artery disease, or heart failure. Patients who had nurse-led care were more satisfied and tended to receive more tests and medications. It is unclear whether specialized nurses improve quality of life or doctor workload.

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List of Abbreviations

ACE	Angiotensin-converting enzyme
APN	Advanced practice nurse
ARB	Angiotensin-receptor blocker
CAD	Coronary artery disease
CHF	Congestive heart failure
CI	Confidence interval(s)
COPD	Chronic obstructive pulmonary disease
ED	Emergency department
HbA1c	Hemoglobin A1c
HRQOL	Health-related quality of life
IQR	Interquartile range
LVSD	Left ventricular systolic dysfunction
MD	Mean difference
MI	Myocardial infarction
NP	Nurse practitioner
OR	Odds ratio
RCT	Randomized controlled trial
RN	Registered nurse
RR	Relative risk
SE	Standard error
SD	Standard deviation
SF-36	Short Form (36) Health Questionnaire

Background

In July 2011, the Evidence Development and Standards (EDS) branch of Health Quality Ontario (HQO) began developing an evidentiary framework for avoidable hospitalizations. The focus was on adults with at least 1 of the following high-burden chronic conditions: chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), atrial fibrillation, heart failure, stroke, diabetes, and chronic wounds. This project emerged from a request by the Ministry of Health and Long-Term Care for an evidentiary platform on strategies to reduce avoidable hospitalizations.

After an initial review of research on chronic disease management and hospitalization rates, consultation with experts, and presentation to the Ontario Health Technology Advisory Committee (OHTAC), the review was refocused on optimizing chronic disease management in the outpatient (community) setting to reflect the reality that much of chronic disease management occurs in the community. Inadequate or ineffective care in the outpatient setting is an important factor in adverse outcomes (including hospitalizations) for these populations. While this did not substantially alter the scope or topics for the review, it did focus the reviews on outpatient care. HQO identified the following topics for analysis: discharge planning, in-home care, continuity of care, advanced access scheduling, screening for depression/anxiety, self-management support interventions, specialized nursing practice, and electronic tools for health information exchange. Evidence-based analyses were prepared for each of these topics. In addition, this synthesis incorporates previous EDS work, including *Aging in the Community* (2008) and a review of recent (within the previous 5 years) EDS health technology assessments, to identify technologies that can improve chronic disease management.

HQO partnered with the Programs for Assessment of Technology in Health (PATH) Research Institute and the Toronto Health Economics and Technology Assessment (THETA) Collaborative to evaluate the cost-effectiveness of the selected interventions in Ontario populations with at least 1 of the identified chronic conditions. The economic models used administrative data to identify disease cohorts, incorporate the effect of each intervention, and estimate costs and savings where costing data were available and estimates of effect were significant. For more information on the economic analysis, please contact either Murray Krahn at murray.krahn@theta.utoronto.ca or Ron Goeree at goereer@mcmaster.ca.

HQO also partnered with the Centre for Health Economics and Policy Analysis (CHEPA) to conduct a series of reviews of the qualitative literature on “patient centredness” and “vulnerability” as these concepts relate to the included chronic conditions and interventions under review. For more information on the qualitative reviews, please contact Mita Giacomini at [gjacomini@mcmaster.ca](mailto:gjacomin@mcmaster.ca).

The Optimizing Chronic Disease Management in the Outpatient (Community) Setting mega-analysis series is made up of the following reports, which can be publicly accessed at <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ohtas-reports-and-ohtac-recommendations>.

- Optimizing Chronic Disease Management in the Outpatient (Community) Setting: An Evidentiary Framework
- Discharge Planning in Chronic Conditions: An Evidence-Based Analysis
- In-Home Care for Optimizing Chronic Disease Management in the Community: An Evidence-Based Analysis
- Continuity of Care: An Evidence-Based Analysis
- Advanced (Open) Access Scheduling for Patients With Chronic Diseases: An Evidence-Based Analysis
- Screening and Management of Depression for Adults With Chronic Diseases: An Evidence-Based Analysis
- Self-Management Support Interventions for Persons With Chronic Diseases: An Evidence-Based Analysis
- Specialized Nursing Practice for Chronic Disease Management in the Primary Care Setting: An Evidence-Based Analysis
- Electronic Tools for Health Information Exchange: An Evidence-Based Analysis
- Health Technologies for the Improvement of Chronic Disease Management: A Review of the Medical Advisory Secretariat Evidence-Based Analyses Between 2006 and 2011
- Optimizing Chronic Disease Management Mega-Analysis: Economic Evaluation
- How Diet Modification Challenges Are Magnified in Vulnerable or Marginalized People With Diabetes and Heart Disease: A Systematic Review and Qualitative Meta-Synthesis
- Chronic Disease Patients’ Experiences With Accessing Health Care in Rural and Remote Areas: A Systematic Review and Qualitative Meta-Synthesis
- Patient Experiences of Depression and Anxiety With Chronic Disease: A Systematic Review and Qualitative Meta-Synthesis
- Experiences of Patient-Centredness With Specialized Community-Based Care: A Systematic Review and Qualitative Meta-Synthesis

Objective of Analysis

The objective of this analysis was to determine the effectiveness of specialized nurses who have a clinical role in patient care in optimizing chronic disease management among adults in the primary health care setting. This evidence-based analysis is part of the larger mega-analysis on optimizing chronic disease management.

Clinical Need and Target Population

A significant increase in the number of patients with complex chronic disease has resulted in increased health care demands and pressures related to access and time constraints on physicians in the primary health care setting. Nurses working in specialized or enhanced roles may be a viable option to improve the management of chronic disease (specifically, congestive heart failure [CHF], coronary artery disease [CAD], chronic obstructive pulmonary disease [COPD], atrial fibrillation, type 2 diabetes, stroke, chronic wounds, or general chronic disease) in the primary health care setting. Specialized nurses working collaboratively with physicians may improve efficiency (by reducing physician demand), improve quality of care and patient outcomes, and reduce health care costs.

Specialized Nursing Practice

In this review, *specialized nursing practice* is used to define nurses with enhanced training, experience, and/or scope of clinical practice, or nurses with a primary clinical role in the care of patients with chronic disease. This includes registered nurses (RNs) with specific knowledge and skills for chronic disease management, or those providing disease-specific nurse-led interventions. Although not specialized in a particular chronic disease, primary health care nurse practitioners (NPs) were also considered to be specialized because they receive advanced, formal training in primary care.

Specialized nurses can supplement or substitute aspects of care provided by physicians in the primary health care setting. *Substitution* refers to specialized nurses providing the same services as physicians, with the intent of reducing physician workload and improving health care efficiency. *Supplementation* refers to specialized nurses providing services that may extend or complement care provided by physicians, thereby improving quality of care and outcomes.

Ontario Context

There is considerable variation between and within countries regarding the specific job titles, education, and experience of nurses. Table 1 summarizes the nursing titles regulated in Ontario, their level of training, and their authorized scope of practice. (1)

In Ontario, RNs receive training at the baccalaureate level. The Canadian Nurses Association defines specialization in nursing as “a focus on 1 field of nursing practice or health care that encompasses a level of knowledge and skill in a particular aspect of nursing greater than that acquired during basic nursing education.” (2) Such specialties can be acquired via clinical experience and can often be validated through certification. For chronic disease management, this can include diabetes educators, respiratory nurse specialists, cardiac nurse specialists, or geriatric nurse specialists.

As well, 2 types of advanced practice nurses—clinical nurse specialists and NPs—have an advanced level of clinical nursing practice based on graduate-level education and in-depth knowledge and expertise in meeting the health care needs of individuals, families, groups, communities, and populations. (3) Clinical nurse specialists are RNs who receive additional training via a Master’s in a clinical nursing speciality. Nurse practitioners are “registered nurses with additional educational preparation and experience who

possess and demonstrate the competencies to autonomously diagnose, order, and interpret diagnostic tests, prescribe pharmaceuticals, and perform specific procedures within their legislated scope of practice.” (3) Primary health care NPs are family or all-ages NPs who work in the community setting.

Table 1: Nursing Specialties and Scope of Practice in Ontario

Regulated Nursing Groups and Specialties	Training	Scope of Practice (Authorized Controlled Acts ^a)
<p>Registered nurse</p> <p>Diabetes educator/ respiratory/heart failure/cardiac/ community/geriatric nurse</p>	<p>Baccalaureate degree</p> <p>Certification in a nursing specialty</p>	<ul style="list-style-type: none"> • Perform a procedure below the dermis or a mucous membrane • Administer a substance by injection or inhalation • Put an instrument, hand, or finger beyond the external ear canal, nasal passages, larynx, opening of the urethra, labia majora, anal verge, or artificial opening of body
<p>Clinical nurse specialist^b</p>	<p>Master’s in nursing, with expertise in a clinical nursing specialty</p>	
<p>Nurse practitioner^b</p> <p>Primary health care nurse practitioner</p> <p>Adult and pediatric nurse practitioner (acute care nurse practitioner)</p>	<p>Post-baccalaureate formal education and licensure</p> <p>Family or all-ages nurse practitioners in community settings</p> <p>Advanced care across continuum of acute care services</p>	<ul style="list-style-type: none"> • Communicate to a patient or patient’s representative, a diagnosis made by the nurse practitioner identifying as the cause of the client’s symptoms, a disease or disorder • Apply or order the application of prescribed form of energy • Set or cast a fracture of a bone or dislocation of a joint • Prescribe, dispense, sell, or compound a drug in accordance with regulations • Order x-rays and laboratory tests as appropriate for patient care • Admit and discharge hospital patients

^aUnder the *Regulated Health Professions Act* and the *Nursing Act*. (1)
^bAdvanced-practice nurses.

Evidence-Based Analysis

Research Question

What is the effectiveness of specialized nursing practice in comparison to usual care in improving patient outcomes and health system efficiencies for chronic disease management in the primary health care setting?

Research Methods

Literature Search

Search Strategy

A literature search was performed on May 3, 2012, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for all studies indexed up to May 3, 2012. There were no limits placed on the start date. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

English language full-reports

- published before May 3, 2012
- randomized controlled trials (RCTs) and systematic reviews
- evaluating specialized nurses (i.e., nurses with additional training, enhanced scope of practice, or providing nurse-led interventions) with a clinical role in patient care
- evaluating nurses in the primary health care setting, including family practice, general practice, general or internal medicine clinics, or primary care clinics
- comparing specialized nursing practice to usual primary care
- in an adult population with chronic disease (i.e., CHF, CAD, COPD, atrial fibrillation, type 2 diabetes, stroke, chronic wounds, general “chronic disease,” or where the average patient was indicated to have chronic disease)

Exclusion Criteria

- studies where the nursing role could not be isolated from the roles of other health care professionals, such as nutritionists, pharmacists, specialists, indirect nurse supervision by members outside the primary care setting, or other interventions (e.g., electronic medical records or web-based tools)
- nursing care primarily provided at home or over the telephone
- primary health care delivery in nursing homes and long-term care
- nurses solely providing patient education, self-management, care coordination, case management, or action plan interventions

Outcomes of Interest

- hospitalizations
- length of stay
- mortality
- emergency department (ED) visits
- specialist visits
- health-related quality of life (HRQOL)
- patient satisfaction
- disease-specific measures
- process measures
 - examinations or medication prescribing
- health-system efficiencies
 - number and length of primary health care visits
 - physician workload

Models of Nursing Care

Studies were stratified by the type of interaction between specialized nurses and primary care physicians based on study design.

Model 1: Nurse Versus Physician (Usual Care)

Studies that directly compared nurses providing autonomous patient care with physicians performing the same tasks (usual care) were classified as *Model 1*. Nurses working in this model were generally NPs who had the legislative authority to perform tasks similar to those of physicians. Studies evaluating this model of nursing care aimed to show comparable outcomes between nurses and physicians.

Model 2: Nurse and Physician Versus Physician (Usual Care)

Studies that compared nurses and physicians working in a partnership, or compared a nursing intervention as part of a primary health care practice with physicians working alone (or usual care), were classified as *Model 2*. Nurses working in this model could be substituting or supplementing aspects of physician care. Studies that compared nurses to physicians but required regular physician consultation were also classified as Model 2. Studies evaluating this model aimed to improve patient quality of care and patient outcomes while maintaining physician workload, or to show comparable patient outcomes while improving efficiency.

Statistical Analysis

Due to clinical heterogeneity in the study populations evaluated, and differences in provider roles and characteristics, the pooling of outcomes was thought to be inappropriate and a meta-analysis was not conducted. Outcomes were summarized descriptively, with significance accepted at $P < 0.05$.

When not provided directly by the authors, relative risks (RRs) for binary outcomes and mean differences (MDs) for continuous outcomes were calculated from raw data using Review Manager 5 version 5.0.25.

Quality of Evidence

The quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (4) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (4) For more detailed information, please refer to the latest series of GRADE articles. (4)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Evidence-Based Analysis

The database search yielded 3,252 citations published before May 3, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded from the analysis.

Five studies (RCTs, published in 6 papers), met the initial inclusion criteria. The reference lists of the included studies were hand searched to identify any additional potentially relevant studies, and 1 additional citation (RCT, published in 2 papers) was identified, for a total of 6 studies (published in 8 papers). Three long-term follow-up studies of the original RCTs included were also identified, but these studies were excluded, as a significant rate of crossover and loss to follow-up had occurred. (5-7)

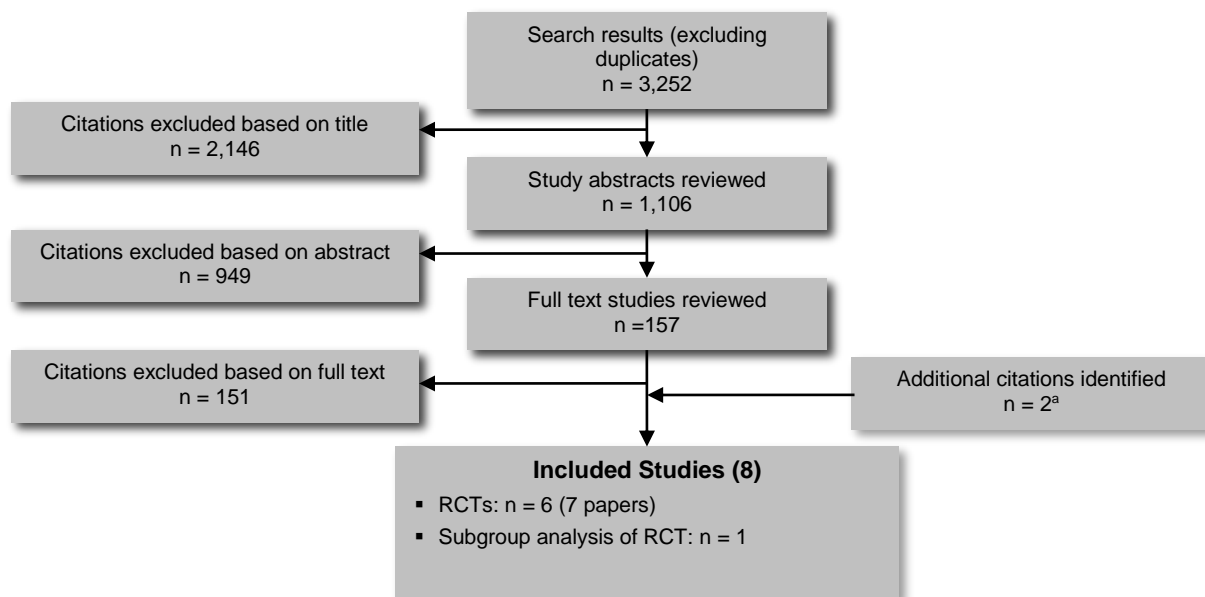


Figure 1: Citation Flow Chart

Abbreviation: RCT, randomized controlled trial.

