Research in Social and Administrative Pharmacy xxx (2017) 1–13

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.rsap.org

The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review

Ankie C.M. Hazen, MSc [a, *], Antoinette A. de Bont, PhD [b], Lia Boelman, MSc [a], Dorien L.M. Zwart, MD PhD [a], Johan J. de Gier Prof [c], Niek J. de Wit Prof [a], Marcel L. Bouvy Prof [d]

[a] Department of General Practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Universiteitsweg 100, 3584 CG, Utrecht, The Netherlands
[b] Institute of Health Policy and Management, Erasmus University, Burgemeester Oudlaan 50, 3062 PA, Rotterdam, The Netherlands
[c] Department of Pharmacotherapy, Epidemiology and Economics, University of Groningen, Antonius Deusinglaan 1, Building 3214, 9713 AV, Groningen, The Netherlands
[d] Department of Pharmaceutical Sciences, Utrecht University, Universiteitsweg 99, 3584 CG, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 23 November 2016
Received in revised form
7 April 2017
Accepted 20 April 2017

Keywords:
Clinical pharmacist
Integrated care
Primary health care
Systematic review

ABSTRACT

Background: A non-dispensing pharmacist conducts clinical pharmacy services aimed at optimizing patients individual pharmacotherapy. Embedding a non-dispensing pharmacist in primary care practice enables collaboration, probably enhancing patient care. The degree of integration of non-dispensing pharmacists into multidisciplinary health care teams varies strongly between settings. The degree of integration may be a determinant for its success.

Objectives: This study investigates how the degree of integration of a non-dispensing pharmacist impacts medication related health outcomes in primary care.

Methods: In this literature review we searched two electronic databases and the reference list of published literature reviews for studies about clinical pharmacy services performed by non-dispensing pharmacists physically co-located in primary care practice. We assessed the degree of integration via key dimensions of integration based on the conceptual framework of Walshe and Smith. We included English language studies of any design that had a control group or baseline comparison published from 1966 to June 2016. Descriptive statistics were used to correlate the degree of integration to health outcomes. The analysis was stratified for disease-specific and patient-centered clinical pharmacy services.

Results: Eighty-nine health outcomes in 60 comparative studies contributed to the analysis. The accumulated evidence from these studies shows no impact of the degree of integration of non-dispensing pharmacists on health outcomes. For disease specific clinical pharmacy services the percentage of improved health outcomes for none, partial and fully integrated NDPs is respectively 75%, 63% and 59%. For patient-centered clinical pharmacy services the percentage of improved health outcomes for none, partial and fully integrated NDPs is respectively 55%, 57% and 70%.

Conclusions: Full integration adds value to patient-centered clinical pharmacy services, but not to disease-specific clinical pharmacy services. To obtain maximum benefits of clinical pharmacy services for patients with multiple medications and comorbidities, full integration of non-dispensing pharmacists should be promoted.

1. Introduction

The aging of the population results in increasingly complex medication-related needs.[1] To sustain the economic viability of health care the majority of elderly patients should be treated in primary care. To incorporate specific pharmaceutical expertise,

* Corresponding author. Universiteitsweg 100, PO box 85500, Room Str. 6.101, 3508 GA, Utrecht, The Netherlands.
E-mail addresses: a.c.m.hazen@umcutrecht.nl (A.C.M. Hazen), debont@bmg.eur.nl (A.A. de Bont), lboelman@gmail.com (L. Boelman), d.zwart@umcutrecht.nl (D.L.M. Zwart), degiercs@wxs.nl (J.J. de Gier), n.j.dewit@umcutrecht.nl (N.J. de Wit), m.l.bouvy@uu.nl (M.L. Bouvy).

http://dx.doi.org/10.1016/j.sapharm.2017.04.014
1551-7411/

some primary care practices have embedded a non-dispensing pharmacist (NDP, also: clinical pharmacist or clinical pharmacy specialist).

NDPs in primary care practice conduct clinical pharmacy services (CPS) that primarily focus on chronic disease management. CPS are usually multifaceted, including medication therapy reviews, counselling and medication education. These services can be aimed at patients with a specific chronic condition such as diabetes, cardiovascular disease or COPD ("disease-specific CPS"), or at a more heterogeneous group of patients at risk of drug related problems, such as patients with multimorbidity and polypharmacy ("patient-centered CPS"). Disease-specific CPS focusses on evidence-based protocolled care, while patient-centered CPS entails a more non-standardized and holistic approach.[2]

Some NDPs are fully integrated into the health care team,[3,4] whereas others only temporarily provide a specific CPS.[5] Common opinion is that integrated care for patients with chronic conditions may improve patient outcomes.[6–8] CPS have been shown to positively affect surrogate outcomes, such as blood pressure, glycemic control and lipid goal attainment.[9–13] Evidence of the effect of CPS on clinical endpoints, such as mortality, hospitalizations and health related quality of life, is less clear probably due to very heterogeneously defined CPS as well as strongly differing study settings.[12,14]

Both aspects are features of the degree of integration of the NDP who delivers the CPS. The degree of integration of NDPs into the health care team may be a determinant for its success, but this association has never been properly assessed. Therefore, we conducted a systematic review to investigate how the degree of integration of an NDP impacts health outcomes in primary care.

2. Methods

The protocol of this systematic review has been published in the PROSPERO register. The registration number is: CRD42016017506.[15]

2.1. Search strategy

We searched PubMed and Embase from 1966 to June 2016. A trained librarian, in consultation with researchers, developed a search strategy (Appendix Table 1). Also, we manually searched the reference list of systematic reviews and background articles about clinical pharmacy interventions in primary care for additional citations.

Potentially relevant studies were identified by two reviewers (AH and LB) based on predetermined inclusion criteria in a two-step procedure: 1) title and abstract, 2) screening of the full text. In case disagreement about inclusion could not be resolved by discussion between the two reviewers, a third reviewer (AB or MB) was consulted to reach consensus. We used the PRISMA checklist to conduct and report the systematic literature review.[16]

2.2. Study selection

Both USA and non-USA comparative studies of any design that had a control group or baseline comparison were included if they met the following criteria:

2.3. The intervention

1. comprised at least one key component of a chronic disease management service aimed at individual ambulatory patients;
2. was conducted by an NDP who had a regular and ongoing relationship with the primary care practice and was at least part-time physically present and at that time not involved in work related to community pharmacy;
3. measured a relevant clinical or patient reported health outcome or a proxy of a relevant health outcome (e.g. improvement of medication errors).

Studies were excluded if the intervention was delivered in a specialty or off-site clinic without collaboration with the general practitioner (GP), or if it was a pilot of an already included study or a secondary analysis. Also, unpublished studies and studies published in languages other than English were not taken into account for analysis.

2.4. Dependant variable: degree of integration

Our main focus was the degree of integration of NDPs, which we assessed via key dimensions of integration from the conceptual framework of Walshe and Smith[17]: organizational, informational, clinical, functional, financial and normative integration (Table 1). The financial integration could not be taken into account as most interventions were project funded studies. The key dimensions were scored dichotomous (yes/no). A positive score on zero to two dimensions of integration was defined as "no integration". A positive score on three or four dimensions of integration was defined as "partial integration" and a positive score on all five dimensions was defined as "full integration". Prescriptive authority was taken into account to assess clinical integration, see Table 3.

2.5. Primary outcome: health outcomes

The primary outcomes of the intervention were either real clinical health outcomes, such as mortality, or surrogate clinical health outcomes, such as HbA1c, lipids and blood pressure. In addition to clinical health outcomes, we included patient reported health outcomes, such as health related quality of life and proxies of health outcomes, such as quality of care performance indicators.

2.6. Data collection process

Other extracted data included the duration of the intervention, study size, primary outcomes, specification of the CPS (disease-specific or patient-centered) and the number of involved practices and NDPs. The primary outcomes of the intervention were categorized as either "positive", "negative" or "no effect". A positive outcome was defined as a statistically significant difference (p value < 0.05) compared to the control group or baseline. A negative outcome being the opposite and no effect as no statistically significant difference between intervention and control group or baseline.

Two authors independently extracted the data and one author cross-checked all extracted data. Differences were resolved in discussion. In case of dissensus, a third researcher was consulted. If we were unable to score the dimensions of integration – despite contacting the corresponding author for additional information and verifying complementary study protocols - the study was excluded for synthesis.

2.7. Quality assessment

We used the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool to assess: selection bias, study design, confounders, data collection methods, withdrawals and dropouts. Given the nature of the included studies, blinding of the participants and outcome assessors was generally not possible. Therefore, this criterion was not included in the quality

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

Table 1
Key dimensions of integrated care for chronic disease management,[17] tailored to the setting of a non-dispensing pharmacist in primary care practice.

Organizational:	Organizational design and governance arrangements *Measurable element*: an umbrella organization or network, or NDP has permanent position within primary care practice
Informational:	Shared access of clinical information systems *Measurable element*: GP and NDP work with integrated clinical information systems
Clinical:	Delivery of rational and continuous clinical care to patients *Measurable elements*: multiprofessional teams, NDP performs patient counselling and follow-up, face-to-face communication between GP and NDP, patient directed activities outside the scope of the intervention, prescribing authority of the NDP
Functional:	Supportive administrative and functional elements *Measurable element*: shared education or administrative support by primary care practice staff
Financial:	Financial arrangements and payment system *Measurable element*: n/a
Normative:	Shared vision, goals and values *Measurable element*: collaboratively designed protocols with shared goals and visions of the pharmaceutical intervention

assessment. Two authors independently assessed each study and resolved disagreement by consensus or by consulting a third reviewer.

2.8. Data synthesis

The included studies were heterogeneous regarding the type of CPS, enrolled participants, number of practices, involved NDPs and measured health outcomes. Therefore, it was inappropriate to perform statistical aggregation of findings. To investigate how the degree of integration of an NDP impacts health outcomes we plotted the number of improved primary outcomes against the total number of assessed primary outcomes. We stratified the analysis for disease-specific CPS and patient-centered CPS.

3. Results

Ninety studies were included for data extraction (Fig. 1). For thirty studies we were unable to determine the degree of integration of the NDP and were excluded (Appendix Table 2a/b). We grouped studies by type of CPS: disease-specific CPS (n = 43) and patient-centered CPS (n = 17).

