Risk Factors for Readmission of Inpatients with Diabetes: A Systematic Review

Dr TD Robbins[1,2], Dr SN Lim Choi Keung[1], Dr S Sankar[2], Prof H Randeva[2], Prof TN Arvanitis[1]

1) Institute of Digital Healthcare, WMG, University of Warwick, Coventry, CV4 7AL, United Kingdom.
2) Warwickshire Institute for the Study of Diabetes, Endocrinology & Metabolism, University Hospitals Coventry & Warwickshire NHS Trust, Clifford Bridge Road, Coventry, CV2 2DX, United Kingdom.

Corresponding Author:

Dr Tim Robbins, Institute of Digital Healthcare, WMG, University of Warwick, Coventry, CV4 7AL, United Kingdom.

t.robbins.2@warwick.ac.uk

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Abstract

Aim

We have limited understanding of which risk factors contribute to increased readmission rates amongst people discharged from hospital with diabetes. We aim to complete the first review of its kind, to identify, in a systematic way, known risk factors for hospital readmission amongst people with diabetes, in order to better understand this costly complication.

Method

The review was prospectively registered in the PROSPERO database. Risk factors were identified through systematic review of literature in PubMed, EMBASE & SCOPUS databases, performed independently by two authors prior to data extraction, with quality assessment and semi-quantitative synthesis according to PRISMA guidelines.

Results

Eighty-three studies were selected for inclusion, predominantly from the United States, and utilising retrospective analysis of local or regional data sets. 76 distinct statistically significant risk factors were identified across 48 studies. The most commonly identified risk factors were; co-morbidity burden, age, race and insurance type. Few studies conducted power calculations; unstandardized effect sizes were calculated for the majority of statistically significant risk factors.

Conclusion

This review is important in assessing the current state of the literature and in supporting development of interventions to reduce readmission risk. Furthermore, it provides an important foundation for development of rigorous, pre-specified risk prediction models.

Key Words:

Diabetes, Inpatient Care, Readmission, Diabetes Complications

1. Introduction

People admitted to hospital have higher rates of diabetes than the general population. In the United Kingdom, 17% of inpatients have a diagnosis of diabetes mellitus [1]. Irrespective of the initial reason for admission, inpatients with diabetes act as a distinct cohort of patients with shared risk factors for adverse events [2]. People with diabetes are at a significantly increased risk of readmission following discharge [3, 4]. Hospital readmissions rates are a psychological and physical burden to patients, and a financial burden on healthcare systems [5]. Despite the importance of readmission amongst people with diabetes, there has been limited research in this area [6]. Specifically, no published studies have attempted to identify, in a systematic way, risk factors relating to readmission for this cohort of patients. There have been attempts to develop and validate risk prediction tools for the readmission of patients with diabetes. Such risk prediction tools report moderate predictive abilities [7, 8], and do not report using the existing research literature to rigorously pre-specify candidate variables.

Understanding risk factors relevant to patients discharged from hospital with diabetes is important to patients, carers, healthcare practitioners and researchers. It supports the delivery and development of individualised medicine, based on each patient's underlying risks; supports our understanding of regional variations in readmission risk, and supports development of evidence based interventions targeted at reducing readmission risks. Interestingly, the paucity of research in this area, for diabetes, is in direct contrast to other medical conditions, such as heart failure [9].

This study therefore aims to identify, systematically, known risk factors for readmission to hospital, among people with diabetes. The intention of the study is to cast a 'broad net', ascertaining all known risk factors, irrespective of whether identified for a specific subset of patients (such as emergency admissions only) or generalised populations of all inpatients with diabetes.

This research will be essential to the planning of future diabetes services, at both an inpatient and community level. It will provide potential targets for improving care, reducing readmission and reducing costs. Identifying a comprehensive list of literature-derived risk factors further facilitates the development of robust pre-specified risk prediction tools. Effective risk prediction models will enable scarce resources to be targeted to patients with the greatest need. Overall, it is hoped that a better understanding of risk factors for people with diabetes will enable the development of discharge planning that is more effective, better patient education interventions, improved risk stratification tools and more targeted interventions.

2. Methods

The systematic review was conducted according to the PRISMA standards[10]. The study protocol was published in advance on the PROSPERO database (Registration Number CRD42017073773).