^aAdditional studies identified via extensive back-searching of all systematic reviews and meta-analyses.

For each included study, the study design was identified and is summarized below in Table 2, a modified version of a hierarchy of study design by Goodman. (8)

Table 2: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCT Studies	
Systematic review of RCTs	
Large RCT	3 ^a
Small RCT	3
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	
Case series	
Retrospective review, modelling	
Studies presented at an international conference	
Expert opinion	
Total	6^a

Abbreviation: RCT, randomized controlled trial.

^aOne RCT published primary results in 2 publications and is counted as 1 eligible study; 1 RCT reported a subgroup analysis in a separate publication and is counted as 1 study.

Systematic Reviews and Meta-Analyses

No systematic reviews met the inclusion criteria. Thirteen systematic reviews and health technology assessments of primarily RCTs that focused on specialized nursing practice for chronic disease management, and/or that included studies of nurses in the primary health care setting, were found (8 through systematic review and 5 through manual searching), but these reviews were not included as they either concentrated on broader nursing interventions for unspecified conditions, were not limited to the primary health care setting, or included studies of nurses without a clinical role in patient care or who provided care primarily over the phone, in-home, or in combination with other health care professionals who were not part of the primary health care team. A summary of these reviews and their applicability to the current analysis is presented in Appendix 2.

Description of Included Studies

Six primary RCTs (8 papers) were identified for inclusion and are summarized in the text below. Campbell et al is referred to as 1 RCT, reporting primary outcomes in 1 paper (9) and secondary outcomes in another. (10) Similarly, Mundinger et al (11) published a secondary analysis among a subgroup of patients with diabetes, which is summarized separately whenever appropriate. (12) Table 3 presents an overview of study characteristics, and Tables 4 and 5 summarize methodological characteristics. Detailed descriptions of study methodologies and patient populations are presented in Appendix 3.

Setting

Two of the 6 RCTs were conducted in the United States, 2 in the United Kingdom, and 2 in the Netherlands. All studies were conducted in the primary health care setting. One was in a general internal medicine clinic in a United States hospital, 1 was in a large medical centre, and the remainder were identified generically as general or primary care practices.

Population

Four RCTs evaluated specific chronic diseases: 1 in a type 2 diabetes population, 1 in a type 2 diabetes plus hypertension population, 1 in a CAD population, and 1 in a combined CAD or CHF population. (9;10;13-15) The study by Mundinger et al (11) evaluated people within a general primary care population, but was included because the study oversampled individuals with asthma, diabetes, and/or hypertension, with 54% of enrolled patients having 1 or more of the chronic diseases of interest. A subgroup analysis was also included, focused only on patients with diabetes at baseline. (12) The study by Laurant et al (16) was conducted at the level of the general practitioner, so patients were not recruited or evaluated. However, NPs were responsible for targeting patients with chronic disease—specifically COPD, asthma, dementia, or cancer.

The mean age across studies ranged from 44.5 to 70.5 years, and 25% to 58% of patients were male. Mundinger et al included a primarily Hispanic population (88%) and Litaker et al had 59% of patients of African-American descent.

Study Design and Randomization

Three studies used parallel group randomization, whereby individual participants were randomly assigned to either the nursing intervention or to usual care. (9-11;15) Two studies used a cluster randomized study design, whereby nurses or nursing interventions were randomly assigned to groups of general practices. (14;16) Among the cluster RCTs, Khunti et al (14) first randomized primary care practices to the intervention or control group, followed by subsequent patient selection and consent to participate in the trial. Laurant et al (16) cluster randomized general practices to receive an NP or to usual care, but did not enrol or identify patients.

Sample sizes among the RCTs that evaluated patient-level data ranged from 157 to 1,981, with follow-up ranging from 6 to 18 months. The study by Laurant et al had a sample size of 48 physicians. (16)

Model of Nursing Care

Model 1

One RCT (2 papers) was classified as Model 1. (11;12) Both arms of the study were staffed with RNs and medical assistants.

Model 2

Five RCTs (6 papers) were classified as Model 2. (9;10;13-16) Nurses in these studies supplemented and/or substituted aspects of care provided by physicians.

Type and Role of Nurse

Titles, roles, and level of nurse training varied significantly across studies (Table 4 and Table 5). Nursing titles were maintained, as reported in the original papers.

In Model 1, specialized nurses were highly trained NPs who worked autonomously providing primary health care. Nurses could diagnose, prescribe, refer, and admit patients. Based on state law, physicians were required to respond to NPs if they needed consultation, but they were not required to be on site. All NPs were faculty from a university medical centre.

Two studies in Model 2 evaluated NPs, (15;16) and 3 studies evaluated RNs or practice nurses (PNs) with disease-specific training. The study by Litaker et al (15) included NPs who received additional training in study treatment algorithms. NPs in this study did not have the authority to broadly prescribe medications, but could prescribe and titrate under the approval of the physician. The education preparedness of NPs in the study by Laurant et al (16) was not provided. However, NPs had post-graduate experience with 2 weeks of training in study protocols prior to the study. NPs in the Laurant et al (16) study were not permitted to prescribe medications. The study by Khunti et al (14) included nurses trained in heart failure management who were not required to follow a protocol and were permitted to prescribe medications, refer patients to secondary care, and order appropriate tests. The studies by Houweling et al (13) and Campbell et al (9;10) included nurses with limited training in chronic disease management. Nurses in the Houweling study were PNs who received minimal training in diabetes protocols and were permitted to prescribe and titrate specific diabetes-related medications. Campbell et al included 1 or 2 health visitors, district nurses, or PNs from the enrolled practices who were trained in CAD clinic protocols.

Outcomes

Table 6 summarizes the primary and secondary outcomes evaluated across studies.

Table 3: Study Characteristics

Author, Year	Country, Setting	Disease	Study Design	Sample Size, # Randomized to Intervention/Comparator	Loss to Follow-Up, N (%) (Intervention/Comparator)	Length of Follow-up, Months
Model 1: Nurse Versus Physician (Usual Care)						
Mundinger et al, 2000 (11)	United States, primary care in medical centre	Primary care, chronic ^a	RCT	1,181/800	Not enrolled (health resource use data): 375 (31.7)/290 (36.2) HRQOL/satisfaction: 532 (45.0)/409 (51.1)	6–12 ^b
Lenz et al, 2002 (12)	United States, primary care in medical centre	Diabetes ^c	RCT (subgroup)	120/94 (10.8% of those randomized in Mundinger et al)	Health resource use/process measures: 70 (32.7) Clinical outcomes: 96 (44.9) to 138 (64.5)	6
Model 2: Nurse and Physician Versus Physician (Usual Care)						
Houweling et al, 2011 (13)	Netherlands, primary care	Diabetes	RCT	116/114	14 (12)/10(8.8)	14
Khunti et al, 2007 (14)	United Kingdom, primary care	CAD ^d or CHF	Cluster RCT	10 practices (505 cases)/10 practices (658 cases)	103 (20.4)/50 (7.6)	12
Laurant et al, 2004 (16)	Netherlands, general practice	Chronic ^e	Cluster RCT	4 local groups (30 GPs)/3 local groups (18 GPs) ^f	10–13 (30–43)/3 (16.7) ^f	6 before/18 after
Litaker et al, 2003 (15)	United States, general internal medicine clinic	Diabetes and hypertension	RCT	79/78	NR	12
Campbell et al, 1998 (9;10)	United Kingdom, general practice	CAD ^g	RCT	673/670	Practice data: 38 (5.6)/40 (6%) Questionnaire data: 80 (11.9)/90 (13.4)	12 (visits every 2–6 weeks based on protocol)

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; GP, general practitioner; HRQOL, health-related quality of life; NR, not reported; RCT, randomized controlled trial.

^aPatients presenting to the emergency department, oversampled those with diabetes, asthma, and/or hypertension.

^b6 months for health outcomes and quality of life, 12 months for health care utilization data.

^cSubgroup analysis of Mundinger study; (11) patients with self-reported diabetes at baseline.

^dDefined as diagnosis of coronary heart disease (angina or past medical history of myocardial infarction).

^eTargeted patients with COPD, asthma, dementia, or cancer.

^fRandomization and loss to follow-up at level of physician; range represents responses for objective and subjective workload, respectively.

^gWorking diagnosis of coronary heart disease.

Table 4: Nursing Interventions and Comparators

Author, Year	Type of Nursing Intervention	Type and Training of Specialized Nurse	Collaboration With Primary Care Physician (Usual Care)	Components of Comparator
Model 1: Nurse Versus Physician (Usual Care)				
Mundinger et al, 2000 (11) and Lenz et al, 2002 (12)	Nurse as first contact and ongoing primary care provider + staffed with RNs and medical assistants	NP	Not required; did not need to be on site and quarterly meetings to review select cases	Care from a physician plus RNs and medical assistants
Model 2: Nurse and Physician Versus Physician (Usual Care)				
Houweling et al, 2011 (13)	Nurse as primary care provider for diabetes (transfer of care from GP to practice nurse)	Practice nurse trained in diabetes treatment/management for 2 weeks; enhanced scope of practice for study	Consulted if necessary	Usual care from GP
Khunti et al, 2007 (14)	Nurse-led disease management program for CAD/CHF (weekly clinics)	Peripatetic nurse specialists trained in heart failure management	Unclear; nurse clinics added to the primary care practice	Usual care from GP and practice nurse
Laurant et al, 2004 (16)	Nurse-targeted chronic disease patients	NP with mean 12.1 years postgraduate experience; special study training program 2 weeks before study	GP referred patient to NP (GP decided specific NP tasks and patients to refer); after consultation, nurse cared for patient, GP and nurse shared patient, or patient referred back to GP	Usual care from GP practice team
Litaker et al, 2003 (15)	Nurse as first-line contact for primary diabetes and hypertension care	NP + additional training on study treatment algorithms	Collaborative care; discussed issues to develop treatment plans, physician signed off on prescriptions, physician evaluated patient if necessary	Usual care from physician (Internist)
Campbell et al, 1998 (9;10)	Nurse-led secondary prevention CAD clinic (clinics incorporated into usual practice)	1 or 2 health visitors (specialized nurse), district nurses (specialized nurse), or practice nurses from the primary care team	Patients referred to GP if drug treatment needed	Usual primary care (including same nurses as intervention arm)

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; GP, general practitioner; NP, nurse practitioner; RCT, randomized, controlled trial; RN, registered nurse.

Table 5: Roles of Specialized Nurses in Chronic Disease Management

Author, Year	Type of Nurse (Title)	Clinical Role								Management Role		
		Follow Protocol	Assess or Screen	Prescribe or Titrate	Order Tests	Refer	Admit	Monitor	Educate	Care Coordination/ Action Plans	Telephone Follow-up	Home Follow-up
Model 1: Nurse Versus Physician (Usual Care)												
Mundinger et al, 2000 (11) and Lenz et al, 2002 (12)	NP	X	✓	✓	✓	✓	✓		✓			
Model 2: Nurse and Physician Versus Physician (Usual Care)												
Houweling et al, 2011 (13)	Practice nurse + training	✓	✓	✓ ^a	✓							
Khunti et al, 2007 (14)	RN + training		✓	✓	✓ ^b	✓ ^b						✓
Laurant et al, 2004 (16)	NP	✓	✓	X ^{cd}	✓ ^{cd}			✓	✓	✓	✓	✓
Litaker et al, 2003 (15)	NP	✓	✓	✓ ^{ce}				✓	✓		✓	✓
Campbell et al, 1998 (9;10)	Health visitor, district nurse or practice nurse	✓	✓	X ^f						✓		

Abbreviations: NP, nurse practitioner; RN, registered nurse.

Note: Blank shaded areas represent tasks that were not reported in the study; shaded areas with Xs represent tasks that were clearly stated as not being part of the nurse's role.

^aPermitted to prescribe 14 medications and adjust dosages for 30; could adjust insulin dosages but not prescribe insulin.

^bNurse could refer patients for echocardiography and assessment in a secondary-care cardiology clinic.

^cConfirmed by author.

^dGPs agreed on range of work for NP, but individual GPs had freedom of choice regarding tasks and patients they would delegate to the NP.

^eNPs did not have autonomous prescribing authority, but followed a titration algorithm under the indirect supervision of the physician. The physician signed prescriptions or the NP called prescriptions into the pharmacy (confirmed by author).

^fNurse reviewed medications and promoted Aspirin use, and referred patients to physician if treatment recommended.

Table 6: Outcomes of Interest Reported in Individual Trials

Author, Year	Health Resource Utilization						Disease-Specific Measures	HRQOL	Patient Satisfaction	Process indicators	Efficiency ^a
	Hospitalizations	LOS	ED/ Urgent Care Visits	Mortality	Specialist Visits	Primary Health Care Visits ^b					
Model 1: Nurse Versus Physician (Usual Care)											
Mundinger et al, 2000 (11)	✓ ^c		✓ ^c		✓ ^c	✓ ^c	✓ ^c	✓ ^{cd}	✓ ^c		
Lenz et al, 2002 (12)	✓ ^c		✓ ^c		✓ ^c	✓ ^c	✓ ^c			✓ ^c	
Model 2: Nurse and Physician Versus Physician (Usual Care)											
Houweling et al, 2011 (13)						✓	✓ ^{cd}	✓	✓	✓	✓
Khunti et al, 2007(14)							✓ ^{cd}	✓		✓ ^{cd}	
Laurant et al, 2004 (16)											✓ ^c
Litaker et al, 2003 ^e (15)						✓	✓	✓	✓	✓	✓
Campbell et al, 1998 (9;10)	✓	✓						✓ ^{cd}		✓ ^c	✓

Abbreviations: ED, emergency department; HRQOL, health-related quality of life; LOS, length of stay.

^aIncludes number of nurse-primary care physician consultations, primary care physician time or workload.

^bOverall number of primary care visits, or number of visits to the randomized group for the condition of interest.

^cStated as primary outcome of interest.

^dPower calculation based on outcome.

^ePowered for outcome of costs rather than effectiveness.

Findings for Model 1: Nurse Alone Versus Physician Alone

Effectiveness of nurses in Model 1 was based on comparability of results between patients receiving primary health care from specialized nurses and physicians.