3.1. Summary of included studies

The included studies consisted of 35 RCTs, 12 two group cohort studies and 13 one group cohort studies. The median of the study population was 140 patients (interquartile range 76–321). The duration of the interventions ranged from 1 to 60 months. The median of the number of involved practices and NDPs was 1

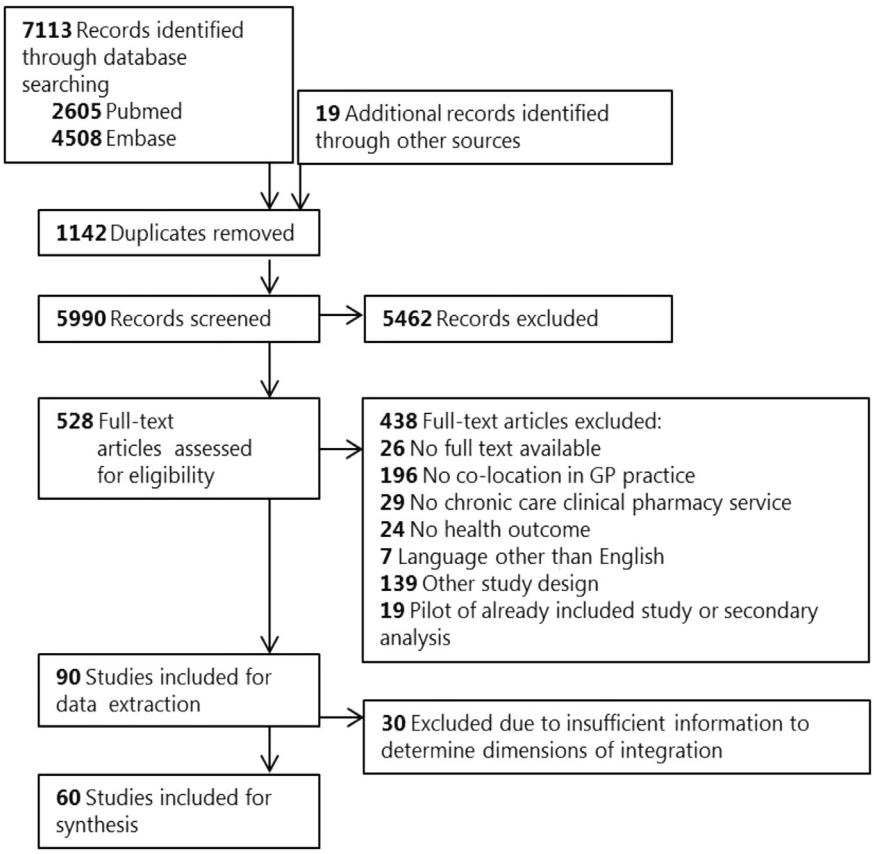

Fig. 1. Flowchart of the study selection.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

(interquartile range 1–6) and 2 (interquartile range 1–4), respectively. The majority of the studies were performed in the United Stated of America (USA) (n = 43) (Tables 2a and 2b).

3.2. Methodological quality

The methodological quality was high in 18 studies (30%), moderate in 34 studies (57%) and low in 8 studies (13%). 35 studies (58%) had a strong design, with described randomization processes. Eight studies (13%) had a high participation rate and were very likely to be representative to the target population. Forty studies (67%) controlled for at least 80% of relevant confounders and 48 studies (80%) used valid and reliable data collection tools. 29 studies (48%) had a follow-up rate of at least 80% (Table 3).

3.3. Synthesis of results

We assessed 89 health outcomes in 60 comparative studies: 54 clinical health outcomes (mainly surrogate health outcomes such as blood pressure or HbA1c), 12 patient reported health outcomes, such as health related quality of life and 23 proxies of health outcomes, such as medication errors (see Table 4). CPS conducted by NDPs showed a significant positive effect on 62% (55/89) of assessed health outcomes. The other 34 health outcomes showed no statistically significant difference compared to control group or baseline. None of the included studies measured a negative impact on health outcomes. The effect of CPS on surrogate clinical health outcomes and proxies of health outcomes was high: 67% (36/54) and 78% (18/23) of these outcomes improved. Patient reported health outcomes were less frequently reported (n = 12) and showed improvement in one trial.

We related the dimensions of integration to the degree of integration. We found 14 studies (23%) in which the NDPs were not or minimally integrated into the health care team (positive score on 0–2 dimensions of integration). 71% (n = 10) of NDPs had shared access to patient medical records (informational integration). Yet, integration on all other dimensions was low: organizational 14% (n = 2), normative 14% (n = 2), functional 7% (n = 1) and clinical 7% (n = 1).

We identified 19 studies (32%) in which the NDPs were partially integrated (positive score on 3–4 dimensions of integration). All but one (95%) had shared access to patient medical records. Integration on the clinical, functional and normative dimension was 68% (n = 13) and 47% (n = 9) of NDPs were permanently employed within the practice or worked within an umbrella organization or network (organizational integration).

We found 27 studies (45%) in which the NDPs were fully integrated within the primary care practice (positive score on 5 dimensions of integration). This involved permanent employment within the organization, or an umbrella organization or network, shared information systems, shared education or administrative support and a profound clinical role with shared goals and visions, such as a collaborative practice agreement to enhance cooperation in the delivery of CPS.

For each level of integration (none-partial-full), we plotted the number of improved primary outcomes against the total number of assessed primary outcomes (Fig. 2). The accumulated evidence from these studies suggests that there is no impact of the degree of integration of NDPs on health outcomes. The percentage of improved health outcomes for none, partial and fully integrated NDPs is respectively 63% (based on 19 assessed health outcomes within 14 different studies), 61% (based on 23 assessed health outcomes within 19 different studies) and 62% (based on 47 assessed health outcomes within 27 different studies). Also, after stratifying the health outcomes into clinical, patient reported and proxies of health outcomes, no association can be identified between the degree of integration of NDPs and an improvement on health outcomes.

3.4. Stratification of the results according to type of CPS

We included 43 studies about disease-specific CPS, in which 61 health outcomes, mainly surrogate clinical health outcomes (n = 51) were assessed, of which 67% showed a significant positive effect. Five patient reported health outcomes and five proxies of health outcomes were reported, of which 20% (n = 1) and 60% (n = 3) showed improvement, respectively. Within this subgroup of CPS services, we found 8 studies (19%) in which the NDPs were not or minimally integrated into the health care team, 14 studies (33%) in which the NDPs were partially integrated and 21 studies (49%) in which the NDPs were fully integrated within the primary care team. For disease-specific CPS the percentage of improved health outcomes in studies with not, partial and fully integrated NDPs is respectively 75%, 63% and 59%. Our data suggest a negative association between integration and improvement on health outcomes for disease-specific CPS (Fig. 2).

We included 17 studies about patient-centered CPS and assessed 28 health outcomes, mainly proxies of health outcomes (n = 18) of which 83% showed a significant positive effect. In total, 7 patient reported health outcomes were reported of which none showed improvement. A small number of surrogate clinical health outcomes was reported (n = 3) and 2 were positively affected by the NDP provided services. We found 6 studies (35%) in which the NDPs were not or minimally integrated into the health care team, 5 studies (29%) in which the NDPs were partially integrated and 6 studies (35%) in which the NDPs were fully integrated within the primary care team. For patient-centered CPS the percentage of improved health outcomes in studies with not, partial and fully integrated NDPs is respectively 55%, 57% and 70%. Therefore, our data suggest a positive association between integration and improvement on health outcomes for patient-centered CPS (Fig. 2).

4. Discussion

We evaluated the impact of the degree of integration of NDPs on health outcomes in primary care. Although we found that the degree of integration of NDPs did not impact health outcomes in the overall group, subgroup analysis suggests that full integration of an NDP may be especially relevant for patient-centered CPS.

An explanation of why full integration of an NDP is more relevant for patient-centered interventions than disease-specific interventions is provided by Weick.[76] Integration enables NDPs to manage interruptions in the care trajectory of an individual patient. Being in close relation with both GPs and patients, NDPs can pick up the small clues that signal lapses in the care trajectory. The degree of integration showed a trend towards a negative association with the health outcomes of disease-specific CPS. The diseases-specific CPS included in this study were based upon a set protocol. These standardized care trajectories are less prone to errors and allowing for variety may not have an added value. Reliability – defined as compliance to the protocols – seems to be more effective.[77]

Almost all studies reported surrogate health outcomes rather than clinical endpoints such as hospitalization or mortality. Disease-specific CPS mainly described surrogate clinical health outcomes (e.g. HbA1c, lipids and blood pressure), while patient-centered CPS

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

Table 2a
Study characteristics of disease-specific clinical pharmacy services (n = 43).

