Guidelines for the Management and Care of Diabetes in the Elderly

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Guidelines for the Management and Care of Diabetes in the Elderly

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Guidelines Methodolgy and Research

The Australian Centre for Diabetes Strategies was appointed by the ADEA to provide the technical expertise in guideline development methods, and to conduct the research underpinning the guideline recommendations. Six questions were developed to lead the research (refer to page 9). Evidence has been graded according to the National Health and Medical Research Council, Levels of Evidence criteria (NHMRC, 1999). These criteria are included in a table in Section 3, Part 1.3.

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Glossary of Acronyms

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ABCD	Appropriate Blood Pressure Control in Diabetes Mellitus
ABPM	Ambulatory Blood Pressure Monitoring
ABS	Australian Bureau of Statistics
ACE	Angiotensin Converting Enzyme
ACR	Albumin Creatinine Ratio
ADA	American Diabetes Association
ADEA	Australian Diabetes Educators Association
ADL	Activities of Daily Living
AER	Albumin Excretion Rate
ALLHAT	Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack
ARB	Angiotensin Receptor Blocker
AusDiab	Australian Diabetes Lifestyle and Obesity Study
BMI	Body Mass Index
CARE	Cholesterol and Recurrent Events
CCB	Calcium Channel Blockers
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
CI	Confidence Interval
CVD	Cardiovascular Disease
DKA	Diabetic Ketoacidosis
EDTRS	Early Treatment Diabetic Retinopathy Study
FPG	Fasting Plasma Glucose
GFR	Glomerular Filtration Rate
GI	Glycaemic Index
HbA_{1c}	Glycosylated/glycated Haemoglobin
HDL	High Density Lipids
HHNC	Hyperglycaemic Hyperosmolar Nonketotic Coma
HOPE	Heart Outcomes Protection Study
HPS	Heart Protection Study
HR	Hazard Ratio
IGT	Impaired Glucose Tolerance
IFG	Impaired Fasting Glucose
IPH	Isolated Postchallenge Hyperglycemia
ISH	Isolated Systolic Hypertension
LDL	Low Density Lipoprotein
LIPID	Long-term Intervention with Pravastatin in Ischaemic Disease
MI	Myocardial Infarction
MMSE	Mini Mental State Exam
MUFA	Mono Unsaturated Fatty Acids
NHANES	National Health and Nutrition Examination Survey
NHMRC	National Health and Medical Research Council
NPDR	Non-proliferative Diabetic Retinopathy
NS	Non significant
OGTT	Oral Glucose Tolerance Test
OHA	Oral Hypoglycaemic Agents

OR	Odds Ratio
PDR	Proliferative Diabetic Retinopathy
PUFA	Poly Unsaturated Fatty Acids
PVD	Peripheral Vascular Disease
RR	Relative Risk
SBGM	Self Blood Glucose Monitoring
SFA	Saturated Fatty Acids
SU	Sulphonylurea
UAC	Urinary Albumin Concentration
UKPDS	United Kingdom Prospective Diabetes Study
VA CSDM	Veterans Affairs Cooperative Study in Diabetes Mellitus
VHA	Veterans Health Administration
WHO	World Health Organisation
WHR	Waist Hip Ratio

Section 1

Overview

1.0 Overview

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The project to develop *Guidelines for the Management and Care of Diabetes in the Elderly* was undertaken by the Australian Diabetes Educators Association (ADEA) in response to the need to document specific standards for older Australians with, or at risk, of diabetes. Novo Nordisk Pharmaceuticals Pty Ltd funded the project, under an educational grant to the ADEA.

1.1 Why do we need guidelines for the elderly?

A set of nine national evidence based guidelines for Type 2 diabetes is being developed under Commonwealth funding by a Diabetes Australia Guideline Development Consortium. Two of these guidelines have already been endorsed by the NHMRC, and four others are available in draft form. With implementation of the Type 2 diabetes guidelines imminent, why does Australia need guidelines for diabetes in the elderly? The answer, which is simple, includes the following:

- The Australian population is ageing;
- Diabetes has a high prevalence, which increases substantially with age;
- Older people are more likely to have co-morbidities and disabilities, which complicate the management of their diabetes;
- There is evidence that the detection and management of diabetes in the elderly is sub-optimal in many settings;
- Available diabetes guidelines rarely address specific care issues for the elderly;
- The National Diabetes Strategy and Implementation Plan (Colagiuri et al, 1998) cites the elderly as a group which requires special consideration in the planning, delivery and co-ordination of diabetes care and prevention services, and
- Although some of the evidence from the systematic reviews for the National Evidence Based Guidelines for Type 2 Diabetes includes data on the elderly, many clinical trials exclude older people from their recruitment process.

The Australian population is ageing. People who reach the age of 65 years are expected to live, on average, a further 19.6 years for women and 15.8 years for men. The proportion of older Australians (those above 65 years) is increasing as shown below (Binns, 1999):

1976	9% (1.2 million)	16% of elderly over 80 years
1996	12% (2.2 million)	20% of elderly over 80 years
2016	16% (3.5 million)	25% of elderly over 80 years

Diabetes is not only the most common chronic condition in the elderly, it is also one of Australia's most challenging health problems. Type 2 diabetes is the most frequent form of diabetes, representing about 80-90% of all cases. The recent AusDiab Study demonstrated that Type 2 diabetes affects 7.4% of the Australian population aged 25 years or older, and confirms that there is one undiagnosed for every diagnosed person

with Type 2 diabetes (Dunstan et al, 2002). AusDiab also reported that 17.9% of people aged between 65 and 74 years and 23.0% aged over 75 years have diabetes. The National Evidence Based Guidelines for Type 2 Diabetes: Case Detection and Diagnosis (Colagiuri S et al, 2002) states that people aged 55 and over are at increased risk of having undiagnosed Type 2 diabetes.

Advancing age does not lessen the requirement for the management of glycaemic control to prevent associated acute and chronic complications and to maintain general well-being. However, the medical treatment and general health care needs of older people with diabetes are different from younger people. The presentation of diabetes in the elderly is often non-specific and hyperglycaemia tends, at least initially, to be milder than it is in younger people, or may be totally asymptomatic (Rosenstock, 2001).