Health Resource Utilization

Hospitalizations

Mundinger et al (11) reported data on the proportion of individuals hospitalized within the medical centre under evaluation (Table 7). There was no significant difference in the proportion of patients hospitalized between groups at 6 months' or 12 months' follow-up (GRADE: moderate). Among patients with diabetes in the subgroup analysis by Lenz et al, (12) there was no significant difference in hospitalizations at 6 months after baseline (GRADE: very low).

Table 7: Hospitalizations With Specialized Nursing Care Versus Physicians Alone

Author, Year	Population	Follow-up, Months	N	Proportion Hospitalized (%)		RR (95% CI) ^a	P Value ^a
				Nurse	Physician		
Mundinger et al, 2000 (11)	Primary care, chronic	6	1,309	33/800 (4.1)	29/509 (5.7)	0.72 (0.45–1.18)	0.19
	Primary care, chronic	12	1,309	68/800 (8.5)	50/509 (9.8)	0.87 (0.61–1.23)	0.41
Lenz et al, 2002 (12)	Diabetes subgroup	6	145	7/86 (8.1)	6/59 (10.2)	0.80 (0.28–2.26)	0.67

Abbreviations: CI, confidence interval; RR, relative risk.

^aValues were not reported in the article; they were calculated using Review Manager.

Emergency Department Visits

The study by Mundinger et al evaluated the proportion of combined ED and urgent care visits in the study medical centre (Table 8). Enrolled patients in both the NP and physician groups made significantly fewer ED/urgent care visits during the 12-month follow-up period compared to the 6 months prior to study enrollment. However, there was no significant difference in the number of ED and urgent care visits between groups at 12-month follow-up (GRADE: moderate). Similar results were observed among the subgroup of patients with diabetes (GRADE: very low).

Table 8: Emergency Department and Urgent Care Visits With Specialized Nursing Care Versus Physicians Alone

Author, Year	Population	Follow-up, Months	N	Proportion (%) With 1 or More ED or Urgent Care Visits		RR (95% CI) ^a	P Value ^a
				Nurse	Physician		
Mundinger et al, 2000 (11)	Primary care, chronic	6	1,309	182/800 (22.7)	127/509 (24.9)	0.91 (0.75–1.11)	0.36
	Primary care, chronic	12	1,309	274/800 (34.3)	172/509 (33.8)	1.01 (0.87–1.18)	0.86
Lenz et al, 2002 (12)	Diabetes subgroup	6	145	21/86 (24.4)	17/59 (28.8)	0.85 (0.49–1.46)	0.55

Abbreviations: CI, confidence interval; ED, emergency department; RR, relative risk.

^aValues were not reported in the article; they were calculated using Review Manager.

Specialist Visits

Specialist visits were evaluated by Mundinger et al (11) and defined as visits to a medical specialty clinic or specialist physician office (Table 9). There were significantly more specialty visits in both groups at 12-month follow-up compared to the 6 months prior to study enrollment. However, there was no significant difference between NPs and physicians at 12-month follow-up (GRADE: moderate). Similar results were observed among the subgroup of patients with diabetes at 6 months (GRADE: very low). (12)

Table 9: Specialist Visits With Specialized Nursing Care Versus Physicians Alone

Author, Year	Population	Follow-up, Months	N	Proportion (%) With 1 or More Speciality Visits		RR (95% CI) ^a	P Value ^a
				Nurse	Physician		
Mundinger et al, 2000 (11)	Primary care, chronic	6	1,309	307/800 (38.4)	188/509 (24.7)	1.04 (0.09–1.20)	0.60
	Primary care, chronic	12	1,309	365/800 (45.6)	230/509 (45.2)	1.01 (0.89–1.14)	0.88
Lenz et al, 2002 (12)	Diabetes subgroup	6	145	47/86 (54.6)	28/59 (47.5)	1.15 (0.83–1.60)	0.40

Abbreviations: CI, confidence interval; RR, relative risk.

^aValues were not reported in the article; they were calculated using Review Manager.

Primary Health Care Visits

The study by Mundinger et al evaluated the number of primary health care visits after the initial visit; only those visits with an NP or physician at the primary health care site were counted as primary care (Table 10). There were significantly more patients with a primary health care visit in the NP group after 6 months, but this difference became nonsignificant at 12 months (GRADE: moderate). Among persons assigned to the NP, 59% saw the same provider for primary health care visits after the initial visit, with 54% of physician patients remaining with their original randomized care provider ($P = 0.11$).

The overall proportion of individuals with a primary health care visit at 6 months was higher among the subgroup of patients with diabetes in both groups. However, there was no significant difference observed between groups. Similarly, patients visited their primary health care provider an average of 3.1 times (standard deviation = 2.38), with no statistical difference between groups (GRADE: very low).

Table 10: Primary Health Care Visits With Specialized Nursing Care Versus Physicians Alone

Author, Year	Population	Follow-up, Months	N	Proportion (%) With Primary Health Care Visits		RR (95% CI) ^a	P Value
				Nurse	Physician		
Mundinger et al, 2000 (11)	Primary care, chronic	6	1,309	635/800 (79.4)	349/509 (68.6)	1.16 (1.08–1.24)	< 0.0001
	Primary care, chronic	12	1,309	658/800 (82.2)	412/509 (80.9)	1.02 (0.96–1.07)	0.55
Lenz et al, 2002 (12)	Diabetes subgroup	6	145	73/86 (84.9)	52/59 (88.1)	0.96 (0.84–1.10)	0.57

Abbreviations: CI, confidence interval; RR, relative risk.

^aValues were not reported in the article; they were calculated using Review Manager.

Disease-Specific Measures

Disease-specific measures were evaluated only among the subgroup of individuals with self-reported chronic disease at baseline (diabetes, hypertension, or asthma) in the Mundinger et al and Lenz et al studies. (11;12) Hemoglobin A1C (HbA1c) data were taken from the diabetes subgroup analysis reported by Lenz et al, (12) and blood pressure and peak flow were taken from the original Mundinger et al study. (11) Measurements were conducted at 6 months only; therefore, a change from baseline could not be calculated.

HbA1c

Final HbA1c was high in both groups at 6-month follow-up (mean 9.72% in the nursing group versus 9.84% in the physician group), but there was no significant difference between patients receiving primary care from nurses and those being treated by physicians ($P = 0.82$) (GRADE: very low).

Blood Pressure

Mean 6-month systolic blood pressure was 139 mm Hg in the nursing group and 137 mm Hg in the physician group ($P = 0.82$). Mean 6-month diastolic blood pressure was significantly lower among patients receiving primary care from nurses compared to physicians (82 mm Hg in the nursing group and 85 mm Hg in the physician group; $P = 0.04$) (GRADE: very low).

Peak Flow

There was no significant difference in peak flow measures among patients with asthma ($P = 0.82$) (GRADE: very low).

Health-Related Quality of Life

SF-36 Scores

The study by Mundinger et al (11) evaluated HRQOL at baseline and 6-month follow-up using the Short Form (36) Health Questionnaire (SF-36). SF-36 scores improved significantly from baseline to follow-up among the entire cohort. However, there were no significant differences between groups in the mean physical component summary score (NP group = 40.53 and physician group = 40.60; $P = 0.92$) or mental component summary score (NP group = 44.55 and physician group = 44.48; $P = 0.92$) when adjusted for age, sex, individual conditions, and baseline subscale scores (GRADE: moderate). Similarly, there was no significant difference between groups for the SF-36 physical component score (NP group = 38.93 and physician group = 36.01; $P > 0.05$) and mental component score (NP group = 45.39 and physician group = 42.15; $P > 0.05$) among the subgroup of diabetes patients (GRADE: very low).

Patient Satisfaction

Patient satisfaction was measured at 6-month follow-up by Mundinger et al (11) using “provider-specific” items from a validated 15-item satisfaction questionnaire. No significant difference in the overall patient satisfaction mean score was found between the NP and physician groups ($P = 0.87$) (GRADE: moderate).

Process Indicators

Documentation of various provider behaviours was assessed via patient chart review in the diabetes subgroup analysis. (12) Nurse practitioners were more likely to document providing education ($P < 0.001$), and monitoring height ($P < 0.01$), urinalysis ($P < 0.01$), and HbA1c levels ($P < 0.05$). There were no significant differences between groups in any assessments of patient history, or in the assessment or monitoring of weight, blood pressure, foot health, blood glucose levels, or creatinine levels. Additionally, there was no significant difference between groups in referrals to an ophthalmologist. The GRADE for this body of evidence was very low.

Results for Model 2: Nurse and Physician versus Physician Alone (or Usual Care)

In Model 2, the effectiveness of specialized nurses plus physicians (or usual care) was assessed by an improvement in patient or health resource use outcomes, or in health care efficiency.

Health Resource Utilization

Hospitalizations

The study by Campbell et al (9) reported on all-cause hospitalizations as a secondary outcome (Table 11). There was a statistically significant decrease in the proportion of patients hospitalized in the first year in the group receiving nurse-led secondary CAD prevention in comparison to usual care alone (GRADE: low). The difference in the hospitalizations was only partly explained by cardiac-related admissions, with 7% in the intervention group and 9% in the control group. Similarly, there was no difference in nonfatal myocardial infarctions (2% in each group).

Table 11: Hospitalizations With Specialized Nursing Care Versus Usual Care

Author, Year	Population	N	Proportion Hospitalized (%)		OR (95% CI)	P Value
			Nursing Intervention	Usual Care		
Campbell et al, 1998 (9)	CAD	1,058	Baseline: 132/540 (24) Follow-up: 106/540 (20) ^a	Baseline: 34/518 (26) Follow-up: 145/518 (28) ^a	0.64 (0.48–0.86) ^b	0.003 ^b

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio.

^aUnadjusted final values.

^bAdjusted for age, sex, general practice, and baseline performance.

Length of Stay

The study by Campbell further commented on hospital length of stay among individuals with CAD. (9) There was no significant difference in the median length of stay at 1 year (6 days in both groups; $P = 0.49$) (GRADE: low).

Disease-Specific Measures

HbA1c

Two studies reported on HbA1c among patients with diabetes. The average patient in the Litaker et al (15) study had elevated HbA1c at baseline (mean 8.5%), with a significant decrease in the mean change from baseline at 1 year in favour of the specialized nurse-physician team (12) (GRADE: moderate).

Table 12: HbA1C With Specialized Nursing Care Versus Usual Care

Author, Year	Population	N	Mean Change From Baseline (SD)		Mean Difference in Mean Change From Baseline (95% CI)	P Value
			Nursing Intervention	Usual Care		
Litaker et al, 2003 (15)	Diabetes and hypertension	157	-0.63 (1.5)	-0.15 (1.0)	-0.48 (-0.88 to -0.08)	0.02

Abbreviations: CI, confidence interval; HbA1c, hemoglobin A1c; SD, standard deviation.

The study by Houweling et al evaluated HbA1c as a primary outcome, observing a nonsignificant decrease in HbA1c among individuals receiving specialized nursing care (MD, -0.12; 95% CI -0.44 to 0.20). This study was not included in the overall body of evidence, as it was underpowered to detect a difference in HbA1c, and 41.7% of patients had controlled HbA1c at baseline (HbA1c < 7%).

Blood Pressure and Lipids

Mean differences from baseline to follow-up in blood pressure and lipids were reported by 4 studies (10;13-15) and are summarized in Table 13. Overall, each study was poorly designed to evaluate these measures, with a large proportion of randomized patients not meeting clinically defined hypertension or high cholesterol levels at baseline. With no subgroup analyses conducted, the clinical relevance of these outcomes could not be assessed.

Table 13: Continuous Blood Pressure and Cholesterol Measures With Specialized Nursing Care Versus Usual Care

Author, Year	Population	N	Mean Change From Baseline (SD)		Mean Difference in Mean Change from Baseline (95% CI)	P Value
			Nursing Intervention	Usual Care		
Systolic Blood Pressure (mm Hg)						
Houweling et al, 2011 (13)	Diabetes	206	-7.40 (17.3)	-5.60 (17.30)	-0.72 (NR)	0.122
Khunti et al, 2007 (14)	CAD	1,152	134.72 (SE 0.86) ^a	139.30 (SE 0.80) ^a	-4.58 (-6.68 to -2.28) ^a	0.001
Diastolic Blood Pressure (mm Hg)						
Houweling et al, 2011 (13)	Diabetes	206	-3.2 (10.18)	-1.0 (9.5)	-2.2 (NR)	0.10
Khunti et al, 2007 (14)	CAD	1,152	75.18 (SE 0.46) ^a	78.71 (SE 0.43) ^a	-3.53 (-4.78 to -2.29) ^a	0.0003
Total Cholesterol (mmol/L)						
Houweling et al, 2011 (13)	Diabetes	206	-0.1 (1.02)	-0.05 (0.77)	-0.05 (NR)	0.69
Litaker et al, 2003 (15)	Diabetes	157	-0.28 (0.87)	-0.26 (0.72)	-0.02 (-0.27 to 0.23)	0.85
Khunti et al, 2007 (14)	CAD	1,152	4.53 (SE 0.05) ^a	4.71 (0.43) ^a	-0.18 (-0.30 to -0.05) ^a	0.01

Abbreviations: CAD, coronary artery disease; CI, confidence interval; NR, not reported; SD, standard deviation; SE, standard error.

^aFinal values adjusted for baseline, age, sex, smoking status, and cluster effect.

Control of Disease-Specific Measures

Three studies provided data on the proportion of individuals meeting predefined targets for HbA1c, (13;15) blood pressure, (13-15) or cholesterol control. (13;14) Each study used a different definition of appropriate control. Results and definitions of target values are reported in Table 14.

The study by Houweling et al (13) found no significant differences in the proportion of diabetes patients receiving specialized nursing care who met target values for HbA1c ($P > 0.05$) or lipid control ($P = 0.46$); and neither Houweling et al (13) nor Litaker et al (15) found a significant difference in hypertension control ($P > 0.05$). All patients in the Litaker et al (15) study had hypertension at baseline and a more

stringent threshold was utilized to define hypertension control. Neither study was powered to detect differences in these measures. The GRADE for each of these outcomes was low.

Khunti et al (14) evaluated cholesterol control as a primary outcome measure, observing a significant improvement in the proportion with total cholesterol < 5 mmol/L at 1-year follow-up ($P = 0.03$) among patients in the nurse-led CAD clinic compared to usual care (GRADE: moderate). This study also found a significant increase in the proportion of patients achieving blood pressure control (< 140/85 mm Hg; $P = 0.01$) compared to usual care (GRADE: moderate).

The study by Campbell et al (10) found a significant increase in the proportion of patients achieving appropriate lifestyle control related to moderate physical activity ($P = 0.001$) and a low-fat diet ($P = 0.009$) (GRADE: low). There was no significant difference in the proportion of patients not currently smoking, although this was greater than 80% in each group (GRADE: low). Baseline performance was found to be a strong predictor of each measure.