2.1 Search Strategy

A literature search was performed using PubMed, EMBASE & SCOPUS databases. The search terms selected were "diabetes" AND "readmission." The search strategy included papers published between August 2006 and August 2018; this wide date range was to ensure that the extracted studies represented current clinical care practices, given historically elongated lengths of stay and differing discharge practices. All study designs were included, with studies limited to English language articles. Due to differing obstetric and paediatric care practices, articles were restricted to adult, non-obstetric patient cohorts. Hand searching of references was performed to identify additional studies for inclusion.

2.2 Study Selection

An initial review of all studies, identified by the literature search, was completed by two authors. Abstracts and titles were reviewed; those papers, not including information regarding risk factors for readmission to hospital in people with diabetes, were removed from the selected studies. Any discrepancies in article selection would be resolved by discussion, involving a third author. All studies selected after the initial screening were reviewed as full text articles, with exclusion of those that did not identify risk factors for readmission, did not consider diabetes, or solely considered diabetes as a risk factor for another condition.

2.3 Data Extraction

Data were extracted to a pre-piloted data collection form. The pro-forma collected information based on the 5 C's (Category, Context, Correctness, Contribution and Clarity), as suggested by the engineering and computing research community and therefore highly relevant to research articles considering extraction of data from clinical information systems [11]. Additional information collected included: the country within which the study was conducted; whether the study was collected at a local, regional or national level; the extent of inpatient data sources, compared to community or social care data sources; the subset of patients with diabetes included in the study; risk factors that were found to be statistically significantly associated with readmission, alongside risk factors that were identified, but not tested for statistical assessment. Data were collected on the definitions of readmission used by different authors, in particular the time periods elapsed between admission and discharge, alongside an evaluation of approaches used to assess effect sizes of the risk factors identified.

2.4 Quality Assessment

Quality assessment for each of the selected papers was performed against pre-determined standards. These included an assessment of sample size, evidence to justify the sample size, appropriateness of any statistical tests applied, a clear description of study recruitment and assessment, with a final overall narrative assessment of each study's quality. The aim of this paper is to assess the state of the literature regarding currently understood risk factors for readmission of people with diabetes, and thus no studies were excluded based on low study quality; rather a description is provided within the results section.

2.5 Data Synthesis

The diversity of definitions of readmission used in the research literature, alongside diverse subsets of people with diabetes in different studies, precludes any attempt at meta-analysis. Rather a narrative summary of risk factors identified was extracted, with subsequent thematic grouping of the risk factors as described below.

2.6 Patient Involvement in Research

This research topic was identified as an area of priority for people with diabetes. This was both through the Diabetes Voices Programme [12], operated by Diabetes UK, and individual patient representatives who were identified through NIHR People in Research [13] and reimbursed for their time contribution.

3. Results

3.1 Search Results

The database search strategy identified 1451 articles, with an additional 10 articles identified through manual reference searching. Following abstract-based screening, a total of 122 articles were included for full text extraction and review. Forty articles were excluded following full text review, with 82 studies remaining for full analysis. The results of the search strategy are shown in figure 1.

