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Comorbidity in the elderly with diabetes: Identification of areas of potential treatment conflicts

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ABSTRACT

Aims: To investigate the prevalence of comorbid conditions in the elderly with diabetes and the prescribing of potentially inappropriate medicines or treatment conflicts.

Methods: A cross-sectional study of diabetics aged ≥65 years, using prescription dispensing data from the Australian Department of Veterans' Affairs. Comorbidities were determined using the comorbidity index Rx-Risk-V. Potentially inappropriate prescribing or treatment conflicts specific for the elderly were determined from guidelines or reference compendia, in addition to the 2003 updated Beers criteria.

Results: Of 18,968 diabetics, the median number of comorbidities was 5 (IQR 3–8). Diabetes and associated cardiovascular medicines accounted for 41.9% of all medicine use. Associated cardiovascular diseases were highly prevalent comorbidities. 46% had gastro-oesophageal reflux disease, 25% depression, 20% chronic airways disease or chronic pain and 15% also had heart failure or inflammation-pain. At least 16% were dispensed a medicine associated with adverse effects in patients with diabetes and 22.7% were dispensed at least one potentially inappropriate medicine.

Conclusion: Significant comorbid conditions in elderly diabetic patients with potential for inappropriate prescribing or treatment conflicts include arthritis, heart failure, chronic airways diseases and diseases treatable with systemic corticosteroids. Appropriate management of comorbidity should be included in guidelines for the elderly with diabetes.

1. Introduction

Diabetes is one of the major challenges for health care systems worldwide. The prevalence of type 2 diabetes is predicted to increase from 171 million in 2000 to 366 million in 2030, with the greatest increase in prevalence in those aged ≥65 years [1]. Multimorbidity, that is the presence of multiple chronic diseases, is common in the elderly population (65–80%) [2–4], further adding to the complexity of treating the elderly patient with diabetes. According to recent studies almost 75% of adults with diabetes have 2 or more comorbid conditions and these account for much of the morbidity and mortality that these patients experience [5–7].

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Some comorbid diseases such as cardiovascular disease (CVD) and retinopathy, are known to be associated with diabetes due to their shared pathophysiological profile and as such are incorporated into diabetes management programs and clinical guidelines. However, there is limited guidance to facilitate the care of concomitant non-related diseases in the diabetic patient [8], and failure to adequately do so may result in ineffective control of diabetes-specific risk factors and may lead to decreased patient quality of life, functioning and potentially increased mortality risk. The major challenge for both the physician and patients is how to best integrate, coordinate and prioritise treatment strategies for all comorbidities, in addition to patient specific diabetes treatment goals [5,9,10].

Previous studies examining diabetes and comorbidity have looked at the effects of individual comorbid conditions [11,12] or provided a count of numbers of conditions related to diabetes and number of independent conditions [5,6]. Increased numbers of comorbid conditions are associated with a decreased prioritisation of diabetes and ability of patients to self-manage their disease [5,6]. Use of diabetes-specific health services does not appear to be affected by the number of comorbid diseases [5,6]. The prevalence of specific comorbid conditions in the elderly with diabetes is less well studied, particularly for those conditions that are not associated with diabetes. Implicit with comorbidity is the use of multiple medicines. Polypharmacy is associated with an increased risk of inappropriate prescribing and adverse drug reactions, resulting in an increase in adverse outcomes, such as falls, hospital admission and mortality [13,14]. Importantly, the characteristics of specific comorbid conditions can potentially impact on how physicians and patients approach their care relative to their diabetes management.

The aims of this study were to investigate the prevalence of specific comorbid conditions in elderly diabetic patients and to examine the prescribing of potentially inappropriate medicines or areas of potential treatment conflicts that physicians commonly encounter in caring for elderly multimorbid diabetic patient.