From a disease management perspective, diabetes in the elderly presents a wide range of additional complexities. Elderly people with diabetes, especially those who live in aged care facilities, often have a number of age-specific issues such as decreased levels of independence, impaired mobility and dexterity, inadequate social support, reduced capability for self care, and co-morbidities which directly impact on glycaemic control, diabetes management and subsequent health outcomes. These factors often limit access to mainstream diabetes services and there are relatively few diabetes specific services for the elderly. To compound this problem, many non-diabetes health professionals significantly underrate the seriousness of diabetes in the elderly and its impact on health status and quality of life.

There is substantial anecdotal evidence and a growing body of documentation regarding the inadequate and/or inappropriate management of diabetes in the elderly, particularly in aged care facilities (Neil et al, 1989; Dornan et al, 1992). This may involve actively inappropriate management but more frequently revolves around the omission of relatively simple treatments or precautions, sometimes with debilitating or even life threatening results.

Unfortunately, there is a worldwide lack of elderly-specific guidelines documenting current evidence and consensus about recommended standards of care for the elderly and, thus, no platform from which to address the identified care deficits.

1.2 The scope of the guidelines

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The brief for *Development of National Guidelines for the Management and Care of Diabetes in the Elderly* was to prepare evidence and consensus based guidelines to describe a set of consistent best practice standards for the diagnosis and care of elderly people in Australia with diabetes.

As there is no scientific data and research specific to elderly Indigenous Australians, no mention is made in the guildeline regarding the management and care of diabetes in this age group. The poorer health status of Indigneous Australians means that their health disadvantage begins at a much earlier age, with their age at death and their life expectancy estimated to be approximately 20 years less than non-Indigneous Australians (Australia's Health, 2003). The major causes of death in Indigenous Australians continue to include cardiovascular disease and diabetes.

Who is 'elderly'?
For the purposes of the project and in line with accepted practice, an elderly person is defined as a person over the age of 65 years. This definition was further classified into two categories:

- The 'young' old i.e. people over 65 and under 75 years
- The 'old' old i.e. people over the age of 75 years

Another important distinction was made between the 'healthy' elderly, defined as those who although ageing are in sound physical, and mental health, and the 'frail' elderly i.e. those with co-morbidities or some form of physical, mental or emotional disability of sufficient magnitude to compromise optimal management of their diabetes and put them at risk of additional diabetes or related health problems.

Who do the guidelines focus on?
It was agreed by the Steering Committee that the guidelines would specifically target the 'healthy' elderly and treatment should be according to the treatments, assessments and clinical targets set out in the National Evidence Based Guidelines for Type 2 Diabetes. However, it was recognised that two specific age-related changes are more common and therefore often present in the elderly person with diabetes. These are cognitive impairment and decreased functional mobility and both may impact on an individuals' ability to manage their diabetes care needs. Either or both conditions are often present in a person considered to be in the 'healthy' elderly group despite a decline or loss of function at an organ level eg blindness, resulting in a disability. Whereas, elderly persons at high risk ie the 'frail' elderly have decreased reserve and resistance to stressors and require individualised decisions and special considerations about their care.

Several key areas were identified and agreed by the Steering Committee members for identification of the available evidence on special considerations and potential differences in diabetes in the elderly with regard to:

- Aged-related issues impacting on diabetes management
- Clinical and laboratory assessments
- Treatment targets
- Medications
- Nutritional issues
- Lifestyle issues
- Self care education

Who are the Guidelines for?
The recommendations contained in this document are a guide to the evidence based best practice information that was available at the time of the development of the document. They were developed to inform health professionals, including general practitioners, community nurses, allied health professionals and aged care workers about diabetes care that works and to promote and encourage standards and consistency in practice nationally. Guidelines are not appropriate to all people in all settings, at all times, therefore application of the Guidelines should be interpreted on an individual basis taking into consideration the social, cognitive and functional status of the elderly person.

1.3 The Consultation Processes

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The initial stages of consultation about these guidelines has involved:

- Notifying key diabetes stakeholder groups such as the Australian Diabetes Society and Diabetes Australia about the development of the guidelines;
- Individual consultation with leading clinicians in the field;
- Close communication between this project and the development of the National Evidence Based Guidelines for Type 2 Diabetes;
- Written communication with relevant groups in New Zealand including the Ministry of Health, Diabetes New Zealand and the New Zealand Guideline Group, and
- Written communication with Commonwealth, State and Territory Health Departments across Australia.

A public consultation document was drafted and launched at the September 2002 joint Annual Scientific Meeting of the Australian Diabetes Educators Association and the Australian Diabetes Society. The guidelines were revised in light of the results of the public consultation. They are published in easily accessible, user-friendly formats and will be widely disseminated to clinicians and consumers.

1.4 Project Management

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An ADEA Steering Committee chaired by the ADEA National President, Ms Erica Wright was convened to direct and guide the project. The Steering Committee comprised five ADEA members experienced either in aged care and/or guideline development, and an Australian Diabetes Society (ADS) member with particular expertise in the medical management of diabetes in the elderly. One of the Steering Committee members, Ms Lynette Brown is a member of both ADEA and the Dietitians Association of Australia, and Ms Patricia Allen is a member of the New Zealand Nurses Specialist Interest Group (Diabetes).

The ADEA appointed the Australian Centre for Diabetes Strategies, Prince of Wales Hospital, Sydney to provide project management services, guidelines methods expertise and a project officer to conduct the literature searches and review and grade the available evidence.

The project funds were held and administered by the ADEA.

References – Overview

Australian Institute of Health and Welfare 2002. Australia's health: the eighth biennial health report of the Australian Institute of Health and Welfare. Canberra: AIHW

Colagiuri S, Colagiuri R, Ward J. National Diabetes Strategy and Implementation Plan. Diabetes Australia, Canberra, 1998

Colagiuri S, Zimmet P, Hepburn A, Holt P, Colagiuri R. Evidence Based Guideline for Type 2 Diabetes: Case Detection and Diagnosis. Diabetes Australia and NHMRC. Canberra, 2002

Dornan TL, Peck GM, Dow JDC, Tattersall RB. A community survey of diabetes in the elderly. Diabet Med 1992;9:860-5

Dunstan DW, .Zimmet PZ, Welborn TA, De Courten MP, Cameron AJ, Sicree RA, Dwyer T, Colagiuri S, Jolley D, Knuman M, Atkins R, Shaw JE. The AusDiab Steering Committee. The rising prevalence of diabetes and impaired glucose tolerance. The Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care 2002;25:1-6

Neil HAW, Thompson AV, Thorogood M, Fowler GH, Mann JI. Diabetes in the elderly: The Oxford Community Diabetes Study. Diabet Med 1989;6:608-13

Binns CW (Ed). National Health and Medical Research Council. Dietary Guidelines for Older Australians. Canberra: NHMRC, 1999

Rosenstock J. Management of type 2 diabetes mellitus in the elderly. Special considerations. Drugs and Ageing 2001:18:31-44

Section 2

Introduction and Guideline Recommendations

1.0 Introduction

1.1 Who is elderly – who is at risk of problems?

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People aged 65 years and over are usually conceptualised as elderly. From a geriatrician's perspective, elderly people are divided into the 'young old' (65-75 years) and the 'old, old' (75 years plus) (Popplewell, 1999).