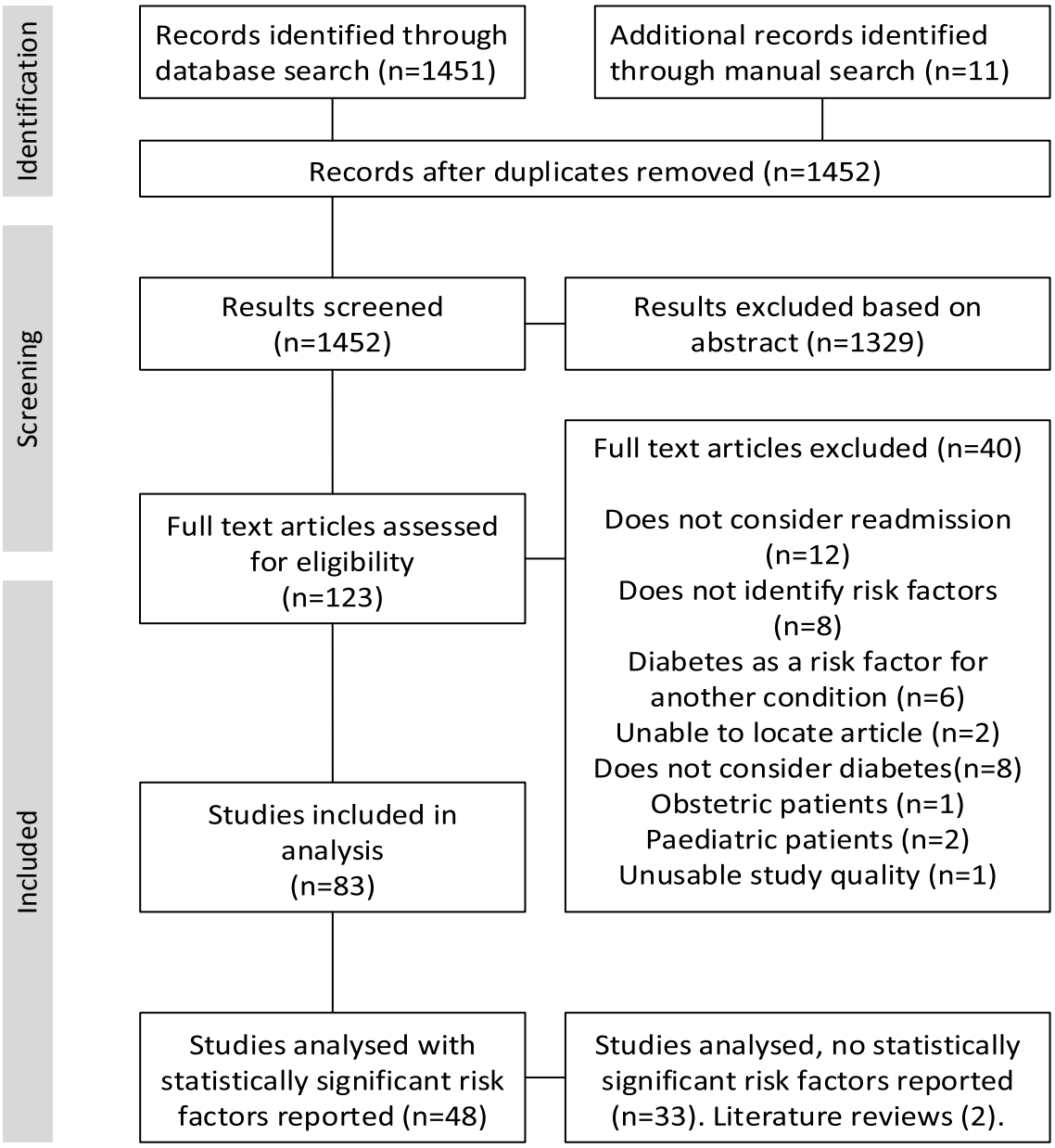

Figure 1: Flow diagram of study selection

3.2 Study Characteristics

From the 83 studies identified, 70 (84%) adopted a retrospective database study design, 2 articles described non-randomised controlled studies, with a single randomised controlled trial. There were 2 prospective pilot studies, 3 prospective cohort studies, 2 case control study, one qualitative study, one systematic review and one narrative review.

The majority of studies were based on patient data from the United States of America (55 studies – 66%), with 9 studies (11%) utilising patient data from the United Kingdom. The remaining studies were conducted based on patient data from Denmark, Australia, Taiwan, Canada, China, Brazil, Italy, Israel, Japan, Saudi Arabia and Spain. One study did not clearly describe the country of origin of the patient population studied.

Studies were predominantly conducted utilising data from a single centre (35 studies, 42%), with 18 studies (22%) utilising data from multiple centres within a single region, and 26 studies using data from a national database (32%). The study setting was unclear in two studies, and not applicable to the review articles. Studies predominantly used inpatient electronic health record sources (68 studies, 83%), with 5 studies (6%) utilising patient data from primary care or community sources and 9 studies (11%) using a combination of both community and inpatient data sources.

Forty-eight studies identified statistically significant risk factors for readmission. The characteristics of these studies are listed in Table 1&2, 20 studies identified risk factors in generalised populations of patients with diabetes (Table 1) and 28 studies identified risk factors for specific sub-populations of patients with diabetes (Table 2). In total, 506 statistically significant risk factors were identified across all analysed studies, including duplicates, with a mean average of 6.10 statistically significant risk factors identified per study. When duplicates were removed, we collated 76 distinct risk factors for readmission of people with diabetes from the published literature. A full breakdown of risk factors identified during the data collection process is shown in Table 3. The risk factors are divided into whether they were identified for only a specific subpopulation of people with diabetes, or whether they were identified for generalised diabetes populations.