2. Methods

2.1. Study sample and design

A retrospective cross-sectional study was undertaken from 1st April to 31 July 2007, which included all veterans aged 65 years and over on 1 April 2007, who had an eligible gold card (entitles veterans to full access to health services) and who had been dispensed at least one medicine for the treatment of diabetes (A10). Data were sourced from prescription dispensing records from the Department of Veterans' Affairs (DVA), Australia. This database contains details of all prescription medicines, medical and allied health services and hospitalisations subsidised by the DVA. The data file contains 80 million pharmacy records, 200 million medical and allied health service records and over 6 million hospital records for a treatment population of 310,000 veterans. The DVA maintain a client file, which includes data on sex, date of birth, date of death and family status. Date of death is sourced from family notifications, death notices and the Australian Government Births, Deaths and Marriages registries. Medicines are coded according to the World Health Organization anatomical and therapeutic chemical (ATC) classification [15] and the Schedule of Pharmaceutical Benefits item codes [16].

Residential status and socioeconomic status was defined at the start date of the study. Residential status was classified as independent or living in residential aged care facility. Socioeconomic status was derived from the index of relative socioeconomic disadvantage from patients' postcode using Socio-Economic Index for Australia (SEIFA) [17].

All analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC) and Microsoft Excel was used to generate the spider-plot graphic.

2.2. Evidence based management of diabetes and comorbidity

Current Australian clinical guidelines for diabetes [18] were used to define evidence-based therapeutic management. For adjunctive cardiovascular risk control, this includes the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (AR2Bs) (ATC code C09A-D), antiplatelet agents (B01AC) and lipid lowering therapies (C10), where appropriate. In addition, the adjunctive use of diuretics (C03) or β-blockers (C07) may also be required for control of hypertension [18]. Comorbidities were determined using the pharmaceutical based comorbidity index Rx-Risk-V, that has been validated in Australia [19], and includes 42 comorbidities as determined by ATC classification (Appendix A).

2.3. Examination of potentially inappropriate medicine issues and treatment conflicts

We sought to examine the prevalence of potentially inappropriate prescribing or areas of potential treatment conflict, specific for the elderly person with diabetes and common comorbid conditions such as chronic airways disease and chronic heart failure [20–22], as identified from the Australian Therapeutic Guidelines: Endocrinology [21] and Australian Medicines Handbook [22] (Table 3).

2.3.1. Potentially inappropriate medicine issues

This included the use of medicines such as:

1. Metformin (A10BA02) generally contraindicated in those aged 85 years or older who are at increased risk of lactic acidosis due to potentially decreased renal function [14,23].
2. Long-acting sulfonylureas, gilbenclamide and glimepiride (A10BB01 or A10BB12), that are exclusively excreted renally and may potentially put the elderly person with decreased renal function at increased risk of hypoglycaemia [24].
3. Thiazolidinediones (A10BG02, A10BG03) in patients with comorbid chronic heart failure (in particular those with moderate to severe heart failure) due to increased risk of peripheral and pulmonary oedema and exacerbation of heart failure [25]
4. β-Blockers (C07) that are recommended for treatment of hypertension in diabetic patients [18] but are contraindicated in patients with chronic airways disease due to

Table 1 – Characteristics of elderly (≥65 years) diabetic cohort (*n* = 18,968).

	Diabetes cohort (*n* = 18,968)
Age years, median (IQR)	82 (79–85)
Gender (% male)	55.9%
Residential aged care status (%, years)	11.7%
SEIFA (%, quartiles)	
Low	21.5%
Low-medium	28.0%
Medium-high	24.9%
High	25.6%
Number of comorbid conditions, median (IQR)	5 (3–8)
Number unique medicines dispensed, median (IQR)	10 (7–14)
Prevalence (%) of polypharmacy[a] (95% CI)	71.3 (70.6–71.9)

[a] Polypharmacy defined as ≥5 unique medicines.

increased risk of inducing bronchoconstriction [26], in particular the non-selective β-blockers (C07AA).

2.3.2. *Comorbid disease treatment conflicts*

Other medicines may be indicated for the treatment of non-related comorbid conditions but may be harmful in patients with diabetes, included:

1. Inhaled (R01AD, R03BA) or systemic corticosteroids (H02AB) that are part of guideline-recommended therapies for patients with chronic airways disease [27] and can increase blood glucose and the risk of hyperglycaemia [28] and non-steroidal anti-inflammatory drugs (NSAIDS, M01A), due to the potential of impaired renal function, increased fluid retention, resulting in increased blood pressure and exacerbation of hypertension [29].
2. The combined use of a thiazolidinedione with an NSAID is not recommended due to an increased risk of fluid retention, elevated blood pressure and exacerbation of heart failure [22].

