National Institute for Health and Care Excellence

Final

Chapter 20 Physician extenders

Emergency and acute medical care in over 16s: service delivery and organisation

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Chapter 20 Physician extenders

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20 Physician Extenders

20.1 Introduction

The term 'Physician Extenders' is used to incorporate a wide range of professions working in roles that would have traditionally been seen as the role of a doctor. The roles include Advanced Nurse Practitioners, Physician Associates and Advanced Clinical Practitioners who may be Physiotherapists and Paramedics with extended training.

Given the increasing pressures within the NHS from an aging population and a lack of front-line health care professionals, it was felt that these roles needed to be further evaluated in order to determine if they – either individually or in combination – could help to alleviate some of this pressure and support the medical workforce.

Some of the roles under the umbrella term 'Physician Extender', such as Advanced Nurse Practitioners, are well established in the UK health service and often provide specialist services, for example, the role of the Diabetes Specialist Nurse or Heart Failure Specialist Nurse; much fewer numbers are working in a generalist setting in secondary care. Other roles, such as Physician Associates, are new to the UK, currently with small numbers which makes it challenging to produce robust evidence to assess the role.

20.2 Review question: Do physician extenders (for example, physician assistants and emergency nurse practitioners) improve outcomes in secondary care?

For full details see review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Adults and young people (16 years and over) at risk of an AME, or with a suspected or confirmed AME

Intervention	Intervention to be stratified by physician extender and specialist nurse
	• Physician extenders in addition to usual care. Roles include:
	  ○ Emergency Nurse Practitioners
	  ○ Advanced Nurse Practitioners
	  ○ Advanced Care Practitioners
	  ○ Physician Assistants/Physician Associates
	  ○ Critical Care Practitioners
	  ○ Critical Care Outreach Nurses
	  ○ Independent prescribing pharmacists
	• Specialist nurse in addition to usual care. Roles include:
	  ○ Diabetes Inpatient Specialist Nurses
	  ○ Heart Failure Specialist Nurses

Comparison	No Physician extenders or specialist nurse Usual care (for example, junior doctors, nurses)
Outcomes	• Mortality (CRITICAL) • Avoidable adverse events (CRITICAL) • Quality of life (CRITICAL) • Patient and/or carer satisfaction (CRITICAL)

	• Length of stay (CRITICAL) • Readmission up to 30 days (IMPORTANT) • Missed or delayed treatments (IMPORTANT) • Staff satisfaction (IMPORTANT)
Study design	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.

20.3 Clinical evidence

We included 4 studies in the physician extender strata,[51,81,163,178] and 2 studies in the specialist nurse strata.[12,55] These are summarised respectively in Table 2 and Table 3 below. Evidence from these studies is summarised in the GRADE clinical evidence summary below (Table 4 and Table 5). See also the study selection flow chart in Appendix B, study evidence tables in Appendix D, forest plots in Appendix C, GRADE tables in Appendix F and excluded studies list in Appendix G.

Table 2: Summary of studies included in the review for the strata physician extender

Study	Intervention and comparison	Population	Outcomes	Comments
Cowan 2006[51] Quasi-RCT USA	Intervention (n=581) Presence of a Nurse Practitioner whose primary role were the following: case management, facilitation of communication and collaboration with physicians and nurses, leading and actively implementing timely processes after the daily multidisciplinary rounds, surveillance of cost-effective measures, twice-daily assessments of cultures for sensitivity with the goal of changing the antibiotic regimen to the narrowest spectrum, review of all medications for drug/drug interactions and side effects, changing intravenous medications to oral, and enforcement of disease-specific care pathways. Continuous care for patients for 8 hours per day. Concurrent medication or care: Increase in multi-disciplinary rounds from weekly to daily (with the NP taking part in the rounds); appointment of a (hospitalist) medical director who was in charge of overseeing NP and physicians. There was 1 medical director for the first 9 months of the study and (assumed) 2 for the final duration. Comparison (n=626) Usual care: Multi-disciplinary rounds once a week. No NP. No further details.	(n=1207) patients admitted to the general medical floor of a tertiary academic medical hospital Inclusion: unclear Exclusion: sickle cell anaemia	Length of stay; in-hospital mortality.	Intervention was a combination of 3 elements: Nurse Practitioner on team; increase in ward rounds; presence of a medical director. Quasi-randomised by intake day. Physicians and RN were randomised into teams and rotated between the 2 groups. Declined to participant on intervention ward intake received NP care.

Study	Intervention and comparison	Population	Outcomes	Comments
Forster 2005[81] RCT Canada	Intervention (n=307) Presence of clinical nurse specialist (nurse team co-ordinator). Role of the nurse was as a team co-coordinator and whose in-hospital role was to facilitate hospital care by retrieving preadmission information, arranging in-hospital consolations and intervention, and organising post discharge follow-up. Comparison (n=313) Usual care	(n=620) consecutive patients admitted from the ED or another service to the general medical service of at 2 sites of tertiary care teaching hospital. Inclusion: All admissions Exclusion: None	Length of stay; in-hospital mortality	Also includes post-discharge outcomes, but intervention also included post-discharge follow-up so these are not included.
Moher 1992[163] RCT Conducted in Canada	Intervention (n=136) Presence of clinical nurse specialist (nurse team co-ordinator). Role is to participate in ward rounds, collaborate with health care professionals, facilitate administrative tasks such as discharge planning, coordinate tests and procedures, and to collect and collate patient information. Comparison (n=131) Usual care without the nurse team co-ordinator	(n=267) patients admitted to general Clinical Teaching Units at a university teaching hospital/ Inclusion: All admissions Exclusion: death expected within 48 hours, those admitted directly to ICU.	Length of stay; in-hospital mortality; readmissions (unknown follow-up); patient and/or carer satisfaction.	
Pioro 2001[178] RCT USA	Intervention (n=193) Nurse practitioner based care. Nurse practitioner's role admission assessment, assembly of patient data, co-ordination of care with patient's attending doctors and implementation of diagnostic and therapeutic plans. NPs were on weekdays 0730 to 2000 and on weekends for morning rounds. NPs were supervised by a medical director who made daily rounds. Comparison (n=188) Usual care by traditional house staff (6 teams consisting of 1 senior or junior medical resident and 2 interns supervised by a teaching attending doctor.	(n=381) patients admitted through out-patient facilities or the emergency room at university hospital. Inclusion: age 18-69. Exclusion: admitted to intensive care or other specialty units and those transferred from the intensive care. For first 5 months patients outside of core admitting times were excluded (not weekdays 0730 to 1700). Rest of duration (~ 1 year) all weekday admissions were included.	Length of stay; in-hospital adverse events; in-hospital mortality; 30 day mortality; quality of life (SF-36 – general health); patient and/or carer satisfaction.	Large asymmetric cross-over of patients: 90/193 crossed over from intervention to control Reasons for cross-over: bed availability (29%), doctor request (22%), NP request (22%), and other (28%). Teams rotated on a monthly basis.

Table 3: Summary of studies included in the review for the strata specialist nurse

Study	Intervention and comparison	Population	Outcomes	Comments
Arts 2012[12] RCT Netherlands	Registered Nurse specialists with extensive experience in diabetes care (Advanced practice nurses). Participants received care from advanced nurse practitioners (Doctoral or Master's prepared registered nurses) who worked according to a protocol (no further details on protocol). Control group: usual care (5 physicians).	People with diabetes mellitus types 1 and 2 treated by an Internist in an academic hospital in Maastricht, the Netherlands.	Mortality; adverse events (diabetes-related complications); quality of life.	
Davies 2001[55] RCT UK	Intervention (n=148) Presence of 1 of 4 diabetes specialist nurse. DSN care included individual structures patient education appropriate to need, and practical management advice including verbal and written case-note feedback to ward-based medical staff. DSN input began on the day of referral and randomisation, and continued until discharge. Comparison (n=152) Usual care without any input from the DSN.	(n=300) sequential, unselected referrals of in-patients to the DSN service (with either type 1 or type 2 diabetes) to a university hospital. Exclusion: patients unable to complete self-reported questionnaire were selectively excluded from that outcome. Reasons for exclusion include: visually impaired, non-English, confused, or had reduced consciousness.	Length of stay; frequency of admission (12 months); patient and/or carer satisfaction; disease specific quality of life; mortality.	If declined to participate patients received DSN input.

