Identifying the need for simplification of type 2 diabetes mellitus treatment in residents of aged-care facilities: a meta-analysis and systematic review of the literature

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Abstract

Background: **The management of type 2 diabetes mellitus (T2DM) in frail older adults is made challenging by the impact of physical and cognitive decline on self-monitoring of blood glucose (BG), administration of medications, especially injectable therapies, and risk of hypoglycaemia.**

Aims and objectives: **(1) To revisit the prevalence of hypoglycaemia in adults with T2DM living in aged-care facilities; (2) to evaluate the impact of simplification of T2DM treatment on quality of life (QOL), morbidity and mortality in this population; and (3) to identify higher risk older adults in whom simplification of therapy will be most appropriate.**

Methods: **MEDLINE was searched using the following concept areas: aged-care facilities, T2DM, anti-diabetic therapies, morbidity, mortality and QOL. Results (and additional literature identified by citation checking) were screened and assessed against pre-defined eligibility criteria. Standardised structures for extracting, appraising and reporting the literature were used.**

Results: **Hypoglycaemia is common in adults with T2DM in aged-care facilities. Glycated haemoglobin (HbA_{1c}) needs to be interpreted cautiously in this cohort, with additional capillary BG monitoring needed to identify individuals at risk of hypo- or hyperglycaemia. Simplification of T2DM treatment can reduce morbidity and mortality in frail older adults.**

Conclusion: **In residents of aged-care facilities, simplification of T2DM treatment can help deliver optimal individualised patient-centred care and improve QOL.**

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Key words: type 2 diabetes mellitus, aged-care facilities, frailty, dementia

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Introduction

Type 2 diabetes mellitus (T2DM) is a significant global healthcare issue – a challenge intensified by our ageing population.[1] By 2030, 5.5 million people in the UK will have T2DM,[2] affecting 17% of those aged over 75 years.[3]

For older adults with T2DM, co-morbidities, polypharmacy and decreased functional reserve equates to greater personal and economic burden of disease: older adults are disproportionally affected by disease complications and hypoglycaemia, which can further impair quality of life (QOL) and accentuate physical and cognitive dependence.[4]

The global prevalence of T2DM in aged-care facilities (including residential and nursing homes) is estimated at 25–33%.[4] Compared with age- and sex-matched controls, residents with T2DM experience accelerated physical and cognitive decline with increased hospital admissions, rapid acquisition of the frail phenotype and reduced life expectancy.[4] Paradoxically, intensive glycaemic control, especially hypoglycaemia, is known to contribute to this decline.[4] The International Diabetes Federation (IDF) recommends a glycated haemoglobin (HbA_{1c}) of 53–64 mmol/mol in functionally dependent older adults, with lenience to <70 mmol/mol in individuals with frailty or dementia.[5] This less intensive glycaemic target aims to balance vascular benefits against the risk of hypoglycaemia in older adults.[5] HbA_{1c} represents the average glycaemic control over an 8–12-week period and is not an ideal parameter for evaluating day-to-day fluctuation in blood glucose (BG) levels. Additionally, anaemia, haemoglobinopathies and renal impairment are relatively more common amongst older adults, resulting in a less reliable marker of glycaemic control in this cohort.

Hypoglycaemia is common and under-recognised in residents of aged-care facilities.[4] This may reflect the dynamic nature of diabetes: disease and age-related changes to body composition, renal

and hepatic dysfunction, reduced nutrition and cognitive impairment result in an increased risk of hypoglycaemia and an impaired ability to respond to lower BG levels. A re-evaluation of glycaemic targets and simplification of treatment can mitigate the risks posed by intensive therapeutic regimens.

Over the last decade, novel oral glucose-lowering therapies have offered simplified treatments and additional cardiovascular and renovascular benefits.[6] However, long-term data outcomes on their safety and efficacy in frail older adults are still to be robustly established.

Aims and objectives

We aimed to evaluate hypoglycaemia prevalence and HbA_{1c} levels as semi-quantitative evidence of overtreatment in residents of aged-care facilities. In addition, we carried out a retrospective review of the literature to evaluate the impact of simplification of T2DM treatment on morbidity, mortality and QOL in this population. Finally, we suggest a possible approach to identify higher risk older adults in whom simplification of therapy will be most appropriate.

Methods

Searching the literature

In April 2020 the MEDLINE database was searched using text word and subject heading functions. The search incorporated the following concept areas: aged-care facilities, T2DM, anti-diabetic therapies, simplification of therapy, morbidity, mortality and QOL. Aged-care facilities include both residential and nursing homes. Appendix 1 (online at www.bjd-abcd.com) details the full search strategy used.

Selecting the literature

Results and additional literature identified through citation checking were screened by title and abstract to exclude literature clearly irrelevant to review. Thereafter, full-text articles were assessed against the following pre-defined eligibility criteria.

Inclusion criteria:

- Evaluates T2DM treatment in residents of aged-care facilities
- Observational or interventional study exploring the impact of simplification of T2DM treatment on morbidity, mortality and QOL
- Observational or interventional study exploring approaches to identify higher risk older adults in whom simplification of therapy will be most appropriate

Exclusion criteria:

- Non-English literature
- Non-peer reviewed literature
- Literature reviews, guidelines, opinions or editorials

Extracting, appraising and reporting the literature

Data extraction was guided by the Cochrane Collaboration's template for data extraction.[7] The Critical Appraisal Skills Programme checklists[8] were used to guide appraisal while the write-up of this review was supported by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[9]

Results

The search strategy yielded 88 results. Following screening by title and abstract, 27 records clearly irrelevant to review were excluded. The remaining 61 full-text articles were assessed for eligibility against the criteria detailed above. Of these, 43 records were excluded. These included 15 records not reflective of review focus, 13 literature reviews, guidelines, opinions or editorials, 10 inaccessible records, and 5 non-English studies (see Figure 1). The remaining 18 studies are included in this review.

We identified 18 studies which evaluated the prevalence of hypoglycaemia and the need for simplification in residents with T2DM in aged-care facilities (see Table 1).[10–27] Based on a retrospective

Figure 1. Adapted PRISMA flow diagram[9] detailing results of methodology.