Table 14: Disease-Specific Measures With Specialized Nursing Care Versus Usual Care

Author, Year	Population	Definition	N	Proportion (%) Meeting Target Values at Follow-Up		OR or RR (95% CI) ^a	P Value
				Nursing Intervention	Usual Care		
HbA1c Control							
Houweling et al, 2011 (13)	Diabetes	< 7%	206	38/102 (34.3)	45/104 (43.3)	RR 0.86 (0.62–1.20)	0.38
		< 8.5%	206	88/102 (86.3)	91/104 (87.5)	RR 0.99 (0.89–1.10)	0.79
Blood Pressure Control							
Houweling et al, 2011 (13)	Diabetes	< 140/90 mm Hg	106	26/102 (25.5)	22/104 (21.2)	RR 1.20 (0.73–1.98)	0.46
Litaker et al, 2003 (15)	Diabetes	< 130/85 mm Hg	157	9/79 (11)	8/78 (10)	RR 1.11 (0.45–2.73)	0.82
Khunti et al, 2007 (14)	CAD	< 140/85 mm Hg	961	250/445 (56.1)	223/516 (43.2)	OR 1.61 (1.22–2.13) ^b	0.01
Lipid Control							
Houweling et al, 2011 (13)	Diabetes	Lipid profile ^c	106	81/102 (79.4)	88/104 (84.6)	RR 0.94 (0.83–1.07)	0.33
Khunti et al, 2007 (14)	CAD	Total < 5 mmol/L	735	249/335 (74.3)	254/400 (63.5)	OR 1.58 (1.05–2.37) ^b	0.03
Lifestyle Control							
Campbell et al, 1998 (9)	CAD	Moderate physical activity	1,155	247/587 (42.1)	177/568 (31.2)	OR 1.67 (1.23–2.26) ^b	0.001
		Low-fat diet	945	271/480 (56.5)	226/465 (48.6)	OR 1.47 (1.10–1.96) ^b	0.009
		Not currently smoking	1,152	483/584 (82.7)	481/568 (84.7)	OR 0.78 (0.47–1.28) ^b	0.32

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio; RR, relative risk.

^aRRs calculated in Review Manager.

^bAdjusted for baseline, age, sex, and practice.

^cTarget values based on Dutch guidelines, in which an indication for treatment in men between 50 to 70 years and women 50 to 75 years with a 25% chance of developing cardiovascular disease in the next 10 years. During treatment, the target value for the cholesterol was < 5 mmol/L.

Health-Related Quality of Life

Generic HRQOL Scores

Both the study by Houweling et al (13) and Litaker et al (15) evaluated generic HRQOL among diabetes patients using the SF-36 or the Short Form 12. Houweling et al (13) found no significant difference in the mental component score (MD, -0.3; $P > 0.05$) and a significant deterioration in the physical component score (MD -3.1; $P = 0.04$) in patients receiving specialized nursing care in comparison to physician care alone. Litaker et al (15) found no significant differences in either the physical component score (MD 1.77; $P = 0.19$) or mental component score (MD 2.14; $P = 0.17$) using the Short Form 12. Overall, these findings were inconsistent based on very low quality evidence.

Both studies evaluating patients with CAD found a trend towards an improvement in SF-36 subscales among patients receiving specialized nursing care in comparison to usual care. (14) No summary scores for the physical and mental component scores were provided. Khunti et al (14) found an improvement in the adjusted mean change score for all subscales, of which 5 out of 8 were statistically significant. Similarly, Campbell et al (9) found a significant improvement in the difference in mean change scores for 6 out of 8 individual SF-36 domains when adjusted for age and baseline performance among patients receiving the nursing intervention. The GRADE for this body of evidence was moderate.

Khunti et al (14) found no significant differences in individual SF-36 domains among patients with confirmed left ventricular systolic dysfunction (LVSD); however this study was underpowered to observe a difference among this subgroup of patients and may be a result of a type 2 error (GRADE: low).

Diabetes-Specific HRQOL

Litaker et al (15) found a significant improvement among patients in the NP-MD team in the Diabetes Quality of Life questionnaire subscale of diabetes satisfaction (MD, 5.42; 95% CI, 4.3-10.41). However, no significant difference was found for diabetes impact (MD, 1.07; 95% CI, -1.37 to 3.51), diabetes social worry (MD, 0.57; 95% CI, -2.49 to 3.64), or diabetes worry (MD, 0.71; 95% CI, -4.58 to 6.00), with higher scores representing better quality of life (GRADE: low). Houweling et al (13) identified significant differences for some of the diabetes symptom score dimensions. However, discrete results were not reported and, as a result, were not included in the body of evidence.

CAD- or CHF-Specific HRQOL

Two studies reported data on HRQOL using CAD- or CHF-specific measures, with inconsistent measures and results. Khunti et al (14) evaluated HRQOL among patients with angina by using the Seattle Angina Questionnaire, while Campbell et al (9) used an Angina Type Specification. There was a significant improvement in the Seattle Angina Questionnaire components of exertional capacity (MD, 5.25; $P = 0.001$) and angina frequency (MD, 2.37; $P = 0.04$) among the nurse-led clinic group in comparison to usual care, and no significant differences in angina stability (MD, 2.37; $P = 0.25$), treatment satisfaction (MD, 2.45; $P = 0.37$), or quality of life (MD, 3.95; $P = 0.06$). Campbell et al (9) found a nonsignificant decrease in chest pain between groups (OR, 0.81; 95% CI, 0.61-1.08; $P = 0.14$) and a significant decrease in worsening chest pain (OR, 0.59; 95% CI, 0.37-0.94; $P = 0.02$). The GRADE for this body of evidence was moderate.

Khunti et al (14) also evaluated HRQOL in patients with LVSD using the Left Ventricular Dysfunction Questionnaire. There was no significant difference in the adjusted 12-month score between the nurse-led clinic and the usual care group (MD -2.44; $P = 0.67$). However, this study was not powered to detect these differences, and these findings may reflect a type 2 error.

Patient Satisfaction

Two studies evaluated patient satisfaction with provider care using different measures. However, only the study by Litaker et al (15) evaluated significance and was included in the body of evidence (Table 15). Litaker et al (15) found a significant increase in the mean change from baseline to follow-up in patient satisfaction among patients receiving specialized nursing care with a physician compared to physician alone (GRADE: moderate). Houweling et al (13) also found an increase in patient satisfaction based on a Patients Evaluation and Diabetes Care survey (satisfaction sum score in nursing group 66.4% and physician group 51.7%).

Table 15: Patient Satisfaction With Specialized Nursing Care Versus Usual Care

Author, Year	Population	N	Satisfaction Tool Used	Mean Patient Satisfaction Score		Mean Difference (95% CI)	P Value
				Nursing Intervention	Usual Care		
Litaker et al, 2003 (15)	Diabetes and hypertension	157	35-item Patient Satisfaction Questionnaire	6.2 ^a	-1.7 ^a	7.9	0.01

Abbreviations: CI, confidence interval; NR, not reported.

^aMean change from baseline to 12 months in general satisfaction, with higher scores representing greater satisfaction.

Process Indicators and Risk Factor Management

Four studies (2 in diabetes (13;15) and 2 in CAD (10;14) evaluated the role of specialized nurses in improving the management of chronic disease risk factors through appropriate examinations and treatment based on disease-specific guidelines.

Disease Management

Campbell et al (10) evaluated appropriate management of blood pressure and lipids, defined as patients receiving attention for their condition (treated, checked or referred) of patients *or* achieving clinical thresholds of appropriate control (Table 16). Based on these definitions, CAD patients receiving care from specialized nurses were 5 times more likely to achieve appropriate blood pressure ($P < 0.001$) management and 3 times more likely to have appropriate lipid management ($P < 0.001$) compared to treatment from physicians alone (GRADE: moderate).

Table 16: Blood Pressure and Lipid Management With Specialized Nursing Care Versus Usual Care

Author, Year	Population	Definition	N	Proportion Managed (%)		OR (95% CI) ^a
				Nursing Intervention	Usual Care	
Campbell et al, 1998 (10)	CAD	Blood pressure managed ^b	1,173	572/593 (96.5)	510/580 (87.9)	5.32 (3.02–9.41)
		Lipids managed ^c	1,173	244/593 (41.1)	125/580 (21.6)	3.19 (2.39–4.26)

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio.

^aAdjusted for baseline, age, sex, and practice.

^bLast blood pressure < 160/90 mm Hg or receiving attention (treated, checked within 3 months).

^cCholesterol < 5.2 mmol/L or receiving attention (treated, checked within 3 months, or referred to a specialist clinic).

Clinical Examinations

Three studies evaluated the proportion of patients receiving appropriate clinical examinations based on guidelines. (13;15) Both diabetes studies (13;15) found patients with diabetes receiving care from specialized nurses to be significantly more likely to receive a foot exam ($P < 0.05$) compared to usual care by a physician (GRADE: moderate). Similarly, patients in the Houweling et al (13) study were significantly more likely to be appropriately referred to an ophthalmologist (if last retina control > 24 months) ($P = 0.01$), with a nonsignificant increase observed in the Litaker et al (15) study ($P = 0.14$) (GRADE: low). This difference may be due to varying definitions of examinations, with Litaker et al (15) evaluating all examinations during the follow-up period rather than appropriate examinations. As well, neither study adjusted for baseline performance.

Khunti et al (14) found a statistically significant increase in the number of referrals for echocardiographs among patients with presumed CHF ($P < 0.01$), as well as the assessment of blood pressure ($P < 0.001$), smoking status ($P < 0.0001$), and body mass index/weight ($P < 0.0001$) among CAD patients receiving secondary prevention from specialized nurses in comparison to usual care. There was no significant difference between groups in the proportion of individuals with cholesterol measured ($P = 0.48$). The GRADE for this body of evidence was moderate.

Table 17: Clinical Examinations Process Measures With Specialized Nursing Care Versus Usual Care

Author, Year	Population	Measure	N	Proportion (%)		RR or OR (95% CI) ^a	P Value
				Nursing Intervention	Usual Care		
Ophthalmologist							
Houweling et al, 2011 (13)	Diabetes	Referred if last exam > 24 months	64	24/34 (70.6)	11/30 (36.7)	RR 1.93 (1.15–3.23) ^a	0.01
Litaker et al, 2003 (15)	Diabetes	Eye exam by ophthalmologist	157	62/79 (78)	53/78 (68)	RR 1.16 (0.95–1.40) ^a	0.14
Foot Exam							
Houweling et al, 2011 (13)	Diabetes	Foot exam, if feet at risk	109	34/60 (56.7)	13/49 (26.5)	RR 2.14 (1.28–3.58) ^a	0.004
Litaker et al, 2003 (15)	Diabetes	Foot exam	157	79/79 (100)	28/78 (36)	RR 2.75 (2.05–3.70) ^a	< 0.0001
Other Measures Taken							
Khunti et al, 2007 (14)	CAD	Blood pressure	1,058	446/450 (99.1)	514/608 (84.5)	OR 22.61 (6.47–70.13)	< 0.001
		Cholesterol	1,059	333/450 (74.0)	403/609 (66.2)	OR 1.21 (0.71–2.08) ^b	0.48
		Body mass index/weight	1,059	396/450 (88.2)	281/609 (46.1)	OR 10.14 (4.99–20.55) ^b	< 0.0001
		Smoking status	1,059	421/450 (93.6)	273/609 (44.8)	OR 33.96 (14.49–79.62) ^b	< 0.0001
	CHF	Echocardiography if CHF presumed but unconfirmed	96	35/96 (36.5)	14/140 (10)	OR 5.64 (2.81–11.31) ^b	< 0.01

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; OR, odds ratio; RR, relative risk.

^aRelative risks calculated using Review Manager.

^bAdjusted for baseline, age, sex, and practice.

Medication Prescribing

Four studies evaluated differences in appropriate or overall number of prescriptions received among specialized nurses and physicians. Results are presented in Table 18.

Among patients with diabetes in the Houweling et al (13) study, specialized nurses were significantly more likely to intensify glucose-lowering therapy ($P = 0.0005$) or intensify blood pressure medications ($P = 0.01$) compared to physicians, if patients were not meeting target values for appropriate control. The number of referrals to an internist for starting insulin therapy was also significantly greater among the nursing group ($P < 0.001$). However, it was not stated how many patients were already on insulin or if this increase reflected more appropriate referrals in comparison to physicians ($P = 0.03$). There was no significant difference in the appropriate prescribing of lipid lowering therapy ($P = 0.07$). The GRADE was moderate for all diabetes medication management outcome measures.

Litaker et al (15) found a significant increase in the proportion of individuals appropriately receiving influenza or pneumovax vaccinations ($P < 0.0001$) (GRADE: moderate), as well as receiving patient education related to smoking, the importance of exercise and diet, and medication side effects ($P < 0.001$) in the nursing intervention group in comparison to usual care. There was no significant difference in education related to medication adherence. However, this was greater than 95% in each group ($P = 0.06$).

Khunti et al (14) reported the proportion of CAD or CHF patients receiving appropriate therapy, 2 of which were evaluated as primary outcomes. There was a statistically significant increase in the primary outcome of the appropriate prescribing of beta-blockers among individuals with a prior myocardial infarction ($P = 0.03$) and no significant difference in the prescribing of an angiotensin converting enzyme (ACE) inhibitor among patients with confirmed LVSD ($P = 0.05$). Among secondary outcomes, there was no significant difference in appropriate prescribing of ACE inhibitors for CAD patients with a history of myocardial infarction (MI), or prescribing of an ACE or angiotensin receptor blocker, beta-blocker, or carvedilol/bisoprolol for patients with LVSD. The GRADE was moderate for cardiac medication management measures.

Two studies reported on Aspirin use, with Khunti et al (14) finding no significant difference in the proportion of patients receiving aspirin ($P = 0.55$), and Campbell et al (10) observing a significant increase in use ($P < 0.001$) (GRADE: low). Differences between the 2 studies may reflect variations in the measure of aspirin use. While Khunti et al (14) assessed use across all patients, Campbell et al (10) accounted for patients who were contraindicated for Aspirin use.