Table 4: Clinical evidence summary: Physician extender versus no physician extender or usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Physician extender versus no physician extender/usual care (95% CI)
Adverse events	709 (2 studies) In-hospital to 34 days follow-up	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.90 (0.64 to 1.28)	Moderate	
				157 per 1000	16 fewer per 1000 (from 57 fewer to 44 more)
Length of stay	1474 (2 studies)	⊕⊕⊖⊖ LOW[a] due to risk of bias	-	The mean length of stay in the control groups was 6.47 days	The mean length of stay in the intervention groups was 1.14 lower (1.83 to 0.45 lower)
Mortality	2475 (4 studies) in hospital to up to 4 months follow-up	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.15 (0.88 to 1.51)	Moderate	
				71 per 1000	11 more per 1000 (from 9 fewer to 36 more)
Satisfaction	290 (1 study) 34 days	⊕⊕⊖⊖ LOW[a] due to risk of bias	-	The mean satisfaction in the control group was 7.6	The mean satisfaction in the intervention groups was 0.6 higher (0.07 to 1.13 higher)
Readmission	1774 (2 studies) 2 weeks to 4 months	⊕⊕⊖⊖ LOW[a] due to risk of bias	RR 1.02 (0.87 to 1.2)	Moderate	
				225 per 1000	4 more per 1000 (from 30 fewer to 45 more)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Narrative findings

Median (IQR) length of stay: Intervention: 6 (3-11) days; Control: 5 (3-10) days, (Forster 2005).

Length of stay during index admission (no SDs reported): Intervention: 5.0 days; Control: 5.3 days, (Pioro 2001).

Mean change in SF-36 at 6 weeks post discharge (no SDs reported): Intervention: 4.7; Control: 2.9, (Pioro 2001).

Table 5: Clinical evidence summary: Specialist nurse versus no specialist nurse or usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Specialist nurse versus no physician extender/usual care (95% CI)
Adverse events	294 (1 studies) 2 year follow-up	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 0.57 (0.27 to 1.21)	Moderate	
				117 per 1000	50 fewer per 1000 (from 85 fewer to 25 more)
Mortality	592 (2 studies) Mortality at 1 year or 2 year follow-up	⊕⊖⊖⊖ VERY LOW[a,b,c] due to risk of bias, imprecision, inconsistency	RR 0.93 (0.42 to 2.07)	Moderate	
				40 per 1000	3 fewer per 1000 (from 23 fewer to 43 more)
Satisfied patients	133 (1 study) 1 week	⊕⊕⊖⊖ LOW[a] due to risk of bias	RR 1.54 (1.24 to 1.91)	Moderate	
				591 per 1000	319 more per 1000 (from 142 more to 538 more)
Readmission	300 (1 studies) at 12 months	⊕⊕⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	RR 1.00 (0.68 to 1.48)	Moderate	
				250 per 1000	0 more per 1000 (from 80 fewer to 120 more)

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
(c) Downgraded by 1 increment because the point estimate varies widely across studies, unexplained by subgroup analysis.

Narrative findings

Median (IQR) length of stay – Intervention: 8 days; Control: 11 days, p<0.01 (Davies 2001).

Audit of Diabetes Dependent Quality of Life (ADDQoL) final score at 1 week after discharge (no details of scale used): Intervention: 0.88; Control: 0.40 (Davies 2001).

Mean EQ-5D quality of life (SD): Intervention: 0.86 (0.22) at baseline and 0.80 at 2 years; Control: 0.82 (0.22) at baseline and 0.82 at 2 years (Arts 2012.)

20.4 Economic evidence

Published literature

No economic evaluations were identified for the first stratum (physician extenders). One economic evaluation was identified with the relevant comparison for the second stratum (specialist nurses) and has been included in this review.[12] This is summarised in the economic evidence profile below (**Error! eference source not found.**) and the economic evidence tables in Appendix E. One study was excluded on the grounds of applicability and another study was selectively excluded – see Appendix H.

The economic article selection protocol and flow chart for the whole guideline can found in Appendix 41A and Appendix 41B.

Table 6: Economic evidence profile: Specialist nurse versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Arts 2012[12] ([Netherlands]	Partially applicable (a)	Potentially serious limitations (b)	• Within RCT analysis • Population: People with diabetes mellitus type 1 and 2 who are treated by an internist in an academic hospital in Maastricht, the Netherlands. • Comparators: diabetes nurse specialists (DNS) versus physicians • Follow-up: 2 years	2 versus 1: £309	2 versus 1: -0.02 QALYs	DNS dominated	Differences in costs and QALYs were not significant. No sensitivity analysis is reported.

Abbreviations: DNS: diabetes nurse specialist ICER: incremental cost-effectiveness ratio; N/A: not applicable; QALY: quality-adjusted life years; RCT: randomised controlled trial.
(a) Some uncertainty regarding the applicability of resource use and costs from the Netherlands (2007) to current NHS context. No discounting reported.

Baseline and relative treatment effects are based on a single RCT, so by definition, does not reflect all evidence in the area. Costs of medications, investigations and other staff groups' time are not included. No sensitivity analysis is reported.

20.5 Evidence statements

Clinical

Physician Extenders

- Four studies comprising 2475 people evaluated the role of physician extenders for improving outcomes in secondary care in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that physician extenders may provide a benefit in reduced length of stay (2 studies, low quality), with a slight reduction in adverse events (2 studies, very low quality). However, the evidence for physician extenders suggested no difference on readmission (2 studies, low quality) or patient and/or carer satisfaction (1 study, low quality) compared to usual care and there was a possible increase in mortality (4 studies, very low quality).

Specialist nurses

- Two studies comprising 592 people evaluated the role of specialist nurses for improving outcomes in secondary care in adults and young people at risk of an AME, or with a suspected or confirmed AME. The evidence suggested that specialist nurses may provide a benefit in reduced adverse events (1 study, very low quality) and improved patient and/or carer satisfaction (1 study, low quality). However, the evidence for specialist nurses suggested no difference to mortality (2 studies, very low quality) or readmission (1 study, very low quality) compared to usual care.

Economic

- One cost utility analysis showed that specialist nurse care was dominated by usual care being more costly (mean £309 per patient) and less effective (0.02 QALYs lost per patient).

20.6 Recommendations and link to evidence

Recommendations	-
Research recommendations	**RR11. What is the clinical and cost effectiveness of providing 'physician extenders' such as advanced nurse practitioners, 'physician associates' and advance clinical practitioners in secondary care?**

Relative values of different outcomes	Mortality, quality of life, length of stay, avoidable adverse events and patient and/or carer satisfaction were considered by the guideline committee to be critical outcomes.
	Readmission, discharges, missed or delayed treatments, and staff satisfaction were considered important outcomes.
	
	The review specifically examined evidence for the effectiveness of:
	• Physician extenders:
	  ○ Emergency Nurse Practitioners
	  ○ Advanced Nurse Practitioners
	  ○ Advanced Care Practitioners
	  ○ Physician Assistants or Physician Associates
	  ○ Critical Care Practitioners
	  ○ Critical Care Outreach Nurses
	  ○ Independent prescribing pharmacists.
	• Specialist nurse:
	  ○ Diabetes in patient specialist nurses
	  ○ Heart failure specialist nurses.

Trade-off between clinical benefits and harms	A total of 6 studies were identified for this review. Four of these studies were in the physician extender strata and 2 studies were assessed in the specialist nurses strata. The 2 including specialist nurses studies were both diabetes specialist nurses as there was a lack of evidence on other specialist nurses such as COPD nurses and oncology nurses. Studies with surgical practitioners were excluded from this review as our remit was limited to medical emergencies. The evidence suggested that physician extenders may provide a benefit in reduced length of stay and patient and/or carer satisfaction. However, the evidence suggested no difference on readmission rates (from 2 weeks to 4 months) or patient and/or carer satisfaction compared to usual care. A possible trend towards fewer adverse events was counterbalanced by a possible increase in mortality. Quality of life was identified only as narrative findings, whilst no evidence was identified for missed or delayed treatments, and staff satisfaction. Evidence from diabetes inpatient specialist nurses may provide a benefit in reduced adverse events and improved patient and/or care satisfaction. The evidence suggested no difference to mortality or readmission at 12 months. Quality of life was identified only as narrative findings, whilst no evidence was identified for length of stay, readmission within 30 days missed or delayed treatments, and staff satisfaction. Although there are several types of physician extender, randomised control trials have only evaluated diabetes specialist nurses, nurse care co-ordinators and nurse practitioners focused on pathway management and improving compliance with best practice. The committee noted the difficulty in making a recommendation without having a broad spectrum of evidence available, as the applicability to the UK system is unclear. The committee noted in particular that there were no RCTs of physician