The presence of chronic heart failure was determined by dispensing of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II antagonist (AR2B) (C09) in addition with the diuretic furosemide (C03CA01) [30] and chronic airways disease by the dispensing of medicines for obstructive airways disease (R03AC02-R03DC03).

2.3.3. *Potentially inappropriate prescribing as defined by 2003 updated Beers criteria*

In addition, the prevalence of potentially inappropriate prescribing as defined by the 2003 updated Beers criteria, for the elderly (≥65 years old), were also assessed [31,32]. Medicines that were not available on the Australian Pharmaceutical Benefits Scheme (PBS) or the Repatriation PBS, were not included, as were those medicines that required diagnostic information (diagnostic data are not available in the DVA prescription dispensing database). In addition, as dosage information is not available in the data set, medicines for which judgment of appropriate use was dependant on dose or duration were excluded. A final list of 26 medicines from the 2003 Beers criteria was examined in our elderly diabetic cohort (Table 4).

3. Results

A total of 18,968 subjects were included in the diabetic cohort, of which 55.9% were men and 44.1% women, with a median age of 82 years (IQR 79–85) (Table 1). The median number of comorbid conditions was 5 (IQR 3–8) and the median number of unique medicines dispensed was 10 (IQR 7–14). Over 70% of the diabetic cohort were dispensed 5 or more unique medicines (Table 1).

Table 2 provides an overview of the prevalence of the number and types of anti-diabetic and cardiovascular medicines dispensed in our study cohort. Anti-diabetic medicines and associated cardiovascular medicines accounted for 41.9% of all medicine use. After exclusion of diabetes and related cardiovascular comorbidities (anti-platelet therapy, hypertension, hyperlipidemia and ischaemic heart disease), the median number of comorbid conditions was 3 (IQR 2–5).

Analysis by comorbidity showed that cardiovascular conditions of known association with diabetes were highly prevalent comorbidities (Fig. 1). Almost half of the diabetes cohort had comorbid gastro-oesophageal reflux disease (GORD), 25% had comorbid depression (as defined by anti-depressant use), approximately 20% had chronic airways disease or chronic pain, 16% had comorbid inflammation/pain, that may be indicative of some form of arthritis and 15% had chronic heart failure. Approximately 10% were identified as having comorbid osteoporosis or anxiety.

Examinations of potentially inappropriate prescribing or treatment conflicts specific for the elderly comorbid person with diabetes are described in Table 3. Over half of those aged 85 years and older were dispensed metformin, whilst only 3.4% of the elderly diabetic cohort (≥65 years old) were dispensed the long-acting sulfonylureas, glibenclamide or glimepiride. One in eight were dispensed a corticosteroid and approximately a sixth were dispensed a non-steroidal anti-inflammatory drug (NSAID). Thiazolidinedione were used by 10% of the comorbid diabetes and CHF population and in this comorbid population only 1% concomitantly were dispensed a thiazolidinedione and a NSAID. Examination of the use of corticosteroids that are part of guideline-recommended therapies for the treatment of chronic airways disease yet are not recommended in patients with comorbid diabetes, showed approximately a third of this diabetic population were dispensed either a systemic or inhaled corticosteroid. The use

Table 2 – Diabetic and recommended cardiovascular medicines dispensed in an elderly (≥65 years) diabetic cohort (*n* = 18,968).