Author (year)	Country	No. intervention practices/No. NDPs	Duration intervention (months)	No. patients in intervention group	Dimension of integration					Primary outcomes (effect)
					Organizational	Informational	Clinical[a]	Functional	Normative	
Diabetes (n=16)										
Choe (2005)[18]	USA	1/1	24	41	Yes	Yes	Yes	Yes	Yes	HbA1C (+)
Coast-Senior (1998)[19]	USA	2/4	3–11	23	Yes	Yes	Yes	Yes	Yes	Glycemic control (+)
Heisler (2012)[4]	UK	5/11	14	1797	Yes	Yes	Yes	Yes	Yes	BP (0)
Henry (2013)[20]	USA	1/2	3	93	Yes	Yes	Yes	Yes	Yes	Guideline adherence (0), HbA1C (+)
Ip (2013)[21]	USA	1/1	12	147	Yes	Yes	Yes	Yes	Yes	HbA1c, LDL-C and BP (+) and goal attainment (+), 10-year CVRR (+)
Irons (2002)[22]	USA	1/2	32	87	Yes	No	Yes	No	Yes	Glycemic control (0)
Jameson (2010)[23]	USA	13/1	12	52	No	Yes	No	Yes	Yes	HbA1c (0)
McAdam-Marx (2015)[24]	USA	10/3	48	303	Yes	Yes	Yes	No	Yes	Glycemic control (+)
McCord (2006)[25]	USA	1/1	4	316	Yes	Yes	Yes	Yes	Yes	HbA1c (+), BP (0), lipids (+)
McFarland (2012)[26]	USA	4/3	6	36	Yes	No	Yes	Yes	Yes	HbA1c (0)
Mourão (2012)[27]	Brazil	6/2	6	50	No	No	No	No	No	HbA1c (0)
Rothman (2005)[28]	USA	1/3	12	112	Yes	Yes	Yes	Yes	Yes	HbA1c (+),LDL-C (0), BP (+)
Salvo (2012)[29]	USA	1/1	18	69	Yes	Yes	Yes	Yes	Yes	HbA1c (+)
Scott (2006)[30]	USA	1/1	9	76	No	Yes	Yes	Yes	Yes	HbA1c (+)
Shane-McWorther (2005)[31]	USA	1/1	36	176	Yes	Yes	Yes	Yes	Yes	HbA1c (0), lipids (0), BP (0)
Simpson (2011)[32]	Canada	5/2	12	131	Yes	Yes	Yes	Yes	No	BP (+)
Hypertension (n=11)										
Bex (2011)[33]	USA	4/6	18	573	Yes	Yes	Yes	Yes	Yes	BP (+)
Bogden (1998)[34]	USA	1/1	6	49	No	Yes	No	No	No	BP (+)
Borenstein (2003)[35]	USA	1/1	12	98	No	Yes	No	Yes	Yes	BP (+)
Carter (2008)[36]	USA	5/2	9	101	Yes	Yes	Yes	Yes	Yes	BP (+)
Hirsch (2014)[37]	USA	1/2	9	166	No	Yes	Yes	Yes	Yes	BP (+)
Hunt (2008)[38]	USA	9/5	12	230	Yes	Yes	Yes	Yes	Yes	BP (+)
Magid (2013)[39]	USA	10/≥10	6	175	Yes	Yes	Yes	Yes	Yes	BP (+)
Margolis (2013)[40]	USA	16/8	18	228	Yes	Yes	Yes	Yes	Yes	BP (+)
Mehos (2000)[41]	USA	1/1	6	18	No	No	No	No	No	BP (+)
O'Neill (2014)[42]	USA	1/1	1	63	Yes	Yes	Yes	Yes	Yes	BP (+)
Wong (2013)[43]	Hong Kong	1/?	6	92	No	No	No	No	No	BP (0)
Dyslipidaemia (n=5)										
Billups (2005)[44]	USA	16/16-48	12	5550	Yes	Yes	No	No	Yes	LDL-C (+)
Bogden (1997)[5]	USA	1/1	6	47	No	Yes	No	No	No	LDL-C (+)
Smith (2013)[45]	USA	2/1	?	213	Yes	Yes	Yes	Yes	Yes	Lipid profile
Straka (2005)[46]	USA	2/2	6	359	No	Yes	Yes	No	Yes	LDL-C (+)
Tahaineh (2011)[47]	Jordan	1/1	6	73	No	No	No	No	Yes	LDL-C (+)
Metabolic syndrome (n=1)										
Hammad (2011)[48]	Jordan	6/2	6	112	Yes	Yes	No	No	No	Metabolic syndrome status (+)
Heart failure (n=1)										
Lowrie (2012)[49]	UK	174/27	60	1090	No	Yes	Yes	No	No	Composite of death or hospital admission for worsening heart failure (0)
Depression (n=3)										
Adler (2004)[50]	USA	9/5	6	268	No	Yes	Yes	Yes	No	Antidepressant use rate (+). depressions severity (0)
Capoccia (2004)[51]	USA	1/2	12	41	Yes	Yes	Yes	Yes	Yes	Depression symptoms (0)
Finley (2003)[52]	USA	1/?	6	75	Yes	Yes	Yes	Yes	Yes	Adherence to antidepressant (+), patient satisfaction (+), clinical and functional severity (0)

(*continued on next page*)

Table 2a (*continued*)

Author (year)	Country	No. intervention practices/No. NDPs	Duration intervention (months)	No. patients in intervention group	Dimension of integration					Primary outcomes (effect)
					Organizational	Informational	Clinical[a]	Functional	Normative	
Osteoporosis (n=1)										
Hall (2009)[53]	USA	1/4	?	22	Yes	Yes	Yes	No	Yes	Compliance with treatment guidelines (+)
Cardiovascular disease (n=1)										
Evans (2010)[54]	Canada	1/1	6	176	No	Yes	Yes	No	Yes	10 year cardiovascular risk reduction (0)
Diabetes + hypertension (n=2)										
Edelman (2010)[55]	USA	2/2	12	133	Yes	Yes	Yes	Yes	No	BP (+),HbA1C (0)
Neto (2011)[56]	Brazil	1/4	36	97	Yes	Yes	Yes	Yes	Yes	10 year cardiovascular risk reduction (+)
Diabetes and/or dyslipidaemia (n=1)										
Hetro (2015)[57]	USA	1/?	6	61	Yes	Yes	Yes	Yes	Yes	HbA1C (+), LDL-C (0), BMI (0)
Diabetes, hypertension, dyslipidaemia or asthma (n=1)										
Koenigsfeld (2012)[58]	USA	3/3	13	131 + 427+299 + 27	Yes	Yes	Yes	Yes	Yes	Achieving goal levels for DM (0), hypertension (+) and % on asthma controller medication (0)

(+) = positive effect, (0) = no effect, BP = Blood Pressure, CVRR = Cardiovascular Risk Reduction, HbA1c = glycosylated haemoglobin, LDL-C = low-density lipoprotein cholesterol.

[a] See Appendix Table 3 for specification.

Table 2b
Study characteristics of patient-centered clinical pharmacy services (n = 17).

Author (year)	Country	No. practices/ No. NDPs	Duration intervention (months)	Study size intervention group (patients)	Dimension of integration					Primary outcome(s) (effect)
					Organizational	Informational	Clinical[a]	Functional	Normative	
Avery (2012)[59]	UK	72/?	12	3812	No	Yes	No	No	No	Three prescribing appropriateness indicators (+)
Berdine (2012)[60]	USA	1/1	36	200	Yes	Yes	Yes	Yes	Yes	Lipids (+), A1C (0) and BMI (+)
Carter (2001)[61]	USA	9/51?	12	523	Yes	Yes	Yes	Yes	No	Patient satisfaction (0), HRQoL (0)
Davis (2007)[62]	USA	6/12	5	79	Yes	Yes	No	Yes	No	MAI (+)
Freeman (2013)[63]	Australia	1/1	0–12	314	Yes	Yes	Yes	Yes	Yes	Uptake of recommendations from medication review (+)
Galt (1998)[64]	USA	1/1	12	336	Yes	Yes	Yes	Yes	Yes	Reduction in use of unessential medications (+)
Hanlon (1996)[65]	USA	1/1	12	105	No	Yes	No	No	No	MAI (+), HRQoL (0), ADE (0)
Hogg (2009)[66]	Canada	1/1	12–18	121	Yes	Yes	Yes	Yes	Yes	QoC for CDM (+)
Isetts (2006)[67]	USA	6/7	12	285	Yes	Yes	Yes	Yes	Yes	Patients' perceptions of care (0), HRQoL (0)
Isetts (2008)[68]	USA	6/7	12	256	Yes	Yes	Yes	Yes	Yes	Quality-of-care performance measures for hypertension and cholesterol (+)
Krska (2001)[69]	UK	?/?	3	168	No	Yes	No	Yes	No	Resolved PCI (+), HRQoL (0)
Lenander (2014)[70]	Sweden	1/1	12	107	No	Yes	No	Yes	Yes	Resolved MRPs (0), No. of medications (+)
Pindolia (2009)[71]	USA	1/7	24	520	Yes	Yes	No	No	No	Improvement on clinical outcome rules (0)
Roth (2013)[72]	USA	½	6	64	No	Yes	No	No	Yes	Resolved MRPs (+)
Sellors (2003)[73]	Canada	24/12	5	431	No	Yes	No	No	No	No. of daily doses (0)
Tan (2014)[74]	Australia	2/2	6	82	No	Yes	Yes	Yes	No	Resolved MRPs (+)
Zermansky (2001)[75]	UK	4/1	12	581	No	Yes	No	Yes	Yes	No. of changes to repeat prescription changes (+)

(+) = positive effect, (0) = no effect, ADE = Adverse Drug Events, BMI = Body Mass Index, BP = Blood pressure, CDM = Chronic Disease Management, HbA1c = glycosylated haemoglobin, HRQoL = Health Related Quality of Life, LDL-C = low-density lipoprotein cholesterol, MAI = Medication Appropriateness Index, MRP = Medication Related Problem, PCI = Pharmaceutical Care Issues, QoC = Quality of Care.

[a] See Appendix Table 3 for specification.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

Table 3
Quality assessment of included studies.