Recommendations	-
Research recommendations	**RR11. What is the clinical and cost effectiveness of providing 'physician extenders' such as advanced nurse practitioners, 'physician associates' and advance clinical practitioners in secondary care?**
	associates or assistants, which is a new profession within the UK and the area in which a recommendation would have a significant impact. Therefore, the committee considered a research recommendation would be appropriate.
Trade-off between net effects and costs	One economic evaluation of diabetes nurse specialists was included. It showed an increase in cost and a decrement in quality of life, which almost reached statistical significance. Another study[180] showed that a diabetes specialist nurse service added to standard care was associated with a substantial cost saving of £436 per admission compared to standard care alone. This was excluded because of the date of the costs, 2003, and because it did not evaluate health outcomes but it is suggestive that in the right form and setting, these specialists could be cost saving. No evidence was identified for any of the other categories of physician extenders in secondary care. There is some evidence that physician extenders as part of a multi-disciplinary team can be cost saving and clinically effective in primary care.[212] The committee considered that the rationale behind physician extenders is to provide equivalent (or better) care at lower staff cost. Given the limited evidence across the whole spectrum of physician extenders, the committee felt that there was a need for more research of high quality into this area to inform policy decisions on whether physician extenders should be adopted on a large scale.
Quality of evidence	Clinical evidence: The physician extender strata included 4 studies: 3 RCTs and 1 quasi-randomised study. All evidence was graded at very low or low quality and evidence was of very high risk of bias, whilst adverse events and mortality were additionally downgraded for imprecision. Two of the trials randomised patients to physician-based care with or without physician extenders; the others randomised patients to either physician-based care or physician extenders. The specialist nurse strata included 2 RCTs. All evidence was graded at very low as all evidence was of very high risk of bias and had high imprecision, whilst mortality was further downgraded for inconsistency. Both trials randomised patients to either physician-based care or specialist nurse care. Economic evidence: The study was assessed to be partially applicable since resource use and costs were from a Netherlands perspective. It was assessed as having potentially serious limitations in that baseline and relative treatment effects are based on a single RCT and costs of medications, investigations and other staff time were not included. Due to the lack of high quality evidence applicable to the UK, the committee decided to make a recommendation for further research.
Other considerations	The committee discussed the contradictory evidence between the economic and clinical evidence, and its applicability to the UK setting. They noted that there may be logistical reasons why a physician extender would be more cost-saving than indicated by the economic evidence identified within this review; for example, they may cover staff shortages, so fewer locums are required, or permit consultant staff to be deployed more effectively on ward rounds or in clinics. The committee did not interpret the clinical evidence as showing that physician extenders had worse clinical

Recommendations	**-**
Research recommendations	**RR11. What is the clinical and cost effectiveness of providing 'physician extenders' such as advanced nurse practitioners, 'physician associates' and advance clinical practitioners in secondary care?**
	outcomes. The committee noted that the workforce planning has left England with insufficient numbers of doctors both in primary and secondary care. Even if an expansion in the number of medical student posts occurred there will be a lag time of more than 5 years to realise the benefit. The training of physician extenders is likely to be shorter (particularly in the case of nurse specialists who focus on a specific disease process rather than act as generalists) and could be used to plug these gaps. The committee noted, with the increasing elderly population, there will be an ever increasing need of staff to manage the demand so increasing the numbers of physician extenders and also increasing medical student places is mutually compatible. The committee had extensive experience of working with all types of physician extenders and anecdotally had found them to be a very positive role within the NHS, however, the evidence as it stood was not sufficient to provide a positive recommendation, despite this. The committee noted that, as a relatively new and diverse group of healthcare professionals in the UK, the role of the physician associate or assistants would be expected to be evaluated in line with the Health Education England Strategic Framework 15-year strategy, supporting the need for a research recommendation. The committee noted that, in the USA, nurse practitioners and physician associates are both post-graduate level, but the training requirements are different. In the UK currently, the Royal College of Nursing position is that any nurse who has been educationally prepared, whether at BSc or MSc level, against the Royal College of Nursing competences, is entitled to be referred to as an Advanced Nurse Practitioner. The training requirement to become a registered physician associate is a post-graduate diploma. Physician extenders with a technical background (non-nursing) cannot, at present, acquire prescribing rights. The committee discussed the need for an evaluation of these professions using randomised controlled trial methodologies to generate more secure evidence, using either parallel cluster or stepped wedge designs. Researchers would need to clarify whether the practitioners were deployed as adjuncts to, or substitutes for, doctors. A trial assessing the contribution of physician associates based in secondary care is ongoing and is due to publish in 2018.[5]

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Appendices

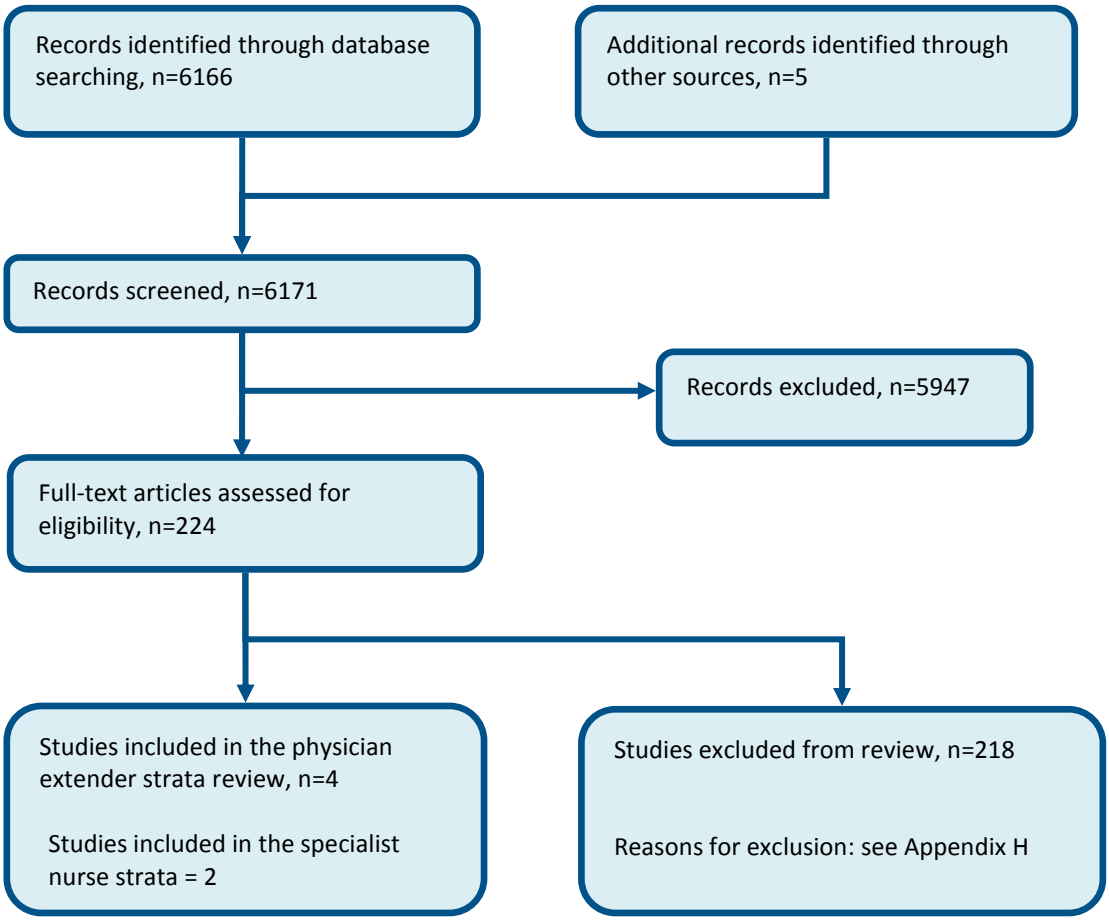
Appendix A: Review protocols

Table 7: Review protocol: physician extenders

Review question	Do physician extenders (for example, physician assistants, and emergency nurse practitioners) improve outcomes in secondary care?
Guideline condition and its definition	Acute medical emergencies. Definition: People with suspected or confirmed acute medical emergencies or at risk of an acute medical emergency
Review population	Adults and young people (16 years and over) at risk of an AME, or with a suspected or confirmed AME
	Adults and young people (16 years and over)
	Line of therapy not an inclusion criterion
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Physician extender in addition to usual care Specialist nurse in addition to usual care No Physician extenders/usual care; No Physician extenders/usual care (for example, junior doctors, staff nurses)
Outcomes	- Quality of life (Continuous) CRITICAL - Length of stay (Continuous) CRITICAL - Readmission up to 30 days (Dichotomous) IMPORTANT - Mortality (Dichotomous) CRITICAL - Avoidable adverse events (Dichotomous) CRITICAL - Patient and/or carer satisfaction (Dichotomous) CRITICAL - Missed or delayed treatments (Dichotomous) IMPORTANT - Staff satisfaction (Dichotomous) IMPORTANT
Study design	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.
Unit of randomisation	Patient
Crossover study	Permitted
Minimum duration of study	Not defined
Other stratifications	Physician extender, Specialist nurse
Subgroup analyses if there is heterogeneity	- Frail elderly (Frail elderly; Not frail elderly); The committee felt this population was significantly different - Type of physician extender (Emergency nurse practitioner; Advanced nurse practitioner; Advanced care practitioner; Physician Assistant/Physician Associate; Critical Care Practitioner; Critical Care Outreach Nurse; Independent prescribing pharmacists); These could show significant differences - Type of specialist nurse; Diabetes inpatient specialist nurse; Heart failure nurse; These could show significant differences
Search criteria	Databases: Medline, Embase, the Cochrane library Date limits for search: None Language: English

Appendix B: Clinical article selection

Figure 1: Flow chart of clinical article selection for the review of Physician extenders



Appendix C: Forest plots

C.1 Physician extender versus no physician extender/usual care

Figure 2: Adverse events.