From the studies identifying statistically significant risk factors there were 12 different definitions of readmission used, ranging from 7-days from index hospital discharge, to 5-years from index hospital discharge. The studies in Table 1 and 2 are ordered by this readmission definition.

In addition to those risk factors found to have a statistically significant impact on research, 19 papers identified risk factors that had an impact on outcomes but did not reach statistical significance. This represented a total of 39 risk factors for readmission, 11 of which were unique and not identified in the list of risk factors recognised as statistically significant. These are outlined in Table 4. None of the 19 studies, identifying these non-significant risk factors, reported a power calculation to ensure they had a sufficient patient population to identify significance, if present.

3.3 Study Quality

Studies typically had large sample sizes of patients, with a median average sample size of 6603 patients. Seven studies, however, included less than 100 participants [14-20]. All quantitative studies described the statistical approach taken to analysing data, and these were appropriate to the study design. One quantitative study did not complete any statistical significance testing [21]. Generally, there was a failure to pre-specify which risk factors would be assessed as primary or secondary outcomes measures, and thus any justification for the selection of these studies. Of central importance, only 2 studies (4%) described or provided the results of a power calculation, in order to justify the sample sizes used and relevance of the subsequent statistical tests. One study was unclear regarding their description of patient recruitment and subsequent patient characteristics [22].

From the studies that identified statistically significant risk factors, 95% reported an effect size related to the risk factors identified. All effect sizes were reported using non-standardised statistical methods (typically Odds Ratio or Hazard Ratio), rather than standardised effect size measures (such as Cohen's D or Phi).

There was a single qualitative study [14], which was rigorously performed with semi-structured interviews and thematic analysis. It, however, was restricted to a single (urban) centre. Twenty-three studies were conducted only in a single centre, potentially restricting their generalisability.

Table 1: Characteristics of studies identifying statistically significant risk factors for readmission in generalised diabetes populations (ordered by definition of readmission)

Ref	First author	Year	Readmission definition (d = day, m = month, yr = year)	Sample size	Country	Study Design	No. of variables		Primary outcome *[* = Multiple primary or composite outcomes]*
							Assessed	Significant	
[23]	X.Liu	2015	7d to >90d	37,620	China	Retrospective cohort analysis	13	13	Readmission
[24]	S.Mokhtar	2012	28d	1125	Saudi Arabia	Retrospective cohort & case-control	11	3	Readmission
[25]	J.Albrecht	2012	30d	26,878	USA	Retrospective cohort analysis	7	7	Readmission
[8]	D.Rubin	2016	30d	44,203	USA	Development & validation of risk tool	46	37	Readmission
[26]	H.Sonmez	2017	30d	102,694	USA	Retrospective cohort analysis	2	2	Readmission and association with admission diagnosis
[27]	J.Robbins	2006	30d	291,752	USA	Retrospective cohort analysis	31	31	Readmission
[28]	F.Zaccardi	2017	30d	101,475	UK	Retrospective case-control study	1	1	Admission, Readmission, length of stay, mortality*
[29]	J.Chen	2012	30d	30,139	USA	Retrospective cohort analysis	39	33	Readmission
[18]	J.Swami	2018	30d	70	USA	prospective observational study	5	2	Readmission
[30]	K.Lipska	2014	30d	33,952,331	USA	Retrospective observational	5	2	Hyper/hypoglycaemia, hospitalization, mortality & readmission*
[31]	K.Bennett	2012	30d	94,121	USA	Retrospective cohort analysis	24	13	Readmission
[32]	D.Rubin	2018	30d	105,791	USA	Retrospective cohort analysis	43	40	Readmission
[33]	A.Karunakaran	2018	30d	17284	USA	Retrospective cohort analysis	51	46	Readmission
[34]	S.Healy	2013	30d & 180d	2265	USA	Retrospective cohort analysis	26	11	Readmission
[35]	X.Liu	2017	30d, 60d & 90d	73,144	China	Cross sectional analysis	18	16	Readmission
[36]	L.Chwastiak	2014	1m	82,060	USA	Retrospective cohort analysis	46	29	Readmission
[37]	H.Kim	2010	3m	124,967	USA	Retrospective cohort analysis	32	18	Scheduled and unscheduled readmissions*
[38]	J.Ena	2018	90d	1977	Spain	Retrospective cohort analysis	21	10	Readmission
[39]	Y.Nishino	2015	Study period	445,504	UK	Cross-sectional analysis	36	24	Admission & readmission*
[22]	S.Cramer	2010	Not declared	2633	USA	Retrospective cohort analysis	10	10	Readmission