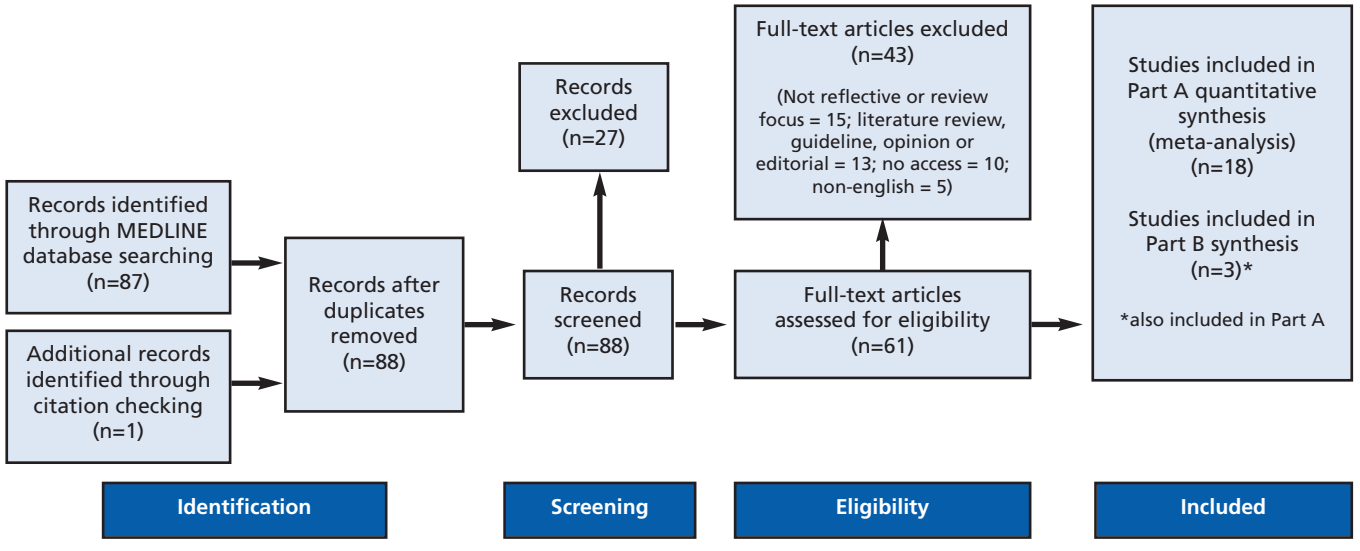

Table 1 Evaluating the need for simplification of T2DM treatment in residents of aged-care facilities

Study details	Study overview	Study design		Key results	Comments
Niznik *et al*, 2020[10]	To explore predictors for diabetes treatment deintensification	Type Population Sample size Intervention Outcome; Comparison	Retrospective cohort study Veteran nursing home residents with advanced dementia or perceived to be at end of life n = 6960 Nil Deintensification of diabetes medication; nil	40% overtreated; 46% deintensified at 90 days. Predictors for deintensification: end of life, non-metformin OAD. Predictors against deintensification: high HbA_{1c}, insulin, obesity, peripheral arterial disease.	Quantifies overtreatment and poor deintensification; insulin as predictor against deintensification may reflect type 1 or Latent Autoimmune Diabetes of Adulthood (LADA).
Umpierrez *et al*, 2018[11]	To explore outcomes of simplifying diabetes treatment with glargine or linagliptin monotherapy	Type Population Sample size Intervention Outcome; Comparison	Open-label randomised controlled trial Aged-care facility residents on OAD or low-dose insulin and HbA_{1c} >58 mmol/mol n = 140 Glargine monotherapy or linagliptin monotherapy Mean daily BG, hypoglycaemia, HbA_{1c}, hospital admission, emergency department visits; baseline, glargine monotherapy, linagliptin monotherapy	Significantly lower mean daily BG with linagliptin and glargine monotherapy compared with baseline. 34% absolute risk reduction in hypoglycaemia with linagliptin compared with glargine. No significant difference in HbA_{1c} at 6 months between linagliptin and glargine. No significant changes to all-cause hospital admissions in any intervention.	Demonstrates safety and efficacy of linagliptin monotherapy for simplification of diabetes treatment.
McCracken *et al*, 2017[12]	To evaluate relationship between polypharmacy and overtreatment	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents n = 214 Nil Number of prescribed medications, HbA_{1c}; nil	48% met definition for polypharmacy. Those with overtreated diabetes prescribed more antidiabetic treatment than those with higher HbA_{1c}.	Polypharmacy common and contributes to functional decline. No significant relationship between number of prescribed medications and overtreatment.
Retornaz *et al*, 2017[13]	To evaluate relationship between HbA_{1c} and hypoglycaemia risk	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 236 Nil HbA_{1c}, hypoglycaemia; nil	Intensive glycaemic control in 60%. 19% affected by hypoglycaemia. Hypoglycaemia and sub-optimal glycaemic control more common in those taking insulin therapy. No significant correlation between HbA_{1c} and hypoglycaemia.	Identifies insulin therapy as most requiring review and simplification. HbA_{1c} levels not sufficient for hypoglycaemia risk detection. Capillary BG monitoring warranted in nursing home residents.
Walfridsson *et al*, 2016[14]	To investigate clinical characteristics and prevalence of hypoglycaemia	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 1350 Nil HbA_{1c}, hypoglycaemia, diabetic complications; nil	Mean HbA_{1c} 56.0 mmol/mol. 43% with HbA_{1c} <52 mmol/mol. 24% affected by hypoglycaemia.	43% overtreated based on IDF HbA_{1c} targets in this population. Hypoglycaemia common.
Dharmarajan *et al*, 2016[15]	To compare safety and efficacy of BB and SS insulin regimens	Type Population Sample size Intervention Outcome; Comparison	Randomised controlled trial Aged-care facility residents with diabetes n = 64 SS insulin regimen, BB insulin regimen Fasting BG, hypoglycaemia, hyperglycaemia, adverse events; BB and SS	Significantly lower fasting BG in those on BB insulin regimens compared to SS. No significant differences in the incidence of hypoglycaemia.	Simplified insulin regimen improves fasting BG. Three-day data collection period not adequate for observation of hypoglycaemic events. Evidence of safety and efficacy of simplified insulin regimens.
Bo *et al*, 2015[16]	To investigate clinical characteristics and prevalence of hypoglycaemia	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 863 Nil Cognitive and functional dependence, HbA_{1c}, hypoglycaemia	Cognitive impairment, functional dependence and co-morbidities are common among residents with diabetes. 55% with HbA_{1c} <53 mmol/mol. 6.6% experience hypoglycaemia.	Individuals who are frail and have dementia are particularly at risk of overtreatment. 55% overtreated based on IDF HbA_{1c} targets in this population.