Author (year)	Selection bias	Study design	Confounders	Data collection	Drop-outs	Global
Adler (2004)[50]	Weak	Strong	Strong	Strong	Strong	Moderate
Avery (2012)[59]	Weak	Strong	Weak	Strong	Strong	Weak
Berdine (2012)[60]	Moderate	Moderate	Weak	Strong	Weak	Weak
Bex (2011)[33]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
Billups (2005)[44]	Moderate	Moderate	Weak	Strong	Strong	Moderate
Bogden (1997)[5]	Moderate	Strong	Strong	Strong	Strong	Strong
Bogden (1998)[34]	Moderate	Strong	Strong	Strong	Strong	Strong
Borenstein (2003)[35]	Weak	Strong	Moderate	Strong	Strong	Moderate
Capoccia (2004)[51]	Moderate	Strong	Strong	Moderate	Strong	Strong
Carter (2001)[61]	Moderate	Strong	Weak	Strong	Weak	Weak
Carter (2008)[36]	Weak	Strong	Strong	Strong	Moderate	Moderate
Choe (2005)[18]	Strong	Strong	Strong	Moderate	Moderate	Strong
Coast-Senior (1998)[19]	Moderate	Weak	Weak	Moderate	Strong	Weak
Davis (2007)[62]	Strong	Moderate	Weak	Strong	Moderate	Moderate
Edelman (2010)[55]	Weak	Strong	Strong	Strong	Strong	Moderate
Evans (2010)[54]	Moderate	Strong	Strong	Strong	Strong	Strong
Finley (2003)[52]	Moderate	Strong	Strong	Strong	Weak	Moderate
Freeman (2013)[63]	Strong	Moderate	Weak	Moderate	Moderate	Moderate
Galt (1998)[64]	Weak	Moderate	Weak	Moderate	Weak	Weak
Hall (2009)[53]	Moderate	Moderate	Strong	Strong	Weak	Moderate
Hammad (2011)[48]	Strong	Strong	Strong	Strong	Strong	Strong
Hanlon (1996)[65]	Strong	Strong	Strong	Moderate	Strong	Strong
Heisler (2012)[4]	Moderate	Strong	Strong	Strong	Weak	Moderate
Henry (2013)[20]	Moderate	Moderate	Weak	Weak	Moderate	Weak
Hetro (2015)[57]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
Hirsch (2014)[37]	Weak	Strong	Strong	Strong	Strong	Moderate
Hogg (2009)[66]	Moderate	Strong	Strong	Moderate	Strong	Strong
Hunt (2008)[38]	Weak	Strong	Strong	Strong	Weak	Weak
Ip (2013)[21]	Moderate	Moderate	Strong	Strong	Moderate	Moderate
Irons (2002)[22]	Moderate	Moderate	Strong	Strong	Moderate	Moderate
Isetts (2006)[67]	Weak	Moderate	Moderate	Strong	Moderate	Moderate
Isetts (2008)[68]	Moderate	Moderate	Strong	Strong	Weak	Moderate
Jameson (2010)[23]	Weak	Strong	Strong	Strong	Strong	Moderate
Koenigsfeld (2012)[58]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
Krska (2001)[69]	Moderate	Strong	Strong	Moderate	Strong	Strong
Lenander (2014)[70]	Moderate	Strong	Strong	Weak	Moderate	Moderate
Lowrie (2012)[49]	Weak	Strong	Strong	Strong	Strong	Moderate
Magid (2013)[39]	Moderate	Strong	Strong	Strong	Strong	Strong
Margolis (2013)[40]	Moderate	Strong	Weak	Strong	Strong	Moderate
McAdam-Marx (2015)[24]	Moderate	Moderate	Strong	Strong	Moderate	Moderate
McCord (2006)[25]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
McFarland (2012)[26]	Moderate	Moderate	Strong	Strong	Moderate	Moderate
Mehos (2000)[41]	Moderate	Strong	Strong	Strong	Strong	Strong
Mourão (2012)[27]	Strong	Strong	Strong	Strong	Moderate	Strong
Neto (2011)[56]	Moderate	Strong	Strong	Strong	Strong	Strong
O'Neill (2014)[42]	Moderate	Weak	Strong	Strong	Moderate	Moderate
Pindolia (2009)[71]	Weak	Moderate	Weak	Strong	Moderate	Weak
Roth (2013)[72]	Moderate	Moderate	Strong	Strong	Strong	Moderate
Rothman (2005)[28]	Moderate	Strong	Strong	Strong	Strong	Strong
Salvo (2012)[29]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
Scott (2006)[30]	Moderate	Strong	Strong	Strong	Strong	Strong
Sellors (2003)[73]	Moderate	Strong	Strong	Strong	Strong	Strong
Shane-McWorther (2005)[31]	Moderate	Moderate	Weak	Strong	Moderate	Moderate
Simpson (2011)[32]	Weak	Strong	Strong	Strong	Strong	Moderate
Smith (2013)[45]	Moderate	Moderate	Strong	Strong	Moderate	Moderate
Straka (2005)[46]	Strong	Strong	Strong	Strong	Strong	Strong
Tahaineh (2011)[47]	Strong	Strong	Weak	Strong	Moderate	Moderate
Tan (2014)[74]	Moderate	Moderate	Strong	Moderate	Moderate	Moderate
Wong (2013)[43]	Moderate	Strong	Strong	Strong	Strong	Strong
Zermansky (2001)[75]	Weak	Strong	Strong	Moderate	Strong	Moderate
Sum weak	14 (23%)	2 (3%)	18 (30%)	2 (3%)	8 (13%)	8 (13%)
Sum moderate	38 (63%)	23 (38%)	2 (3%)	10 (17%)	23 (38%)	34 (57%)
Sum strong	8 (13%)	35 (58%)	40 (67%)	48 (80%)	29 (48%)	18 (30%)

often used process outcomes (e.g. quality of care performance indicators) to measure the effect of the intervention. Also, we found a low impact of CPS on health related quality of life.[51,61,65,67,69] The effects of a multifaceted quality improvement service often do not extend as far as to health related quality of life.[78]

Fully integrated NDPs are permanently employed or work within a network or umbrella organization (organizational integration), they usually have shared access to clinical information systems (informational integration), work in multiprofessional teams with face-to-face collaboration with the GP (clinical integration), have shared education and/or support staff for administrative functions (functional integration) and share a vision on

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

Table 4
The impact of the degree on integration of NDPs on health outcomes in primary care.

	All outcomes (n = 89)			Disease-specific CPS (no. of assessed outcomes: 61)			Patient-centered CPS (no. of assessed outcomes: 28)		
	No integration	Partial integration	Full Integration	No integration	Partial integration	Full integration	No integration	Partial integration	Full integration
Clinical health outcomes									
Death or hospitalization	0/1 (1090)			0/1 (1090)					
Surrogate clinical health outcomes									
HbA1c	1/1 (50)	2/6 (687)	8/11 (1369)	1/1 (50)	2/6 (687)	8/10 (1169)			0/1 (200)
Lipids	2/2 (120)	2/2 (5909)	4/7 (1225)	2/2 (120)	2/2 (5909)	3/6 (1025)			1/1 (200)
BP	2/3 (159)	4/4 (430)	7/11 (4198)	2/3 (159)	4/4 (430)	7/11 (4198)			
BMI			1/2 (261)			0/1 (61)			1/1 (200)
Metabolic syndrome status	1/1 (112)			1/1 (112)					
Cardiovascular risk reduction		0/1 (176)	2/2 (244)		0/1 (176)	2/2 (244)			
Subtotal	6/8 (75%)	8/13 (62%)	22/33 (68%)	6/8 (75%)	8/13 (62%)	20/30 (67%)			2/3 (67%)
Patient reported health outcomes									
HRQoL	0/2 (273)	0/1 (523)	0/2 (453)			0/1 (168)	0/2 (273)	0/1 (523)	0/1 (285)
Patient satisfaction, perceptions of care	0/1 (105)	0/1 (523)	1/2 (360)			1/1 (75)	0/1 (105)	0/1 (523)	0/1 (285)
Depression severity		0/1 (268)	0/2 (116)		0/1 (268)	0/2 (116)			
Subtotal	0/3 (0%)	0/3 (0%)	1/6 (17%)		0/1 (0%)	1/4 (25%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
Proxies of health outcomes									
Adherence rate		1/1 (268)	1/1 (75)		1/1 (268)	1/1 (75)			
Reduction of (unwanted) medications	0/1 (431)	2/2 (688)	1/1 (336)				0/1 (431)	2/2 (688)	1/1 (336)
Medication errors, pharmaceutical care issues, prescribing appropriateness	6/7 (12.293)	3/4 (290)	3/5 (753)		1/1 (22)	0/2 (120)	6/7 (12.293)	2/3 (268)	3/3 (633)
Uptake of recommendations from MR			1/1 (314)						1/1 (314)
Subtotal	6/8 (67%)	6/7 (86%)	6/8 (75%)		2/2 (100%)	1/3 (33%)	6/8 (75%)	4/5 (80%)	5/5 (100%)
Total	**12/19 (63%)**	**14/23 (61%)**	**29/47 (62%)**	**6/8 (75%)**	**10/16 (63%)**	**22/37 (59%)**	**6/11 (55%)**	**4/7 (57%)**	**7/10 (70%)**

No. of improved outcomes/no. of assessed outcomes (no.of intervention patients).
For each health outcome, the number of studies that demonstrated significant improvement is divided by the total number of assessed studies. Since studies can include more than one primary outcome, the total number of assessed outcomes (89) exceeds the total number of included studies (60).
The numbers in parentheses reflect the accumulated number of intervention patients in studies assessing the specific health outcome.
BP = Blood pressure, BMI = Body Mass Index, HbA1c = glycosylated haemoglobin, HRQoL = Health Related Quality of Life, MR = Medication Review.

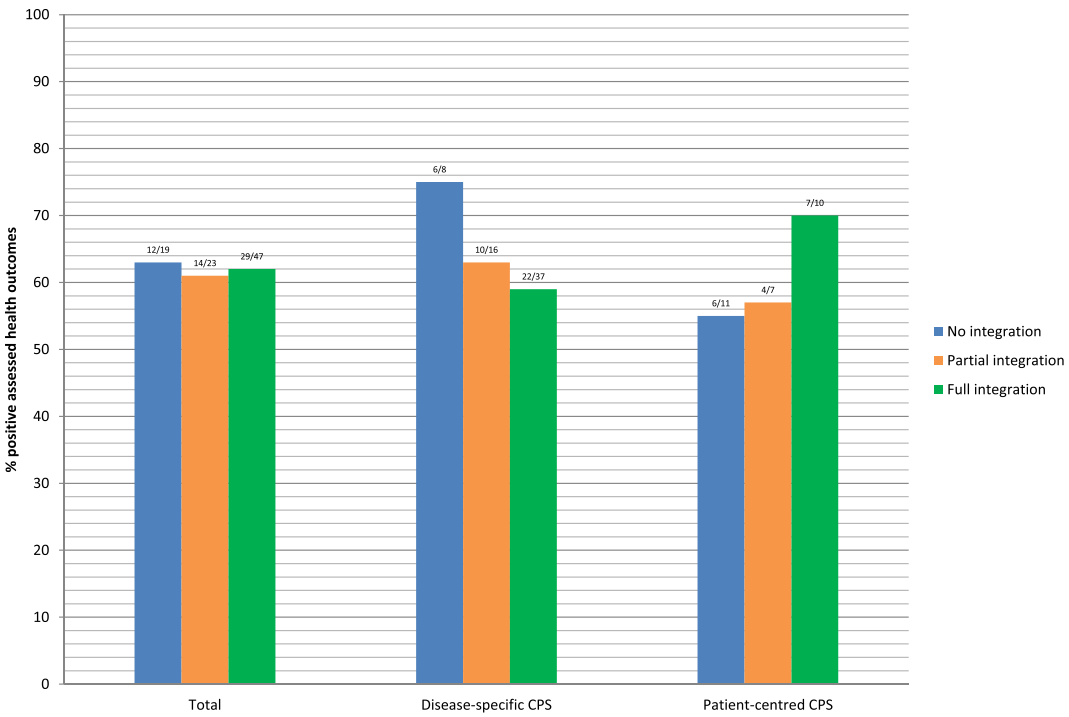

Fig. 2. Outcomes by degree of integration of NDPs on health outcomes in primary care. For each category of integration the total number of significant improved outcomes is divided by the total number of assessed outcomes. The results are also stratified by disease-specific CPS and patient-centered CPS.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

patient care with clinicians (normative integration). Clinical integration into a multidisciplinary primary care team provides greater opportunities for both formal and informal communication, probably enhancing patient care.[63] Also, expanding the clinical role of the NDP by allocating prescribing privileges might be beneficial.[79] Within disease-specific CPS, more than half of the NDPs were authorized to make medication changes within a defined scope of practice. Within patient-centered CPS, only 2 studies showed NDPs with prescribing authority. In these kind of services, with a more holistic approach to pharmaceutical care, prescribing authority would entail the whole spectrum of medications. The current absence of prescribing authority might have restricted the impact of the CPS on health outcomes.