Table 2: Characteristics of studies identifying statistically significant risk factors for specific subpopulations of people with diabetes (ordered by definition of readmission)

Ref	First author	Year	Specific diabetes sub-population	Readmission definition (d = day, m = month, yr = year)	Sample size	Country	Study Design	No. of variables		Primary outcome *[* = Multiple primary or composite outcomes]*
								Assessed	Significant	
[40]	N.Wei	2013	T2DM	30d	1949	USA	Retrospective cohort analysis	1	1	Readmission & emergency department attendance*
[41]	M.Engoren	2014	Diabetes and CABG	30d	880	USA	Retrospective cohort analysis	3	3	Readmission
[42]	F.Lovecchio	2014	IDDM & NIDDM post arthroplasty	30d	43299	USA	Retrospective cohort analysis	1	1	Medical / surgical complications & readmission*
[19]	P.Lee	2014	T2DM & Elevated Hba1c	90d	83	USA	Retrospective cohort analysis	1	1	Readmission & emergency department visit*
[43]	Z.Ries	2015	Diabetes & lower limb amputation	30d	439	USA	Retrospective cohort analysis	20	5	Readmission
[44]	Z.Li	2015	Diabetes and CABG	30d	7348	USA	Retrospective cohort analysis	1	1	Major adverse events
[45]	A.Raval	2015	T2DM aged over 65 years	30d	202,496	USA	Retrospective cohort analysis	37	20	Readmission
[46]	H.Chen	2015	Diabetes & ambulatory care	30d	120208	USA	Andersen's Behavioural Model	40	17	Readmission
[47]	D.Rubin	2017	Cardiovascular disease	30d	8,189	USA	Retrospective cohort analysis	43	36	Readmission
[48]	G.Caughey	2017	Diabetes & elderly	30d	848	USA	Retrospective cohort analysis	40	9	Readmission
[49]	J.Collins	2017	T2DM	30d	63237	USA	Development of risk prediction model	20	14	Readmission
[50]	C.Holscher	2018	Diabetic foot disease	30d	206	USA	Retrospective cohort analysis	43	6	Readmission

Ref	First author	Year	Specific diabetes sub-population	Readmission definition (d = day, m = month, yr = year)	Sample size	Country	Study Design	No. of variables		Primary outcome *[* = Multiple primary or composite outcomes]*
								Assessed	Significant	
[51]	N.Shohat	2018	Diabetes & orthopaedic surgery	90d	3302	USA	Retrospective cohort analysis	1	1	Length of stay, readmission & mortality*
[52]	D.Yu	2018	T2DM and cardiovascular disease	90d	5195	UK	Prospective study	16	15	Hospitalisation and rehospitalisation*
[53]	H.Mochari-Greenberger	2014	Diabetes and cardiovascular disease	30d and 1 yr	1126	USA	Prospective study	18	1	Readmission
[54]	C.Hsieh	2015	T2DM on clopidogrel	3m, 6m & 12m	6603	Taiwan	Retrospective cohort analysis	1	1	Acute coronary syndrome and revascularisation readmission*
[55]	G.Rumenapf	2013	Diabetic foot disease	1 yr	376	Germany	Retrospective cohort analysis	1	1	Readmission
[20]	L.Azevedo	2014	Diabetic ketoacidosis admitted ITU	1 yr	76	Canada	Retrospective matched cohort study	30	7	ICU admission with DKA
[56]	P.Heaton	2016	T2DM	1 yr	13,500,000	USA	Retrospective cohort analysis	17	3	Readmission
[57]	M.Kennedy	2016	Diabetes post myocardial infarction	2 yr	294	Netherlands	Multi-modal	1	1	Major adverse cardiovascular event, including readmission
[58]	E.Wu	2012	T2DM on insulin pre-admission	3 yr	2160	USA	Observational, retrospective analysis	1	1	Glycaemic control, readmission, hypoglycaemia, survival & cost*
[59]	F.Hsiao	2010	T2DM & heart failure	Study period	8139	Taiwan	Retrospective cohort analysis	1	1	Death, all cause readmission, first admission heart failure*
[60]	M.Isidro	2013	Diabetic ketoacidosis	Study period	152	Spain	Retrospective analysis	1	1	Multiple
[61]	E.Wu	2012	T2DM, on insulin	Study period	732	USA	Retrospective cohort analysis	1	1	Hba1c, hypoglycaemia & readmission*
[62]	M.Dhamoon	2018	Stroke	Study period	25,495	Canada	Retrospective cohort analysis	2	2	Mortality, recurrent stroke, readmission*