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Table 1 Evaluating the need for simplification of T2DM treatment in residents of aged-care facilities (continued)

Study details	Study overview	Study design		Key results	Comments
Neumark *et al*, 2016[17]	To explore clinical characteristics of older people with diabetes living at home (with and without additional care) and in nursing care homes	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged ≥80 with diabetes n = 277 Nil HbA_{1c}; residing at home, residing in residential care homes, residing in nursing care homes	Lower HbA_{1c} in residents of nursing homes. HbA_{1c} <52 mmol/mol in 48% of nursing homes residents, 35% of those living at home with additional care, and 29% of those living at home independently. Insulin use more prevalent in nursing care homes.	48% overtreated based on IDF HbA_{1c} targets in this population.
Abatecola *et al*, 2015[18]	To investigate clinical characteristics and prevalence of hypoglycaemia	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 2258 Nil Fasting BG, postprandial BG, HbA_{1c}, ADLs; anti-diabetic treatments	Hypoglycaemia observed in 18% of nursing home residents with dementia compared to 8% in residents without dementia. Residents on sulfonylurea therapy had increased odds ratio (8.8, CI 4.2 to 18.2) of severe hypoglycaemia. Rapid and analogue insulin therapy associated with reduced odds ratio (0.333, CI 0.184 to 0.602 and 0.248, CI 0.070 to 0.882 respectively) of severe hypoglycaemia.	Individuals with dementia are particularly at risk of hypoglycaemia. Cautious use of sulfonylurea therapy required. Rapid and analogue insulin therapy relatively safer.
Andreassen *et al*, 2014[19]	To investigate clinical characteristics and prevalence of hypoglycaemia	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 742 Nil HbA_{1c}; nil	32% on insulin monotherapy. Mean HbA_{1c} 57 mmol/mol. HbA_{1c} <53 mmol/mol in 46%. 60% identified at risk of hypoglycaemia based on capillary BG measurement.	Insulin therapy common - proportion who are insulin dependent unknown. 46% overtreated based on IDF HbA_{1c} targets in this population. Capillary BG measurement has a broader reach to identify those at risk of developing hypoglycaemia.
Bouillet *et al*, 2010[20]	To determine clinical characteristics by antidiabetic therapy	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes aged ≥65 years n = 100 Nil HbA_{1c}; antidiabetic therapy	32% with HbA_{1c} <47.5 mmol/mol.	32% overtreated based on IDF HbA_{1c} targets in this population.
Sjoblom *et al*, 2008[21]	To compare safety and efficacy of deintensification of diabetes treatment	Type Population Sample size Intervention Outcome; Comparison	Open-label non-randomised controlled trial Aged-care facility residents with diabetes and HbA_{1c} ≤42 mmol/mol n = 98 Cessation of OADs, cessation of insulin <20 units and halving of insulin >20 units HbA_{1c}, hypoglycaemia; baseline	6-month 7 mmol/mol mean HbA_{1c} increase in those undergoing deintensification. 6-month post-intervention mean remained low at 40 mmol/mol. Deintensification caused no significant changes to all-cause hospital admissions or mortality.	Demonstrates safety and efficacy of deintensification of diabetes treatment.
Meyers *et al*, 2007[22]	To investigate variability of HbA_{1c}	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 168 Nil HbA_{1c}; nil	Mean HbA_{1c} 54.1 mmol/mol. Age correlation with HbA_{1c} lowest among the oldest. Higher HbA1c with insulin use. No correlation between HbA_{1c} and self-perceived health and life expectancy.	Suggests the oldest and frailest at increased risk of hypoglycaemia. HbA_{1c} may not have self-perceived impact on quality of life.

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Table 1 Evaluating the need for simplification of T2DM treatment in residents of aged-care facilities (continued)

Study details	Study overview	Study design		Key results	Comments
Gill *et al*, 2006[23]	To investigate clinical characteristics and glycaemic control	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 54 Nil HbA_{1c}; nil	Mean HbA_{1c} 56 mmol/mol. Co-morbidities and polypharmacy common. 27% on insulin.	Co-morbidities and polypharmacy contribute to disease and age-mediated decline. Insulin therapy common - proportion who are insulin dependent unknown.
Pham *et al*, 2003[24]	To investigate clinical characteristics and outcomes	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 240 nursing home residents; n = 80 residential home residents Nil	Insulin treatment in 36%. OAD in 40%.	Insulin therapy common - proportion who are insulin dependent unknown.
Wolffenbuttel *et al*, 1991[25]	Investigate clinical characteristics and outcomes of aged-care facility residents with diabetes	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 38 Nil HbA_{1c}, diabetic complications; nil	Mean HbA_{1c} 58 mmol/mol. No difference between HbA_{1c} in those with diabetes in the community or in aged-care facilities. Those in aged-care facilities more likely to experience general decline: ulcers, necrosis, recurrent infections, peripheral arterial disease.	Emphasises general propensity towards frailty in residents of aged-care facilities.
Davis *et al*, 2014[26]	Investigate clinical characteristics and outcomes of individuals receiving basal insulin	Type Population Sample size Intervention Outcome; Comparison	Retrospective observational study Aged-care facility residents with diabetes n = 2096 Nil Hypoglycaemia; nil	60% of residents receive insulin therapy. 17% affected by hypoglycaemia.	Insulin therapy common - proportion who are insulin dependent unknown. Hypoglycaemia relatively common. Basal insulin under-utilised.
Newton *et al*, 2013[27]	To determine clinical characteristics by antidiabetic therapy	Type Population Sample size Intervention Outcome; Comparison	Cross-sectional observational study Aged-care facility residents with diabetes n = 1409 Nil Antidiabetic therapy	34% received insulin, 26% received insulin and OAD, 5% on OAD alone, 10% diet-controlled.	Insulin therapy common - proportion who are insulin dependent unknown.