Number and type of medicine dispensed	Diabetes cohort (*n* = 18,968)
Number of anti-diabetic medicines dispensed (prevalence, %)	
1	58.6
2	34.0
≥3	7.4
Number of anti-diabetic medicines dispensed, median (IQR)	1 (1–2)
Type of anti-diabetic medicine	
Metformin (A10BA02)	66.0
Sulfonamides (A10BB)	59.8
Metformin + sulfonamide (A10BA02 + A10BB)	29.8
Metformin and Sulfonamide combination formulation (A10BD)	1.8
Acarbose (A10BF)	0.9
Insulin (A10A)	17.5
Thiazolidinediones (glitazones, A10BG02, A10BG03)	9.6
Number of CV medicine classes dispensed, median (IQR)	3 (2–4)
Type of CV medicine classes dispensed (prevalence, %)	
Anti-platelet (B01AC)	46.0
Lipid lowering therapy (C10)	66.0
ACE or AR2B (C09A-D)	77.5
Diuretic (C03)	51.7
β-Blocker (C07)	33.2
Number of anti-diabetic and CV medicines dispensed, median (IQR)	4 (3–5)

CV, cardiovascular; ACE, angiotensin-converting enzyme inhibitors; AR2B, angiotensin II receptor blockers.

of β-blockers in this comorbid population is associated with an increased risk of bronchoconstriction and almost a quarter were co-dispensed this medicine. Only 3% were dispensed the non-selective β-blockers that are more commonly associated with this adverse effect (Table 3).

Almost 23% of the elderly diabetic cohort was found to have been dispensed at least one potentially inappropriate medicine, as defined by the 2003 updated Beers criteria (Table 4) and 3.4% were dispensed two or more. The medicines most commonly implicated included long-acting benzodiazepines (5.9%), amitriptyline (4.1%), nifedipine (3.3%) and amioderone (2.8%) and the most common combination was long-acting benzodiazepines and amtiriptyline (0.4%).

4. Discussion

This large population based study show a high level of comorbidity and associated polypharmacy in elderly Australian diabetic patients. This includes both those cardiovascular comorbidities of known association with diabetes and non-related comorbid diseases. Overall 40% of the comorbidity could be attributed to associated cardiovascular conditions and 40% of all medicine use was attributed to the dispensing of diabetes guideline treatments, which includes the management of both diabetes and associated cardiovascular comorbidities. The most prevalent non-related comorbid conditions were gastro-oesophageal reflux disease, depression, chronic

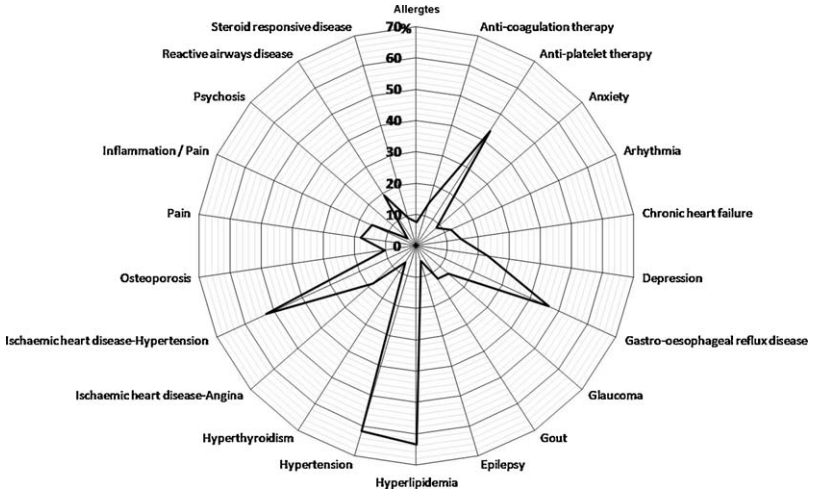

Fig. 1 – Prevalence of comorbid conditions in an elderly (≥65 years) diabetic cohort (*n* = 18,968)[a].
[a]Only those comorbidities with a prevalence of ≥5% are presented.

Table 3 – Potentially inappropriate medicine issues or comorbid disease treatment conflicts in an elderly (≥65 years) diabetic cohort (*n* = 18,968).