Ref	First author	Year	Specific diabetes sub-population	Readmission definition (d = day, m = month, yr = year)	Sample size	Country	Study Design	No. of variables		Primary outcome *[* = Multiple primary or composite outcomes]*
								Assessed	Significant	
[63]	M.Arguello	2018	T2DM with sepsis	Not reported	395	Unknown	Retrospective cohort analysis	2	1	Readmission & length of stay*
[64]	N.Shohat	2017	Diabetes & joint arthoplasty	Not reported	119	USA	Prospective cohort study	1	1	Surgical site infection
[65]	F.Cosmi	2018	Heart failure	Not reported	Multiple studies	Italy	Multiple studies	1	1	Mortality & heart failure hospitalisation rate*

Risk factors for specific diabetes subpopulations		Risk factors identified in general diabetes population	
Risk factor	Number of studies & Ref	Risk factor	Number of studies & Ref
Demographic			
Age	4 [45, 46, 49, 52]	Age	9 [23, 25, 29, 30, 32, 35-38]
Race	4 [27, 46, 47, 53]	Race	5 [30, 32-34, 36, 37, 39]
Sex	4 [45, 49, 52, 62]	Sex	3 [22, 37, 38]
Marital status	2 [47, 56]	Marital status	1 [32, 33]
		Year of discharge	1 [33]
		Language	1 [33]
Socioeconomic status			
Insurance type	2 [47, 49]	Insurance type	5 [23, 33-37]
Education level	1 [47]	Neighbourhood affluence	2 [37, 39]
Employment status	1 [47]	Urban home environment	2 [31, 37]
		Employment status	4 [8, 23, 32, 33, 35]
		Education level	1 [32, 33]
Lifestyle			
Illicit substance use	2 [27, 60]	Illicit substance use	3 [22, 29, 33, 36]
Smoking status	2 [43, 50]		
Geographic location	1 [49]		
Patient medical factors			
Co-morbidity[1]	5 [41, 43, 46, 49, 63]	Mental illness	6 [22, 25, 29, 32, 33, 36, 37]
Insulin dependent diabetes	2 [42, 44]	Co-morbidity[2]	10 [22, 23, 26, 29, 32, 33, 35-38, 47]
Macro/microvascular disease	2 [43, 46, 47, 56]	Previous admission	5 [8, 32, 36, 37]
Mental illness	2 [46, 47]	Macro/microvascular disease	2 [8, 32, 33]
Raised Body Mass Index	2 [46, 52]	Hypogylcaemia admission	1 [28]
Hypertension	2 [50, 52]	Family history of diabetes	1 [35]
Previous DKA	1 [47]	Prior diabetes screening	1 [35]
Previous admission	2 [47, 48]	Disability index	1 [38]
Cognitive impairment	1 [45]	Cognitive impairment	1 [38]
Falls	1 [45]	Body mass index	1 [32, 33]
		Previous DKA / HHS	1 [32, 33]
		Outpatient follow up	1 [33]
Inpatient Stay Factors			
Active case management	1 [55]	Length of stay	7 [25, 32-37, 45]
Distance from hospital	1 [47]	Diabetes specific admission	1 [45]
Surgical procedure type	1 [57]	Diabetes education	2 [18, 34]
Penalty if re-admitted	1 [46]	Discharge destination	3 [25, 32, 33, 37]
Support post-discharge	1 [46]	Distance from hospital	2 [8, 32, 33]
Cardiovascular admission	1 [48]	Non-adherence to guidelines	1 [24]
Diabetes specific admission	1 [48]	Hypoglycaemia	3 [30, 37, 38, 45]
Inpatient blood transfusion	1 [47]	Failure to record DM diagnosis	1 [27]
Enteral/parenteral nutrition	1 [47]	Hospital type	2 [23, 35]
Most extreme blood glucose	1 [47]	Previous emergency care use	2 [45, 49]
Intensive care admission	1 [47]	Cardiovascular admission	1 [45]
Glycaemic variability	1 [51]	Cost of index hospitalisation	1 [35]
Discharge care management	1 [63]	Emergency admission	1 [33, 36]
		Inpatient blood transfusion	1 [33]
		Enteral/parenteral nutrition	1 [33]
		Diabetes inpatient consult	1 [33]