Study or Subgroup	Physician extender Events	Total	No PE/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Forster 2005	37	157	39	171	69.7%	1.03 [0.70, 1.53]
Pioro 2001	10	193	16	188	30.3%	0.61 [0.28, 1.31]
Total (95% CI)		**350**		**359**	**100.0%**	**0.90 [0.64, 1.28]**
Total events	47		55			

Heterogeneity: Chi² = 1.47, df = 1 (P = 0.23); I² = 32%
Test for overall effect: Z = 0.56 (P = 0.58)

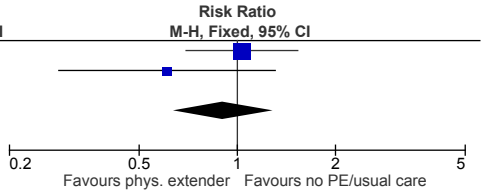


Figure 3: Length of stay.

Study or Subgroup	Physician extender Mean	SD	Total	No PE/usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Cowan 2006	5	6.3	581	6.01	6.9	626	86.3%	-1.01 [-1.75, -0.27]
Moher 1992	7.43	6.33	136	9.4	8.97	131	13.7%	-1.97 [-3.84, -0.10]
Total (95% CI)			**717**			**757**	**100.0%**	**-1.14 [-1.83, -0.45]**

Heterogeneity: Chi² = 0.88, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 3.23 (P = 0.001)

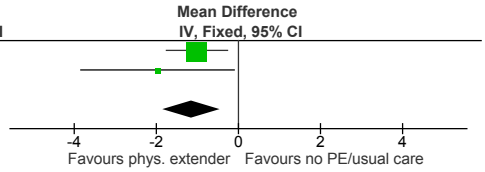


Figure 4: Mortality.

Study or Subgroup	Physician extender Events	Total	No PE/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cowan 2006	58	581	50	626	54.7%	1.25 [0.87, 1.79]
Forster 2005	28	307	30	313	33.8%	0.95 [0.58, 1.55]
Moher 1992	10	136	8	131	9.3%	1.20 [0.49, 2.96]
Pioro 2001	3	193	2	188	2.3%	1.46 [0.25, 8.65]
Total (95% CI)		**1217**		**1258**	**100.0%**	**1.15 [0.88, 1.51]**
Total events	99		90			

Heterogeneity: Chi² = 0.86, df = 3 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.00 (P = 0.32)

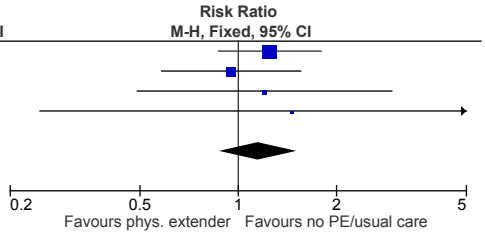


Figure 5: Satisfaction.

Study or Subgroup	Physician extender Mean	SD	Total	No PE/usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Forster 2005	8.2	2.2	135	7.6	2.4	155	100.0%	0.60 [0.07, 1.13]
Total (95% CI)		**135**				**155**	**100.0%**	**0.60 [0.07, 1.13]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.22 (P = 0.03)

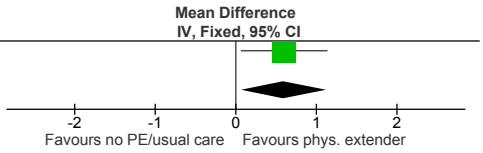
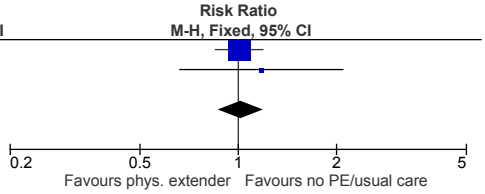


Figure 6: Readmission

Study or Subgroup	Physician extender Events	Total	No PE/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cowan 2006	183	581	196	626	91.1%	1.01 [0.85, 1.19]
Moher 1992	22	136	18	131	8.9%	1.18 [0.66, 2.09]
Total (95% CI)		**717**		**757**	**100.0%**	**1.02 [0.87, 1.20]**
Total events	205		214			

Heterogeneity: Chi² = 0.27, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 0.26 (P = 0.80)



C.2 Specialist nurse versus no specialist nurse/usual care

Figure 7: Adverse events

Study or Subgroup	Specialist nurse Events	Total	No specialist nurse/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arts 2012	10	149	17	145	100.0%	0.57 [0.27, 1.21]
Total (95% CI)		**149**		**145**	**100.0%**	**0.57 [0.27, 1.21]**
Total events	10		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.14)

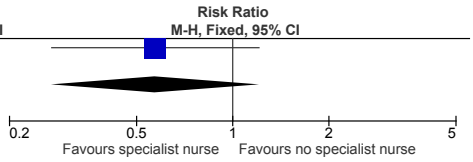


Figure 8: Mortality

Study or Subgroup	Specialist nurse Events	Total	No specialist nurse/usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Arts 2012	5	147	4	145	38.9%	1.23 [0.34, 4.50]
Davies 2001	6	148	8	152	61.1%	0.77 [0.27, 2.17]
Total (95% CI)		**295**		**297**	**100.0%**	**0.93 [0.41, 2.08]**
Total events	11		12			

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.19 (P = 0.85)

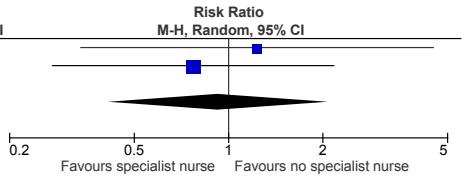


Figure 9: Satisfied patients

Study or Subgroup	Physician extender Events	Total	No PE/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davies 2001	61	67	39	66	100.0%	1.54 [1.24, 1.91]
Total (95% CI)		**67**		**66**	**100.0%**	**1.54 [1.24, 1.91]**
Total events	61		39			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.95 (P < 0.0001)

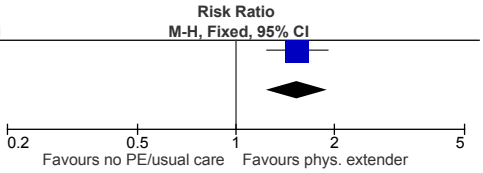
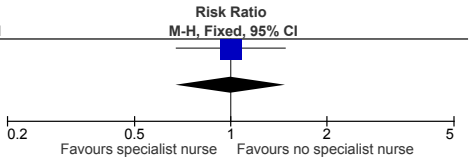


Figure 10: Readmission

Study or Subgroup	Specialist nurse Events	Total	No specialist nurse/usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davies 2001	37	148	38	152	100.0%	1.00 [0.68, 1.48]
Total (95% CI)		**148**		**152**	**100.0%**	**1.00 [0.68, 1.48]**
Total events	37		38			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



Appendix D: Clinical evidence tables

Study	Arts 2012[12]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=337)
Countries and setting	Conducted in Netherlands; Setting: Academic hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 10 months + 2 year follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Specialist nurse: Diabetes mellitus types 1 and 2 patients
Subgroup analysis within study	Not applicable
Inclusion criteria	Required treatment with either insulin or oral blood-glucose medication combined with 1 or more of the following conditions: inadequate regulation of blood glucose, blood pressure, or lipids
Exclusion criteria	Disturbed renal function (Creatinine > 180 mmol/L), pregnant or planned pregnancy, treated with continuous subcutaneous insulin infusion, recent cardiovascular event (<6 months before inclusion), Co-morbidity necessitating treatment from an internist, active or recurrent foot ulcer(s), hypertension that requires treatment including more than 4 medications
Recruitment/selection of patients	People with diabetes from the area of Maastricht, who were under the care of the 5 physicians and 2 resident endocrinologists involved in the study
Age, gender and ethnicity	Age - Mean (SD): Group 1: 59.5 (13.8), Group 2: 58.4 (14.1). Gender (M:F): 101:193. Ethnicity: NR
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear
Extra comments	study reports EQ-5D scores at baseline, but insufficiently reports final scores ("EQ-5D scores remained similar over time in both groups (p=0.058)")
Indirectness of population	No indirectness
Interventions	(n=169) Intervention 1: Specialist nurse in addition to usual care. Participants received care from advanced nurse practitioners, who worked according to a protocol (no further details on protocol). Duration until discharge. Concurrent medication/care: no details given Further details: 1. Type of specialist nurse: Diabetes specialist nurses which were defined in the study as an advanced practice nurse who focus on a specific patient population in specialised area of nursing practice (Doctoral or Master's prepared registered nurses).