Risk Population	Medicine	Potential risk	Prevalence % (95%, CI)
Potentially inappropriate medicine issues			
Diabetes ≥85 years (*n* = 5620)	Metformin in those aged ≥85 years old	Elderly have decreased renal function [14] placing the very old at increased risk of lactic acidosis [23].	*n* = 2966, 52.8 (51.5–54.1)
Diabetes ≥65 years (*n* = 18,968)	Glibenclamide or Glimepiride in elderly	The long-acting sulfonylureas that are exclusively excreted renally put the elderly at increased risk of hypogylcaemia [24] due to decreased renal function [14].	*n* = 647, 3.4 (3.2–3.7)
Diabetes ≥65 years (*n* = 18,968)	Corticosteroids—inhaled Corticosteroids—systemic	Can increase blood glucose potentially increasing risk of hyperglycaemia [28].	*n* = 795, 4.2 (3.9–4.5) *n* = 1736, 9.1 (8.7–9.6)
Diabetes ≥65 years (*n* = 18,968)	NSAIDs[a]	Impair renal function, increase fluid retention and may exacerbate hypertension [29].	*n* = 2958, 15.6 (15.1–16.1)
Comorbid disease treatment conflicts			
Diabetes and chronic heart failure (CHF) (*n* = 3657)	Thiazolidinediones (glitazones) in CHF	Increased fluid retention and expansion of plasma volume leading to peripheral and pulmonary oedema [25].	*n* = 357, 9.7 (8.8–10.8)
Diabetes and CHF (*n* = 3657)	Concomitant use of thiazolidinediones and NSAIDs	Increased risk of fluid retention with both NSAIDs and thiazolidinediones in an already at risk population.	*n* = 45, 1.23 (1.14–1.39)
Diabetes and chronic airways disease (*n* = 3626)	Corticosteroids—inhaled Corticosteroids—systemic	Can increase blood glucose potentially increasing risk of hyperglycaemia [28] but are part of treatment recommendations for chronic airways disease [27].	*n* = 519, 14.3 (13.2–15.5) *n* = 740, 20.4 (19.1–21.7)
Diabetes and chronic airways disease (*n* = 3626)	β-Blockers—all β-Blockers—non-selective	β-Blockers are recommended for treatment of comorbid hypertension in diabetic patients [18] but are contraindicated in patients with chronic airways disease due to increased risk of inducing bronchoconstriction [26].	*n* = 902, 24.9 (23.5–26.3) *n* = 112, 3.1 (2.5–3.7)

[a] NSAIDs: non-steroidal anti-inflammatory drugs.

airways disease and chronic pain/inflammatory disease. Examination of potential treatment conflicts that physicians may encounter when looking after the multimorbid elderly diabetic patient, revealed that arthritis, chronic heart failure, chronic airways diseases and those diseases treatable with systemic corticosteroids such as inflammatory disorders, are the comorbidities of most concern. Further, one in five of our study cohort were dispensed a potentially inappropriate medicine, as defined by the Beers criteria.

In our study the median number of comorbid conditions was 5 (IQR 3–8), higher than in previous studies that have examined comorbidity in diabetes, generally around three comorbid conditions [5,12,33]. However, in contrast to our study, those included were either in younger diabetic patients [5,12,33] or examined only a smaller number specified comorbid conditions [5,12] or used the Charlson comorbidity index, that is derived from hospital encounters [6] and so may be less reflective of total chronic disease burden [19]. Implicit with the ''count of comorbidity'' approach is the assumption that all comorbid conditions are equal in terms of their effects on overall health status and importance to the patient. This approach cannot take into account the effects of individual comorbid diseases nor does it provide any guidance or insight for the prescribing physician in terms of diseases that are the most commonly observed in the elderly patient with diabetes.

A recent review of comorbidity in chronic diseases in Australian studies reported lower prevalence of all comorbid diseases examined, than our results show here, except for osteoporosis and arthritis (which could only be identified by proxy in our study with the use of analgesics/NSAIDs), in elderly diabetic patients [20]. Rather than being a real difference this may reflect the fact that most studies to date have focused only on one comorbid condition. The most common non-related comorbid conditions in our study were those that were highly symptomatic conditions which may have had a more debilitating impact on the patients' health status and may have potentially resulted in treatment prioritisation over diabetes. In a US study, an increasing number of comorbidities resulted in a decreased prioritisation of diabetes and resulted in worse self-management scores [5].

Table 4 – Inappropriate medication use as defined by the 2003 updated Beers criteria[a] in the elderly diabetic cohort (≥65 years) (*n* = 18,968).