Risk factors for specific diabetes subpopulations		Risk factors identified in general diabetes population	
Risk factor	Number of studies & Ref	Risk factor	Number of studies & Ref
Medication related			
Combined PPI & clopidogrel	1 [54]	Sulfylnourea exposure	2 [32, 37]
Discharge on antibiotics	1 [43]	Insulin use prior to admission	2 [8, 32, 33]
Medication non-compliance	1 [27]	Statin exposure	2 [29, 32, 33]
Number of prescribers	1 [48]	Insulin during admission	2 [29, 38]
Thiazolidonide exposure	2 [47, 59]	Glucocorticoid exposure	2 [32, 33, 38]
Insulin exposure	4 [47, 58, 61, 65]	Thiazolidonide exposure	1 [32, 33]
Glucocorticoid exposure	1 [47]	Antihypertensive exposure	1 [32, 33]
Statin exposure	1 [47]	Metformin exposure	1 [32, 33]
Sulfylnourea exposure	2 [47, 56]		
Anti-hypertensive exposure	1 [47]		
Medication intensification	2 [19, 40]		
Speciality of physician prescribing anti-diabetic medications in community	1 [49]		
Gap in medication prescriptions	1 [45]		
Polypharmacy	1 [45]		
Laboratory Results			
Hba1c	2 [41, 52]	Hba1c	2 [32, 34]
Fructosamine level	1 [64]	Raised haematocrit	2 [8, 32, 33]
Electrolyte abnormalities	1 [47]	Electrolyte abnormalities	3 [8, 29, 32, 33, 38]
Serum cholesterol	1 [52]	Serum Cholesterol	2 [29, 32]
Admission elevated WBC	1 [47]	Admission elevated WBC	1 [32, 33]
Serum haematocrit	1 [47]	Serum albumin	1 [33]
Serum albumin	1 [47]		

Table 3: Statistically significant risk factors identified

[1] *Specified co-morbidities: Chronic kidney disease, chronic obstructive pulmonary disease, congestive cardiac failure, deficiency anaemia, diseases of the heart, diseases of the urinary system, diseases of white blood cells, fluid and electrolyte disorders, gastrointestinal haemorrhage, haemodialysis, hypertension, liver diseases, obesity, other lower respiratory diseases, other nervous system disorders, pressure or stasis ulcer, respiratory failure, stroke, valvular disease.*

[2] *Specified co-morbidities: Anaemia, arrhythmia, asthma, chest pain, chronic obstructive pulmonary disease, coagulopathy, digestive disorders, fluid and electrolyte disorders, heart failure, hypertension, hypothyroidism, infection, implant, ischaemic heart disease, liver disease, lymphoma, malignant neoplasm, number of chronic conditions, other neurological disorders, paralysis, primary hypertension, pulmonary circulation disease, renal failure, rheumatoid arthritis/collagen vascular disease, stroke, valvular disease*

Additional risk factors with non-significant impact on readmission rates	Article ref
Number of primary care physicians	[46]
Living alone	[46]
Alcohol use	[66]
Failure to attend clinic appointment	[66]
Use of variable rate intravenous insulin infusion during admission	[15]
Immigration status	[67]
Elevated transaminases	[43]
Number of clinic visits	[29]
Absence of multidisciplinary team input at point of discharge	[17]
Type of beta-blocker drug	[68]
Type of community practice	[49]
Body mass index	[47]
SGLT2 exposure	[69]
Insulin type	[70]

Table 4: Additional risk factors with non-significant impact on readmission rate

4. Discussion

Reducing readmission risk following hospital discharge, is a key priority for patients and policy makers across healthcare systems. People with diabetes are at an increased risk of hospital readmission. This article represents the first review of its kind, aiming to identify, in a systematic way, risk factors for readmission to hospital, amongst both generalised and specific populations of people with diabetes. A total of 76 distinct statistically significant risk factors were identified, with the most commonly identified being co-morbidities (16 studies), age (13 studies), race (10 studies), insurance type (8 studies), sex (7 studies). A requirement for insulin was a widely reported risk factor either before admission, during admission or subsequent to discharge.