A more clinically relevant approach may be to classify older people according to their physical and mental status i.e. the healthy elderly and the frail elderly. For example, a healthy elderly person is independent, mentally alert and sufficiently dextrous and mobile to perform routine activities of daily living such as feeding, showering and dressing. Such people will be in reasonable physical and mental health as defined by the absence of cognitive impairment or dementia, and will have few difficulties with mobility or self-care. Frailty, on the other hand, is considered highly prevalent in old age and carries a high risk for falls, disability, comorbidities, hospitalisation, and mortality.

Frailty has been variously described but a standardised definition has not yet been established. Nonetheless, it is recognised by many as a distinct clinical syndrome. Formal definitions of frailty range from simply renaming as frail those who are dependent on others to perform activities of daily living for them to more complex definitions. Rockwood et al (1996) proposes that frailty should be understood as a vulnerable state resulting from the balance and interplay of medical and social factors. In a later study Rockwood et al (2000) further argues that definitions of frailty must include multisystem impairment, instability, change over time, an association with ageing, and an association with increased risk of adverse outcomes.

Many geriatricians consider frailty as decreased reserve and resistance to stresses resulting from cumulative declines across multiple physiologic systems and causing vulnerability to adverse outcomes. The markers of frailty include age-associated declines in lean body mass, strength, endurance, balance, walking performance, and low activity (Fried, 2001).

Definitions of the concept of frailty have often included a dependence on others, or being at substantial risk of dependency, experiencing the loss of physiologic reserve, experiencing 'uncoupling from the environment', having many chronic illnesses, having complex medical and psychosocial problems, having atypical disease presentations, being able to benefit from specialised geriatric programs, and most simply, experiencing accelerated ageing (Rockwood et al, 2000).

Brown et al (1995) considered frailty to exist when there are indications of:

- poor physical health, such as chronic or acute illness;
- poor mental health and functioning, such as depression or cognitive impairment and dementia;
- disability or mobility impairment;
- people living in states of dependency, such as being housebound or in an institution, and
- people who are simply very old.

Brown et al (1995) further detailed two factors of frailty:

Personal factors:
- Cognitive factors - diminished intellectual functioning, memory loss, or reduced attentive ability
- Physical factors - reduced mobility and agility, pain, loss of energy, or diminished hearing and sight
- Psychological factors - depression, emotional disturbance, psychiatric disorders, or a decreased sense of self-worth
- Spiritual factors - loss of hope or meaning in life, or a decrease in altruistic behaviour

Environmental factors:
- Financial factors - diminished funds to live on, a decrease in material possessions, or a reduction of material resources available from the environment
- Interpersonal factors - the availability of family, friends, acquaintances, or social activities
- Living situation factors - danger in one's neighbourhood, or distance from stores
- Legal factors - not being allowed to drive a car because of age, or losing control over personal finances through power of attorney
- Institutional factors - lack of control over daily routines, food, and clothing, or lack of access to different environments outside the institution

These examples suggest that many factors might contribute to frailty. For clinical and practical purposes, these guidelines focus on those elderly people with diabetes who could be categorised as the 'healthy' elderly. Further, clinical judgement in treating "frail" elderly people with diabetes will need to take account of the wide variations which may occur between individuals who may be considered frail. For example, Rodriguez-Manas highlights some of the difficulties of defining frailty by comparing the difference between an 80-year old who plays twice weekly golf but needs assistance in the bath, with an elderly person who is blind or bedridden. He also wisely points out that the current challenge in managing diabetes in elderly people comes not so much from particular characteristics of diabetes but from the characteristics of elderly individuals themselves.

The *Guidelines for the Management and Care of Diabetes in the Elderly* should be used in this spirit, tempered with clinical wisdom and accommodating the unique needs, capabilities and circumstances of each individual.

References – Introduction

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Brown I, Renwick R, Raphael D. Frailty: constructing a common meaning, definition, and conceptual framework. Int J Rehabil Res 1995;18:93-102

Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: Evidence for a phenotype. J Gerontol 2001;56A:M146-56

Popplewell P. Diabetes in the elderly. In: Phillips P, Brown L, Dunning T, Ayers B eds. Diabetes and You. The essential guide. Canberra: Diabetes Australia; 1999. p. 82-5

Rockwood K, Stolee P, McDowell I. Factors associated with institutionalization of older people in Canada: Testing a multifactorial definition of frailty. J Am Geriatr Soc 1996;44:578-82

Rockwood K, Hogan DB, MacKnight C. Conceptualisation and measurement of frailty in elderly people. Drugs and Aging 2000;17:295-302

Rodriguez-Manas L. Management of frail Type 2 diabetic patients. Literature Review Service. Diabetes (year unknown)

1.2 Research questions

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1. Is case detection and diagnosis for Type 2 diabetes in the elderly worthwhile?

2. What clinical and laboratory assessments should be recommended for elderly people with diabetes, and are there differences in treatment targets for the elderly?

3. Are there specific treatments/managements that should be encouraged or discouraged in elderly people with diabetes?

4. What are the barriers to diabetes education and health care in elderly people with diabetes?

5a. Are there special considerations for elderly people with diabetes with regard to loss of symptoms/early detection of hypoglycaemia?

5b. Are there special considerations for elderly people with diabetes with regard to hyperglycaemia?

6. Are primary prevention strategies for Type 2 diabetes effective in the elderly?

1.3 Summary of recommendations

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Recommendation - Case Detection and Diagnosis

- Asymptomatic elderly people should be screened for undiagnosed diabetes by measurement of fasting plasma glucose as recommended for the general population

Recommendations – Assessments and Targets

A. Elderly people with diabetes should have regular comprehensive clinical and laboratory evaluation of their metabolic control and screening for complications as follows:

1. Glycaemic control:
- Should be assessed by HbA_{1c} six monthly if glycaemic control is stable, and quarterly in people with inadequate glycaemic control
- The general treatment target for HbA_{1c} is ≤ 7.0% but may require upward adjustment to avoid hypoglycaemia.