Table 18: Number of Appropriate Prescriptions With Specialized Nursing Care Versus Usual Care

Author, Year	Population	Definition	N	Proportion (%) Prescribed Appropriate Therapy at Follow-Up		RR or OR (95% CI) ^a	P Value
				Nursing Intervention	Usual Care		
Glucose-Lowering Therapy							
Houweling et al, 2011 (13)	Diabetes	Intensification of glucose lowering therapy if HbA1c ≥ 7	120	53/64 (82.8)	28/56 (50)	RR 1.66 (1.26–2.20) ^a	0.0005 ^a
		Referred to internist for insulin	206	10/102 (9.8)	2/104 (1.9)	RR 5.10 (1.15–22.7) ^a	0.03 ^a
Blood Pressure Medications							
Houweling et al, 2011 (13)	Diabetes	Intensified blood pressure medication if > 140/90 mm Hg	170	42/85 (49.4)	24/85 (28.2)	RR 1.75 (1.17–2.61) ^a	0.01 ^a
Lipid Medications							
Houweling et al, 2011 (13)	Diabetes	Intensified cholesterol therapy if not at target	55	13/29 (44.8)	13/26 (50.0)	RR 0.90 (0.51–1.57) ^a	0.70 ^a
Khunti et al, 2007 (14)	CAD	Lipid lowering	1,080	275/461 (59.6)	322/419 (52.0)	OR 1.99 (1.06–3.74) ^b	0.03
Aspirin Therapy							
Khunti et al, 2007 (14)	CAD	Aspirin	1,080	314/461 (68.1)	411/619 (66.4)	OR 1.08 (0.84–1.40) ^b	0.55
Campbell et al, 1998 (10)	CAD	Aspirin taken or contraindicated	1,137	466/575 (81)	373/562 (66.4)	OR 3.22 (2.15–4.80) ^b	< 0.001
Cardiac Medications (Primary Outcomes)							
Khunti et al, 2007 (14)	CAD + prior MI	Beta-blocker	586	125/249 (50.2)	141/337 (41.8)	OR 1.43 (1.19–1.99) ^b	0.03
	LVSD	ACE inhibitor	126	33/51 (64.7)	51/68 (68.0)	OR 0.57 (0.14–2.32)	0.15
Cardiac Medications (Secondary Outcomes)							
Khunti et al, 2007 (14)	CAD + prior MI	ACE inhibitor	489	84 (39.4)	117 (42.4)	OR 0.97 (0.68–1.43)	0.93
		LVSD	ACE or ARB	126	43/51 (84.3)	62/68 (82.7)	OR 0.57 (0.14–2.32)
	LVSD	Beta-blocker	126	20/51 (39.2)	28/68 (37.3)	OR 1.72 (0.25–11.82)	0.58
		Carvedilol or bisoprolol	126	17/51 (33.3)	18/68 (24.0)	OR 2.75 (0.63–11.86)	0.17
Vaccinations							
Litaker et al, 2003 (15)	Diabetes	Influenza vaccination	157	62/79 (78)	37/78 (47)	RR 1.91 (1.43–2.56) ^a	< 0.0001
		Pneumovax (if unvaccinated)	93	32/44 (72.7)	12/52 (23.1)	RR 3.15 (1.86–5.34) ^a	< 0.0001

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CI, confidence interval; LVSD, left ventricular systolic dysfunction; MI, myocardial infarction; OR, odds ratio; RR, relative risk.

^aRelative risks and P values calculated using Review Manager.

^bAdjusted for baseline, age, sex, and practice.

Efficiency

Number of Visits

Two studies commented on the number of visits to allocated providers among patients with type 2 diabetes. Houweling et al (13) found a mean increase of 3.3 visits to the practice nurse group (6.1 versus 2.8) in comparison to the physician group ($P < 0.001$) (GRADE: low). Litaker et al (15) stated there was a significant increase in the number of visits related to hypertension or diabetes among patients randomized to the NP–physician team compared to the physician alone ($P < 0.001$). However, no estimates were provided and, as a result, these outcomes were not included in the body of evidence.

Length of Visits

Both the studies (13) provided data on the mean length of visits with each provider or the average contact time (Table 19). Houweling et al (13) found a significant increase of 11 minutes in the average length of visit with the practice nurse in comparison to the general practitioner ($P < 0.001$). The study also found a significant increase of 100 minutes in average contact time. It was not stated if visits with the physician were only those related to diabetes, or all-cause visits. Litaker et al (15) found a significant increase in the average contact time (MD 95 minutes; $P < 0.0001$) related to diabetes or hypertension in patients seeing the nurse–physician team compared to the physician alone.

Table 19: Mean Length of Visits With Specialized Nursing Care Versus Usual Care

Author, Year	Population	Measure	N	Time, Minutes		P Value
				Nursing Intervention	Usual Care	
Houweling et al, 2011 (13)	Diabetes	Average length of visit	206	21	10	< 0.001
		Average contact time		128	28	Significant difference
Litaker et al, 2003 (15)	Diabetes	Average contact time	157	180 ^a	85 ^a	< 0.001

^aExcluding time spent managing problems by telephone.

Physician Workload

Physician workload or collaboration between nurses and physicians was assessed in 4 studies (2 diabetes, 1 CAD, 1 chronic disease). (10;13;15;16) Two studies provided data on the amount of nurse-physician collaboration in the intervention arm, and 2 studies reported on the change in physician workload before and after the introduction of a nursing intervention.

Diabetes

Table 20 presents the amount of nurse-physician collaboration for diabetes patients receiving specialized nursing care. In the study by Litaker et al, (15) a physician addressed diabetes or hypertension in approximately 40% of patient visits. However, these were stated to be for low-complexity issues generally related to medication addition, deletion, or titration. The total number of visits was not provided. Physicians in the Houweling et al (13) study had a median of 1.4 consultations per patient with the nurse (interquartile range 1–2) in the nursing arm, with a median time of 1 minute. Overall, it remains unclear if the addition of a specialized nurse improved efficiency in these studies.

Table 20: Amount of Collaboration Between Specialized Nurses and Physicians

Author, Year	Population	Measure	N	Estimate (IQR)
Houweling et al, 2011 (13)	Diabetes	Median number of physician consultations with nurse, per patient	206	1.4 (0–2)
		Median time per physician-nurse consultation		1 minute (0–3.3)
Litaker et al, 2003 (15)	Diabetes	Percentage of visits physician addressed diabetes or hypertension	157	40%

Abbreviation: IQR, interquartile range.

CAD

Campbell et al (10) found no significant difference in the change in mean number of physician consultations between groups after the introduction of the nurse-led CAD clinics (mean of 1 consultation/patient in both groups at 1 year; $P = 0.488$). It is uncertain how the estimation of physician consultations was determined (GRADE: low).

Chronic Disease

Laurant et al (16) was the only study to directly evaluate objective and subjective physician workload as a primary outcome before and after the addition of an NP to the general practice team. Results are presented in Table 21.

Objective workload was measured by diary, where over 28 consecutive days general practitioners (GPs) recorded the start and end of their working day, and the number of patient consultations. Overall, there was a nonsignificant increase in the mean difference in number of contacts per week by GPs during surgery hours among practices with the NP intervention. This was reflected by a nonsignificant decrease in mean number of out-of-hours contacts in the intervention group. This pattern was similarly observed when looking at time spent consulting for COPD or asthma patients, where GPs had significantly more surgery hour contacts per week after the addition of the NP (MD 2.82; $P = 0.006$), and a nonsignificant decrease in out-of-hours contacts. The GRADE for the objective workload body of evidence was low.

Table 21: Mean Difference in Change in Objective Workload After Adding a Nurse Practitioner

Author, Year	Population	Measure	N	Change in Mean Number of Contacts/Week (95% CI)		Mean Difference in Change ^c	P Value
				Nursing Intervention	Usual Care		
Laurant et al, 2004 (16)	Chronic: COPD, asthma, dementia, or cancer	Surgery hours ^a	30 GPs (4 groups, 20 practices)/ 19 GPs (3 groups, 14 practices)	Total: 4.5 (0.6–8.3)	Total: 0.1 (–1.9 to 2.2)	4.4	0.06
				COPD/asthma: 2.8 (0.3–5.3)	COPD/asthma: –0.2 (–1.4 to 1.1)	2.8	0.01
		Out of hours ^b		Total: –1.5 (–3.9 to 0.9)	Total: 2.1 (–1.3 to 5.5)	–3.6	0.22
				COPD/asthma: –1.5 (–3.0 to –0.03)	COPD/asthma: 0.7 (–0.9 to 2.2)	–2.2	0.09

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; GP, general practitioner.

^aStandardized by median number of days worked.

^bStandardized by mean number of shifts.

Subjective physician workload was assessed via validated questionnaire. There was no significant difference in any of the 4 subjective workload components of available time, job satisfaction, inappropriate demands, or cost benefit when a NP was added to the general practitioner practice (GRADE: low).

Summary

An overall summary of outcomes for nursing Models 1 and 2 is presented in Table 22.

Table 22: Summary of Outcomes

Population	Health Resource Utilization	Disease-Specific Measures	HRQOL/Patient Satisfaction	Process Indicators	Efficiency
Model 1: Nurse Versus Physician (Usual Care)					
Primary care population oversampled with chronic disease	No significant difference in hospitalizations, ED visits, specialist visits, or primary care visits	No significant difference in systolic blood pressure or peak flow; significant decrease in diastolic blood pressure	No significant difference in SF-36	NR	Nurses directly substituted care provided by physicians
GRADE	Moderate	Very Low	Moderate	NA	
Diabetes subgroup	No significant difference in hospitalizations, ED visits, specialist visits, or primary care visits	No significant difference in HbA1c	No significant difference in SF-36	Significant increase or no significant difference in education and monitoring of health	
GRADE	Very low	Very low	Very low	Very low	
Model 2: Nurse and Physician Versus Physician (Usual Care)					
Diabetes	Significant increase in number of visits	Significant decrease in HbA1c; no significant difference in target HbA1c, blood pressure, or cholesterol	Inconclusive HRQOL; significant increase in patient satisfaction	Trend toward significant improvement	Indeterminate
GRADE	Low	Low–Moderate	Low–Moderate	Low–Moderate	—
CAD/coronary heart disease	Significant increase in hospitalizations; no significant difference in length of stay	Significant increase in achievement of target blood pressure, cholesterol, and lifestyle control, and management of blood pressure and cholesterol	Inconclusive HRQOL	Trend toward significant improvement	No difference in change in number of physician consultations
GRADE	Low	Low–Moderate	Moderate	Low–Moderate	Low
Chronic disease	NR	NR	NR	NR	No significant difference in total surgery hours or out of hours and significant increase in COPD/asthma hours; no difference in subjective physician workload
GRADE	NA	NA	NA	NA	Low

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ED, emergency department; HbA1c, hemoglobin A1c; HRQOL, health-related quality of life; LOS, length of stay; SF-36, Short Form (36) Health Questionnaire.

Limitations

There are several limitations that need to be considered when evaluating the strength of this evidence-based analysis. Although all studies included were randomized controlled trials, there was heterogeneity in the roles and training of specialized nurses, and the types of primary health care practices and settings in which the studies were conducted. None of the studies was conducted in Canada, and, as a result, there are limitations to the applicability of the results to the Ontario context, particularly related to the degree of training and scope of practice of nurses. Additionally, most outcomes were evaluated over a 12-month follow-up period, which may not be adequate time to observe an impact.

Only 1 study was identified under Model 1, which was not designed to assess equivalence across all outcomes. This study population was oversampled with chronic disease and, therefore, may not represent a true chronic disease population. A subgroup analysis was undertaken, limited to diabetes patients. However, this analysis was underpowered and may comprise type 2 errors. Additionally, the majority of patients in this study were Hispanic, which limits the generalizability.

Overall, it was unclear in the studies examining Model 2 whether the nurses were substituting or supplementing the role of the physician. The improvement of efficiency in the primary health care setting was only directly evaluated by one study. This study observed an increase in the mean number of physician consultations per week during practice hours, and a trend towards a decrease in out-of-hours time. There remains uncertainty in these estimates as the physicians were responsible for determining which patients were referred to the nurses, and no data was provided on the number of patients referred to the nurse, the characteristics of the patients they dealt with, or the type of collaboration between the nurse and the physicians. Additionally, although nurses in this study were stated as being NPs, they had a limited scope of practice compared to NPs in Ontario.

Conclusions

Model 1

The effectiveness of specialized nurses working under Model 1 was evaluated based on comparable outcomes between nurses and physicians (usual care). This model aims to improve efficiency by directly substituting the role of the physician with a specialized nurse. Results from the evidence-based analysis found specialized nurses providing autonomous patient care to a primary health care population oversampled with chronic disease demonstrated comparable outcomes to physician care alone. Outcomes were similarly comparable among the subgroup of patients with diabetes. Specialized nurses in this model most closely resemble NPs in the Ontario context.

Based on moderate quality of evidence, there was no significant difference among patients receiving primary health care from NPs in comparison to physicians alone for outcomes related to:

- health resource utilization (hospitalizations, ED or urgent care visits, specialist visits, and primary health care visits)
- HRQOL based on the SF-36
- patient satisfaction with care

Diabetes Subgroup

Based on very low quality of evidence, there was no significant difference between patients receiving primary health care from specialized nurses and those being cared for by physicians for:

- health resource utilization (hospitalizations, ED or urgent care visits, specialist visits, and primary health care visits)
- HbA1c

Model 2

When compared to physicians alone or usual care, specialized nurses working with physicians showed a general increase in process measures related to clinical examinations and medication management based on guidelines. This was reflected by a significant reduction in HbA1c among diabetes patients, and a significant increase in the proportion of CAD patients with controlled blood pressure and total cholesterol. Patients receiving secondary prevention for CAD from a nurse-led secondary prevention clinic were significantly less likely to be hospitalized after 1 year. Patients were more satisfied with care provided by the nurse plus physician intervention compared to the physician alone. However, there was inconsistency regarding outcomes related to HRQOL. No outcomes indicated specialized nursing interventions to be more harmful than physicians alone.

The specific role of the specialized nurse in supplementing or substituting physician care was unclear, making it difficult to determine the impact on efficiency. Further research is needed to understand the impact of specialized nurses on primary health care efficiency.