Medicine concern	*n*	%
High severity		
Indomethacin	167	0.88
Oxybutynin	414	2.18
Amitriptyline	768	4.05
Doxepin	274	1.44
Long-acting benzodiazepines (diazepam, nitrazepam, flunitrazepam)	1118	5.89
Disopyramide	10	0.05
Methyldopa	194	1.02
Propantheline	0	–
Anticholinergics and antihistamines (cyproheptadine, promethazine)	206	1.09
Primidone	21	0.11
Ticlopidine	4	0.02
Dexamphetamine	6	0.03
Long half-life, high dose NSAIDs		
Naproxen	42	0.22
Piroxicam	68	0.36
Ketoprofen	68	0.36
Fluoxetine	177	0.93
Amiodarone	527	2.78
Nifedipine (short acting)	629	3.31
Thioridazine	6	0.03
Imipramine	127	0.69
Low severity		
Propoxyphene	110	0.58
Dipyridamole (short acting)	58	0.31
Clonidine	33	0.17
Cimetidine	18	0.10
Ethacrynic acid	5	0.03
Ergot alkaloids	0	–
Total dispensed at least one potentially inappropriate medicine % (95 CI)	*n* = 4317, 22.7% (22.2–23.4)	

[a] Medications defined as potentially inappropriate on the basis of the 2003 updated Beers criteria [32]. Severity was defined by the combination of the likelihood that an adverse event might occur and the clinical significance of that outcome should it occur [31].

Furthermore, those conditions such as depression, arthritis (pain/inflammation) and chronic airways disease have the potential to impair the patients' ability to self-manage, by limiting physical functioning, and thus pose barriers to lifestyle change or impact on medication adherence. Depression specifically, has been shown to be associated with decreased medication adherence, increased functional impairment and higher health care costs in diabetic patients [11]. Diabetes with comorbid osteoarthritis has been reported to be associated with a significant lower quality of life than diabetes alone [12].

Comorbidity has been identified as a potential factor contributing to the discordance between recommended guideline treatments and the actual practices observed [9,10]. Comorbidities can have a profound effect on managing the elderly patient with diabetes both in terms of treatment regimens, balancing competing recommendations and on patients' self-care. The incidence of adverse drug reactions, many of which require hospitalisation, is increasing, particularly in the elderly population, where polypharmacy and comorbidity are common [14]. The identification of the most prevalent treatment conflicts or potentially inappropriate prescribing that may occur in our comorbid elderly diabetic population may help to prepare targeted clinical guidance. The two most commonly dispensed anti-diabetic medicines in our study and in accord with clinical guidelines [18] were metformin and sulfonylureas. Both these medicines may pose potential problems in the elderly population where renal function may be comprimised [14]. Whilst current Australian guidelines recommend metformin be avoided in the very elderly (≥85 years) [23] due to an increased risk of lactic acidosis, we observed that over 50% of this age group were dispensed metformin. Whilst lactic acidosis is associated with substantial mortality and the risk increases with age and duration of diabetes, two very recent studies, a meta-analysis and an observational population based study have reported a low risk of lactic acidosis with metformin use [23,34] and as such have called for the warning to be removed.

In addition to their adverse gastrointestinal and cardiovascular profile, NSAIDs are also associated with adverse renal effects and exacerbation of hypertension [29]. We found a sixth of our elderly diabetic cohort were dispensed a NSAID during the study period, and whilst this may be reflective of the high level of comorbid osteoarthritis in the elderly population, it does not negate the increased risk of an adverse drug event or poorer hypertension control. Osteoarthritis is painful and disabling and consequently associated with high disease burden. Treatment of such a debilitating condition may result in the greatest impact on the patients' quality of life but this may place patients at increased risk of adverse drug reactions. Use of a NSAID has been reported to double the risk of hospital admission for CHF [35] and is associated with a four-five fold increased risk of upper gastrointestinal harm [36]. For the patient with osteoarthritis, effective pain management and mobility may be the most important priority in terms of treatment and is willing to take the increased risk of notional adverse events in the future. The prescribing physician must be able to balance these risks while giving precedence to the patients' priorities. Ideally, these NSAIDs should be used for rescue analgesia, not used chronically, and close monitoring by the physician for adverse renal and gastrointestinal effects and elevated hypertension may reduce the risk of an adverse event.