2. Blood pressure:
- Should be assessed at least every 3 months in hypertensive people, every 6 months in normotensive people
- The treatment target for blood pressure in elderly people is <140/90mmHg

3. Lipid profile:
- Should be assessed annually in people with normal lipid profile, and every 3-6 months in those with an abnormal lipid profile or treated with lipid-lowering agents
- The treatment targets should be LDL cholesterol <2.5mmol/L and triglyceride <2.0mmol/L

4. Renal function:
- Microalbuminuria/proteinuria should be assessed annually in all people with diabetes and 3-6 monthly in people with microalbuminuria or proteinuria. Serum creatinine should be measured annually

5. Eye examination:
- Initial examination should be performed at diagnosis. If no retinopathy is present, repeat every two years; if minimal Non Proliferative Diabetic Retinopathy (NPDR) is found, repeat yearly; at the stage of moderate NPDR or proliferative diabetic retinopathy, refer to an ophthalmologist as soon as possible

6. Foot assessment:
- Feet should be assessed annually in people who have no history of foot complications and every 3-6 months in people with at risk feet, and appropriate management or referral if necessary

7. Cognitive function assessment:
- The Mini Mental State Exam (MMSE) should be used to assess elderly people with diabetes as an adjunct to the planning of diabetes care and education

B. These recommendations also apply to the frail elderly. However, the frequency of assessments and the targets may need to be adjusted according to the physical and mental status of the individual

Recommendations - Special Treatments

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- Elderly people with diabetes should have initial and routine nutrition assessments and be encouraged to follow the *NHMRC Dietary Guidelines for Older Australians*. In addition, attention to the intake and distribution of carbohydrate is important
- Weight loss in elderly people is not recommended unless they are at least 20% overweight
- Elderly people with diabetes should be encouraged to follow the *National Physical Activity Guidelines for Australians* which recommend 30 minutes of physical activity each day (aerobic exercise and/or strength training). Prescription of exercise in the frail elderly should be tailored to the individual
- Alcohol intake in elderly people who are current drinkers is recommended not to exceed one standard drink in women or two standard drinks in men per day
- Smoking cessation is recommended for all elderly people
- The choice of hypoglycaemic agent for an elderly person with diabetes should take into account comorbidities, contraindications and potential side effects, especially hypoglycaemia
- A range of antihypertensive agents can be used to control blood pressure in elderly people with diabetes
- Lipid lowering therapy should be considered in elderly people, especially in those who have had a previous vascular event

Recommendations – Barriers to Health Care and Education

- Special attention should be given to ensuring that elderly people with diabetes and their carers receive diabetes education and have access to general and specialist health services required for optimal diabetes care
- Models and systems of care should be structured to ensure that elderly people with diabetes receive recognised standards of diabetes care and comprehensive assessments to assist care planning where necessary
- Diabetes education for elderly people with diabetes should be individualised and should be specifically designed to address barriers which are common in the elderly - visual, hearing and cognitive impairment, depression, reduced mobility and manual dexterity, and social and financial problems

- Professional training and continuing education programs in diabetes care should be recommended for health professionals caring for elderly people with diabetes
- Government and community health and social services for the elderly should ensure that their staff have at least basic training in the special needs of elderly people with diabetes

Recommendations - Hypoglycaemia

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- Reduced glucose counterregulation and awareness of hypoglycaemia with ageing, and overall health status, should be considered when making treatment plans. Increased blood glucose monitoring may be required to detect unrecognised hypoglycaemia in elderly people with diabetes
- Elderly people with diabetes and their carers should receive a specific individualised education about managing hypoglycaemia, with any change in medication, environment, cognitive or functional status
- When prescribing sulphonylurea and/or insulin treatment in elderly people with diabetes, caution should be taken (including a review of current medication) because of the increased risk of hypoglycaemia

Recommendation - Hyperglycaemia

- The possibility of hyperosmolar hyperglycaemic nonketotic state should be considered in elderly people with extremely high blood glucose levels

Recommendation - Primary Prevention

- Elderly people should be encouraged to exercise regularly and to lose excess weight in order to reduce their risk of developing Type 2 diabetes

2.0 Guideline Recommendations

2.1 Case Detection and Diagnosis

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Is case detection and diagnosis for Type 2 diabetes worthwhile in the elderly?

Answer

Yes

Why

- Type 2 diabetes and Impaired Glucose Tolerance (IGT) are prevalent in the elderly
  NHMRC Evidence Level III
- Type 2 diabetes and IGT are associated with increased cardiovascular disease and mortality in the elderly
  NHMRC Evidence Level III
- A significant proportion of elderly people have undiagnosed Type 2 diabetes
  NHMRC Evidence Level III
- The protocol for case detection and diagnosis of Type 2 diabetes in elderly people should be the same as used in the general population
  NHMRC Evidence Level I

Recommendation

Asymptomatic elderly people should be screened for undiagnosed diabetes by measurement of fasting plasma glucose as recommended for the general population

Background – Case Detection and Diagnosis

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The prevalence of Type 2 diabetes increases with age and this applies to both diagnosed and undiagnosed diabetes. People aged 55 and over are at increased risk of having undiagnosed Type 2 diabetes (Colagiuri et al, 2002). The elderly, who have a much higher prevalence of diabetes than the general population, fall into this high-risk category. The recent AusDiab study (Dunstan et al, 2002) revealed that Type 2 diabetes affects 17.9% of the Australian population aged 65-74 years and 23.0% in people aged ≥75 years. This study also showed that half of all those identified as having diabetes were undiagnosed, and this varied little across age groups.

The potential benefits of case detection for Type 2 diabetes were reviewed in the Case Detection and Diagnosis Guideline (Colagiuri et al, 2002). The benefits included:

- Identifying undiagnosed diabetes may prompt earlier and more appropriate treatment for individuals with a higher risk for cardiovascular diseases;
- Testing for Type 2 diabetes enables the detection of people with impaired glucose tolerance (IGT) and impaired fasting glucose (IGF) which are both associated with increased morbidity and mortality due to cardiovascular diseases and their detection provides an opportunity to implement interventions which may improve outcomes, and
- The rate of progression of IGT to Type 2 diabetes can be reduced by lifestyle interventions.

The NHMRC endorsed *Australian Guidelines for the Case Detection and Diagnosis of Type 2 Diabetes* do not specifically address the elderly population. This section reviews the evidence with regard to the early detection of Type 2 diabetes in the elderly.