ADLs, activities of daily living; BB, basal bolus; BG, blood glucose; CI, confidence interval; HbA_{1c}, glycated haemoglobin; IDF, International Diabetes Federation; OAD, oral antidiabetic drug; SS, sliding scale.

analysis of data from 10 observational studies, our systematic review suggests that hypoglycaemia remains common: hypoglycaemia was reported in 6.6–43%,[10,11,13,14,16,18,19,24,26,27] clearly identifying it as a preventable factor contributing to increased morbidity and mortality in this cohort.

We could identify only three studies which evaluated a strategy for simplification of T2DM treatment in residents of aged-care facilities (see Table 2). Based on our meta-analysis, older adults with T2DM were more prone to experience hypoglycaemia at both ends of the HbA_{1c} spectrum.[10,13,14]

Discussion

Part A: Evaluating the need for simplification of T2DM treatment in residents of aged-care facilities

Management of T2DM in frail older adults poses special challenges as a reduction in functional capacity, development of co-morbidities, polypharmacy, cognitive decline and frailty warrants dynamic re-evaluation of glycaemic targets. The vascular benefits of intensive control need to be weighed against risks posed by hypoglycaemia, with focus on simplification of the therapeutic regimen and adaptation of an individualised approach.

Multiple observational and cross-sectional studies have investigated the prevalence of hypoglycaemia and used HbA_{1c} as a marker of glycaemic control.[10–28] We identified 16 studies (collectively involving 7,869 aged-care residents with T2DM) in which data on HbA_{1c} were collected and compared to evaluate glycaemic control. Among these studies, the mean HbA_{1c} was 51.9 mmol/mol (95% CI 52.0 to 51.8 mmol/mol); Figure 2). However, of the five studies reporting grouped values, HbA_{1c} <53 mmol/mol was seen in 43–55%.[14–16,19,22] With the IDF recommending a target HbA_{1c} of

Table 2 Simplification of type 2 diabetes mellitus treatment in aged-care facility residents

Study details	Study overview	Study design		Key results	Comments
Umpierrez *et al*, 2018[11]	To explore outcomes of simplifying diabetes treatment with glargine or linagliptin monotherapy	Type Population Sample size Intervention Outcome; Comparison	Open-label randomised controlled trial Aged-care facility residents on OAD or low-dose insulin and HbA_{1c} >58 mmol/mol n = 140 Glargine monotherapy or linagliptin monotherapy Mean daily BG, hypoglycaemia, HbA_{1c}, hospital admission, emergency department visits; baseline, glargine monotherapy, linagliptin monotherapy	Significantly lower mean daily BG with linagliptin and glargine monotherapy compared with baseline. 34% absolute risk reduction in hypoglycaemia with linagliptin compared with glargine. No significant difference in HbA_{1c} at 6 months between linagliptin and glargine. No significant changes to all-cause hospital admissions in any intervention.	Demonstrates safety and efficacy of linagliptin monotherapy for deintensification of diabetes treatment.
Dharmarajan *et al*, 2016[15]	To compare of safety and efficacy of BB and SS insulin regimens	Type Population Sample size Intervention Outcome; Comparison	Randomised controlled trial Aged-care facility residents with diabetes n = 64 SS insulin regimen, BB insulin regimen Fasting BG, hypoglycaemia, hyperglycaemia, adverse events; BB and SS	Significantly lower fasting BG in those on BB insulin regimens compared with SS. No significant differences in the incidence of hypoglycaemia.	Simplified insulin regimen improves fasting BG. Three-day data collection period not adequate for observation of hypoglycaemic events. Evidence of safety and efficacy of simplified insulin regimens.
Sjoblom *et al*, 2008[21]	To compare the safety and efficacy of deintensification of diabetes treatment	Type Population Sample size Intervention Outcome; Comparison	Open-label non-randomised controlled trial Aged-care facility residents with diabetes and HbA_{1c} ≤42 mmol/mol n = 98 Cessation of OADs, cessation of insulin <20 units and halving of insulin >20 units; HbA_{1c}, hypoglycaemia; baseline	6-month 7 mmol/mol mean HbA_{1c} increase in those undergoing deintensification. 6-month post-intervention mean remained low at 40 mmol/mol. Deintensification caused no significant changes to all-cause hospital admissions or mortality.	Demonstrates safety and efficacy of deintensification of diabetes treatment.

BB, basal bolus; BG, blood glucose; HbA_{1c}, glycated haemoglobin; OAD, oral antidiabetic drug; SS, sliding scale.

53–64 mmol/mol in functionally dependent older adults, with lenience to <70 mmol/mol in those frail or living with dementia,[9] this suggests significant overtreatment of this population cohort.

Interestingly, higher HbA_{1c} levels were also associated with an increased risk of developing hypoglycaemia,[10,13,14] reflecting poor glycaemic control at both ends of the HbA_{1c} spectrum. HbA_{1c} is a poor marker of glucose variability and needs to be interpreted cautiously in older adults (especially those dependent on carers for nutrition and injectable therapy) due to their susceptibility to BG fluctuation. HbA_{1c} levels can also be falsely high or low due to anaemia, polycythaemia or renal impairment, which become more prevalent with ageing. Andreassen *et al*[19] found capillary BG measurements to have a broader reach in identifying older adults at risk of developing hypoglycaemia than HbA_{1c} levels.