Specialized nurses plus physicians had a positive significant impact when compared to usual care:

- based on moderate quality of evidence for the CAD or CHF population
 - proportion meeting appropriate threshold of blood pressure and cholesterol control
 - proportion with appropriate blood pressure management and cholesterol management
 - number of clinical examinations for blood pressure, BMI and smoking status

- number of echocardiography assessments for confirmation of CHF, among unconfirmed cases
- number of prescriptions for a beta-blocker among individuals with a prior MI
- based on moderate quality of evidence for the diabetes population
 - HbA1c
 - patient satisfaction
 - number of foot examinations
 - number with intensification of glucose lowering therapy if uncontrolled HbA1c, intensification of blood pressure lowering therapy if uncontrolled blood pressure, or referral to internist for insulin
- based on low quality of evidence for the CAD population
 - all-cause hospitalizations
 - proportion achieving lifestyle control related to physical activity and low-fat diet
- based on low quality of evidence for the diabetes population
 - number of primary healthcare visits to randomized group

There was no significant difference in patients receiving chronic disease management from specialized nurses compared to usual care for:

- based on moderate quality of evidence for the CAD or CHF population
 - number of clinical examination of cholesterol
 - number of prescriptions for an ACE inhibitor if confirmed LVSD
- based on moderate quality of evidence for the diabetes population
 - number with intensification of cholesterol therapy if not controlled
- based on low quality of evidence for the diabetes population
 - proportion of patients meeting HbA1c, blood pressure, or total cholesterol target values
- based on low quality of evidence for the CAD or CHF population
 - length of hospital stay
 - proportion of non-smokers
 - mean difference in the number of physician consultations before and after the introduction of the nurse-led clinic
- based on low quality of evidence for the chronic disease population
 - objective and subjective physician workload

There was indeterminate or inconsistent evidence, with a trend towards improved outcomes among the nurse-led group, for:

- based on moderate quality of evidence for the CAD or CHF population
 - SF-36 measures of HRQOL
 - angina-specific measures of HRQOL
- based on low quality of evidence for the diabetes population
 - SF-36 and SF-12 measures of HRQOL
 - diabetes-specific measures of HRQOL
 - ophthalmologist exam

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Expert Panel for Health Quality Ontario: Optimizing Chronic Disease Management in the Community (Outpatient) Setting

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Theresa Agnew	Executive Director	Nurse Practitioners' Association of Ontario
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Arlene Bierman	Ontario Women's Health Council Chair in Women's Health	Department of Medicine, Keenan Research Centre in the Li Ka Shing Knowledge Institute, St. Michael's Hospital, University of Toronto
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Moira Stewart	Director	Centre for Studies in Family Medicine, University of Western Ontario
Walter Wodchis	Associate Professor	Institute of Health Management Policy and Evaluation, University of Toronto

Appendices

Appendix 1: Literature Search Strategies

OID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE

Search date: May 3, 2012

Database: Ovid MEDLINE(R) <1946 to April Week 4 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <May 02, 2012>, Embase <1980 to 2012 Week 17>

Search Strategy:

-
- 1 exp Coronary Artery Disease/ (223512)
 - 2 exp Myocardial Infarction/ use mesz (135828)
 - 3 exp heart infarction/ use emez (226111)
 - 4 (coronary artery disease or cad or heart attack).ti. (46076)
 - 5 ((myocardi* or heart or cardiac or coronary) adj2 (atheroscleros* or arterioscleros* or infarct*)).ti. (154179)
 - 6 or/1-5 (560881)
 - 7 exp Atrial Fibrillation/ use mesz (29058)
 - 8 exp heart atrium fibrillation/ use emez (58501)
 - 9 ((atrial or atrium or auricular) adj1 fibrillation*).ti,ab. (77417)
 - 10 or/7-9 (104258)
 - 11 exp heart failure/ (312234)
 - 12 ((myocardi* or heart or cardiac) adj2 (failure or decompensation or insufficiency)).ti,ab. (244965)
 - 13 11 or 12 (397186)
 - 14 exp Stroke/ (185400)
 - 15 exp Ischemic Attack, Transient/ use mesz (16571)
 - 16 exp transient ischemic attack/ use emez (20600)
 - 17 exp stroke patient/ use emez (5831)
 - 18 exp brain infarction/ or exp cerebrovascular accident/ use emez (105307)
 - 19 (stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA).ti,ab. (295295)
 - 20 or/14-19 (409281)
 - 21 exp Diabetes Mellitus, Type 2/ use mesz (70992)
 - 22 exp non insulin dependent diabetes mellitus/ use emez (108768)
 - 23 exp diabetic patient/ use emez (13793)
 - 24 (diabetes or diabetic* or niddm or t2dm).ti,ab. (801951)
 - 25 or/21-24 (828073)
 - 26 exp Skin Ulcer/ (74585)
 - 27 ((pressure or bed or skin) adj2 (ulcer* or sore* or wound*)).ti,ab. (29869)
 - 28 (decubitus or bedsore*).ti,ab. (8754)
 - 29 or/26-28 (94113)
 - 30 exp Pulmonary Disease, Chronic Obstructive/ use mesz (17962)
 - 31 exp chronic obstructive lung disease/ use emez (57639)
 - 32 (chronic obstructive adj2 (lung* or pulmonary or airway* or airflow or respiratory) adj (disease* or disorder*)).ti,ab. (57361)
 - 33 (copd or coad).ti,ab. (48369)
 - 34 chronic airflow obstruction.ti,ab. (1087)
 - 35 exp Emphysema/ (38390)
 - 36 exp chronic bronchitis/ use emez (7071)

37 ((chronic adj2 bronchitis) or emphysema).ti,ab. (52147)
38 or/30-37 (165549)
39 exp Chronic Disease/ (353302)
40 ((chronic* adj2 disease*) or (chronic* adj2 ill*)).ti,ab. (231548)
41 39 or 40 (527877)
42 6 or 10 or 13 or 20 or 25 or 29 or 38 or 41 (2716853)
43 exp nursing discipline/ or exp nurse/ or exp Team Nursing/ or exp nurse attitude/ or exp nurse patient relationship/ or exp doctor nurse relation/ or exp nursing staff/ use emez (341407)
44 exp Nursing/ or exp nurse's practice patterns/ or exp nursing, team/ or exp nurses/ or exp nursing staff/ or exp Nurse's Role/ or exp Nurse-Patient Relations/ or exp physician-nurse relations/ or exp Nursing Process/ or exp nursing care/ or exp nursing services/ or exp Nursing Faculty Practice/ use mesz (784042)
45 (nurse or nurses or nursing).ti,ab. (614066)
46 or/43-45 (1006663)
47 42 and 46 (62317)
48 exp Intermediate Care Facilities/ use mesz (601)
49 (intermedia* adj2 care).ti,ab. (2489)
50 exp ambulatory care/ (77241)
51 exp Ambulatory Care Facilities/ use mesz (40298)
52 exp ambulatory care nursing/ use emez (9)
53 exp Outpatients/ use mesz (7332)
54 exp Outpatient Department/ use emez (33551)
55 exp outpatient care/ use emez (18025)
56 exp Community Health Services/ use mesz (450632)
57 exp community care/ use emez (88690)
58 exp Community Medicine/ (3924)
59 exp Subacute Care/ use mesz (711)
60 exp General Practice/ (125169)
61 exp Primary Health Care/ (158229)
62 exp Physicians, Family/ or exp general practitioners/ or exp Physicians, Primary Care/ use mesz (64103)
63 exp general practitioner/ use emez (48542)
64 exp family medicine/ use emez (5963)
65 exp Group Practice/ use mesz (22251)
66 exp Team Nursing/ use emez (23)
67 exp Primary Care Nursing/ use mesz (39)
68 exp Patient Care Team/ use mesz (49665)
69 exp Teamwork/ use emez (9390)
70 *Patient Care Management/ use mesz (1274)
71 ((primary or family or community or outpatient* or ambulatory) adj2 (care* or physician* or nurs* or service* or clinic* or facility or facilities)).ti,ab. (343246)
72 ((transitional or multidisciplin* or multifacet* or multi-disciplin* or multi-facet* or cooperat* or cooperat* or interdisciplin* or inter-disciplin* or collaborat* or multispecial* or multi-special* or share or sharing or shared or integrat* or joint or multi-modal or multimodal) adj2 (care or team*)).ti,ab. (50531)
73 (team* or liaison).ti,ab. (185842)
74 ((general or family or primary care or community) adj2 (practic* or clinic* or program* or doctor* or nurse* or physician*)).ti,ab. (221390)
75 or/48-74 (1391621)
76 47 and 75 (21187)
77 limit 76 to (controlled clinical trial or meta analysis or randomized controlled trial) (1745)
78 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ use mesz (65746)

- 79 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ use emez (561797)
 80 (health technology adj2 assess\$).ti,ab. (3321)
 81 exp Random Allocation/ or exp Double-Blind Method/ or exp Control Groups/ or exp Placebos/ use mesz (393767)
 82 Randomized Controlled Trial/ or exp Randomization/ or exp RANDOM SAMPLE/ or Double Blind Procedure/ or exp Triple Blind Procedure/ or exp Control Group/ or exp PLACEBO/ use emez (944772)
 83 (random* or RCT).ti,ab. (1316536)
 84 (placebo* or sham*).ti,ab. (430858)
 85 (control* adj2 clinical trial*).ti,ab. (36726)
 86 meta analysis/ use emez (62532)
 87 (meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (270753)
 88 or/77-87 (2267776)
 89 76 and 88 (3579)
 90 limit 89 to english language (3366)
 91 remove duplicates from 90 (2472)

CINAHL

#	Query	Results
S54	S50 and S53 Limiters - English Language	589
S53	S51 or S52	157536
S52	random* or sham* or rct* or health technology N2 assess* or meta analy* or metaanaly* or pooled analysis or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane or control* N2 clinical trial*	149343
S51	(MH "Random Assignment") or (MH "Random Sample+") or (MH "Meta Analysis") or (MH "Systematic Review") or (MH "Double-Blind Studies") or (MH "Single-Blind Studies") or (MH "Triple-Blind Studies") or (MH "Placebos") or (MH "Control (Research)")	84296
S50	S31 and S49	5113
S49	S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48	217022
S48	((general or family or primary care or community) N2 (practic* or clinic* or program* or doctor* or nuse* or physician*))	42038
S47	(team* or liaison)	51641
S46	((transitional or multidisciplin* or multifacet* or multi-disciplin* or multi-facet* or cooperat* or co-operat* or interdisciplin* or inter-disciplin* or collaborat* or multispecial* or multi-special* or share or sharing or shared or integrat* or joint or multi-modal or multimodal) N2 (care or team*)).	30029
S45	((primary or family or community or outpatient* or ambulatory) N2 (care* or physician* or nurs* or service* or clinic* or facility or facilities))	120243
S44	(MH "Team Nursing") OR (MH "Primary Nursing")	1283
S43	(MH "Multidisciplinary Care Team+")	18485
S42	(MH "Group Practice+")	5857
S41	(MH "Physicians, Family")	7173

S40	(MH "Primary Health Care")	24977
S39	(MH "Family Practice")	9153
S38	(MH "Community Medicine")	22
S37	(MH "Community Programs")	3902
S36	(MM "Community Health Services") OR (MH "Community Health Nursing+") OR (MH "Community Networks") OR (MH "Family Services") OR (MH "Occupational Health Services+")	31665
S35	(MH "Outpatients")	27057
S34	(MH "Outpatient Service")	3001
S33	(MH "Ambulatory Care") OR (MH "Ambulatory Care Facilities+") OR (MH "Ambulatory Care Nursing")	13382
S32	(MH "Subacute Care")	975
S31	S27 or S26 or S29 or S33 or S31 or S28 or S27 or S30	30611
S30	S28 or S29	28893
S29	chronic*N2 disease* or chronic* N2 ill*	7650
S28	(MH "Chronic Disease")	24261
S27	(S27 or S26 or S25 or S26)	1861
S26	chronic N2 bronchitis or emphysema	1849
S25	(MH "Emphysema")	908
S24	chronic obstructive N2 disease* or chronic obstructive N2 disorder* or copd or coad	7641
S23	(MH "Pulmonary Disease, Chronic Obstructive+")	5670
S22	S30 or S29	51
S21	pressure N1 ulcer* or bedsore* or bed N1 sore* or skin N1 ulcer* OR pressure N1 wound* OR decubitus	9771
S20	(MH "Skin Ulcer+")	15062
S19	S34 or S33 or S32	45
S18	diabetes or diabetic* or niddm or t2dm	71792
S17	(MH "Diabetic Patients")	3627
S16	(MH "Diabetes Mellitus, Type 2")	18872
S15	S30 or S31 or S32	74
S14	stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA	38660
S13	(MH "Cerebral Ischemia, Transient")	1948
S12	(MH "Stroke") OR (MH "Stroke Patients")	26348
S11	S27 OR S28	25
S10	myocardi*failure OR myocardial decompensation OR myocardial insufficiency OR cardiac failure OR cardiac decompensation or cardiac insufficiency OR heart failure OR heart decompensation OR heart insufficiency	19281

S9	(MH "Heart Failure+")	14847
S8	S26 OR S25	53
S7	atrial N1 fibrillation* OR atrium N1 fibrillation* OR auricular N1 fibrillation*	8328
S6	(MH "Atrial Fibrillation")	6741
S5	S31 OR S30 OR S29 OR S28	76
S4	TI myocardi* N2 infarct* or TI heart N2 infarct* or TI cardiac N2 infarct* OR TI coronary N2 infarct* or TI arterioscleros* or TI atheroscleros*	9820
S3	coronary artery disease OR cad OR heart attack*	7863
S2	(MH "Myocardial Infarction+")	19665
S1	(MH "Coronary Arteriosclerosis")	4863

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Line	Search	Hits
1	MeSH DESCRIPTOR coronary artery disease EXPLODE ALL TREES	300
2	(coronary artery disease or cad or heart attack*):TI	223
3	((myocardi* or heart or cardiac or coronary) adj2 (atheroscleros* or arterioscleros* or infarct*)):TI	232
4	MeSH DESCRIPTOR Atrial Fibrillation EXPLODE ALL TREES	277
5	((atrial or atrium or auricular) adj1 fibrillation*):TI	0
6	((atrial or atrium or auricular) adj1 fibrillation*):TI	181
7	MeSH DESCRIPTOR heart failure EXPLODE ALL TREES	500
8	((myocardi* or heart or cardiac) adj2 (failure or decompensation or insufficiency)):TI	293
9	MeSH DESCRIPTOR stroke EXPLODE ALL TREES	668
10	MeSH DESCRIPTOR Ischemic Attack, Transient EXPLODE ALL TREES	42
11	(stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA):TI	640
12	MeSH DESCRIPTOR Diabetes Mellitus, Type 2 EXPLODE ALL TREES	631
13	(diabetes or diabetic* or niddm or t2dm):TI	1276
14	MeSH DESCRIPTOR Skin Ulcer EXPLODE ALL TREES	280
15	((pressure or bed or skin) adj2 (ulcer* or sore* or wound*)):TI	76
16	(decubitus or bedsore*):TI	0
17	MeSH DESCRIPTOR Pulmonary Disease, Chronic Obstructive EXPLODE ALL TREES	291
18	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow or respiratory)):TI	228
19	(copd or coad):TI	116
20	(chronic airflow obstruction):TI	0
21	MeSH DESCRIPTOR Emphysema EXPLODE ALL TREES	11
22	((chronic adj2 bronchitis) or emphysema):TI	48
23	MeSH DESCRIPTOR Chronic Disease EXPLODE ALL TREES	773
24	((chronic* adj2 disease*) or (chronic* adj2 ill*)):TI	265
25	MeSH DESCRIPTOR Comorbidity EXPLODE ALL TREES	170
26	(comorbid* OR co-morbid* OR multimorbid* OR multi-morbid* OR (complex* adj1 patient*) OR "patient* with multiple" OR (multiple adj2 (condition* OR disease*)))	25
27	#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 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	5011
28	MeSH DESCRIPTOR nursing EXPLODE ALL TREES	311
29	MeSH DESCRIPTOR Nurse-Patient Relations EXPLODE ALL TREES	20