Type 2 diabetes and IGT are prevalent in the elderly

NHMRC Gradeable Evidence

The recently published AusDiab study (Dunstan et al, 2002) examined a nationally representative sample of 11,247 individuals aged ≥25 years and reported an overall diabetes prevalence (using the 1999 World Health Organisation (WHO) criteria) in Australia of 7.4%, and an additional 16.4% with IGT or IFG. The prevalence of diabetes and impaired glucose metabolism (IGT and IFG) increases with age, from 0.3% and 5.4%, respectively in the 25-34 age group, to 17.9% and 28.8% in the 65-74 age group, to 23.0% and 30.0% in the 75+ age group. The prevalence of diabetes has more than doubled, compared with the Busselton 1981 survey using the 1980 WHO criteria (Glatthaar et al, 1985) which reported prevalence rates in people aged ≥25 years of 3.4% for both known and undiagnosed diabetes, and 2.9% for IGT. All categories of abnormal glucose tolerance (known as diabetes, newly diagnosed diabetes, and IGT) increased from 1.4% for men and 1.6% for women in the 25-34 age group, to 14.3% for men and 14.5% for women in the 65-74 age group, and to 26.8% for men and 23.6% for women in the 75+ age group.

The US NHANES II survey (Harris et al, 1987) reported an age-related increase in diabetes prevalence. The prevalence of diabetes increased from 1.7% in people aged 20-44 years to 17.9% in people aged 65-74 years. Furthermore, the prevalence of undiagnosed diabetes was 11.7% in people with three risk factors (older age, family history and obesity) compared with 0.4% for people without these risk factors. The prevalence of IGT was 11.2% in the study population, increasing from 6.4% in the 20-44 year age group to 22.8% in the 65-74 year age group.

The prevalence of diabetes was investigated in a cohort of people aged 65-85 years in Melton Mowbray, United Kingdom (Croxson et al, 1991). Among 861 study participants, 52 had previously been diagnosed with diabetes. A modified oral glucose tolerance test (OGTT) using 1985 WHO criteria was performed on 583 participants. Of these 19 had diabetes, 44 had IGT and 520 were normal. The prevalence of previously diagnosed diabetes was assessed using a 95% Confidence Interval (CI) and found to be 6.0% (CI 4.3-8.1) and the prevalence of previously undiagnosed diabetes was 3.3% (CI 2.0-5.0). The acceptance rate for OGTT fell from 80% in the 65-year-old subjects to 54% in the 85-year-olds. Therefore the age-specific total prevalence of diabetes in Melton Mowbray was 6.3% (CI 3.5-10.3), 10.5% (CI 6.0-16.9), 9.7% (CI 5.4-15.7), 11.1% (CI 4.8-21.4), and 13.8% (CI 4.6-30.4) in 65, 70, 75, 80, 85-year-old subjects, respectively.

Type 2 diabetes and IGT are associated with increased cardiovascular disease and mortality in the elderly

NHMRC Gradeable Evidence

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The prospective Dubbo Study of Australian Elderly people has confirmed the excess all-causes mortality, Coronary Heart Disease (CHD) and stroke in those with diabetes, especially in women (Simons et al, 1996). In the study where 2,627 elderly (aged 60 years and older) were followed over 62 months, 9.2% of males and 6.9% of females had diabetes. In the presence of diabetes, all-cause mortality was increased twofold in both sexes (diabetes vs. no diabetes, 31.2% vs. 16.9% in men, and 22.8% vs. 10.2% in women). The incidence of CHD was increased twofold in men (31.9% vs. 17.5%) and threefold in women (32.7% vs. 12.2%). Stroke incidence was increased twofold in women (9.2% vs. 4.7%) but was similar in men (8.2% vs. 6.2%).

In the Melton Mowbray study (Croxson et al, 1994), residents aged 65, 70, 75, 80, and 85 years were screened by OGTT and followed up for 4.5 years. Death occurred in 56 of 520 subjects with normal glucose tolerance, 9 of 44 subjects with IGT, 7 of 19 subjects with newly diagnosed diabetes, and 27 of 52 subjects with known diabetes. There was an excess of vascular deaths among the diabetic subjects, but this was not significant. The age and sex adjusted Relative Risk (RR) of death compared with people with normal glucose tolerance was 5.2 (3.2-8.5) in people with known diabetes, 3.0 (1.3-6.6) in people newly diagnosed diabetes and 1.7 (0.8-3.5) in people with IGT.

In a Danish study (de Fine Olivarius and Andreasen, 1997) the five-year all cause mortality of 1,323 middle aged and elderly people with newly diagnosed diabetes was compared with the general Danish population. The median age at diagnosis was lower

in men (63.6 years) than for women (67.5 years), but more men than women had died. Excessive mortality amongst males occurred in the 60-79 year age group (p=0.002). With increasing duration of diabetes, both males and females exhibited an increasing excess mortality compared to the general Danish population. For men this excess mortality became statistically significant 4 years after diagnosis for the 40-59 year age group and 6 years after diagnosis for the 60-79 age group. For women and very old men, excess mortality was not significant, although there was a tendency for the survival curve in the 40-79 female age group to separate from the general Danish population.

The Cardiovascular Heart Study (Barzilay et al, 1999) demonstrated that people found to have Type 2 diabetes diagnosed by an OGTT screening program had an excess of MI, stroke and cardiovascular death. Four thousand, five hundred and fifteen elderly individuals (mean age 73 years) participated in this cohort study. During a mean of 5.9 years of follow-up, among the 3,984 individuals without baseline CHD or CVD, there were 581 new cardiovascular events or deaths. Of 581 participants, 20% had newly diagnosed diabetes using 1985 WHO criteria or 10% had new diabetes using the fasting American Diabetes Association (ADA) criteria. The RR for cardiovascular events or death was higher in individuals with newly diagnosed diabetes, RR 1.55 (CI 1.23-1.95) by 1985 WHO criteria and RR 1.46 (CI 1.09-1.94) by the fasting ADA criteria, compared with those with normal glucose tolerance on both criteria.