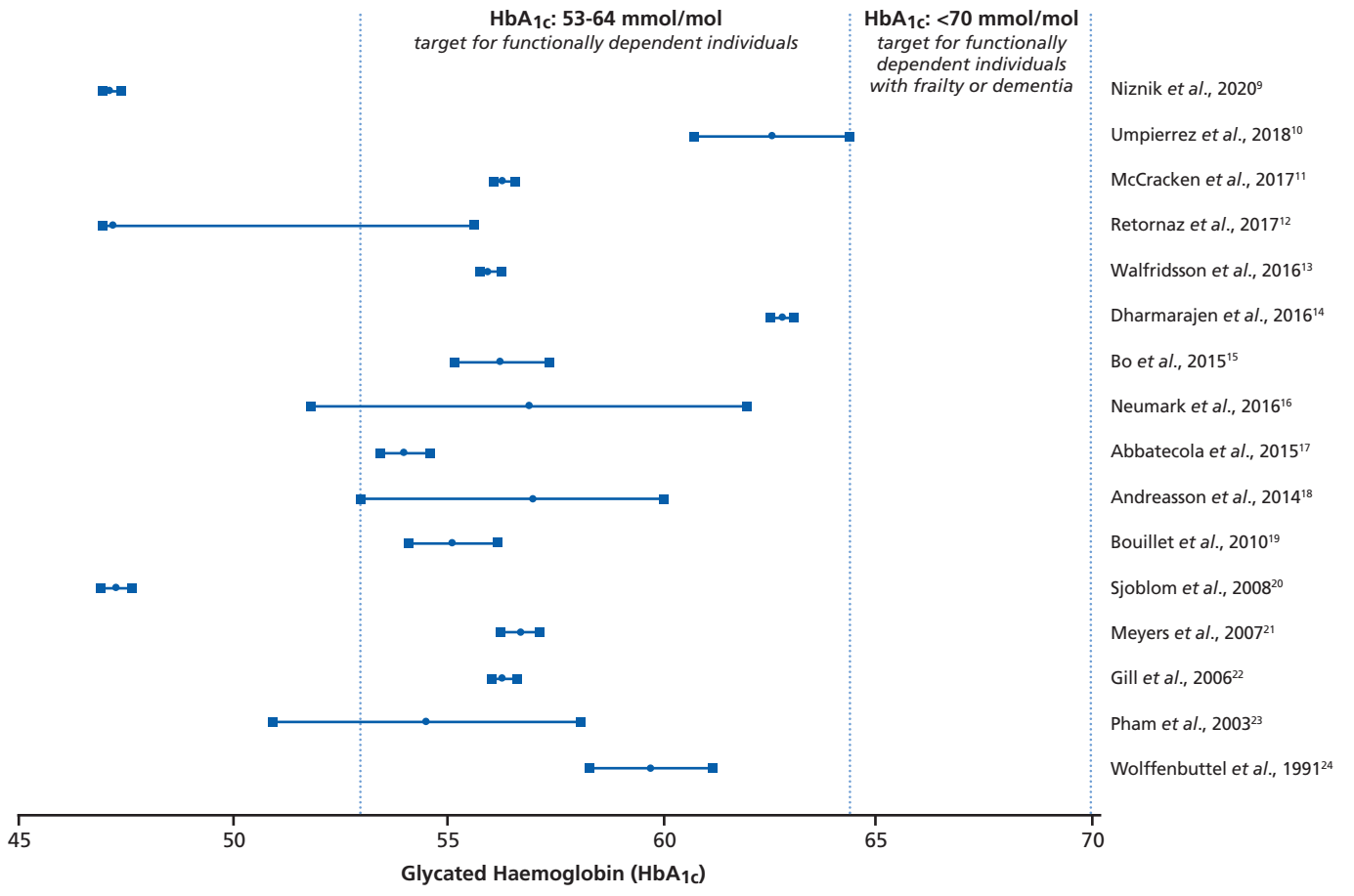
We identified 10 observational studies which have reported on the prevalence of hypoglycaemia in aged-care facility residents. The prevalence of hypoglycaemia based on these studies ranged from 6.6% to 60%,[10,11,13,14,16,18,19,24,26,27] reflecting it to be a common and avoidable risk factor associated with increased morbidity in this age group. Indeed, of the 44 nursing homes approached by Hurley *et al*, 19% reported hypoglycaemic evens as "frequent" among its residents.[28]

Insulin therapy was commonly associated with the greatest risk of hypoglycaemia compared with other treatment modalities,[10,11,13,14,16,24,27] highlighting this therapy as the most in need of review and simplification. An exception to this was a study by Abbatecola *et al* who observed a lower risk of severe hypoglycaemia associated with rapid and analogue insulin (OR 0.333, 95% CI 0.184 to 0.602 and OR 0.248, 95% CI 0.070 to 0.882, respectively) compared with sulfonylurea therapy (OR 8.8, 95% CI 4.2 to 18.2).[18] This study also reported residents with dementia (18%) to be especially vulnerable to developing severe hypoglycaemia compared with residents without dementia (8%).[18] Multiple other studies have reported an increased risk of sulfonylurea-induced hypoglycaemia in residents with dementia.[16,18]

Part B: Simplification of T2DM treatment in residents of aged-care facilities

There is limited literature exploring simplification of T2DM treatment in this population. We identified three such studies which provide a regimen for simplification of T2DM management in residents of aged-care facilities. These studies showed marked heterogeneity in population selection, intervention used for simplification and reported outcomes, making direct comparison non-viable. For example, Sjoblom et al explored different strategies for simplification including switching insulin to oral antidiabetic drugs, cessation of insulin <20 units and halving of insulin >20 units.[21] Dharmarajan *et al* explored simplifying insulin regimens from sliding scale (SS) to

Figure 2. Forest plot showing mean HbA_{1c} and 95% confidence intervals (CI) of aged-care facility residents with diabetes. Overall pooled studies mean 51.9 mmol/mol (95% CI 51.8 to 52.0).



basal bolus (BB).[15] A study by Umpierrez *et al* was the only one to compare basal insulin (glargine) with DPP4 inhibitor (linagliptin) monotherapy.[11]

Of the two studies reporting BG levels, both showed reduced glycaemic variability with simplified treatment. For example, compared with baseline, linagliptin monotherapy resulted in significantly lower mean daily BG.[11] A 34% absolute risk reduction in residents affected by hypoglycaemia was also demonstrated when compared with those receiving insulin.[11] Similarly, Dharmarajan *et al* demonstrated significantly lower fasting BG in those on BB insulin regimens compared with SS.[15] Here, there were no significant differences in the incidence of hypoglycaemia, although data collection for this occurred over a three-day period only.[15]

Two of the studies used HbA_{1c} to report the impact of simplification on glycaemic control. Although Sjoblom *et al* reported a 7 mmol/mol mean HbA_{1c} increase, the 6-month post-intervention mean remained low at 40 mmol/mol.[21] When compared with insulin therapy, linagliptin showed no significant difference in HbA_{1c} at 6 months.[11] In addition, simplification caused no significant changes to all-cause hospital admissions[11,21] or mortality.[21]