CPS performed in isolation may negatively influence the quality of care.[80] There is one systematic review that described the effectiveness of NDPs co-located in primary care practice.[9] The importance of follow-up and face-to-face communication with the patient's GP (clinical integration) is highlighted. Other available studies described the effectiveness of CPS in different outpatient settings.[10–14] This study is the first to unravel the association between the extent of NDP integration in clinical care and drug related health outcomes.

4.1. Limitations

This review has a number of limitations. Similar to most literature reviews, there might have been publication bias. Also, CPS can like all cognitive interventions be subject to the Hawthorne-effect. The Hawthorne-effect might, at least partly, explain the absence of any negative health outcome in the included studies. The interventions and outcomes assessed in this review were heterogeneous. Also, we were unable to assess the impact of health care systems on the degree of integration of NDPs and on the success of the provided services. Moreover, the study population, duration of the intervention, number of practices and involved NDPs differed widely, limiting our options to assess the independent effect of integration and to pool data. The problem of heterogeneity in clinical pharmacy intervention studies has been previously addressed.[9,12,14,81–83] Hence, we cannot draw too strong conclusions about the impact of integration – as reflected by the wording we choose. Lastly, the positive association we found between the degree of integration and the effect of patient-centered CPS was based upon a limited number of studies (n = 17). Random effects cannot be ruled out. Additional research is required when new studies about integrated clinical pharmacy services in primary care become available.

4.2. Implications

This study has several implications for practitioners and policymakers. Integration on *all* dimensions for *all* types of chronic disease management services performed by NDPs in primary care practice may not be necessary. Integration on *all* dimensions should be promoted for individually tailored, i.e. patient-centered CPS.

5. Conclusion

To obtain maximum benefits of CPS for patients with multiple medications and comorbidities, full integration of NDPs should be stimulated.

Funding

This study is part of the POINT intervention study which is funded by The Netherlands Organization for Health Research and Development (ZonMW) and by the Dutch health insurance company Agis/Achmea. ZonMW and Agis/Achmea were not involved in the design of this systematic review, nor in the decision to submit this article for publication.

Appendix A

Table 1
Search strategies for Pubmed and Embase

Pubmed search June 2016	Embase search June 2016
("pharmacist"[Title/Abstract] OR "pharmacists"[Title/Abstract] OR "pharmaceutical service"[Title/Abstract] OR "pharmaceutical services"[Title/Abstract] OR "pharmacy"[Title/Abstract]OR "pharmacists"[MeSH Terms] OR "pharmaceutical services"[MeSH Terms])	pharmacist:ti,ab OR pharmacists:ti,ab OR pharmacy:ti,ab OR 'pharmaceutical service':ti,ab OR 'pharmaceutical services':ti,ab OR 'pharmacist'/exp OR 'pharmacy'/exp
("family practice"[Title/Abstract] OR "general practitioner"[Title/Abstract] OR "primary care"[Title/Abstract] OR "general practitioners"[Title/Abstract] OR "general practice"[Title/Abstract] OR "family physician"[Title/Abstract] OR "physicians, family"[MeSH Terms] OR "family practice"[MeSH Terms] OR "general practitioners"[MeSH Terms] OR "general practice"[MeSH Terms])	'family practice':ti,ab OR 'general practitioner':ti,ab OR 'general practitioners':ti,ab OR 'general practice':ti,ab OR 'community dwelling':ti,ab OR 'family physician':ti,ab OR 'community dwelling':ti,ab OR 'ambulatory patient':ti,ab OR 'ambulatory elderly':ti,ab OR 'ambulatory patients':ti,ab OR 'primary care':ti,ab OR 'general practice'/exp OR 'general practitioner'/exp
("patient care"[Title/Abstract]) OR "interprofessional relation"[Title/Abstract] OR "interprofessional relations"[Title/Abstract] OR "cooperation"[Title/Abstract] OR "collaboration"[Title/Abstract] OR "consultation"[Title/Abstract] OR "referral"[Title/Abstract] OR "refer"[Title/Abstract] OR "home medicines review"[Title/Abstract] OR "medication review"[Title/Abstract] OR "medication reviews"[Title/Abstract] OR "community dwelling"[Title/Abstract] OR "ambulatory patient"[Title/Abstract] OR "ambulatory elderly"[Title/Abstract] OR "ambulatory patients"[Title/Abstract] OR "pharmaceutical care"[Title/Abstract] OR "drug utilization review"[Title/Abstract] OR patient care[MeSH Terms] OR interprofessional relations[MeSH Terms]OR cooperative behaviour [MeSH Terms]OR counselling[MeSH Terms]OR professional role [MeSH Terms] OR (referral and consultation[MeSH Terms] OR "drug utilization review"[MeSH Terms] OR "review"[Title/Abstract])	'patient care':ti,ab OR 'interprofessional relation':ti,ab OR 'interprofessional relations':ti,ab OR cooperation:ti,ab OR collaboration:ti,ab OR consultation:ti,ab OR referral:ti,ab OR refer:ti,ab OR 'home medicines review':ti,ab OR 'medication review':ti,ab OR 'medication reviews':ti,ab OR review:ti,ab OR 'pharmaceutical care':ti,ab OR 'drug utilization review':ti,ab OR 'patient care'/exp OR 'patient referral'/exp

Table 2a
excluded studies with disease-specific CPS

Author (year)	Dimension of integration				
	Organizational	Informational	Clinical	Functional	Normative
Anaya (2008)[84]	No	Yes	Yes	N/A	Yes
Barnes (2014)[85]	Yes	Yes	No	N/A	N/A
Bruhn (2013)[86]	Yes	Yes	Yes	N/A	N/A
Carter (2015)[87]	Yes	Yes	Yes	No	N/A
Chung (2014)[88]	Yes	Yes	N/A	N/A	Yes
Cording (2002)[89]	Yes	Yes	N/A	Yes	Yes
Duran-Parrondo (2011)[90]	No	N/A	Yes	N/A	Yes
Erickson (1997)[91]	Yes	Yes	No	N/A	No
Gums (2014)[92]	Yes	Yes	Yes	No	N/A
Gums (2015)[93]	Yes	Yes	Yes	No	N/A
Jacobs (2012)[94]	No	Yes	No	N/A	No
Jamieson (2010)[95]	No	Yes	N/A	N/A	N/A
Johnson (2010)[96]	No	N/A	N/A	N/A	N/A
Kelly Hester (2000)[97]	No	N/A	N/A	No	No
Monte (2009)[98]	No	N/A	No	Yes	N/A
Shane-McWorther (2015)[99]	N/A	No	N/A	No	Yes
Solomon (1998)[100]	Yes	N/A	No	N/A	N/A
Stading (2009)[101]	Yes	Yes	N/A	N/A	N/A
Thumar (2014)[102]	No	Yes	No	Yes	N/A
Tobari (2010)[103]	Yes	Yes	No	N/A	N/A
Trompeter (2009)[104]	No	Yes	N/A	Yes	N/A
Villa (2009)[105]	N/A	N/A	N/A	N/A	N/A

Table 2b
excluded studies with patient-centered CPS

Author (year)	Dimension of integration				
	Organizational	Informational	Clinical	Functional	Normative
Hamley (1997)[106]	Yes	N/A	N/A	N/A	N/A
Harris (2009)[107]	Yes	Yes	No	N/A	N/A
Jameson (1995)[108]	N/A	N/A	No	N/A	N/A
Jameson (2001)[109]	N/A	Yes	No	N/A	N/A
Laucka (1996)[110]	No	Yes	No	N/A	N/A
Lowe (2000)[111]	No	No	No	N/A	N/A
Morrison (2015)[112]	No	Yes	No	N/A	Yes
Taylor (2003)[113]	No	Yes	No	N/A	N/A

Table 3
Clinical integration based upon six measurable elements. The NDP was considered clinical integrated when the result on ≥ four elements was positive ("Yes").

Ref.	Patient counselling by NDP	Follow-up by NDP	Face-to-face communication GP and NDP	Multiprofessional collaboration (≥3 care providers)	Other patient directed activities outside scope of intervention	Prescribing authority
Adler (2004)[50]	Yes	Yes	Yes	Yes	Yes	No
Avery (2012)[59]	No	Yes	Yes	No	No	No
Berdine (2012)[60]	Yes	Yes	Yes	No	Yes	Yes
Bex (2011)[33]	Yes	Yes	Yes	Yes	Yes	No
Billups (2005)[44]	No	Yes	No	No	Yes	No
Bogden (1997)[5]	Yes	No	No	No	No	No
Bogden (1998)[34]	Yes	No	Yes	No	No	No
Borenstein (2003)[35]	Yes	Yes	No	No	No	No
Capoccia (2004)[51]	Yes	Yes	Yes	Yes	Yes	Yes
Carter (2001)[61]	Yes	Yes	Yes	Yes	Yes	Yes
Carter (2008)[36]	Yes	Yes	Yes	Yes	Yes	No
Choe (2005)[18]	Yes	Yes	Yes	Yes	Yes	No
Coast-Senior (1998)[19]	Yes	Yes	Yes	Yes	Yes	Yes
Davis (2007)[62]	Yes	Yes	No	No	Yes	No
Edelman (2010)[55]	Yes	Yes	Yes	Yes	Yes	No
Evans (2010)[54]	Yes	Yes	Yes	No	Yes	No
Finley (2003)[52]	Yes	Yes	Yes	Yes	Yes	Yes
Freeman (2013)[63]	Yes	No	Yes	Yes	Yes	No
Galt (1998)[64]	Yes	Yes	Yes	Yes	Yes	No
Hall (2009)[53]	Yes	Yes	No	Yes	No	Yes
Hammad (2011)[48]	Yes	Yes	Yes	No	No	No
Hanlon (1996)[65]	Yes	No	Yes	No	No	No
Heisler (2012)[4]	Yes	Yes	Yes	Yes	Yes	Yes
Henry (2013)[20]	Yes	Yes	Yes	Yes	Yes	No