The research remains at a relatively early stage of maturity, with the majority of studies representing retrospective reviews of local or regional datasets. The research is dominated by studies from the USA, which itself has a unique insurance-based approach to healthcare, and thus may not be representative of readmission patterns in other countries.

There were only two review articles that considered risk factors for readmission, one study was for a particularly specific subset of patients following cardiac surgery [71], and the other a narrative review article considering generalised diabetes readmission and preventions opportunities [6]. One study took a qualitative approach to data collection [14]. Given the nature of diabetes, as a disease of self-management, it is important that we gain a greater qualitative understanding of factors affecting readmission. The absence of qualitative studies may explain the relative paucity of psychological and patient-educational factors in the list of statistically significant risk factors extracted into Table 2.

The methodological and statistical approaches, to identifying risk factors, are also at an early stage of maturity. Whilst studies have relatively large sample sizes, there was rarely any attempt to identify the required sample sizes to meet significance testing through appropriate power calculations. This may explain the relatively low average number of statistically significant risk factors identified per study. It is a particular concern that, this approach to statistical planning for studies may mean that a number of risk factors, which could be statistically significant, were an appropriate sample size was selected, could have been missed. Conversely, the significant risk factors identified in Table 1 & 2 include those based on univariate comparisons, and it is important to note that univariate significance may disappear after adjustment for confounders in multivariable modelling. We have included risk factors identified through univariate comparison in order to provide a comprehensive overview of the current literature.

The underlying variation in the patient populations described (both in the generalised patient populations and specific patient populations), alongside significant variation in the definition of readmission and use of unstandardized effect size statistical tools, precludes a meaningful quantitative meta-analysis of the effect sizes described, in order to create a "hierarchy" of risk factors, or to assess the consistency across studies identifying the same risk factors. The further comprehensive, quantitative evaluation of risk factors, in properly powered multi-centre studies will be essential to better understanding and modifying the risk factors, most relevant to patients diagnosed from hospital with diabetes.

The risk factors acknowledged in this review, demonstrate a truly diverse set of factors that significantly contribute to readmission risks in patients with diabetes. Interestingly, relatively little overlap exists between studies, with 29 risk factors (38%) being identified in just one study. Risk factors are relatively evenly distributed across the demographic, socio-economic, lifestyle, patient medical, medication related and pathology result categories described above. Forty-one percent of risk factors (31 risk factors) were identified in both studies examining a subset of populations with diabetes, and those identifying risk factors for generalised populations of patients with diabetes. This overlap potentially raises the argument that people with diabetes can be treated as a distinct population within the inpatient setting.

This study has a number of strengths including pre-registration in PROSPERO; a clearly defined, two-person search across three databases; assessment of study quality; semi-quantitative data synthesis; and patient and public involvement demonstrating the research question as a priority for patients. There are, however, a number of limitations that should be considered, including the fact that the study only considers English Language papers. There is also a potential limitation in the grouping of risk factors identified as statistically significant in Table 2; for example, mental health diagnoses have been grouped separately, whilst some might argue they could be considered together. The groupings have, however,

been decided across the research team, and individualised references provided to support future researchers.

This study identifies a number of key research priorities to better support patients at discharge from hospital with diabetes. Many of the studies reported mortality outcomes following discharge alongside readmission outcomes, and it will be important to assess the extent to which the research literature has considered mortality outcomes, given a lack of systematic review in this area. Similarly, the inability to perform a quantitative meta-analysis of effect sizes, related to individual risk factors identified, demonstrates and important gap in the research literature.

Taken together, the literature demonstrates that risk factors can, and have been identified for people with diabetes, being readmitted to hospital. This is a valuable resource to patients, clinicians and academics looking to improve the process of inpatient discharge from hospital. There is a clear need for statistically rigorous studies, which incorporate data from both inpatient, community and qualitative sources to understand further these diverse risk factors, matched to meaningful effect sizes, to be developed. Such research would act as the foundation for both cohorting at risk patient populations and introducing targeted personalised interventions, in order to improve the quality of care for provided for people with diabetes.

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