Our systematic review of the literature provides further evidence to support a well-formed consensus: residents with T2DM in aged-care facilities are often subject to intensive glycaemic control and hypoglycaemia. In older adults with T2DM, intensive glycaemic control, especially hypoglycaemia, contributes to accelerated physical and cognitive decline, hospital admissions, frailty and reduced life expectancy.[4] Although limited by scarcity of randomised controlled trials, this review suggests that simplification of T2DM treatment can effectively reduce hypoglycaemia risk without compromising glycaemic control in this population.[11,15,21] Additionally, simplification may also benefit QOL by reducing tablet, injection and BG monitoring burden for both residents and carers.[29]

Part C: Identification of residents most likely to benefit from simplification of T2DM treatment

Identifying aged-care facility residents most likely to benefit from simplification of therapy has not received much focus. Evaluating glycaemic control in this cohort is challenging as factors such as cognitive impairment, frailty, reduced functional reserve and depression may make self-monitoring of BG and reporting of osmotic symptoms difficult.

HbA_{1c} measurement remains a relatively insensitive tool to screen those at risk of developing hypoglycaemia.[10,13,14] Capillary BG monitoring should supplement HbA_{1c} monitoring in identifying

Key messages

- Hypoglycaemia is a common and preventable cause of increased morbidity and mortality in residents of aged-care facilities
- Capillary blood glucose monitoring should supplement HbA_{1c} monitoring in evaluating glycaemic control in frail adults
- Continuous glucose monitoring in older adults deemed at high risk of hypoglycaemia offers a novel and pragmatic approach with potential to improve quality of life
- Simplification of type 2 diabetes therapy should be considered in most residents of aged-care facilities, especially in the presence of frailty and dementia

older adults most vulnerable to develop hypoglycaemia. Short- or medium-term continuous glucose monitoring in aged-care facility residents deemed at high risk of hypoglycaemia offers a pragmatic approach and a far more comprehensive reflection of glycaemic control.

The number of antidiabetic prescriptions has not been observed to show correlation with hypoglycaemia risk.[12] Care is needed to avoid cessation of insulin in those with type I diabetes mellitus or Latent Autoimmune Diabetes of Adulthood (LADA). As such, further work is needed to explore whether an insulinopenic phenotype as suggested by history, low or low-normal body mass index, previous diabetic ketoacidosis, presence of anti-GAD or anti-islet cell antibodies or strong personal history of autoimmune conditions correctly identifies those with insulin dependency. Similarly, preserved urinary C-peptide:creatinine can give biochemical reassurance of residual pancreatic β cell function and confidence to simplify diabetic treatment.

Selecting a safe and individualised regimen for simplification remains integral in delivering biological, not chronological, patient-centred care – a principal central to all discussions in this review.

Conclusions

In summary, simplification of treatment should be considered in most residents with T2DM living in aged-care facilities, especially in the presence of dementia and frailty. Treatment regimens need to be individualised with simplification of the insulin regimen and/or switching to oral glucose-lowering medications wherever possible. At the time of writing this review, the COVID-19 pandemic reminds us that keeping our older adults with diabetes safe, reducing their dependence on caregivers for administration of tablets, injections and BG monitoring, is far more important now than it has been ever before.

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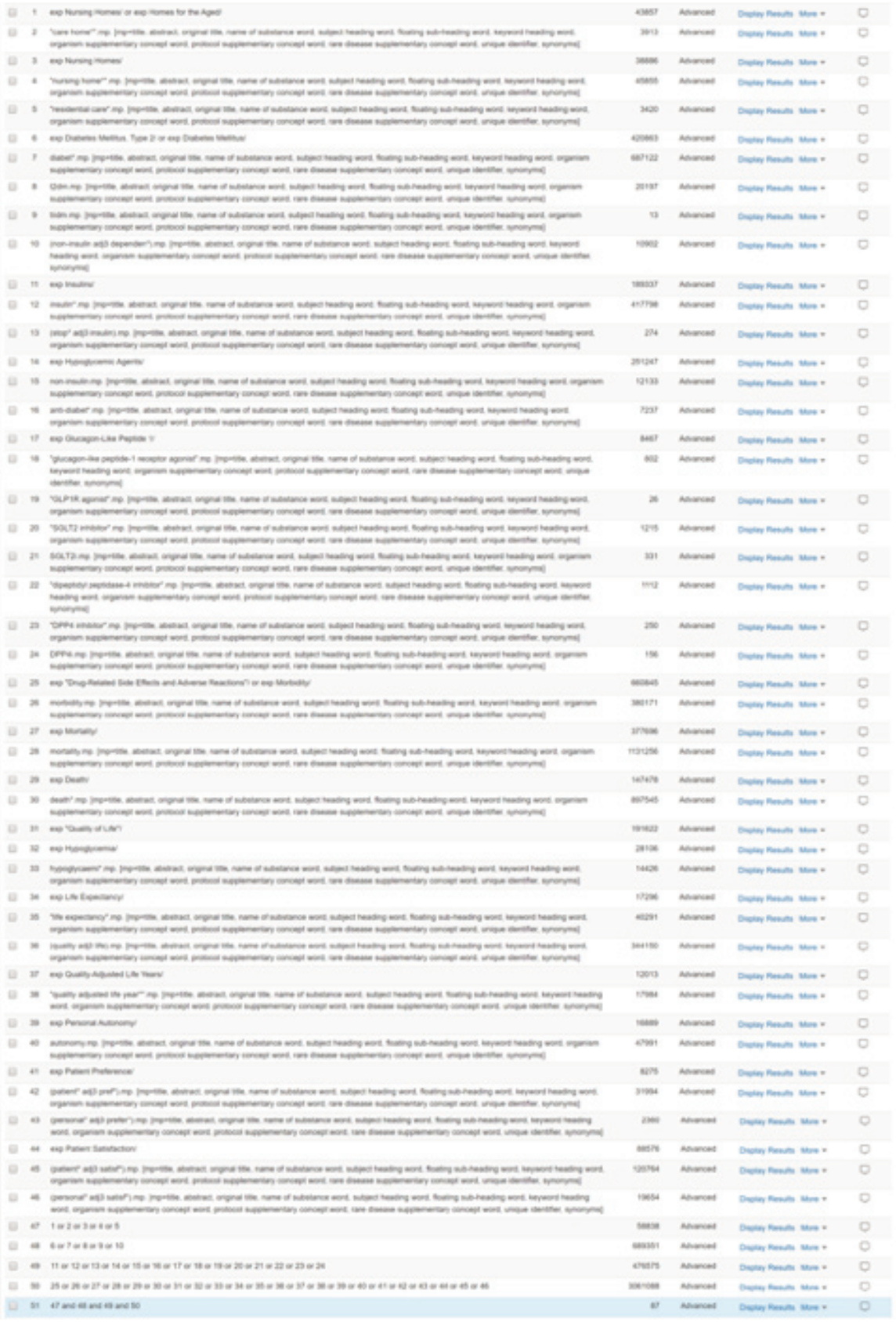
References