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

Table 3 (*continued*)

Ref.	Patient counselling by NDP	Follow-up by NDP	Face-to-face communication GP and NDP	Multiprofessional collaboration (≥3 care providers)	Other patient directed activities outside scope of intervention	Prescribing authority
Hetro (2015)[57]	Yes	Yes	Yes	Yes	Yes	Yes
Hirsch (2014)[37]	Yes	Yes	Yes	No	No	Yes
Hogg (2009)[66]	Yes	Yes	Yes	Yes	Yes	No
Hunt (2008)[38]	Yes	Yes	Yes	No	No	Yes
Ip (2013)[21]	Yes	Yes	Yes	Yes	Yes	Yes
Irons (2002)[22]	Yes	Yes	No	No	Yes	Yes
Isetts (2006)[67]	Yes	Yes	Yes	Yes	No	No
Isetts (2008)[68]	Yes	Yes	Yes	Yes	Yes	No
Jameson (2010)[23]	Yes	Yes	Yes	No	No	No
Koenigsfeld (2012)[58]	Yes	Yes	Yes	No	Yes	No
Krska (2001)[69]	Yes	Yes	No	Yes	No	No
Lenander (2014)[70]	Yes	No	Yes	Yes	No	No
Lowrie (2012)[49]	Yes	Yes	Yes	Yes	No	Yes
Magid (2013)[39]	Yes	Yes	No	Yes	Yes	Yes
Margolis (2013)[40]	Yes	Yes	No	Yes	Yes	Yes
McAdam-Marx (2015)[24]	Yes	Yes	Yes	Yes	No	Yes
McCord (2006)[25]	Yes	Yes	Yes	Yes	Yes	Yes
McFarland (2012)[26]	No	Yes	No	Yes	No	Yes
Mehos (2000)[41]	Yes	Yes	No	No	No	No
Mourão (2012)[27]	Yes	Yes	No	No	No	Yes
Neto (2011)[56]	Yes	Yes	Yes	Yes	Yes	No
O'Neill (2014)[42]	Yes	Yes	Yes	Yes	Yes	Yes
Pindolia (2009)[71]	Yes	Yes	Yes	No	No	No
Roth (2013)[72]	Yes	Yes	Yes	No	No	No
Rothman (2005)[28]	Yes	Yes	Yes	Yes	No	Yes
Salvo (2012)[29]	Yes	Yes	No	Yes	Yes	Yes
Scott (2006)[30]	Yes	Yes	No	Yes	No	Yes
Sellors (2003)[73]	Yes	Yes	Yes	No	No	No
Shane-McWorther (2005)[31]	Yes	Yes	No	Yes	Yes	No
Simpson (2011)[32]	Yes	Yes	Yes	Yes	No	No
Smith (2013)[45]	Yes	Yes	Yes	Yes	Yes	Yes
Straka (2005)[46]	Yes	Yes	Yes	No	No	Yes
Tahaineh (2011)[47]	Yes	Yes	No	No	Yes	No
Tan (2014)[74]	Yes	No	Yes	Yes	Yes	No
Wong (2013)[43]	Yes	No	No	No	No	No
Zermansky (2001)[75]	Yes	Yes	Yes	No	No	No

References

1. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet*. 2012;380(9836):37–43. http://dx.doi.org/10.1016/S0140-6736(12)60240-2.
2. Stewart M. Towards a global definition of patient centred care. *BMJ*. 2001;322(7284):444–445. http://dx.doi.org/10.1136/bmj.322.7284.444.
3. Nadrash TA, Plushner SL, Delate T. Clinical pharmacists' role in improving osteoporosis treatment rates among elderly patients with untreated atraumatic fractures. *Ann Pharmacother*. 2008;42(3):334–340. http://dx.doi.org/10.1345/aph.1K541.
4. Heisler M, Hofer TP, Schmittdiel JA, et al. Improving blood pressure control through a clinical pharmacist outreach program in patients with diabetes mellitus in 2 high-performing health systems: the adherence and intensification of medications cluster randomized, controlled pragmatic trial. *Circulation*. 2012;125:2863–2872. http://dx.doi.org/10.1161/CIRCULATIONAHA.111.089169.
5. Bogden PE, Koontz LM, Williamson P, Abbott RD. The physician and pharmacist team. An effective approach to cholesterol reduction. *J Gen Intern Med*. 1997;12(3):158–164. http://dx.doi.org/10.1046/j.1525-1497.1997.012003158.x.
6. Leape L, Berwick D, Clancy C, et al. Transforming healthcare: a safety imperative. *Qual Saf Health Care*. 2009;18(6):424–428. http://dx.doi.org/10.1136/qshc.2009.036954.
7. Strandberg-Larsen M, Krasnik A. Measurement of integrated healthcare delivery: a systematic review of methods and future research directions. *Int J Integr Care*. 2009;9(February):e01.
8. Martínez-González NA, Berchtold P, Ullman K, Busato A, Egger M. Integrated care programmes for adults with chronic conditions: a meta-review. *Int J Qual Health Care*. 2014;26(5):561–570. http://dx.doi.org/10.1093/intqhc/mzu071.
9. Tan ECK, Stewart K. Elliott R a., George J. Pharmacist services provided in general practice clinics: a systematic review and meta-analysis. *Res Soc Adm Pharm*. 2014;10(4):608–622. http://dx.doi.org/10.1016/j.sapharm.2013.08.006.
10. Santschi V, Rodondi N, Bugnon O, Burnier M. Impact of electronic monitoring of drug adherence on blood pressure control in primary care: a cluster 12-month randomised controlled study. *Eur J Intern Med*. 2008;19:427–434. http://dx.doi.org/10.1016/j.ejim.2007.12.007.
11. Houle SKD, Chatterley T, Tsuyuki RT. Multidisciplinary approaches to the management of high blood pressure. *Curr Opin Cardiol*. 2014;29(4):344–353. http://dx.doi.org/10.1097/HCO.0000000000000071.
12. Greer N, Bolduc J, Geurkink E, et al. Pharmacist-led chronic disease management: a systematic review of effectiveness and harms compared with usual care. *Ann Intern Med*. 2016. http://dx.doi.org/10.7326/M15-3058.
13. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy*. 2008;28(4):421–436. http://dx.doi.org/10.1592/phco.28.4.421.
14. Viswanathan M, Kahwati LC, Golin CE, et al. Medication therapy management interventions in outpatient settings. *JAMA Intern Med*. 2014;175(138):76–87. http://dx.doi.org/10.1001/jamainternmed.2014.5841.
15. Hazen A. *The Impact of the Degree of Integration of Non-dispensing Clinical Pharmacists in Primary Care Clinics on Patient Outcomes*. Prospero; 2015. Available at:: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016017506 [Accessed 25 July 2016].
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2014;151(2):264–269. http://dx.doi.org/10.1371/journal.pmed1000097.
17. Walshe, Smith. Chronic disease and integrated care. In: *Healthcare Management*. second ed. McGraw-Hill Education; 2011.
18. Choe HM, Mitrovich S, Dubay D, Hayward RA, Krein SL, Vijan S. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. *Am J Manag Care*. 2005;11(4):253–260.
19. Coast-Senior. Management of patients with type 2 diabetes by pharmacists in primary care clinics. *Ann Pharmacother*. 1998;32:636–641.
20. Henry TM, Smith S, Hicho M. Treat to goal: impact of clinical pharmacist referral service primarily in diabetes management. *Hosp Pharm*. 2013;48(8):656–661. http://dx.doi.org/10.1310/hpj4808-656.
21. Ip EJ, Shah BM, Yu J, Chan J, Nguyen LT, Bhatt DC. Enhancing diabetes care by adding a pharmacist to the primary care team. *Am J Health Syst Pharm*. 2013;70(10):877–886. http://dx.doi.org/10.2146/ajhp120238.
22. Irons BK, Lenz RJ, Anderson SL, et al. A retrospective cohort analysis of the clinical effectiveness of a physician-pharmacist collaborative drug therapy management diabetes clinic. *Pharmacotherapy*. 2002;22:1294–1300.
23. Jameson JP, Baty PJ. Pharmacist collaborative management of poorly controlled diabetes mellitus: a randomized controlled trial. *Am J Manag Care*.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