Study	Arts 2012[12]
	(n=168) Intervention 2: No specialist nurse/usual care (for example, junior doctors, staff nurses). Usual care provided by the 5 physicians participating in this trial. Duration until discharge. Concurrent medication/care: no details given. Further details: 1. Type of physician extender: Not applicable / Not stated / Unclear.
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES) Protocol outcome 1: Mortality during the study period - Actual outcome: Mortality at 2 years; Group 1: 5/147, Group 2: 4/145; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in baseline diabetes-related complications (Group 1: 47%, Group 2: 42%), and smokers: (Group 1: 19.3%, Group 2: 27.6%); Group 1 Number missing: 20, Reason: dropped out; Group 2 Number missing: 23, Reason: dropped out Protocol outcome 2: Avoidable adverse events during the study period - Actual outcome: Diabetes-related complications at 2 years; Group 1: 10/149, Group 2: 17/145; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in baseline diabetes-related complications (Group 1: 47%, Group 2: 42%), and smokers: (Group 1: 19.3%, Group 2: 27.6%); Group 1 Number missing: 20, Reason: dropped out; Group 2 Number missing: 23, Reason: dropped out Protocol outcome 3: Quality of life - Actual outcome: Mean EQ-5D quality of life (SD): Group 1: 0.86 (0.22) at baseline and 0.80 at 2 years; Group 2: 0.82 (0.22) at baseline and 0.82 at 2 years; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in baseline diabetes-related complications (Group 1: 47%, Group 2: 42%), and smokers: (Group 1: 19.3%, Group 2: 27.6%); Group 1 Number missing: 20, Reason: dropped out; Group 2 Number missing: 23, Reason: dropped out	
Protocol outcomes not reported by the study	Readmission during the study period; Patient and/or carer satisfaction during the study period; Discharges during the

Study	Arts 2012[12]
	study period; Missed or delayed treatments during the study period; Staff satisfaction during the study period; Length of stay during the study period

Study	Cowan 2006[51]
Study type	Quasi-RCT (General medicine floor divided into control unit and experimental unit; Parallel)
Number of studies (number of participants)	1 (n=1207)
Countries and setting	Conducted in the USA; Setting: tertiary academic medical hospital
Line of therapy	First line
Duration of study	Intervention + follow up: intervention to hospital discharge + 30 days after discharge + 4 months follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: hospitalised, acutely ill general medicine patients
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted to the general medical floor of a tertiary academic medical hospital
Exclusion criteria	Sickle cell anaemia
Recruitment/selection of patients	Patients admitted to the general medical floor of a tertiary academic medical hospital
Age, gender and ethnicity	Age - Mean (SD): Group 1:55 (19), Group 2: 55 (19). Gender (M:F): 554:653. Ethnicity: White 820; African-American 205; Asian 67; Other 115
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear
Extra comments	
Indirectness of population	No indirectness
Interventions	(n=581) Intervention 1: Presence of a Nurse Practitioner whose primary role for inpatient care were the following: case management, facilitation of communication and collaboration with physicians and nurses, leading and actively implementing timely processes after the daily multidisciplinary rounds, surveillance of cost-effective measures (that is, rational use of cardiac monitors, indwelling lines and catheters), twice-daily assessments of cultures for sensitivity with the goal of changing the antibiotic regimen to the narrowest spectrum, review of all medications for drug/drug interactions and side effects, changing intravenous medications to oral, and enforcement of disease-specific care pathways and expedition of discharge planning with post-discharge follow up. Continuous care for patients for 8 hours per day.

Study	Cowan 2006[51]
	After discharge: follow-up phone calls (2 calls in first week, once a week for the next 3 weeks); assessed issues such as medication compliance and side effects, follow up appointments with primary physician, symptom management, pain management and resumption of functional activities of daily living. They advised primary physicians to change medication orders if necessary, Home visits were offered to all patients who lived within a 20-mile geographic radius of the hospital (around 7% had home visits). Concurrent medication/care: Increase in multi-disciplinary rounds from weekly to daily (with the NP taking part in the rounds); appointment of a (hospitalist) medical director who was in charge of overseeing NP and physicians. There was 1 medical director for the first 9 months of the study and (assumed) 2 for the final duration. Duration: in hospital and for 30 days after discharge. Further details: 1. Type of physician extender: (n=626) Intervention 2: No Physician extenders/usual care - No Physician extenders/usual care (for example. junior doctors, staff nurses). Usual care provided by attending physician, 2 residents, 3 interns, medical students and nurses. Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Not applicable / Not stated / Unclear
Funding	Agency for Health Care Policy and Research

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES)

Protocol outcome 1: Length of stay

- Actual outcome: Length of stay (index admission); Group 1: 5 (6.3) days; Group 2: 6.01 (6.9) days; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality

- Actual outcome: Mortality at 4 months; Group 1: 58/581, Group 2: 50/626; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Readmission

- Actual outcome: Readmission at 4 months; Group 1: 183/581, Group 2: 196/626; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high,

Study	Cowan 2006[51]
Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life during the study period; Avoidable adverse events during the study period; Patient and/or carer satisfaction during the study period; Discharges during the study period; Missed or delayed treatments during the study period; Staff satisfaction during the study period

Study	Davies 2001[55]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=300)
Countries and setting	Conducted in UK; Setting: secondary care
Line of therapy	1st line
Duration of study	Intervention + follow up: intervention during hospitalisation + 12 months follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Specialist nurse: type 1 or type 2 diabetes patients
Subgroup analysis within study	Not applicable
Inclusion criteria	Sequential, unselected referrals of in-patients to the DSN service (with either type 1 or type 2 diabetes) to a university hospital
Exclusion criteria	Patients unable to complete self-reported questionnaire were selectively excluded from that outcome. (reasons for exclusion include: visually impaired, non-English, confused, or had reduced consciousness)
Recruitment/selection of patients	Sequential, unselected referrals of in-patients to the DSN service (with either type 1 or type 2 diabetes) to a university hospital
Age, gender and ethnicity	Age - Median (IQR): Group 1: 63.4 (19.1), Group 2:63.6 (19.5). Gender (M:F): 159:139. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear
Extra comments	If declined to participate patients received DSN input
Indirectness of population	No indirectness
Interventions	(n=148) Intervention 1: Specialist nurse in addition to usual care. Presence of 1 of 4 diabetes specialist nurse. DSN care included individual structures patient education appropriate to need, and practical management advice including verbal and written case-note feedback to ward-based medical staff. DSN input began on the day of referral and randomisation, and continued until discharge

Study	Davies 2001[55]
	Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Diabetes specialist nurse (n=152) Intervention 2: No specialist nurse /usual care (for example, junior doctors, and staff nurses). Usual care from medical, general nursing and dietetic health professionals without any input from the DSN Duration Concurrent medication/care: Not stated Further details: 1. Type of specialist nurse extender: diabetic specialist nurse
Funding	Welsh Office for Research and Development for Health and Social Care, Welsh Assembly, Cardiff, Wales, UK

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES)

Protocol outcome 1: Quality of life

- Actual outcome: Audit of Diabetes Dependent Quality of Life (ADDQoL) final score at 1 week after discharge (no details of scale used): Group 1: 0.88 (no SD, n=67); Group 2: 0.40 (no SD, n=66); Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Length of stay

- Actual outcome: Median length of stay during index admission: Group 1: 8.0 days; Group 2: 11.0 days, p<0.01; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Mortality during the study period

- Actual outcome: Mortality at 12 months; Group 1:6/148, Group 2: 8/152; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Patient and/or carer satisfaction

- Actual outcome: Modified Diabetes Clinic Satisfaction Questionnaire (% satisfied) at 1 week post discharge; Group 1: 91% (n=67), Group 2: 59% (n=66); Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Study	Davies 2001[55]
Protocol outcome 5: Readmission - Actual outcome: Readmission within 12 months; Group 1: 37/148; Group 2: 38/152; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Discharges during the study period; Missed or delayed treatments during the study period; Staff satisfaction during the study period

Study	Forster 2005[81]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=620)
Countries and setting	Conducted in Canada; Setting: Tertiary teaching hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: intervention during discharge and to 3 days after discharge + follow-up to a median of 34 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: undifferentiated acute multi-system medical illness
Subgroup analysis within study	Not applicable
Inclusion criteria	Consecutive patients admitted from the ED or another service to the general medical service of at 2 sites of tertiary care teaching hospital
Exclusion criteria	None
Recruitment/selection of patients	Consecutive patients admitted from the ED or another service to the general medical service of at 2 sites of tertiary care teaching hospital
Age, gender and ethnicity	Age - Mean (SD): Group 1: 68.8 (18.7), Group 2: 69.9 (18.5). Gender (M:F): 306:324. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear
Extra comments	
Indirectness of population	No indirectness
Interventions	(n=307) Intervention 1: Presence of clinical nurse specialist (nurse team co-ordinator). Role of the nurse was as a team