A significant proportion of elderly people have undiagnosed Type 2 diabetes

NHMRC Gradeable Evidence

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The total diabetes prevalence in Australia (known and newly diagnosed) is 7.4% (Dunstan et al, 2002). Of this group - 3.7% have known diabetes and 3.7% have newly diagnosed diabetes, indicating that half of all those identified with diabetes were previously undiagnosed. In the 65-74 year age group, the prevalence of known diabetes and newly diagnosed diabetes was 9.4% and 8.5%, respectively; while in the 75+ year age group, the figure was 10.9% and 12.1% respectively, and the percentage of newly diagnosed diabetes was even higher than that of known diabetes.

Harris et al (1987) reported that the prevalence of undiagnosed diabetes (3.4%) in a US population aged 20-74 years was equal to that of previously diagnosed diabetes (3.4%). Moreover, the prevalence of undiagnosed diabetes increased significantly from 0.9% in the 20-44 year age group to 9.4% in 65-74 year age group.

Franse et al (2001) studied 3,075 well-functioning people aged 70-79 years using an OGTT. Diabetes was defined according to the 1985 WHO criteria and the 1997 ADA criteria. The prevalence of diagnosed and undiagnosed diabetes was 15.6% and 8.0%, respectively. A multivariate analyses, compared with people without diabetes, found that individuals with undiagnosed diabetes were more likely to be men (Odds Ratio (OR) 1.4, CI 1.1-1.9, $p<0.05$), and have a history of hypertension (OR 1.7, CI 1.3-2.2, $p<0.001$), higher Body Mass Index (BMI) (OR 2.6 for the highest quartile, CI 1.7-3.8, p trend <0.001), and larger waist circumference (OR 2.7 for the highest quartile, CI 1.8-4.1, p trend <0.001). The study concluded that screening for diabetes may be

more efficient among men and individuals with hypertension, high BMI, and large waist circumference.

The protocol for case detection and diagnosis of Type 2 diabetes in elderly people should be the same as used in the general population

NHMRC Gradeable Evidence

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The *National Evidence Based Guideline for Case Detection and Diagnosis of Type 2 Diabetes* advocates testing for undiagnosed Type 2 diabetes in all people aged 55 years and over for the general Australian population. The guideline commented that setting an upper age limit was difficult because there were no data to indicate an age limit at which benefits might not be expected from treating previously undiagnosed Type 2 diabetes.

Diagnosing diabetes in asymptomatic elderly people presents special considerations and challenges. In the general population, fasting plasma glucose is recommended as the initial test for undiagnosed Type 2 diabetes in people with risk factors because it has a high sensitivity and specificity, and provides a simple and reliable method of screening for undiagnosed Type 2 diabetes. However, since a substantial proportion of people with undiagnosed diabetes have a fasting glucose value in the equivocal range of 5.5 to 6.9mmol/L, diabetes can only be diagnosed in this group by a 2hour (2h) glucose value during an OGTT (Colagiuri et al, 2002).

However it is well recognised that while FPG changes little with age, the 2hour post glucose load increases with increasing age. Harris et al (1987) studied 5,826 people aged 20-74 years without a history of diabetes with an OGTT. The mean FPG values showed a slight upward trend with age - 4.97mmol/L for the 20-44 year age group, 5.40mmol/L for the 45-64 year age group, and 5.44mmol/L for the 65-74 year age group. In contrast, the mean 2hour plasma glucose showed a larger increase with age - 5.67, 6.62, and 7.41mmol/L for the three different age groups, respectively.

Wahl and colleagues (1998) reported that compared with 1985 WHO criteria, the prevalence of undiagnosed diabetes in older people was significantly underestimated using ADA fasting criteria. In the Cardiovascular Health Study, glucose concentrations were measured during fasting and 2hour after a 75g OGTT in 4,515 participants (aged 65-100 years) without a previous diagnosis of diabetes. The prevalence of undiagnosed diabetes using ADA diagnostic fasting criteria was 7.7%, while the prevalence was 14.8% using 1985 WHO criteria. The difference in prevalence ($p< 0.0001$) was due to the stronger correlation with age of the 2hour glucose compared with the fasting glucose (Wahl et al, 1998).

Isolated post challenge hyperglycaemia (IPH), defined as an elevated 2hour post glucose load plasma glucose but a normal FPG, is common in older people and its prevalence increases with age. IPH is a risk factor for CVD and this diagnosis will be missed by measurement of FPG alone (Barrett-Connor and Ferrara, 1998).

Other studies have shown that people whose only abnormality was an evaluated 2hour glucose have increased mortality. The DECODE study which included 18,048 men and 7,316 women aged ≥ 30 years from 13 European prospective cohort studies found that within each fasting glucose classification (< 6.1, 6.1-6.9, 7.0-7.7, and

≥7.8mmol/L) mortality increased with increasing 2hour glucose. There was a small increase in mortality associated with IFG in men (Hazard Ratio (HR) 1.21, CI 1.05-1.41) but not women (HR 1.08, CI 0.76-1.66) but a greater increase in both men (HR 1.51, CI 1.32-1.72) and women (HR 1.60, CI 1.22-2.10) with IGT. This study suggested that fasting glucose concentrations alone did not identify individuals at increased risk of death associated with hyperglycaemia, with the OGTT providing additional prognostic information (The DECODE study group, 1999).

Compared with people without diabetes, people with IPH had an increased risk of all-cause mortality (HR 2.7, CI 1.8-3.9 in men; 2.0, CI 1.3-3.3 in women), and of cardiovascular mortality (HR 2.3, CI 1.2-4.2 in men; 2.6, CI 1.3-5.1 in women) (Shaw et al, 1999).

Practical issues also require consideration in deciding the most appropriate strategy for detecting undiagnosed diabetes in asymptomatic elderly people. While there is strong evidence that an isolated elevation of the 2h post glucose challenge plasma glucose is the only abnormality diagnostic of diabetes in the elderly, using an OGTT to screen for undiagnosed diabetes in all elderly people is impractical. Furthermore, since the diagnosis of diabetes in an asymptomatic individual requires confirmation, this would almost certainly require repeating the OGTT in a substantial proportion of elderly people. Therefore, while it is recognised that the diagnosis of diabetes in some elderly people with OGTT defined diabetes will be missed, it is felt on balance that the current guidelines advocated for the general population should also be used in the elderly population. Clearly what is required is a more sensitive screening test which can detect people who might have IPH without the necessity to perform an OGTT in everyone.

Furthermore, it should be recognised that apart from the inconvenience of the test, the OGTT has its own limitations, mainly related to reproducibility. The overall reproducibility of the OGTT is approximately 65%. Most of the problems with OGTT reproducibility relate to people with IGT, and a few people with normal glucose tolerance are misclassified as having diabetes (Colagiuri et al, 2002).