The dispensing of thiazolidinediones to 10% of the diabetic cohort with comorbid chronic heart failure was also of particular concern as these medicines are associated with an increased risk of cardiovascular events including heart failure and acute myocardial infarction and mortality [25]. Their use in patients with moderate to severe heart failure is contraindicated and the harms of thiazolidinediones clearly outweigh their benefits, particularly in these high risk patients. It is unclear from our study if the use of thiazolidinediones precipitated the heart failure or if they were introduced to patients with existing heart failure, but highlights the need for physicians to be judicious when prescribing these medicines, particularly when specific comorbid conditions are present and where safer alternatives should be considered.

Chronic airways disease was comorbid with one in five of our elderly diabetes cohort and this disease combination poses several treatment dilemmas for the prescribing physician that may complicate the management of both diseases. Whilst the use of both inhaled and systemic corticosteroids are advocated in guidelines for the prevention and treatment of acute exacerbations in chronic obstructive pulmonary disease (COPD), respectively [27,37], these agents can increase blood glucose potentially placing the diabetic patient at increased risk of hyperglycaemia [28]. Again, in elderly patients with diabetes, tight glycaemic control may take lesser priority in the short-term management of comorbid respiratory diseases excacerbations, as much diabetes management is to prevent future micro- and macrovascular complications. A recent meta-analysis of glycaemic control on CVD and all-cause mortality found that intensive glycaemic control reduced non-fatal stroke by 17% and coronary heart disease by 15% but did not impact on stroke or all-cause mortality [38]. These studies were largely undertaken in younger subjects, largely free if the comorbidities seen so frequently among older diabetic patients. Therefore, the optimum extent of glycaemia reduction in this elderly cohort cannot be clearly inferred from such studies in different populations. We reported over a third of this comorbid population concomitantly received a corticosteroid and clinicians should anticipate an increase in glucose levels and closely monitor glucose levels in these patients. The benefits of β-blockers (particularly the cardio-selective) in terms of improved survival are clear across the cardiovascular spectrum, including those patients with diabetes. However, the use of these agents in patients with diabetes and comorbid COPD or asthma is the subject of much debate [39] due to their potential to precipitate bronchoconstriction [27,37]. Whilst studies, including a meta-analysis have established the relative safety of cardio-selective β-blockers in patients with asthma [40] and COPD [41], there is a paucity of long-term studies from which safety and efficacy can be inferred. In the mean time physicians must carefully weigh the cardiovascular benefits of β-blocker therapy against an increased risk of respiratory exacerbations.

We also identified potentially inappropriate prescribing in our study cohort using the most commonly used measure of mediation appropriateness for those aged 65 years and older, the Beers criteria [32]. Consistent with previous studies, one in five of the elderly diabetic patients were dispensed a potentially inappropriate medicine, with long-acting benzodiazepines and amitriptyline the most commonly implicated [42,43]. Despite the widespread use of the Beers criteria as a measure of health care quality and safety, the evidence for its association with adverse health outcomes is mixed. A recent systematic review found that medicines identified by the Beers criteria were associated with an increased risk of hospitalisation in community dwelling elderly and adverse drug reactions, whereas no impact on mortality, quality of life or health care use was found [44]. Further, Beers criteria medicines were identified to account for 3.6% of all emergency department visits for adverse drug reactions in the elderly [45]. In a recent study, comparison of individualised expert review of over 250 patients with the Beers criteria found that 61% of medicines identified as potentially inappropriate by the Beers criteria were not judged to be problematic by expert review [46]. Whilst such criteria may serve to warn physicians of potential problems, it is clear individualised and judicious medicine prescription and regular review in the elderly particularly in the setting of comorbidity is vital.