Study	Forster 2005[81]
	co-coordinator and whose in-hospital role was to facilitate hospital care by retrieving preadmission information, arranging in-hospital consolations and intervention, organising post discharge follow-up and providing patients education; and telephoning patients early after discharge (average 3 days) to answer questions and address early problems. Duration In hospital and to 3 days after discharge Concurrent medication/care: Not stated Further details: 1. Type of physician extender: clinical nurse specialist (n=313) Intervention 2: No Physician extenders/usual care - No Physician extenders/usual care (for example, junior Doctors, staff nurses). Usual care Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Not applicable / Not stated / Unclear
Funding	Ottawa Internists Research Group

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES)

Protocol outcome 1: Adverse events

- Actual outcome: Adverse event (not defined) at a median of 34 days after discharge: Group 1: 37/157; Group 2: 39/171; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Length of stay

- Actual outcome: Median (IQR) length of stay: Group 1: 6 (3-11) days; Group 2: 5 (3-10) days; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Mortality in hospital

- Actual outcome: Mortality in hospital; Group 1: 28/307, Group 2: 30/313; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Mortality after discharge

Study	Forster 2005[81]
- Actual outcome: Mortality up to median 34 days after discharge; Group 1: 3/135, Group 2: 4/155; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 5: Patient and/or carer satisfaction - Actual outcome: Satisfaction with overall quality of care (no details of scale used) at 34 days after discharge: Group 1: 8.2 (2.2); Group 2: 7.6 (2.4); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 6: Readmission - Actual outcome: Readmission at median 34 days after discharge; Group 1: 30/157, Group 2: 22/171; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life during the study period; Readmission during the study period; Patient and/or carer satisfaction during the study period; Discharges during the study period; Missed or delayed treatments during the study period; Staff satisfaction during the study period; Length of stay during the study period

Study	Moher 1992[163]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=267)
Countries and setting	Conducted in Canada; Setting: university teaching hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: intervention during discharge + 2 weeks follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: Most patients had diseases of the circulatory, respiratory or digestive system
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted to general Clinical Teaching Units at a university teaching hospital
Exclusion criteria	Death expected within 48 hours, those admitted directly to ICU
Recruitment/selection of patients	Patients admitted to general Clinical Teaching Units at a university teaching hospital
Age, gender and ethnicity	Age - Mean (SD): Group 1: 66.3 (18.6), Group 2: 64.3 (19.9). Gender (M:F): 112:155. Ethnicity: Not stated
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear

Study	Moher 1992[163]
Extra comments	
Indirectness of population	No indirectness
Interventions	(n=136) Intervention 1: Presence of clinical nurse specialist (nurse team co-ordinator). Role is to participate in ward rounds, collaborate with health care professionals, facilitate administrative tasks such as discharge planning, coordinate tests and procedures, and to collect and collate patient information. Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: "medical team coordinator" – baccalaureate nurse (n=131) Intervention 2: No Physician extenders/usual care - No Physician extenders/usual care (for example, junior doctors, and staff nurses). Usual care without the nurse team co-ordinator Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Not applicable / Not stated / Unclear
Funding	Ontario Ministry of Health
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES) Protocol outcome 1: Length of stay - Actual outcome: Length of stay during index admission: Group 1: 7.43 (6.33); Group 2: 9.40 (8.97); Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Mortality during the study period - Actual outcome: Mortality in hospital; Group 1: 10/136, Group 2: 8;131; Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Readmission - Actual outcome: Readmission within 2 weeks; Group 1: 22/136, Group 2: 18/131; Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life during the study period; Patient and/or carer satisfaction during the study period; Discharges during the study period; Missed or delayed treatments during the study period; Staff satisfaction during the study period

Study	Pioro 2001[178]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=381)
Countries and setting	Conducted in USA; Setting: University hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: intervention in hospital + follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: general medical patients (abdominal pain, pneumonia, acute dyspnoea, asthma, fever, gastrointestinal bleeding, congestive heart failure, diabetes mellitus, infection/cellulitis)
Subgroup analysis within study	Not applicable
Inclusion criteria	General medical patients aged 18-69
Exclusion criteria	Admitted to intensive care or other specialty units and those transferred from the intensive care. For first 5 months patients outside of core admitting times were excluded (not weekdays 0730 to 1700). Rest of duration (~ 1 year) all weekday admissions were included
Recruitment/selection of patients	Patients admitted through out-patient facilities or the emergency room at university hospital
Age, gender and ethnicity	Age - Mean (SD): Group 1: 48.0 (14.9), Group 2: 47.7 (14.4). Gender (M:F): 149:232. Ethnicity: 40% White
Further population details	1. Frail elderly: Not applicable / Not stated / Unclear
Extra comments	90/193 crossed over from intervention to control. Reasons for cross-over: bed availability (29%), doctor request (22%), NP request (22%), and other (28%)
Indirectness of population	No indirectness
Interventions	(n=193) Intervention 1: Nurse practitioner based care. Nurse practitioner's role admission assessment, assembly of patient data, co-ordination of care with patient's attending doctors and implementation of diagnostic and therapeutic plans. NPs were on weekdays 0730 to 2000 and on weekends for morning rounds. NPs were supervised by a medical director who made daily rounds. Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Nurse practitioner (n=188) Intervention 2: No Physician extenders/usual care - No Physician extenders/usual care (for example, junior doctors, and staff nurses). Usual care by traditional house staff (6 teams consisting of 1 senior or junior medical

Study	Pioro 2001[178]
	resident and 2 interns, supervised by a teaching attending doctor). Duration: in hospital Concurrent medication/care: Not stated Further details: 1. Type of physician extender: Not applicable / Not stated / Unclear
Funding	Robert Wood Johnson Foundation's Health Care Financing and Organization Initiative
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHYSICIAN EXTENDER IN ADDITION TO USUAL CARE versus NO PHYSICIAN EXTENDERS/USUAL CARE (FOR EXAMPLE, JUNIOR DOCTORS, STAFF NURSES) Protocol outcome 1: Quality of life - Actual outcome: Change in SF-36 at 6 weeks post discharge: Group 1: 4.7; Group 2: 2.9 (no SDs reported); Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Adverse events - Actual outcome: 1 or more hospital-acquired complication: Group 1: 10/193; Group 2: 16/188; Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Length of stay - Actual outcome: Length of stay (index admission): Group 1: 5.0 days; Group 2: 5.3 days (no SDs given); Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 4: Mortality in hospital - Actual outcome: Mortality in hospital; Group 1: 3/193, Group 2: 2/188; Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 5: Mortality after discharge - Actual outcome: Mortality at 30 days post discharge; Group 1: 7/193, Group 2: 6/188; Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 6: Patient and/or carer satisfaction - Actual outcome: Overall rating of "overall care given at hospital" – rated using 5 response categories ranging from "poor" to "excellent" which were transformed to 0-100 scales for analysis: Group 1: 84.7; Group 2: 80.7 (no SDs given); Risk of bias: All domain – Very high, Selection – Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectnessgro	
Protocol outcomes not reported by the study	Readmission during the study period; Discharges during the study period; Missed or delayed treatments during the

Study	Pioro 2001[178]
	study period; Staff satisfaction during the study period

Appendix E: Economic evidence tables

E.1 Physician extender versus no physician extender or usual care

No studies were included.

E.2 Specialist nurse versus no specialist nurse or usual care

Study	Arts 2012[12]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** economic evaluation alongside a randomised controlled study (RCT) **Approach to analysis:** Individual patient level cost and QALY data were analysed and ICER calculated. Two cost analyses were presented, 1 of costs directly affected by the intervention and another of overall costs. The former is used here. **Perspective:** Dutch Healthcare perspective **Follow-up:** 2 years	**Population:** People with diabetes mellitus type 1 and 2 who are treated by an internist at an academic hospital in Maastricht, the Netherlands. **Cohort settings: (n=285)** Mean age: Intervention 1: 58.4 years Intervention 2: 59.5 years Male: Intervention 1: 35.2% Intervention 2: 37.6% **Intervention 1: (n=145)**	**Total costs (mean per patient):** Intervention 1: £5,593 Intervention 2: £5,902 Incremental (2−1): £309 (95% CI: NR; p=0.6) **Currency & cost year:** 2007 euro (presented here as 2007 UK pounds[(b)]) **Cost components incorporated:** Outpatient visits Diabetes-related admissions	**QALYs (mean per patient):** Intervention 1:0.82 Intervention 2: 0.80 Incremental (2−1): -0.02 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Reported as £15 per QALY gained however, the results as presented show that intervention 2 is dominated **Analysis of uncertainty:** Differences in costs and QALYs were not significant. No sensitivity analysis is reported.