2010;16(4):250–255.
24. McAdam-Marx C, Dahal A, Jennings B, Singhal M, Gunning K. The effect of a diabetes collaborative care management program on clinical and economic outcomes in patients with type 2 diabetes. *J Manag Care Pharm*. 2015;21(6):452–468. http://dx.doi.org/10.18553/jmcp.2015.21.6.452.
25. Mccord AD, Pharm D. Clinical impact of a pharmacist-managed diabetes mellitus drug therapy management service. *Pharmacotherapy*. 2006;26(2):248–253.
26. McFarland M, Davis K, Wallace J, et al. Use of home telehealth monitoring with active medication therapy management by clinical pharmacists in veterans with poorly controlled type 2 diabetes mellitus. *Pharmacotherapy*. 2012;32(5):420–426.
27. Mourão AOM, Ferreira WR, Martins MAP, et al. Pharmaceutical care program for type 2 diabetes patients in Brazil: a randomised controlled trial. *Int J Clin Pharm*. 2013;35(1):79–86. http://dx.doi.org/10.1007/s11096-012-9710-7.
28. Rothman RL, Malone R, Bryant B, et al. A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes. *Am J Med*. 2005;118(3):276–284. http://dx.doi.org/10.1016/j.amjmed.2004.09.017.
29. Salvo MC, Brooks AM. Glycemic control and preventive care measures of indigent diabetes patients within a pharmacist-managed insulin titration program vs standard care. *Ann Pharmacother*. 2012;46(1):29–34. http://dx.doi.org/10.1345/aph.1Q512.
30. Scott DM, Boyd ST, Stephan M, Augustine SC, Reardon TP. Outcomes of pharmacist-managed diabetes care services in a community health center. *Am J Health Syst Pharm*. 2006;63(21):2116–2122. http://dx.doi.org/10.2146/ajhp060040.
31. Shane-McWhorter L, Oderda GM. Providing diabetes education and care to underserved patients in a collaborative practice at a Utah community health center. *Pharmacotherapy*. 2005;25(1):96–109. http://dx.doi.org/10.1592/phco.25.1.96.55623.
32. Simpson SH, Majumdar SR, Tsuyuki RT, Lewanczuk RZ, Spooner R, Johnson JA. Effect of adding pharmacists to primary care teams on blood pressure control in patients with type 2 diabetes a randomized controlled trial. *Diabetes Care*. 2011;34(1):20–26. http://dx.doi.org/10.2337/dc10-1294.
33. Bex SD, Boldt AS, Needham SB, et al. Effectiveness of a hypertension care management program provided by clinical pharmacists for veterans. *Pharmacotherapy*. 2011;31(1):31–38. http://dx.doi.org/10.1592/phco.31.1.31.
34. Bogden PE, Abbott RD, Williamson P, Onopa JK, Koontz LM. Comparing standard care with a physician and pharmacist team approach for uncontrolled hypertension. *J Gen Intern Med*. 1998;13(11):740–745. http://dx.doi.org/10.1046/j.1525-1497.1998.00225.x.
35. Borenstein JE, Graber G, Saltiel E, et al. Physician-pharmacist comanagement of hypertension: a randomized, comparative trial. *Pharmacotherapy*. 2003;23(2):209–216. http://dx.doi.org/10.1592/phco.23.2.209.32096.
36. Carter BL, Bergus GR, Dawson JD, et al. A cluster randomized trial to evaluate physician/pharmacist collaboration to improve blood pressure control. *J Clin Hypertens (Greenwich)*. 2008;10(4):260–271. http://dx.doi.org/10.1111/j.1751-7176.2008.07434.x.
37. Hirsch JD, Steers N, Adler DS, et al. Primary care–based, pharmacist–physician collaborative medication-therapy management of hypertension: a randomized, pragmatic trial. *Clin Ther*. 2014;36(9):1244–1254. http://dx.doi.org/10.1016/j.clinthera.2014.06.030.
38. Hunt JS, Siemienczuk J, Pape G, et al. A randomized controlled trial of team-based care: impact of physician-pharmacist collaboration on uncontrolled hypertension. *J Gen Intern Med*. 2008;23(12):1966–1972. http://dx.doi.org/10.1007/s11606-008-0791-x.
39. Magid DJ, Olson KL, Billups SJ, Wagner NM, Lyons EE. Kroner B a. A pharmacist-led, American heart association Heart360 web-enabled home blood pressure monitoring program. *Circ Cardiovasc Qual Outcomes*. 2013;6(2):157–163. http://dx.doi.org/10.1161/CIRCOUTCOMES.112.968172.
40. Margolis KL, Asche SE, Bergdall AR, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. *Jama*. 2013;310(1):46–56. http://dx.doi.org/10.1001/jama.2013.6549.
41. Mehos BM, Saseen JJ, MacLaughlin EJ. Effect of pharmacist intervention and initiation of home blood pressure monitoring in patients with uncontrolled hypertension. *Pharmacotherapy*. 2000;20:1384–1389. http://dx.doi.org/10.1592/phco.20.17.1384.34891.
42. O'Neill JL, Cunningham TL, Wiitala WL, Bartley EP. Collaborative hypertension case management by registered nurses and clinical pharmacy specialists within the patient aligned care teams (PACT) model. *J Gen Intern Med*. 2014;29(S2):675–681. http://dx.doi.org/10.1007/s11606-014-2774-4.
43. Wong MCS, Liu KQL, Wang HHX, et al. Effectiveness of a pharmacist-led drug counseling on enhancing antihypertensive adherence and blood pressure control: a randomized controlled trial. *J Clin Pharmacol*. 2013;53(7):753–761. http://dx.doi.org/10.1002/jcph.101.
44. Billups SJ, Plushner SL, Olson KL, Koehler TJ, Kerzee J. Clinical and economic outcomes of conversion of simvastatin to lovastatin in a group-model health maintenance organization. *J Manag Care Pharm*. 2005;11(8):681–686.
45. Smith MC, Boldt AS, Walston CM, Zillich AJ. Effectiveness of a pharmacy care management program for veterans with dyslipidemia. *Pharmacotherapy*. 2013;33(7):736–743. http://dx.doi.org/10.1002/phar.1273.
46. Straka RJ, Taheri R, Cooper SL, Smith JC. Achieving cholesterol target in a managed care organization (ACTION) trial. *Pharmacotherapy*. 2005;25(3):360–371. http://dx.doi.org/10.1592/phco.25.3.360.61601.
47. Tahaineh L, Albsoul-Younes A, Al-Ashqar E, Habeb A. The role of clinical pharmacist on lipid control in dyslipidemic patients in North of Jordan. *Int J Clin Pharm*. 2011;33(2):229–236. http://dx.doi.org/10.1007/s11096-011-9479-0.
48. Hammad E, Yasein N, Tahaineh L, Albsoul-Younes A. A randomized controlled trial to assess pharmacist-physician collaborative practice in the management of metabolic syndrome in a university medical clinic in Jordan. *J Manag Care Pharm*. 2011;17(4):295–303.
49. Lowrie R, Mair FS, Greenlaw N, et al. Pharmacist intervention in primary care to improve outcomes in patients with left ventricular systolic dysfunction. *Eur Heart J*. 2012;33(3):314–324. http://dx.doi.org/10.1093/eurheartj/ehr433.
50. Adler DA, Bungay KM, Wilson IB, et al. The impact of a pharmacist intervention on 6-month outcomes in depressed primary care patients. *Gen Hosp Psychiatry*. 2004;26:199–209. http://dx.doi.org/10.1016/j.genhosppsych.2003.08.005.
51. Capoccia KL, Boudreau DM, Blough DK, et al. Randomized trial of pharmacist interventions to improve depression care and outcomes in primary care. *Am J Heal Pharm*. 2004;61:364–372.
52. Finley PR, Rens HR, Pont JT, et al. Impact of a collaborative care model on depression in a primary care setting: a randomized controlled trial. *Pharmacotherapy*. 2003;23(9):1175–1185. http://dx.doi.org/10.1592/phco.23.10.1175.32760.
53. Hall LN, Shrader SP, Ragucci KR. Evaluation of compliance with osteoporosis treatment guidelines after initiation of a pharmacist-run osteoporosis service at a family medicine clinic. *Ann Pharmacother*. 2009;43(11):1781–1786. http://dx.doi.org/10.1345/aph.1M366.
54. Evans CD, Eurich DT, Taylor JG, Blackburn DF. The collaborative cardiovascular risk reduction in primary care (CCARP) study. *Pharmacotherapy*. 2010;30(8):766–775. http://dx.doi.org/10.1592/phco.30.8.766.
55. Edelman D, Fredrickson SK, Melnyk SD, et al. Medical clinics versus usual care for patients with both diabetes. *Ann Intern Med*. 2010;152(11):689–696.
56. Neto PRO, Marusic S, de Lyra DP, et al. Effect of a 36-month pharmaceutical care program on coronary heart disease risk in elderly diabetic and hypertensive patients. *J Pharm Pharm Sci*. 2011;14(2):249–263.
57. Hetro A, Rossetto J, Bahlawan N, Ryan M. Clinical pharmacists supporting patients with diabetes and/or hyperlipidemia in a military medical home. *J Am Pharm Assoc*. 2015;55(1):73. http://dx.doi.org/10.1331/JAPhA.2015.14103.
58. Koenigsfeld CF, Horning KK, Logemann CD, Schmidt GA. Medication therapy management in the primary care setting: a pharmacist-based pay-for-performance project. *J Pharm Pract*. 2011;45(5):573–579. http://dx.doi.org/10.1177/0897190011416671.
59. Avery AJ, Rodgers S, Cantrill JA, et al. A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis. *Lancet*. 2012;379(9823):1310–1319. http://dx.doi.org/10.1s016/S0140-6736(11)61817-5.
60. Berdine HJ, Skomo ML. Development and integration of pharmacist clinical services into the patient-centered medical home. *J Am Pharm Assoc*. 2012;52(5):661–667. http://dx.doi.org/10.1331/JAPhA.2012.10206.
61. Carter BL. Interpreting the findings of the IMPROVE study. *Am J Heal Syst Pharm*. 2001:58.
62. Davis RG, Hepfinger CA, Sauer KA, Wilhardt MS. Retrospective evaluation of medication appropriateness and clinical pharmacist drug therapy recommendations for home-based primary care veterans. *Am J Geriatr Pharmacother*. 2007;5(1):40–47. http://dx.doi.org/10.1016/j.amjopharm.2007.03.003.
63. Freeman CR, Cottrell WN, Kyle G, Williams ID, Nissen L. An evaluation of medication review reports across different settings. *Int J Clin Pharm*. 2013;35(1):5–13. http://dx.doi.org/10.1007/s11096-012-9701-8.
64. Galt KA. Cost avoidance, acceptance, and outcomes associated with a pharmacotherapy consult clinic in a Veterans Affairs Medical Center. *Pharmacotherapy*. 1998;18(5):1103–1111.
65. Hanlon JT, Weinberger M, Samsa GP, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *Am J Med*. 1996;100(4):428–437. http://dx.doi.org/10.1016/S0002-9343(97)89519-8.
66. Hogg W, Lemelin J, Dahrouge S, et al. Randomized controlled trial of anticipatory and preventive multidisciplinary team care: for complex patients in a community-based primary care setting. *Can Fam Physician*. 2009;55(12):e76–85, 55/12/e76 [pii].
67. Isetts BJ, Schondelmeyer SW, Heaton AH, Wadd WB, Hardie NA, Artz MB. Effects of collaborative drug therapy management on patients' perceptions of care and health-related quality of life. *Res Soc Adm Pharm*. 2006;2(1):129–142. http://dx.doi.org/10.1016/j.sapharm.2005.12.002.
68. Isetts BJ, Schondelmeyer SW, Artz MB, et al. Clinical and economic outcomes of medication therapy management services: the Minnesota experience. *J Am Pharm Assoc (2003)*. 2008;48(2):203–211. http://dx.doi.org/10.1331/JAPhA.2008.07108, 3 pp. following 211.
69. Krska J, Cromarty J a, Arris F, et al. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. *Age Ageing*. 2001;30(3):205–211. http://dx.doi.org/10.1093/ageing/30.3.205.
70. Lenander C, Elfsson B, Danielsson B, Midlöv P, Hasselström J. Effects of a pharmacist-led structured medication review in primary care on drug-related problems and hospital admission rates: a randomized controlled trial. *Scand J Prim Health Care*. 2014;32(4):180–186. http://dx.doi.org/10.3109/02813432.2014.972062.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014