30	MeSH DESCRIPTOR nursing staff EXPLODE ALL TREES	44
31	MeSH DESCRIPTOR nurses EXPLODE ALL TREES	118
32	MeSH DESCRIPTOR nursing, team EXPLODE ALL TREES	3
33	MeSH DESCRIPTOR physician-nurse relations EXPLODE ALL TREES	3
34	MeSH DESCRIPTOR Nursing Process EXPLODE ALL TREES	147
35	MeSH DESCRIPTOR Nursing care EXPLODE ALL TREES	219
36	MeSH DESCRIPTOR nursing services EXPLODE ALL TREES	281
37	MeSH DESCRIPTOR nursing faculty practice EXPLODE ALL TREES	0
38	MeSH DESCRIPTOR Nurse's Role EXPLODE ALL TREES	62
39	(nurse or nurses or nursing)	3334
40	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	3497
41	MeSH DESCRIPTOR Intermediate Care Facilities EXPLODE ALL TREES	4
42	(intermedia* adj2 care)	39
43	MeSH DESCRIPTOR ambulatory care EXPLODE ALL TREES	346
44	MeSH DESCRIPTOR Ambulatory Care Facilities EXPLODE ALL TREES	205
45	MeSH DESCRIPTOR Outpatients EXPLODE ALL TREES	73
46	MeSH DESCRIPTOR Community Health Services EXPLODE ALL TREES	4099
47	MeSH DESCRIPTOR Community Medicine EXPLODE ALL TREES	3
48	MeSH DESCRIPTOR Subacute Care EXPLODE ALL TREES	7
49	MeSH DESCRIPTOR Primary Health Care EXPLODE ALL TREES	673
50	MeSH DESCRIPTOR Physicians, Family EXPLODE ALL TREES	50
51	MeSH DESCRIPTOR Group Practice EXPLODE ALL TREES	65
52	MeSH DESCRIPTOR Patient Care Team EXPLODE ALL TREES	207
53	MeSH DESCRIPTOR Patient Care Management EXPLODE ALL TREES	2512
	((primary or family or community or outpatient* or ambulatory) adj2 (care* or physician* or nurs* or service* or clinic* or facility or facilities))) OR (((transitional or multidisciplin* or multifacet* or multi-disciplin* or multi-facet* or cooperat* or co-operat* or interdisciplin* or inter-disciplin* or collaborat* or multispecial* or multi-special* or share or sharing or shared or integrat* or joint or multi-modal or multimodal) adj2 (care or team*))) OR (team* or liaison) OR (general or family or primary care or community) adj2 (practic* or clinic* or program* or doctor* or nuse* or physician*))	
54		2135
55	#41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54	7583
56	#27 AND #40 AND #55	297

Cochrane

ID	Search	Hits
#1	MeSH descriptor Coronary Artery Disease explode all trees	2250
#2	MeSH descriptor Myocardial Infarction explode all trees	7854
#3	(myocardi* or heart or cardiac or coronary) NEAR/2 (atheroscleros* or arterioscleros* or infarct*):ti or (coronary artery disease or cad or heart attack*):ti	8562
#4	MeSH descriptor Atrial Fibrillation explode all trees	2159
#5	(atrial NEAR/2 fibrillation* or atrium NEAR/2 fibrillation* or auricular NEAR/2 fibrillation*):ti	2357
#6	MeSH descriptor Heart Failure explode all trees	4818
#7	(myocardi* NEAR/2 (failure or decompensation or insufficiency)):ti or (heart NEAR/2 (failure or decompensation or insufficiency)):ti or (cardiac NEAR/2 (failure or	5347

	decompensation or insufficiency)):ti	
#8	MeSH descriptor Stroke explode all trees	4020
#9	MeSH descriptor Ischemic Attack, Transient explode all trees	469
#10	(stroke or tia or transient ischemic attack or cerebrovascular apoplexy or cerebrovascular accident or cerebrovascular infarct* or brain infarct* or CVA):ti	10009
#11	MeSH descriptor Diabetes Mellitus, Type 2 explode all trees	7179
#12	(diabetes or diabetic* or niddm or t2dm):ti	16895
#13	MeSH descriptor Skin Ulcer explode all trees	1599
#14	(pressure or bed or skin) NEAR/2 (ulcer* or sore* or wound*):ti	673
#15	(decubitus or bedsore*):ti	100
#16	MeSH descriptor Pulmonary Disease, Chronic Obstructive explode all trees	1804
#17	(chronic obstructive NEAR/2 (lung* or pulmonary or airway* or airflow or respiratory)):ti	2436
#18	(copd or coad):ti	3352
#19	(chronic airflow obstruction):ti	72
#20	MeSH descriptor Emphysema explode all trees	92
#21	(chronic NEAR/2 bronchitis) or emphysema:ti	1184
#22	MeSH descriptor Chronic Disease explode all trees	10019
#23	(chronic* NEAR/2 disease* or chronic* NEAR/2 ill*):ti	1702
#24	MeSH descriptor Comorbidity explode all trees	1987
#25	(comorbid* OR co-morbid* OR multimorbid* OR multi-morbid* OR (complex* NEXT patient*) OR "patient* with multiple" OR (multiple NEAR/2 (condition* OR disease*))) :ti	654
#26	(#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 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25)	69160
#27	MeSH descriptor Intermediate Care Facilities explode all trees	13
#28	(intermedia* NEAR/2 care):ti or (intermedia* NEAR/2 care):ab	95
#29	MeSH descriptor Ambulatory Care Facilities explode all trees	1424
#30	MeSH descriptor Outpatients explode all trees	692
#31	MeSH descriptor Community Health Services explode all trees	19917
#32	MeSH descriptor Community Medicine explode all trees	34
#33	MeSH descriptor Subacute Care explode all trees	16
#34	MeSH descriptor General Practice explode all trees	2113
#35	MeSH descriptor Primary Health Care explode all trees	2928
#36	MeSH descriptor Physicians, Family explode all trees	445
#37	MeSH descriptor General Practitioners explode all trees	31
#38	MeSH descriptor Physicians, Primary Care explode all trees	21
#39	MeSH descriptor Group Practice explode all trees	378
#40	MeSH descriptor Primary Care Nursing explode all trees	1

#41	MeSH descriptor Patient Care Team explode all trees	1177
#42	MeSH descriptor Patient Care Management explode all trees	13149
#43	((primary or family or community or outpatient* or ambulatory) NEAR/2 (care* or physician* or nurs* or service* or clinic* or facility or facilities)):ti and ((primary or family or community or outpatient* or ambulatory) NEAR/2 (care* or physician* or nurs* or service* or clinic* or facility or facilities)):ab	2110
#44	(transitional or multidisciplin* or multifacet* or multi-disciplin* or multi-facet* or cooperat* or co-operat* or interdisciplin* or inter-disciplin* or collaborat* or multispecial* or multi-special* or share or sharing or shared or integrat* or joint or multi-modal or multimodal) NEAR/2 (care or team*):ti or (transitional or multidisciplin* or multifacet* or multi-disciplin* or multi-facet* or cooperat* or co-operat* or interdisciplin* or inter-disciplin* or collaborat* or multispecial* or multi-special* or share or sharing or shared or integrat* or joint or multi-modal or multimodal) NEAR/2 (care or team*):ab	1115
#45	((general or family or primary care or community) NEAR/2 (practic* or clinic* or program* or doctor* or nuse* or physician*)):ti or ((general or family or primary care or community) NEAR/2 (practic* or clinic* or program* or doctor* or nuse* or physician*)):ab	8087
#46	(team* or liaison):ti or (team* or liaison):ab	3183
#47	(#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46)	39299
#48	(#26 AND #47)	5315
#49	MeSH descriptor Nurse's Role explode all trees	269
#50	MeSH descriptor Nursing explode all trees	2702
#51	MeSH descriptor Nurse's Practice Patterns explode all trees	17
#52	MeSH descriptor Nurses explode all trees	824
#53	MeSH descriptor Nursing, Team explode all trees	18
#54	MeSH descriptor Nursing Staff explode all trees	447
#55	MeSH descriptor Nurse-Patient Relations explode all trees	265
#56	MeSH descriptor Physician-Nurse Relations explode all trees	19
#57	MeSH descriptor Nursing Process explode all trees	1741
#58	MeSH descriptor Nursing Care explode all trees	1437
#59	MeSH descriptor Nursing Services explode all trees	1373
#60	MeSH descriptor Nursing Faculty Practice explode all trees	4
#61	(nurse or nurses or nursing):ti and (nurse or nurses or nursing):ab	2300
#62	(#49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61)	6577
#63	(#48 AND #62)	871

Appendix 2: Summary of Systematic Reviews

Table A1: Summary of Systematic Reviews

Author, Year	Type of Review	Search Dates	Number of Studies	Type of Intervention and Nurse	Disease	Setting	Outcomes Evaluated	Conclusions	Overall Relevance to Current Review
Nurses in Primary Care (General)									
Browne et al, 2012 (17)	Review of high-quality systematic reviews and studies	2004–2011	27 reviews, 29 studies	Stratified by model of intervention (nurse-involved versus nurse-led and nurse training) All nurses (mainly NPs)	All	All; stratified by acute, community/primary care or long-term care	Mortality, morbidity, access, waiting time, QOL, hospitalizations, length of stay, ED visits, economics	Effect/cost reviews: 13 more/less; 6 more/same; 4 equal/less; 3 equal/equal; 1 more/more Effect/cost studies: 12 more/less; 2 more/equal; 7 equal/less; 5 equal/equal; 3 equal/more	Mixture of settings, conditions, and type of nurses Very few primary care plus chronic disease studies
Newhouse et al, 2011 (18)	Systematic review of United States studies	1990–2008	69 studies (20 RCTs; 37 NPs, 11 clinical nurse specialists)	APNs (NPs, clinical nurse specialists, nurse midwives, nurse anesthetists)	All	All	Patient satisfaction, perceived health, functional status, disease-specific, ED visits, hospitalizations, length of stay, mortality	APNs provide effective and high-quality patient care in the United States	Mixed populations, setting and interventions Both observational and RCTs included
Laurant et al, 2009 (19)	Systematic review and meta-analysis	Up to 2002	16 studies (13 RCTs)	Substitution of doctors All types of nurses	All (4 in specific chronic conditions)	Primary care	Patient-level, process of care, resource utilization, direct and indirect costs	Nurses can produce as high quality care as primary care doctors and as good health outcomes	Mixed populations, mainly general primary care
Keleher et al, 2009 (20)	Systematic review	1966–2007	Substitution: 2 reviews, 7 RCTs Supplementation: 1 review 19 RCTs	Substitution and supplementation All types of nurses	All	Primary care (included community)	Mortality, QOL, compliance, knowledge, satisfaction, resource use	Nurses can provide effective care and achieve positive health outcomes for patients similar to doctors Nurses are effective in diverse range of roles Insufficient evidence about nurses roles and impact on patient outcomes	Mixed diseases, included community interventions, excluded NPs with autonomous assessment of patients or diabetes/respiratory nurses, included nurses solely providing education/coaching

Dennis et al, 2009 (21)	Systematic review (tally of positive outcome measures)	1999–2007	46 papers (30 RCTs); 21 studies of nurses	Substitution of GPs Nurses (all types) or pharmacists involved in the planning and delivery of continuous care	Adults aged 65 years and over living in the community	Community	Adherence to guidelines, patient service use, disease-specific measures, QOL, health status, patient satisfaction, functional status	Nurses can effectively provide disease management and/or health promotion for older people with chronic disease in primary care While there were improvements in patient outcomes, no reduction in health service use was evident It is important that health professional roles be complementary, otherwise they may duplicate tasks	Not all primary care studies, not all chronic diseases of interest; mixed interventions with specific nursing roles unclear
Horrocks et al, 2002 (22)	Systematic review and meta-analysis	1966–2001	23 observational, 11 RCTs	Substitution of physicians by NPs	All	Primary care	Satisfaction, process measures (length of visit, prescriptions, investigations, return consultations, referrals)	Increasing availability of NPs in primary care is likely to lead to high levels of patient satisfaction and high quality of care	Studies primarily in general primary care without chronic disease
Nurses for Specific Diseases									
Clark et al, 2011 (23)	Systematic review and meta-analysis	2002–2009	11 RCTs	Any intervention conducted by nurses compared to usual doctor-led care (primarily nurse-led clinics)	Hypertension and diabetes	Primary and secondary care	Blood pressure (absolute, changes, proportion reaching target and proportion taking meds)	Some evidence for improved blood pressure outcomes with nurse-led interventions; nurses require an algorithm to structure care; more work is needed	Combination of settings, interventions variable: education multiple providers, home care, lifestyle advice, group self-management
Allen et al, 2010 (24)	Systematic review	2000–2008	55 RCTs	Interventions with a major nursing component	CAD or heart failure	All	Reported all primary clinical outcome measures from each trial (outcomes not prespecified for review)	Most trials demonstrated a beneficial impact of nursing interventions for secondary prevention in CAD or heart failure; optimal combination of intervention components remains unknown	All settings; variable interventions (case management, medication management, education, counselling and support, clinics, home-based, telephone or technology-based)

Loveman et al, 2009 (25)	Systematic review	Up to 2002	6 studies (5 RCTs)	Diabetes specialist nurses (in addition to routine care)	Type 1 and 2 diabetes (3 RCTs in type 2)	Hospital, community, home (mixed)	HbA1c; ED visits, hospitalizations, QOL	Diabetes specialist nurse/nurse case manager may improve diabetes control over short time periods, but effects over longer periods not evident. No significant differences in glycemic episodes, hospitalizations or QOL	Type 1 and 2 diabetes; all settings; among studies of nurses in primary care for type 2 diabetes mainly provided telephone follow-up
McHugh et al, 2009 (26)	Narrative systematic review	1999–2009	6 systematic reviews, 9 empirical studies (5 RCTs)	Specialist community nurses (specialist training within community and primary care)	COPD and musculoskeletal conditions	Community and primary care	Patient outcomes	In patients with COPD, there was evidence of effectiveness of some interventions carried out by nurses, particularly in relation to hospital at home/early discharge roles. Findings were mixed for case management or programs to promote self-care	Not all primary care; COPD studies primarily of nurses providing in-home or phone care, discharge planning, case management or care coordination
Jonsdottir et al, 2007 (27)	Integrated review	1996–2006	16 studies (11 RCTs or reviews of RCTs)	Nursing care in clinics for COPD	COPD	Community, outpatient, and primary care	Not prespecified	Nurse clinics for COPD is in its infancy, more research needed	Primarily home care, telephone calls, education, or self-management
Taylor et al, 2005 (28)	Systematic review	1980–2005	9 RCTs	Interventions for chronic disease management, led, coordinated or delivered by nurses	COPD	Inpatient, outpatient, or community	QOL, exacerbations, pulmonary function, mortality, ED visits, outpatient visits, knowledge, readmission, symptoms	Little evidence to support the implementation of nurse led management interventions for COPD, but data too sparse to exclude benefit or harm	Primarily nurse case managers with discharge planning, home care or self-management/ education programs
Halcomb et al, 2004 (29)	Descriptive systematic review	1980–2004	16 RCTs	Role of practice nurses in HF management	Heart failure	Community	No synthesis of results, general summary of findings	Practice nurses represent a potentially useful adjunct to current models of service provision in heart failure management	Most nurses providing telephone or home care, care coordination or discharge planning

Abbreviations: APN, advance practice nurse; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ED, emergency department; GP, general practitioner; HbA1c, hemoglobin A1c; NP, nurse practitioner; QOL, quality of life; RCT, randomized controlled trial.