This issue was examined in the Hoorn study (Mooy et al, 1996). Repeat testing with an OGTT was performed over a 2 to 6 week period and the diagnostic categories compared in 555 people without known diabetes. The reproducibility of normal glucose tolerance was 91%, 48% for IGT and 78% for diabetes. Most of the movement was in the IGT category in which prevalence decreased from 11.5% on the first test to 5.6% on the second test with most people moving from IGT to normal. Only one person moved from the diabetic to normal category and that occurred between the first and second tests. The screening procedure should be performed as shown in Table 1 (adapted from Colagiuri et al, 2002):

Table 1: Measurement of fasting plasma glucose (FPG): Index

FPG < 5.5mmol/L →	Diabetes unlikely	Retest after 3 years
FPG 5.5-6.9mmol/L →	Diabetes possible	Perform OGTT
FPG ≥ 7mmol/L →	Diabetes likely	Repeat FPG unless diagnosis unequivocal

NHMRC Gradeable Evidence table for Case Detection and Diagnosis

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Barrett-Connor and Ferrara, 1998	Cohort	II	IPH
Barzilay et al, 1999	Cohort	II	Comparison of 1997 ADA criteria with 1985 WHO criteria
Colagiuri et al, 2002	Systematic review	I	Case detection and diagnosis
Croxson et al, 1991	Cross-sectional	II	Prevalence of diabetes
Croxson et al, 1994	Cohort	II	Mortality in elderly people with diabetes
DECODE Study Group, 1999	Cross-sectional	III	Glucose tolerance and mortality
De Fine Olivarius and Andreasen, 1997	Cohort	III	All cause mortality in newly diagnosed diabetes
Dunstan et al, 2002	Cross-sectional	III	Prevalence of diabetes and IGT
Franse et al, 2001	Cross-sectional	III	The prevalence of diagnosed and undiagnosed diabetes
Glatthaar et al, 1985	Cross-sectional	III	Prevalence of diabetes and IGT
Harris et al, 1987	Cross-sectional	III	Prevalence of diabetes and IGT
Mooy et al, 1996	Cross-sectional	III	Reproducibility of the OGTT
Shaw et al, 1999	Cross-sectional	III	IPH and mortality
Simons et al, 1996	Cohort	III	Comparison of all-cause mortality, incidence of CHD and stroke between diabetics and nondiabetics
Wahl et al, 1998	Cross-sectional	III	Comparison of 1997 ADA criteria with 1985 WHO criteria

Barrett-Connor E, Ferrara A. Isolated postchallenge hyperglycemia and the risk of fatal cardiovascular disease in older women and men - The Rancho Bernardo Study. Diabetes Care 1998;21(8):1236-9

Barzilay JI, Spiekerman CF, Wahl PW, Kuller LH, Cushman M, Furberg CD, Dobs A, Polak JF, Savage PJ. Cardiovascular disease in older adults with glucose disorders: comparison of American Diabetes Association criteria for diabetes mellitus with WHO criteria. Lancet 1999;354:622-5

Colagiuri S, Zimmet P, Hepburn A, Holt P, Colagiuri R. Evidence Based Guideline for Type 2 Diabetes: Case Detection and Diagnosis. Diabetes Australia and NHMRC. Canberra, 2002.

Croxson SCM, Burden AC, Bodington M, Botha JL The prevalence of diabetes in elderly people. Diabetic Med 1991;8:28-31

Croxson SCM, Price DE, Burden M, Jagger C, Burden AC. The mortality of elderly people with diabetes. Diabetic Med 1994;11:250-2

DECODE Study Group. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. Lancet 1999;354:617-21

de Fine Olivarius N, Andreasen AH. Five-year all-cause mortality of 1323 newly diagnosed middle-aged and elderly diabetic patients. Data from the population-based study, diabetes care in general practice, Denmark. J Diabetes Complications 1997;11:83-9

Dunstan DW, Zimmet PZ, Welborn TA, De Courten MP, Cameron AJ, Sicree RA, Dwyer T, Colagiuri S, Jolley D, Knuman M, Atkins R, Shaw JE. The AusDiab Steering Committee. The rising prevalence of diabetes and impaired glucose tolerance. The Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care 2002;25:1-6

Franse LV, Di Bari M, Shorr RI, Resnick HE, van Eijk JTM, Bauer DC, Newman AB, Pahor M. Type 2 diabetes in older well-functioning people: Who is undiagnosed? Data from the Health, Aging and Body Composition Study. Diabetes Care 2001;24:2065-70

Glatthaar C, Welborn TA, Stenhouse NS, Garcia-Webb P. Diabetes and impaired glucose tolerance. A prevalence estimate based on the Busselton 1981 survey. Med J Aust 1985;143:436-40

Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. Diabetes 1987;36:523-34

Mooy JM, Grootenhuis PA, de Vries H, Kostense PJ, Popp-Snijders C, Bouter LM, Heine RJ. Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general Caucasian population: the Hoorn Study. Diabetologia 1996;39:298-305

Shaw JE, Hodge AM, de Courten M, Chitson P, Zimmet PZ. Isolated post-challenge hyperglycaemia confirmed as a risk factor for mortality. Diabetologia 1999;42:1050-4

Simons LA, McCallum J, Friedlander Y, Simons J. Diabetes, mortality and coronary heart disease in the prospective Dubbo study of Australian elderly. Aust NZ J Med 1996;26:66-74

Wahl PW, Savage PJ, Psaty BM, Orchard TJ, Robbins JA, Tracy RP. Diabetes in older adults: comparison of 1997 American Diabetes Association classification of diabetes mellitus with 1985 WHO classification. Lancet 1998:352:1012-5

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2.2 Assessments and Targets

Index

What clinical and laboratory assessments should be recommended for elderly people with diabetes and are there differences in treatment targets for the elderly?

Answer

The same clinical and laboratory assessments as recommended for all adults with diabetes should be performed in the elderly.

The same general treatment targets apply in the elderly, however individual targets may need to be relaxed. Target HbA_{1c} may need to be higher to avoid potentially dangerous hypoglycaemia and a slightly higher target systolic blood pressure may need to be accepted because of the increased prevalence of isolated systolic hypertension in the elderly.