71. Pindolia VK, Stebelsky L, Romain TM, Luoma L, Nowak SN, Gillanders F. Mitigation of medication mishaps via medication therapy management. *Ann Pharmacother*. 2009;43(4):611–620. http://dx.doi.org/10.1345/aph.1L591.
72. Roth MT, Ivey JL, Esserman DA, Crisp G, Kurz J, Weinberger M. Individualized medication assessment and planning: optimizing medication use in older adults in the primary care setting. *Pharmacotherapy*. 2013;33(8):788–797. http://dx.doi.org/10.1002/phar.1274.
73. Sellors J, Kaczorowski J, Sellors C, et al. A randomized controlled trial of a pharmacist consultation program for family physicians and their elderly patients. *CMAJ*. 2003;169(1):17–22.
74. Tan ECK, Stewart K, Elliott RA, George J. Pharmacist consultations in general practice clinics: the Pharmacists in Practice Study (PIPS). *Res Soc Adm Pharm*. 2014;10(4):623–632. http://dx.doi.org/10.1016/j.sapharm.2013.08.005.
75. Zermansky AG, Petty DR, Raynor DK, Freemantle N, Vail A, Lowe CJ. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. *BMJ*. 2001;323(7325):1340–1343. http://dx.doi.org/10.1136/bmj.323.7325.1340.
76. Weick E, Sutcliffe K. *Managing the Unexpected. Resilient Performance in an Age of Uncertainty*. San Francisco: Jossey-Bass; 2007.
77. Renn O. *Risk Governance: Coping with Uncertainty in a Complex World*. Earthscan; 2008.
78. Brown C, Hofer T, Johal A, et al. An epistemology of patient safety research: a framework for study design and interpretation. Part 3. End points and measurement. *Qual Saf Heal Care*. 2008;17(3):170–177. http://dx.doi.org/10.1136/qshc.2007.023655.
79. Shojania KG, Ranji SR, McDonald KM, et al. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. *JAMA*. 2006;296(4):427–440. http://dx.doi.org/10.1001/jama.296.4.427.
80. Holland R. Does home based medication review keep older people out of hospital? The HOMER randomised controlled trial. *BMJ*. 2005;330(7486):293–300. http://dx.doi.org/10.1136/bmj.38338.674583.AE.
81. Holland R, Desborough J, Goodyer L, Hall S, Wright D, Loke YK. Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis. *Br J Clin Pharmacol*. 2008;65(3):303–316. http://dx.doi.org/10.1111/j.1365-2125.2007.03071.x.
82. Nkansah N, Mostovetsky O, Yu C, et al. Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. *Cochrane database Syst Rev*. 2010;7:CD000336. http://dx.doi.org/10.1002/14651858.CD000336.pub2.
83. Royal S. Interventions in primary care to reduce medication related adverse events and hospital admissions: systematic review and meta-analysis. *Qual Saf Heal Care*. 2006;15(1):23–31. http://dx.doi.org/10.1136/qshc.2004.012153.
84. Anaya JP, Rivera JO, Lawson K, Garcia J, Luna J, Ortiz M. Evaluation of pharmacist-managed diabetes mellitus under a collaborative drug therapy agreement. *Am J Heal Pharm*. 2008;65(19):1841–1845. http://dx.doi.org/10.2146/ajhp070568.
85. Barnes KD, Tayal NH, Lehman AM, Beatty SJ. Pharmacist-driven renal medication dosing intervention in a primary care patient-centered medical home. *Pharmacotherapy*. 2014;34(12):1330–1335. http://dx.doi.org/10.1002/phar.1508.
86. Bruhn H, Bond CM, Elliott AM, et al. Pharmacist-led management of chronic pain in primary care: results from a randomised controlled exploratory trial. *BMJ Open*. 2013;3(4):e002361. http://dx.doi.org/10.1136/bmjopen-2012-002361.
87. Carter BL, Levy BT, Gryzlak B, et al. A centralized cardiovascular risk service to improve guideline adherence in private primary care offices. *Contemp Clin Trials*. 2015;43:25–32. http://dx.doi.org/10.1016/j.cct.2015.04.014.
88. Chung N. Impact of a clinical pharmacy program on changes. *J Manag Care Spec Pharm*. 2014;20(9):914–919.
89. Cording MA, Engelbrecht-Zadvorny EB, Pettit BJ, Eastham JH, Sandoval R. Development of a pharmacist-managed lipid clinic. *Ann Pharmacother*. 2002;36(5):892–904.
90. Duran-Parrondo C, Vazquez-Lago JM, Campos-Lopez AM, Figueiras A. Impact of a pharmacotherapeutic programme on control and safety of long-term anticoagulation treatment: a controlled follow-up study in Spain. *Drug Saf*. 2011;34(6):489–500. http://dx.doi.org/10.2165/11588520-000000000-00000.
91. Erickson SR, Slaughter R, Halapy H. Pharmacists' ability to influence outcomes of hypertension therapy. *Pharmacotherapy*. 1997;17(1):140–147.
92. Gums TH, Carter BL, Milavetz G, et al. Physician-pharmacist collaborative management of asthma in primary care. *Pharmacotherapy*. 2014;34(10):1033–1042. http://dx.doi.org/10.1126/scisignal.2001449.Engineering.
93. Gums TH, Uribe L, Vander Weg MW, James P, Coffey C, Carter BL. Pharmacist intervention for blood pressure control: medication intensification and adherence. *J Am Soc Hypertens*. 2015;9(7):569–578. http://dx.doi.org/10.1016/j.jash.2015.05.005.
94. Jacobs M, Sherry PS, Taylor LM, Amato M, Tataronis GR, Cushing G. Pharmacist assisted medication program enhancing the regulation of diabetes (PAMPERED) study. *J Am Pharm Assoc*. 2012;52:613–621.
95. Jamieson LH, Scally AJ, Chrystyn H. A randomised comparison of practice pharmacist-managed hypertension providing Level 3 Medication Review versus usual care in general practice. *J Appl Ther Res*. 2010;7(3):77–86.
96. Johnson KA, Chen S, Cheng IN, et al. The impact of clinical pharmacy services integrated into medical homes on diabetes-related clinical outcomes. *Ann Pharmacother*. 2010;44(12):1877–1886. http://dx.doi.org/10.1345/aph.1P380.
97. Kelly C, Rodgers P. Implementation and evaluation of a pharmacist-managed diabetes service. *J Manag Care Pharm*. 2000;6(6):488–493. Available at http://www.amcp.org/data/jmcp/research_v6_488-493.pdf.
98. Monte SV. Clinical and economic impact of a diabetes clinical pharmacy service program in a university and primary care-based collaboration model. *J Am Pharm Assoc*. 2009;49:200–208.
99. Shane-McWorther L, McAdam-Marx C, Lenert L, et al. Pharmacist-provided diabetes management and education via a telemonitoring program. *J Am Pharm Assoc*. 2015;55(5):516–526.
100. Solomon DK, Portner TS, Bass GE, et al. Part 2. Clinical and economic outcomes in the hypertension and COPD arms of a multicenter outcomes study. *J Am Pharm*. 1998;38:574–585.
101. Stading J, Herrmann J, Walters R, Destache C, Chock A. Impact of pharmacist intervention on diabetes patients in an ambulatory setting. *Pharm Ther*. 2009;22(4):241–246.
102. Thumar R, Zaiken K. Impact of live medication therapy management on cholesterol values in patients with cardiovascular disease. *J Am Pharm Assoc*. 2014;54(5):526–529. http://dx.doi.org/10.1331/JAPhA.2014.13205.
103. Tobari H, Arimoto T, Shimojo N, et al. Physician-pharmacist cooperation program for blood pressure control in patients with hypertension: a randomized-controlled trial3187. *Am J Hypertens*. 2010;23(10):1144–1152. http://dx.doi.org/10.1038/ajh.2010.127.
104. Trompeter JM, Havrda DE. Impact of obtaining medications from pharmaceutical company assistance programs on therapeutic goals. *Ann Pharmacother*. 2009;43(3):469–477. http://dx.doi.org/10.1345/aph.1L420.
105. Villa LA, von Chrismar AM, Oyarzun C, Eujenin P, Fernandez ME, Quezada M. Pharmaceutical care program for dyslipidemic patients at three health care centers: impacts and outcomes. *Lat Am J Pharm*. 2009;28(3):415–420.
106. Hamley J, MacGregor S, Dunbar J, Cromarty J. Integrating clinical pharmacists into the primary health care team: a framework for rational and cost-effective prescribing. *Scott Med J*. 1997;42:4–7.
107. Harris IM, Westberg SM, Frakes MJ, van Vooren JS. Outcomes of medication therapy review in a family medicine clinic. *J Am Pharm Assoc*. 2009;49(5):624–627.
108. Jameson J, VanNoord G, Vanderwoud K. The impact of a pharmacotherapy consultation on the cost and outcome of medical therapy. *J Fam Pract*. 1995;41(5):469–473.
109. Jameson JPP, VanNoord GRR. Pharmacotherapy consultation on polypharmacy patients in ambulatory care. *Ann Pharmacother*. 2001;35(7/8):835–840. http://dx.doi.org/10.1345/aph.10259.
110. Laucka Paul V. Pharmacist review to simplify medication regimens in a VAMC primary care clinic. *J Pharm Technol*. 1996;12:62–66.
111. Lowe CJ, Raynor DK, Purvis J, Farrin A, Hudson J. Effects of a medicine review and education programme for older people in general practice. *Br J Clin Pharmacol*. 2000;50(2):172–175. http://dx.doi.org/10.1046/j.1365-2125.2000.00247.x.
112. Morrison C, MacRae Y. Promoting safer use of high-risk pharmacotherapy: impact of pharmacist-led targeted medication reviews. *Drugs - Real World Outcomes*. 2015;2(3). http://dx.doi.org/10.1007/s40801-015-0031-8.
113. Taylor CT, Byrd DC, Krueger K. Improving primary care in rural Alabama with a pharmacy initiative. *Am J Heal Pharm*. 2003;60:1123–1129.

Please cite this article in press as: Hazen ACM, et al., The degree of integration of non-dispensing pharmacists in primary care practice and the impact on health outcomes: A systematic review, Research in Social and Administrative Pharmacy (2017), http://dx.doi.org/10.1016/j.sapharm.2017.04.014