Appendix 3: Summary of Included Studies

Table A2: Summary of Included Studies

Author, Year	Population	Setting	Patient Selection	Inclusion	Exclusion	Randomization	Average Baseline Characteristics	Data Collection/Measurements
Houweling et al, 2011 (13)	Type 2 diabetes	5 GPs from group practice in 1 region of the Netherlands	GPs patient information system and local pharmacy	Diagnosis of diabetes, medication for diabetes, HbA1c measured in last 3 years	No diagnosis of diabetes, type 1 diabetes, not treated in primary care, inability to participate, not willing to return for follow-up	Independent medical investigators Non-transparent, closed envelopes Sequential numbers (even and odd randomized)	Male, 48%; age, 68 years; diabetes duration, 7.5 years; HbA1c, 7.5%; systolic blood pressure/diastolic blood pressure, 159/87 mm Hg; total cholesterol, 5.4 mmol/L; BMI, 30 kg/m ² ; feet at risk, 56%	All measures taken prior to randomization and 14 months QOL: SF-36, Patients' Evaluation of the Quality of Diabetes Care Visits: practice nurse kept records for intervention group, patient questioned for GP Process measures: not stated
Khunti et al, 2007 (14)	CAD/CHF	20 volunteer primary care practices (53 GPs) in 1 region of United Kingdom	Practice databases using disease registers and medication searches	Diagnosis of coronary heart disease (angina or past MI) or CHF was recorded or suggested by medications	None	Computer-generated case-control pairs (list size, number GPs, Jarman score, teaching status) randomly allocated nurses to practices Patients enrolled after	Male, 53%; age, 70.5 years; prior MI, 42%; mean years since MI, 8.9; angina, 87.5%; presumed HF, 31%; diabetes, 20%; peripheral vascular disease, 7.5%; hypertension, 53%	Process of care: general practice records QOL: SF-36 and Left Ventricular Dysfunction 36
Laurant et al, 2004 (16)	Chronic disease	Volunteer local groups and GPs in Netherlands	No patient selection (only GPs) 7 of 21 local groups volunteered to participate	None	None	Grouped local groups into matched pairs using deprivation of population and rurality Independent researchers randomly assigned 1 group from each pair with sealed opaque envelopes	No patient-level data; physician characteristics	Objective workload: 28-day diary Subjective workload: questionnaire
Litaker et al, 2003 (15)	Type 2 diabetes and hypertension	Department of general internal medicine in Ohio, United States	Direct physician referrals or advertisements within the institution	Type 2 diabetes and mild to moderate hypertension, received primary care at study site, resident of Cleveland	None	Randomly allocated	Female, 58%; age 61 years; African-American, 59% HbA1c, 8.4%; total cholesterol, 5.5 mmol/L; blood pressure < 130/85 mm Hg, 9%; comorbid conditions, 1; Charlson comorbidity, 3.1	Process indicators from patient medical records QOL: SF-12, Diabetes Quality of Life Questionnaire Satisfaction: patient satisfaction questionnaire Clinical outcomes: measured at baseline and 12 months

Munding et al, 2000 (11)	General primary care (>50% chronic disease)	4 community-based primary care clinics (17 GPs) and 1 academic centre clinic (7 NPs)	Consecutive recruitment at ED/urgent care; prior diagnosis of asthma/diabetes/hypertension oversampled	No current primary care provider at the time of recruitment and planned to be in area for next 6 months	None	Randomly and blindly assigned in 2:1 ratio; later 1:1 ratio	Male, 25.5%; age, 44.5 years; 1 or more chronic disease listed, 51%; ethnicity, 88% Hispanic, 9.3% black, 1.1% white	Recruitment: SF-36 and patient demographics Satisfaction: telephone satisfaction questionnaire 6 month interview: SF-36, satisfaction Physiologic measures: taken by nurse Utilization data: medical system
Lenz et al, 2002 (Mundinger subgroup) (12)	Type 2 diabetes	As above	As above; subgroup self-reported type 2 diabetes	As above	As above	As above	Male 33.8%; age, 54.8 years; hypertension, > 50%; ethnicity, 91.5% Hispanic; Medicaid enrolled, 84.1	As above
Campbell et al, 1998 (9;10)	CAD	Randomly selected practices in Scotland	General practice case notes	Working diagnosis of coronary heart disease	Terminally ill, dementia, house-bound, or excluded at request of GP	Eligible patients stratified by age, sex, general practice, and randomized using tables of random numbers	Male, 58.4%; age, 66.1 years; prior MI, 45%; median years since MI, 5.5; angina, 50%; 1-year hospitalizations, 25%	QOL: SF-36, angina-type specification Hospitalizations: angina-type specification Clinical data: medial records Lifestyle factors: postal questionnaire

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; ED, emergency department; GP, general practitioner; QOL, quality of life; MI, myocardial infarction; SF-36, Short Form (36) Health Survey.

Appendix 4: GRADE Tables

Table A3: GRADE Evidence Profile for Comparison of Specialized Nurses and Physicians (Model 1)

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality
Hospitalizations, Chronic Disease						
1 (RCT)	Serious limitations (–1) ^a	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Hospitalizations, Diabetes Subgroup						
1 (RCT)	Very serious limitations (–2) ^b	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low
ED Visits, Chronic Disease						
1 (RCT)	Serious limitations (–1)	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
ED Visits, Diabetes Subgroup						
1 (RCT)	Very serious limitations (–2) ^b	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low
Specialist/Outpatient Visits, Chronic Disease						
1 (RCT)	Serious limitations (–1) ^a	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Specialist/Outpatient Visits, Diabetes Subgroup						
1 (RCT)	Very serious limitations (–2) ^b	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low
Primary Care Visits, Chronic Disease						
1 (RCT)	Serious limitations (–1) ^a	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Primary Care Visits, Diabetes Subgroup						
1 (RCT)	Very serious limitations (–2) ^b	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low
Health-Related Quality of Life, Chronic						
1 (RCT)	Very serious limitations (–2) ^b	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
HbA1c, Diabetes Subgroup						
1 (RCT)	Very serious limitations (–2) ^{bde}	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low
Process Measures (Education, History, and Examinations)						
1 (RCT)	Very serious limitations (–2) ^{bde}	No serious limitations	No serious limitations	Serious limitations (–1) ^c	Undetected	⊕ Very Low

Abbreviations: ED, emergency department; No., number; RCT, randomized controlled trial.

^aLarge and unbalanced loss to follow-up between arms; patients not enrolled in the study differed significantly from enrolled patients.

^bResults from a single subgroup analysis based on patient self-report of diabetes at baseline; major loss to follow-up with no intention-to-treat or comparison of patients who were enrolled and not enrolled.

^cLow event rates and study does not meet optimal information size and therefore is likely underpowered.

^dOnly final HbA1c measured; no baseline measurement.

^eLack of blinding of nurses and physicians to enrolled patients may bias the recording of process measures.

Table A4: GRADE Evidence Profile for Comparison of Specialized Nurses + Physicians and Physicians (Model 2)—Health Resource Utilization and Disease-Specific Measures

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality
Hospitalizations						
1 (RCT), CAD	Very serious limitations (–2) ^{ab}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Hospital Length of Stay						
1 (RCT), CAD	Very serious limitations (–2) ^{ab}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Number of Visits						
1 (RCT), diabetes	Very serious limitations (–2) ^{cd}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Mean Change in HbA1c						
1 (RCT), diabetes	Serious limitations (–1) ^e	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
HbA1c Below Threshold						
1 (RCT), diabetes	Serious limitations (–1) ^c	No serious limitations	No serious limitations	Serious limitations (–1) ^f	Undetected	⊕⊕ Low
Blood Pressure Below Threshold						
2 (RCTs), diabetes	Serious limitations (–1) ^{ec}	No serious limitations	No serious limitations	Serious limitations (–1) ^f	Undetected	⊕⊕ Low
1 (RCT), CAD	Serious limitations (–1) ^h	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Lipids Below Threshold						
1 (RCT), diabetes	Serious limitations (–1) ^c	No serious limitations	No serious limitations	Serious limitations (–1) ^f	Undetected	⊕⊕ Low
1 (RCT), CAD	Serious limitations (–1) ^e	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Lifestyle Control						
1 (RCT), exercise, CAD	Very serious limitations (–2) ^{ag}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
1 (RCT), low-fat diet, CAD	Very serious limitations (–2) ^{ag}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
1 (RCT), not smoking, CAD	Very serious limitations (–2) ^{ag}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Health-Related Quality of Life						
2 (RCTs), SF-36/SF-12, diabetes	Serious limitations (–1) ^{ce}	Serious limitations (–1)	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
2 (RCTs), SF-36, CAD	Serious limitations (–1) ^{ah}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate

1 (RCT), diabetes-specific	Serious limitations (-1) ^e	No serious limitations	No serious limitations	Serious limitations (-1) ^f	Undetected	⊕⊕ Low
2 (RCTs), CAD- specific	Serious limitations (-1) ^{ah}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Patient Satisfaction						
1 (RCT), diabetes	Serious limitations (-1) ^c	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate

Abbreviations: CAD, coronary artery disease; RCT, randomized controlled trial; SF-36, Short Form (36), Health Survey.

^aNo blinding and unknown allocation concealment; potential contamination with same nurses and physicians in both arms.

^bHospitalizations assessed based on patient self-report from health-related quality of life instrument.

^cNo blinding and no intention-to-treat analysis conducted.

^dNumber of visits based on patient self-report in physician arm and nurse report in other.

^eNo allocation concealment and blinding not stated; potential contamination as physicians had patients in both arms of the study.

^fStudy was not powered to look at this outcome.

^gLifestyle control based on patient questionnaire which is likely biased.

^hKhunti, general: potential recruitment bias as patients recruited by physician *after* cluster randomization; a large proportion of patients were already meeting appropriate disease-specific control and thresholds at baseline.

Table A5: GRADE Evidence Profile for Comparison of Specialized Nurses + Physicians and Physicians (Model 2)—Process Measures

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality
Blood Pressure Management						
1 (RCT), CAD	Serious limitations (-1) ^a	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Cholesterol Management						
1 (RCT), CAD	Serious limitations (-1) ^a	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Foot Exams						
2 (RCTs), diabetes	Serious limitations (-1) ^{bc}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Ophthalmologist Referral						
2 (RCTs), diabetes	Serious limitations (-1) ^{bc}	Serious limitations (-1)	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Clinical Examinations (Blood Pressure, cholesterol, BMI, smoking, echocardiography)						
1 (RCT), CAD	Serious limitations (-1) ^d	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Medication Management (Appropriate glucose lowering therapy, insulin referral, Blood Pressure medication, lipid medication)						
1 (RCT), diabetes	Serious limitations (-1) ^{bc}	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Medication Management (Vaccinations)						
1 (RCT), diabetes	Serious limitations (-1) ^d	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Medication Management (Cardiac Medications)						
1 (RCT), CAD	Serious limitations (-1) ^d	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕⊕ Moderate
Medication Management (Aspirin)						
2 RCTs - CAD	Serious limitations (-1) ^{ad}	Serious limitations (-1)	No serious limitations	No serious limitations	Undetected	⊕⊕ Low

Abbreviations: CAD, coronary artery disease; RCT, randomized controlled trial.

^aNo blinding and unknown allocation concealment; potential contamination with same nurses and physicians in both arms.

^bNo allocation concealment and blinding not stated; potential contamination as physicians had patients in both arms of the study.

^cNo intention-to-treat analysis conducted; more patients with feet at risk or foot issues at baseline.

^d Potential recruitment bias as patients recruited by physician after cluster randomization.

Table A6: GRADE Evidence Profile for Comparison of Specialized Nurses + Physicians and Physicians (Model 2)—Efficiency Measures

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality
Objective Workload						
CAD	Serious limitations (-1) ^a	No serious limitations	No serious limitations	Serious limitations (-1) ^b	Undetected	⊕⊕ Low
Chronic disease	Very serious limitations (-2) ^b	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low
Subjective Workload						
Chronic disease	Very serious limitations (-2) ^b	No serious limitations	No serious limitations	No serious limitations	Undetected	⊕⊕ Low

Abbreviation: CAD, coronary artery disease.

^aUnknown allocation concealment; potential contamination with the same nurses and physicians in both arms.

^bVery small event rate, study was not powered to look at workload and unclear how this was measured.

^cUnbalanced response rates between groups; use of an unvalidated diary to assess workload; potential variations between practices in relation to the role of the nurse.

Table A7: Risk of Bias for All Included Studies

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Houweling et al, 2011 (13)	No limitations	Limitations ^a	Limitations ^b	No limitations	Limitations ^c
Khunti et al, 2007 (14)	No limitations	Limitations ^a	No limitations	No limitations	Limitations ^d
Laurant et al, 2004 (16)	No limitations	Limitations ^a	Limitations ^e	No limitations	Limitations ^f
Litaker et al, 2003 (15)	Limitations ^g	Limitations ^h	No limitations	No limitations ⁱ	Limitations ^j
Mundinger et al, 2000 (11)	No limitations	Limitations ^k	No limitations ^l	No limitations	No Limitations
Lenz et al, 2002 (12) (subgroup of Mundinger)	No limitations	Limitations ^k	Limitations ^m	No limitations	Serious Limitations ⁿ
Campbell et al, 1998 (9;10)	Limitations ^g	Limitations ^h	No limitations	No limitations	Limitations ^o

^aNot feasible to blind physicians, nurses or patients, however assessors were not stated as being blinded. Downgraded for subjective outcomes.

^b10.4% loss to follow-up, with no intention-to-treat analysis conducted.

^cUnbalanced number of patients with feet at risk at baseline, may effect process measures and health-related quality of life; number and length of visits based on patient self-report for the physician arm and average length of visit was applied whereas nurses reported length of visits in nursing arm.

^dPotential recruitment bias as patients recruited by physician *after* cluster randomization.

^eUnbalanced in nonresponse rates of physicians, with no intention-to-treat analysis conducted.

^f Use of unvalidated diary to assess objective workload; number of patients with chronic disease in practices not reported and number of NP visits with patients not reported; physicians responsible for choosing which patients the nurse practitioner sees and the specific role of the nurse practitioner in the practice.

^gAllocation concealment not stated.

^hNot feasible to blind physicians, nurses or patients; however assessors were appropriately blinded to patients. Downgraded for subjective outcomes.

ⁱNumber of visits to emergency departments and outside providers was stated as being assessed, but results not reported; and selective reporting of estimates, confidence intervals and *P*-values; however, not downgraded as bias could not be confirmed.

^jPotential contamination as physicians had patients in both arms of the study; powered to look at costs rather than outcomes.

^kPatients and providers not blinded, but it was stated that no attempt was made to differentiate study patients in practice. Downgraded for subjective outcomes.

^lSignificant loss to follow-up, however subgroup analyses were stated as being conducted among all patients with data and intention-to-treat conducted on all health resource utilization outcomes.

^mNo intention-to-treat analysis stated, unclear if same methods as Mundinger were used.

ⁿChronic disease based on patient self-report of disease at baseline; 6-month follow-up is likely limited to see an improved difference; study not powered to look at subgroup analysis.

^oPotential contamination by presence of intervention in control group practices; self-reported behavioural practices, hospitalizations based on patient self-report from angina health-related quality of life questionnaire.

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