1. Gojka R. WHO Global report on diabetes: a summary. *Int J Noncommun Dis* 2016;**1**(1):3–8.
2. Diabetes UK. How many people are at risk of type 2 diabetes? London: The British Diabetic Association. 2019. Available at: https://www.diabetes.org.uk/about_us/news/new-stats-people-living-with-diabetes (accessed 6 May 2020).
3. Diabetes UK. Diabetes in the UK 2010: Key statistics on diabetes. 2010. Available at: https://www.diabetes.org.uk/resources-s3/2017-11/diabetes_in_the_uk_2010.pdf (accessed 5 May 2020).
4. Sinclair AJ, Gadsby R, Abdelhafiz AH, Kennedy M. Failing to meet the needs of generations of care home residents with diabetes: a review of the literature and a call for action. *Diabet Med* 2018;**35**(9):1144–56. https://doi.org/10.1111/dme.13702
5. Dunning T, Sinclair A, Colagiuri S. New IDF guideline for managing type 2 diabetes in older people. *Diabetes Res Clin Pract* 2014;**103**(3):538–40. https://doi.org/10.1016/j.diabres.2014.03.005
6. American Diabetes Association. 12. Older Adults: Standards of Medical Care in Diabetes—2020. *Diabetes Care* 2020;**43**(Suppl 1):S152–S162. https://doi.org/10.2337/dc20-S012
7. Ryan R, Synnot A, Prictor M, Hill S. Data extraction template for included studies. 2016. Available at: https://figshare.com/articles/Data_extraction_template/6818852 (accessed 30 April 2020).
8. Critical Appraisal Skills Programme. CASP Checklists. 2018. Available at: https://casp-uk.net/casp-tools-checklists/ (accessed 30 April 2020).
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta- analyses: the PRISMA statement. *BMJ* 2009;**339**:b2535. https://doi.org/10.1136/bmj.b2535
10. Niznik JD, Hunnicutt JN, Zhao X, *et al*. Deintensification of diabetes medications among Veterans at the end of life in VA nursing homes. *J Am Geriatr Soc* 2020;**68**(4):736–45. https://doi.org/10.1111/jgs.16360
11. Umpierrez GE, Cardona S, Chachkhiani D, *et al*. A randomized controlled study comparing a DPP4 inhibitor (linagliptin) and basal insulin (glargine) in patients with type 2 diabetes in long-term care and skilled nursing facilities: Linagliptin-LTC Trial. *J Am Med Dir Assoc* 2018;**19**(5):399–404.e3. https://doi.org/10.1016/j.jamda.2017.11.002
12 McCracken R, McCormack J, McGregor MJ, *et al*. Associations between polypharmacy and treatment intensity for hypertension and diabetes: a cross-sectional study of nursing home patients in British Columbia, Canada. *BMJ Open* 2017;**7**(8):e017430. https://doi.org/10.1136/bmjopen-2017-017430
13. Retornaz F, Grino M, Mari L, Oliver C. Assessment of glycemic control in nursing home residents with diabetes. *J Nutr Health Aging* 2017;**21**(4):457–63. https://doi.org/10.1007/s12603-016-0776-0
14. Walfridsson A, Sehlberg M, Gillespie U, *et al*. Diabetes treatment and hypoglycaemic episodes in elderly patients at nursing homes in Uppsala County. *Uppsala J Med Sci* 2016;**121**(3):179–83. https://doi.org/10.1080/03009734.2016.1198441
15. Dharmarajan TS, Mahajan D, Zambrano A, *et al*. Sliding scale insulin vs basal-bolus insulin therapy in long-term care: a 21-day randomized controlled trial comparing efficacy, safety and feasibility. *J Am Med Dir Assoc* 2016;**17**(3):206–13. https://doi.org/10.1016/j.jamda.2015.08.015
16. Bo M, Gallo S, Zanocchi M, *et al*. Prevalence, clinical correlates, and use of glucose-lowering drugs among older patients with type 2 diabetes living in long-term care facilities. *J Diabetes Res* 2015;**2015**:174316. https://doi.org/10.1155/2015/174316
17. Neumark A-SN, Brudin L, Neumark T. Adherence to national diabetes guidelines through monitoring quality indicators—A comparison of three types of care for the elderly with special emphasis on HbA1c. *Primary Care Diabetes* 2015;**9**(4):253–60. https://doi.org/10.1016/j.pcd.2015.03.002
18. Abbatecola AM, Bo M, Barbagallo M, *et al*. Severe hypoglycemia is associated with antidiabetic oral treatment compared with insulin analogs in nursing home patients with type 2 diabetes and dementia: results from the DIMORA Study. *J Am Med Dir Assoc* 2015;**16**(4):349.e7–e12. https://doi.org/10.1016/j.jamda.2014.12.014
19. Andreassen LM, Sandberg S, Kristensen GBB, *et al*. Nursing home patients with diabetes: prevalence, drug treatment and glycemic control. *Diabetes Res Clin Pract* 2014;**105**(1):102–09. https://doi.org/10.1016/j.diabres.2014.04.012