The lack of clinical diagnoses within our dataset limits any conclusions one can draw regarding the appropriateness of all therapies dispensed, the rationale driving the prescribing or the effects on health outcomes in our diabetes cohort. Nor did we examine the prevalence of adverse drug events or health outcomes that may have been associated with potentially inappropriate prescribing or treatment conflicts within our study. It is also important to recognise that treatment with pharmacological therapies alone does not necessarily equate to clinically meaningful outcomes.

The complexity in managing the older diabetic patient with many comorbidities is becoming increasing recognised, with the recent publication of guidelines aimed at improving the care of the elderly patient with diabetes [10]. These guidelines provide a rationale for prioritisation of therapies and treatment preferences of older persons with diabetes and include comorbid conditions such as depression, cognitive impairment in addition to common geriatric conditions [10]. Whilst this is an important step towards providing better guidance for caring for diabetic patients with comorbidities, it is clear from this study that there are common comorbid conditions in the elderly with diabetes for which treatment decisions should be addressed in the development of future clinical guidelines.

It is time to provide integrated disease management guidance which takes account of the most common comorbidities increasingly observed among older people with diabetes. It is no longer adequate to only focus on cardiovascular comorbidity in this population. Until then, where significant comorbidity co-exists with increasingly common chronic conditions like diabetes, it is imperative that treatment decisions must remain individualised. Prioritisation of common comorbid conditions and the potential benefits and harms of these treatment decisions need to be clearly considered holistically, by combining evidence and clinical judgement balanced by patient specific information, preference and circumstance.

Conflicts of interest

The authors declare no conflict of interest.

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Appendix A. Appendix

Comorbidities were determined using the pharmaceutical based comorbidity index Rx-Risk-V, that has been validated in Australia [19]. It includes 42 comorbidities as determined by ATC classification; alcohol dependence (N07BB03–N07BB04

V03AA01), allergies (R01AC01–R01AD60, R06AD02–R06AX26), anti-coagulation therapy (B01AA03–B01AB06), anti-platelet therapy (B01AC04–B01AC30), anxiety (N05BA01–N05BA12), arrhythmia (C01AA05, C01BA01–C01BD01), benign prostate hypertrophy (G04CA02–G04CA03) bipolar disorder (N06AX), chronic heart failure (C03CA01–C03CC01) and (C09AA01–C09AA10, C09CA06–C09CA07), dementia (N06DA02–N06DA04), depression (N06AA01–N06AG02, N06AX03–N06AX18), diabetes (not included in our analyses) (A10AA01–A10BG03), end stage renal disease (B03XA01–B03XA02, A11CC01–A11CC04,V03AE02), epilepsy (N03AA01–N03AX14), gastric-oesophageal reflux disorder (A02BA01–A02BX05), glaucoma (S01EA01–S01EB03, S01EC03–S01EX), gout (M04AA01–M04AC01), hepatitis C (J05AB54), HIV (J05AE–J05AE08, J05AF01–J05AG03, J05AR, J05AX07), hyperkalaemia (V03AE01), hyperlipidemia (C10AA01–C10BX03), hypertension (C03AA01–C03BA11, C03DA01–C03EA01, C09BA02–C09BA09, C09DA02–C09DA07, C02AB01–C02AC05, C02DB02–C02KX01), hyperthyroidism (H03AA01–H03AA02),/angina (C01DA02–C01DA14), ischaemic heart disease/hypertension (C07AA01–C07AB03, C07AG01–C08DB01), irritable bowel syndrome (A07EC01–A07EC04, A07EA01–A07EA02), liver failure (A06AD11), malignancies (L01AA01–L01XX31), malnutrition (B05BA03), migraine (N02CA01–N02CX01), osteoporosis/pagets (M05BA01–M05BB03), pain (N02AA01–N02AX02), inflammation/pain (M01AB01–M01AH06), pancreatic insufficiency (A09AA02), parkinsons disease (N04AA01–N04BX02), psoriasis (D05AA, D05BB01–D05BB02, D05AX02), psychotic illness (N05AA01–N05AB02, N05AB06–N05AX12), chronic airways disease (R03AC02–R03DC03), smoking cessation (N07BA01–N07BA02), steroid responsive diseases (H02AB01–H02AB10), transplant (L04AA01–L04AA21), tuberculosis (J04AB04–J04AK02).

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