Treatment effect duration[(a)]: 2 years **Discounting:** No	Usual care provided by physicians (5 physicians) **Intervention 2: (n=149)** Care provided by diabetes nurse specialists (DNSs) (convenience sample of 4 nurses with advanced training in diabetes)			
Data sources				
Health outcomes: Within trial analysis with data collected at baseline and after 2 years of follow-up. **Quality-of-life weights:** EQ-5D, tariff not specified. **Cost sources:** National tariff (DBC system) was used to calculate the costs of hospital-based care.				
Comments				
Source of funding: None. **Applicability and limitations:** Some uncertainty regarding the applicability of resource use and costs from the Netherlands (2007) to current NHS context. No discounting reported. Baseline and relative treatment effects are based on a single RCT, so by definition, does not reflect all evidence in the area. Costs of medications, investigations and other staff groups' time are not included. No sensitivity analysis is reported.				
Overall applicability[(c)]:partially applicable **Overall quality[(d)]:** potentially serious limitations				

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; N/A: not applicable; NR: not reported; QALYs: quality-adjusted life years.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and, if so, for how long?

(b) Converted using 2007 purchasing power parities.[172]

(c) Directly applicable/Partially applicable/Not applicable.

(d) Minor limitations/Potentially serious limitations/Very serious limitations.

Appendix F: GRADE tables

Table 8: Clinical evidence profile: Physician extender versus no physician extender/usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physician extender versus no physician extender/usual care s	Control	Relative (95% CI)	Absolute		
Adverse events (follow-up In-hospital to 34 days)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	47/350 (13.4%)	15.7%	RR 0.90 (0.64 to 1.28)	16 fewer per 1000 (from 57 fewer to 44 more)	⊕OOO VERY LOW	CRITICAL
Length of stay (Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	717	757	-	MD 1.14 lower (1.83 to 0.45 lower)	⊕⊕OO LOW	CRITICAL
Mortality (follow-up in hospital to up to 4 months)												
4	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	99/1217 (8.1%)	7.1%	RR 1.15 (0.88 to 1.51)	11 more per 1000 (from 9 fewer to 36 more)	⊕OOO VERY LOW	CRITICAL
Satisfaction (follow-up 34 days; range of scores: 0-10; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	135	155	-	MD 0.6 higher (0.07 to 1.13 higher)	⊕⊕OO LOW	IMPORTANT
Readmission (follow-up 2 weeks to 4 months)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	205/717 (28.6%)	22.5%	RR 1.02 (0.87 to 1.2)	4 more per 1000 (from 29 fewer to 45 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

Table 9: Clinical evidence profile: Specialist nurse versus no specialist nurse/usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Specialist nurse	No specialist nurse/usual care	Relative (95% CI)	Absolute		
Adverse events (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10/149 (6.7%)	11.7%	RR 0.57 (0.27 to 1.21)	50 fewer per 1000 (from 85 fewer to 25 more)	⊕OOO VERY LOW	CRITICAL
Mortality (follow-up 1-2 years)												
2	randomised trials	very serious[1]	serious[3]	no serious indirectness	very serious[2]	none	11/295 (3.7%)	4%	RR 0.93 (0.42 to 2.07)	3 fewer per 1000 (from 23 fewer to 43 more)	⊕OOO VERY LOW	CRITICAL
Satisfied patients (follow-up 1 weeks)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	61/67 (91%)	59.1%	RR 1.54 (1.24 to 1.91)	319 more per 1000 (from 142 more to 538 more)	⊕⊕OO LOW	IMPORTANT
Readmission (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	37/148 (25%)	25%	RR 1 (0.68 to 1.48)	0 fewer per 1000 (from 80 fewer to 120 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
[3] Downgraded by 1 increment because the point estimate varies widely across studies, unexplained by subgroup analysis.

Appendix G: Excluded clinical studies

Table 10: Studies excluded from the clinical review

Study	Reason for Exclusion
Ahern 2004[6]	Unclear setting. Study design (Observational)
Ahmed 2002[7]	Systematic review - no eligible papers
Allen 2009[11]	Not secondary care (post-discharge care)
Allen 2011[8]	Not secondary care (community care)
Allen 2011A[9]	Not secondary care (community clinics). Study design (Observational)
Allen 2013A[10]	Study design (Qualitative)
Allen 2013A[10]	Study design (Qualitative)
Anon 1994[1]	Not secondary care (primary care). Study design (Descriptive)
Anon 2001[2]	Study design (case-control). Study design (Observational)
Anon 2006[3]	Review protocol
Anon 2015A[4]	Study design (Descriptive)
Anon 2015G [5]	Study design (Observational)
Bakewellsachs 1991[13]	Study design (Descriptive)
Ball 2007[14]	Study design (Observational)
Banerjee 1998[15]	Cross-sectional. Study design (Observational)
Barton 2011[16]	No comparator. Study design (Observational)
Bevis 2008[17]	Not AME (trauma surgeons for tube thoracotomies). Study design (Observational)
Black 2013[18]	No relevant comparator. Study design (Observational)
Black 2014[19]	Not AME (trauma)
Blue 2001[20]	Not secondary care (home care)
Brandon 2009[21]	Not secondary care (post-discharge care)
Broers 2009[22]	Study design (Observational)
Bryant-Lukosius 2015[23]	Systematic review - no eligible papers
Burgess 2010[24]	Study design (Literature review)
Butler 2011[25]	All eligible papers ordered
Calder 2002[26]	Unable to locate a copy
Callaghan 2008[27]	Study design (Literature review)
Carberry 2013[28]	Low n number. Study design (Observational)
Carey 2008[29]	Low n number. Study design (Observational)
Carlson 2004[30]	Unable to locate a copy
Carroll 2007[31]	Not secondary care (community care)
Carter 2007[32]	Systematic review - no eligible papers
Caserta 2007[33]	Study design (Descriptive)
Cheng 2013[34]	Incorrect intervention (physician-nurse team)
Christmas 2005[35]	Not AME (trauma). Study design (Observational)
Clark 2015[36]	Protocol/abstract only
Cockayne 2014[37]	Unable to locate a copy

Study	Reason for Exclusion
Cole 2014[38]	Unable to locate a copy
Colligan 2011[39]	Study design (Observational)
Comiskey 2014[40]	Cross-sectional. Low n number. Study design (Observational)
Connolly 2015[41]	Not secondary care (residential care facilities)
Considine 2006[44]	Study design (Observational)
Considine 2010[42]	Study design (Observational)
Considine 2012[43]	No relevant comparison (compared with other physician extenders). Study design (Observational)
Cook 2015[45]	Systematic review - no eligible papers
Cooper 2002[46]	Study design (Observational)
Cooper 2008[47]	No comparator. No outcomes of interest. Study design (Observational)
Cope 2015[48]	Study design (Observational)
Corner 2003[49]	Systematic review - no eligible papers. Study design (literature review)
Counsell 2007[50]	Not secondary care (home care)
Dacey 2007[52]	Study design (Observational)
David 2015[53]	Study design (Observational)
Davidson 2010[54]	Not secondary care (outpatient clinic)
Dawes 2007[56]	Not AME (elective surgery)
Dean 2012A[58]	Study design (Descriptive)
Dean 2014[59]	Not secondary care (community care)
Debroe 2001[57]	Systematic review - no eligible papers
Derksen 2007[60]	Not AME (trauma)
Dewar 2008[62]	Not secondary care (outpatient clinic). Study design (Observational)
Dewar 2008A[61]	Low n number. Study design (Observational)
Dinh 2012[63]	Not AME (emergency department fast-track / trauma)
Dinh 2013[64]	Not AME (trauma). Low n number. Study design (Observational)
Doan 2011[65]	Systematic review of emergency department / trauma
Domingo 2012[66]	Protocol only
Donaghy 1995[67]	Not secondary care (outpatient clinic)
Donald 2013[68]	Systematic review - no eligible papers
Donald 2014[70]	Systematic review - no eligible papers
Donald 2015[69]	Systematic review - no eligible papers
Driscoll 2008[71]	Not secondary care (primary care and clinic)
Dyar 2012[72]	Not secondary care (palliative care)
Ellis 2003[73]	Not secondary care (outpatient clinic)
Ellis 2004[74]	Unable to locate a copy
Ellis 2005[76]	Not secondary care (outpatient clinic)
Ellis 2005C[75]	Duplication of Ellis2005
Ezra 2005[77]	Low n number. Study design (Observational)
Fanta 2006[78]	Paediatric. Not AME (trauma)
Farmer 2011[79]	Study design (Qualitative)
Forbes 2003[80]	Systematic review - no eligible papers
Fotheringham 2011[82]	Study design (Observational)