20. Bouillet B, Vaillant G, Petit JM, *et al*. Are elderly patients with diabetes being overtreated in French long-term-care homes? *Diabetes Metab* 2010; **36**(4):272–7. https://doi.org/10.1016/j.diabet.2010.01.009
21. Sjöblom P, Anderstengblad U-B, Löfgren C, *et al*. Can diabetes medication be reduced in elderly patients? An observational study of diabetes drug withdrawal in nursing home patients with tight glycaemic control. *Diabetes Res Clin Pract* 2008;**82**(2):197–202. https://doi.org/10.1016/j.diabres.2008.08.014
22. Meyers RM, Broton JC, Woo-Rippe KW, *et al*. Variability in glycosylated hemoglobin values in diabetic patients living in long-term care facilities. *J Am Med Dir Assoc* 2007;**8**(8):511–14. https://doi.org/10.1016/j.jamda.2007.02.002
23. Gill EA, Corwin PA, Mangin DA, Sutherland MG. Diabetes care in rest homes in Christchurch, New Zealand. *Diabet Med* 2006;**23**(11):1252–6. https://doi.org/10.1111/j.1464-5491.2006.01976.x
24. Pham M, Pinganaud G, Richard-Harston S, *et al*. Prospective audit of diabetes care and outcomes in a group of geriatric French care homes. *Diabetes Metab* 2003;**29**(3):251–8. https://doi.org/10.1016/s1262-3636(07)70034-4
25. Wolffenbuttel BHR, van Vliet S, Knols AJF, *et al*. Clinical characteristics and management of diabetic patients residing in a nursing home. *Diabetes Res Clin Pract* 1991;**13**(3):199–206. https://doi.org/10.1016/0168-8227(91)90064-k
26. Davis KL, Wei W, Meyers JL, *et al*. Use of basal insulin and the associated clinical outcomes among elderly nursing home residents with type 2 diabetes mellitus: a retrospective chart review study. *Clin Interv Aging* 2014;**9**:1815–22. https://doi.org/10.2147/CIA.S65411
27. Newton CA, Adeel S, Sadeghi-Yarandi S, *et al*. Prevalence, quality of care, and complications in long term care residents with diabetes: a multicenter observational study. *J Am Med Dir Assoc* 2013;**14**(11):842–6. https://doi.org/10.1016/j.jamda.2013.08.001
28. Hurley L, O'Donnell M, O'Caoimh R, Dinneen SF. Investigating the management of diabetes in nursing homes using a mixed methods approach. *Diabetes Res Clin Pract* 2017;127:156–62. https://doi.org/10.1016/j.diabres.2017.03.010
29. Barnhart C, McClymont K, Smith AK, *et al*. "Everyone else gets ice cream here more often than I do--It burns me up"-perspectives on diabetes care from nursing home residents and their doctors. *BMC Geriatrics* 2016;**16**:28. https://doi.org/10.1186/s12877-016-0199-0

Appendix 1. Full MEDLINE search



1	exp Nursing Homes/ or exp Homes for the Aged/	43657	Advanced	Display Results	More	
2	"care home*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3913	Advanced	Display Results	More	
3	exp Nursing Homes/	38886	Advanced	Display Results	More	
4	"nursing home*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	45855	Advanced	Display Results	More	
5	"residential care".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3420	Advanced	Display Results	More	
6	exp Diabetes Mellitus, Type 2/ or exp Diabetes Mellitus/	420863	Advanced	Display Results	More	
7	diabet*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	687122	Advanced	Display Results	More	
8	t2dm.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	20197	Advanced	Display Results	More	
9	t1dm.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	13	Advanced	Display Results	More	
10	(non-insulin adj3 dependen*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	10902	Advanced	Display Results	More	
11	exp Insulins/	189337	Advanced	Display Results	More	
12	insulin*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	417798	Advanced	Display Results	More	
13	(stop* adj3 insulin).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	274	Advanced	Display Results	More	
14	exp Hypoglycemic Agents/	251247	Advanced	Display Results	More	
15	non-insulin.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	12133	Advanced	Display Results	More	
16	anti-diabet*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	7237	Advanced	Display Results	More	
17	exp Glucagon-Like Peptide 1/	8467	Advanced	Display Results	More	
18	"glucagon-like peptide-1 receptor agonist".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	802	Advanced	Display Results	More	
19	"GLP1R agonist".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	26	Advanced	Display Results	More	
20	"SGLT2 inhibitor".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1215	Advanced	Display Results	More	
21	SGLT2i.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	331	Advanced	Display Results	More	
22	"dipeptidyl peptidase-4 inhibitor".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1112	Advanced	Display Results	More	
23	"DPP4 inhibitor".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	250	Advanced	Display Results	More	
24	DPP4i.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	156	Advanced	Display Results	More	
25	exp "Drug-Related Side Effects and Adverse Reactions"/ or exp Morbidity/	660845	Advanced	Display Results	More	
26	morbidity.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	380171	Advanced	Display Results	More	
27	exp Mortality/	377696	Advanced	Display Results	More	
28	mortality.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1131256	Advanced	Display Results	More	
29	exp Death/	147478	Advanced	Display Results	More	
30	death*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	897545	Advanced	Display Results	More	
31	exp "Quality of Life"/	191822	Advanced	Display Results	More	
32	exp Hypoglycemia/	28106	Advanced	Display Results	More	
33	hypoglycaem*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	14426	Advanced	Display Results	More	
34	exp Life Expectancy/	17296	Advanced	Display Results	More	
35	"life expectancy".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	40291	Advanced	Display Results	More	
36	(quality adj3 life).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	344150	Advanced	Display Results	More	
37	exp Quality-Adjusted Life Years/	12013	Advanced	Display Results	More	
38	"quality adjusted life year*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	17984	Advanced	Display Results	More	
39	exp Personal Autonomy/	16889	Advanced	Display Results	More	
40	autonomy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	47991	Advanced	Display Results	More	
41	exp Patient Preference/	8275	Advanced	Display Results	More	
42	(patient* adj3 pref*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	31994	Advanced	Display Results	More	
43	(personal* adj3 prefer*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2360	Advanced	Display Results	More	
44	exp Patient Satisfaction/	88578	Advanced	Display Results	More	
45	(patient* adj3 satisf*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	120764	Advanced	Display Results	More	
46	(personal* adj3 satisf*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	19654	Advanced	Display Results	More	
47	1 or 2 or 3 or 4 or 5	59838	Advanced	Display Results	More	
48	6 or 7 or 8 or 9 or 10	989351	Advanced	Display Results	More	
49	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24	476575	Advanced	Display Results	More	
50	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	3061088	Advanced	Display Results	More	
51	47 and 48 and 49 and 50	87	Advanced	Display Results	More	