Study	Reason for Exclusion
Fry 2011[83]	Study design (Literature review)
Furze 2012[84]	Incorrect comparison (lay-facilitated angina management)
Gershengorn 2011[85]	Study design (Observational)
Gillard 2011[86]	Not AME (major trauma). Study design (Observational)
Goessens 2006[87]	Not secondary care (community)
Goldie 2012[88]	Not AME (inclusion of elective patients, exclusion of emergency patients)
Goldman 2014[89]	Not secondary care (post-discharge follow-up)
Goodwin 2011[90]	Study design (Qualitative)
Gracias 2008[91]	No outcomes of interest. Study design (Observational)
Gracias 2008A[91]	Duplicate of Gracias 2008
Gradwell 2002[92]	Not guideline condition (Dermatology). Not secondary care (outpatient clinic)
Greving 2015[93]	Not secondary care (outpatient clinic)
Griffiths 2001[94]	Not AME (medically stable)
Haan 2007[95]	Not AME (trauma). Study design (Observational)
Hamden 2014[96]	Study design (Observational)
Harbman 2014[97]	Study design (Observational)
Harris 2005A[98]	Study design (Observational)
Harrison 2001[99]	Study design (News report)
Hartford 2005[100]	Not secondary care (post-discharge care)
Hawkins 1994[101]	Cross-sectional survey. Study design (Observational)
Hayden 2014[102]	Incorrect intervention (primary care physician in the ED). Study design (Observational)
Henry 2011[103]	Systematic review - no eligible papers
Ho 2013[104]	Not AME (nasogastric insertions)
Hoffman 2005[105]	Study design (Observational)
Hooker 2005[106]	Not secondary care (primary care). Study design (Observational)
Hooker 2011[107]	Systematic review - no eligible papers
Hoskins 2011[108]	Study design (Literature review)
Houweling 2004[109]	Unable to locate a copy
Houweling 2009[110]	Not secondary care (outpatient clinic)
Hylka 1995[111]	No outcomes of interest. Study design (Observational)
Imhof 2012[112]	Not secondary care (primary care)
Innes 2015[113]	Integrative review
Jaarsma 2008[114]	Not secondary care (outpatient clinic)
Jeanmonod 2013[115]	Incorrect intervention (not physician extender). Study design (Observational)
Jennings 2008[119]	Not AME (trauma). Study design (Observational)
Jennings 2009[118]	Low n number. Not AME (trauma). Study design (Observational)
Jennings 2014[117]	Protocol. Not AME (fast track ED / trauma)
Jennings 2015A[116]	Systematic review - no eligible papers
Jones 2005A[120]	Systematic review - no eligible papers
Jonsson 2014[121]	Unable to locate a copy
Kannusamy 2006[122]	Study design (Observational)
Kartha 2014[123]	Study design (Observational)

Study	Reason for Exclusion
Kawar 2011[124]	Study design (Observational)
Keane 2008[125]	Study design (Observational)
Kilpatrick 2015[126]	Systematic review - no eligible papers
Kinley 2001[127]	Not AME (elective surgery)
Kinsman 2008[128]	Not AME (trauma / fast track). Study design (Observational)
Kirton 2007[129]	No outcomes of interest. Step-up, Step-down. Study design (Observational)
Kleinpell 2006[130]	Cross-sectional survey. Study design (Observational)
Kleinpell 2008[131]	Study design (Observational)
Kroese 2008[132]	Not AME (diagnosis of fibromyalgia)
Kuethe 2011[133]	Paediatric. Not secondary care (outpatient clinic)
Kuethe 2013[134]	Protocol only
Lalor 2013[135]	Study design (Qualitative)
Lambing 2004[136]	Study design (Observational)
Larkin 2010[137]	No intervention
Laroche 2000[138]	Unable to locate a copy
Latour 2006[139]	Not secondary care (home-based care)
Lau 2013[140]	Not AME (trauma). Low n numbers. Study design (Observational)
Lewis 2014[141]	Systematic review - no eligible papers
Lilja 1998[142]	Not AME (Total hip replacement or breast cancer surgery)
Limogesgonzalez 2011[143]	Not AME (NP delivered elective endoscopy)
Lohr 2013[144]	Study design (Observational)
Loveman 2003[145]	Systematic review - no eligible papers
Lutze 2014[146]	Study design (Observational)
Mahoney 1994[148]	Not secondary care (primary care)
Mahoney 1995[147]	Study design (Descriptive)
Martinezgonzalez 2014A[149]	Systematic review - no eligible papers
Mason 2005[150]	No outcomes of interest
Mason 2007C[152]	Study design (Observational)
Mason 2008A[151]	Not AME (trauma). Study design (Observational)
Mccarthy 2012[153]	Not secondary care (trauma / fast track). Study design (Observational)
Mccauley 2006[154]	Not secondary care (home-care)
Mcclellan 2012[155]	Not AME (soft tissue injury)
Mcclellan 2013[156]	Not AME (soft tissue injury)
Mccord 2009[157]	Incorrect intervention (not comparable to UK physician extenders as they performed unsupervised emergency obstetrical surgery). Study design (Observational)
Mccorkle 2009[158]	Not secondary care (post-discharge care)
Mcdonnell 2015[159]	Study design (Qualitative)
Melis 2005[160]	Not secondary care (community care)
Mergenhagen 2012[161]	Study design (Observational)
Meyer 2005[162]	Study design (Observational)
Motherwell 2007[164]	Study design (Observational)
Nash 2007[165]	Study design (Observational)
Nathan 2006[166]	Not secondary care (outpatient clinic)

Study	Reason for Exclusion
Naylor 2004[167]	Not secondary care (home care)
Nestler 2012[168]	Study design (Observational)
Newhouse 2011[169]	Systematic review - no eligible papers
Okeeffe 2014[170]	Study design (Observational)
Oneill 2014[171]	Not secondary care (primary care and clinic). Study design (Observational)
Owens 2011[173]	Protocol only
Page 2005[174]	Systematic review - no eligible papers
Patel 2008[175]	Not secondary care (home-based care)
Pear 2009[176]	Study design (Observational)
Peeters 2014[177]	Not secondary care (outpatient clinic)
Pirret 2008[179]	Low N number. Study design (Observational)
Quattrini 2011[181]	Systematic review - no eligible papers
Ranzenbach 2012[182]	Study design (Observational)
Rao 2007[183]	Not secondary care (clinic and community care)
Reynolds 2000[184]	Not secondary care (outpatient clinic)
Ridsdale 2000[185]	Not secondary care (outpatient clinic)
Robles 2011[186]	Study design (Observational)
Roche 2015[187]	Protocol only. Full study not yet published
Rowe 2011[188]	Systematic review - no eligible papers
Roy 2008[189]	Study design (Observational)
Russell 2010A[190]	Study design (Observational)
Sackett 2009[191]	Study design (Descriptive)
Sandhu 2009[192]	Not AME ('primary care problems' in the ED)
Sarkissian 1999[193]	Not secondary care (tertiary care, epilepsy monitoring unit). Study design (observational)
Sawatzky 2013[194]	Not secondary care (post-discharge care)
Shah 2013[195]	Incorrect intervention (pharmacist was not independently prescribing)
Shum 2000[196]	Not secondary care (primary care). Study design (Observational)
Skinner 2013[197]	Study design (Observational)
Snyder 1994[198]	Study design (Descriptive)
Sonday 2010[199]	Study design (Observational)
Sridhar 2008[200]	Not secondary care (outpatient clinic and home follow-up)
Stables 2004[201]	Not AME (elective surgery)
Stanikhutt 2013[202]	Systematic review - no eligible studies
Stewart 2001[203]	Not secondary care (home care)
Stoller 2001[204]	Study design (literature review)
Strand 2011[205]	Not secondary care (outpatient follow-up)
Takeda 2012[206]	Systematic review - no eligible papers
Thomas 2005[207]	Systematic review - no eligible papers
Thompson 2005[208]	Not secondary care (outpatient clinic and home-based care)
Thourani 2006[209]	Study design (Descriptive)
Timmermans 2014[210]	Protocol only. Study design (Observational)
Vadher 1997[211]	Not secondary care (outpatient care)

Study	Reason for Exclusion
Vanderbiezen 2016[212]	Incorrect population (primary care patients)
Vanderlinden 2010[213]	Study design (diagnostic accuracy study)
Vanderlinden 2010A[213]	Duplicate of Vanderlinden 2010
Vanzuilen 2005[216]	Not secondary care (outpatient clinic)
Vanzuilen 2008[217]	Not secondary care (unclear - assumed to be outpatient clinic)
Vanzuilen 2011[214]	Not secondary care (unclear - assumed to be outpatient clinic)
Vanzuilen 2012[215]	Not secondary care (outpatient clinic)
Webb 1997[219]	Unable to locate a copy
Weeks 2016[220]	Cochrane review (different PICO)
Wheeler 1999[221]	Study design (literature review)
Wierzchowiecki 2006[222]	Not secondary care (outpatient clinic)
Williams 2009[223]	Not AME (nurse delivered diagnostic endoscopy)
Wright 2003B[224]	Not secondary care (home care)

Appendix H: Excluded economic studies

Table 11: Studies excluded from the clinical review

Study	Reason for Exclusion
Pledger 2005[180]	Selectively excluded because it did not evaluate health outcomes and costs were dated.
Walsh 2005[218]	Excluded because it evaluates hospital-based nurse-led care rather than physician extenders.