Why

- The prevalence of diabetes and its complications increases with age, and with the increase in the average life expectancy of Australians aged 65 years (15 years for males and 19 years for females), many elderly people now live long enough to experience the complications of diabetes
  Consensus – National Diabetes Strategy and Implementation Plan

- In order to reduce diabetes complications and to maximise the quality of life in elderly people, appropriate clinical and laboratory assessment should be performed regularly to identify preventable/treatable complications
  Consensus – National Diabetes Strategy and Implementation Plan

- Good glycaemic control can be achieved in elderly people with Type 2 diabetes and should be assessed by regular measurement of HbA_{1c}
  NHMRC Evidence Level III

- Isolated systolic hypertension (ISH) which is common in the elderly, increases the difficulty in achieving the general blood pressure target for people with Type 2 diabetes
  NHMRC Evidence Level I

- Lipid abnormalities are common and are strong predictors of cardiovascular events in elderly people with Type 2 diabetes
  NHMRC Evidence Level II

- Albuminuria predicts cardiovascular events, mortality and renal disease in elderly people with Type 2 diabetes
  NHMRC Evidence Level III

- Duration of diabetes and diabetes control significantly affect the risk of developing retinopathy
  NHMRC Evidence Level I

- Elderly people are at increased risk of developing foot ulcers or amputation, compared to younger people with Type 2 diabetes
  NHMRC Evidence Level I

- Diabetes is associated with a decline in cognitive function
  NHMRC Evidence Level III

Recommendations

A. Elderly people with diabetes should have regular comprehensive clinical and laboratory evaluation of their metabolic control and screening for complications as follows:

Glycaemic control:
- Should be assessed by HbA_{1c} twice a year if glycaemic control is stable, and quarterly in people with inadequate glycaemic control
- The general target for HbA_{1c} is ≤ 7.0% but may require upward adjustment to avoid hypoglycaemia

Blood pressure:
- Should be assessed at least every 3 months in hypertensive people; every 6 months in normotensive people
- The treatment target for blood pressure in elderly people is <140/90mmHg

Lipid profile:
- Should be assessed annually in people with normal lipid profile and every 3-6 months in those with an abnormal lipid profile or treated with lipid-lowering agents
- The treatment targets should be LDL cholesterol <2.5mmol/L and triglyceride <2.0mmol/L

Renal function:
- Microalbuminuria/proteinuria should be assessed annually in all people with diabetes, and 3-6 monthly in people with microalbuminuria or proteinuria. Serum creatinine should be measured annually

Eye examination:
- Initial examination should be performed at diagnosis. If no retinopathy is present, repeat every two years; if minimal non proliferative diabetic retinopathy (NPDR) is found, repeat yearly; at the stage of moderate NPDR or proliferative diabetic retinopathy, refer to ophthalmologist as soon as possible

Foot assessment:
- Feet should be assessed annually in people who have no history of foot complications and every 3-6 months in people with at risk feet, and appropriate management or referral if necessary

Cognitive function assessment:
- The MMSE should be used to assess elderly people with diabetes as an adjunct to the planning of diabetes care and education

B. These recommendations also apply to the frail elderly. However, the frequency of assessments and the targets may need to the physical and mental status of the individual

Background – Assessments and Targets

Index

In Australia a person of age 65 can expect to live on average a further 19 years for women and 15 years for men (Binns, 1999). Due to increasing age and an increasing incidence of diabetes in the elderly, many elderly people with diabetes may experience some diabetes complications in their lives. In order to reduce diabetes complications and to maximise the quality of life in the elderly, all elderly people with diabetes should have a regular clinical review and undergo appropriate laboratory investigations to evaluate their metabolic control. The presence of diabetes complications including microvascular (retinopathy, neuropathy and nephropathy) and macrovascular complications (CHD, cerebrovascular and peripheral vascular disease), and their overall nutritional status should also be reviewed.

The principles of managing Type 2 diabetes in the elderly are not different from those in younger people, but the priorities and therapeutic strategies need to be cautiously individualised (Rosenstock et al, 2001). Age and life expectancy, comorbid conditions and severity of vascular complications influence treatment decisions. There is a lack of evidence, specifically in the elderly, but:

1. duration of diabetes is a major determinant for the development of microvascular complications, and
2. increasing age is a major factor in the development of macrovascular complications.

Ongoing assessment and management is therefore appropriate to reduce the impact of diabetes in the elderly.

Glycaemic control

Good glycaemic control can be achieved in elderly people with Type 2 diabetes and should be assessed by regular measurement of HbA_{1c}

NHMRC Gradeable Evidence

A cross-sectional study of the Third National Health and Nutrition Examinations Survey (NHANES III) (Shorr et al, 2000), assessed 1,482 people aged 20 years or older (categorised into 4 age groups: 20-54, 55-64, 65-74, and ≥75 years) who had self-reported Type 2 diabetes. Four hundred and fifty people (30%) were aged 65 to 74 years, and 362 (24%) were aged 75 years and older. The mean HbA_{1c} was 7.7±0.1% and 7.3±0.1% in people aged 65-74 years and ≥75 years, respectively. The percentage of these groups achieving an HbA_{1c} value less than 7% was similar: 38.3% of people aged 65-74 years, 55.2% of people aged >75 years of age, 45.6% of people aged 20-54 years and 42.7% of people aged 55-64 years. Also the percentage of people who required further action (HbA_{1c} >8.0%) to improve blood glucose control

was 37.2%, 26.9%, 41.5% and 38.2%, respectively. Overall, among people aged 65 years or older, HbA_{1c} <7% was achieved by 71%, 44%, and 27% of people using no drug therapy, OHAs, and insulin, respectively. Although some elderly people did not achieve ADA targets for glycaemic control, there was no evidence to suggest that elderly people were treated less vigorously than younger people with diabetes.

Bruce et al (2000) conducted a cross-sectional study among 1,205 people with a mean duration of Type 2 diabetes of 4.2 years in order to investigate whether glycaemic control changed with increasing age. Of the participants, 33.3% were over 70 years of age and 6.9% were over 80 years of age. In multiple regression analysis, age was negatively associated with glycaemic control ($p<0.001$) whereas duration of diabetes and treatment with either OHA's or insulin were positively associated with glycaemic control (both $p<0.001$). The proportion of people with HbA_{1c} >8% by treatment type (diet, OHA, insulin) were: 13.7%, 47.4%, and 71.4% in the 40-69 year age group; 14.3%, 40.2%, and 64.4% in the 70-79 year age group; and 15.4%, 35.6%, and 36.4% in the ≥80 year age group. The proportion of people with HbA_{1c} >8% by diabetes duration (0-4 yrs, 4+ yrs) were: 26.6% and 52.5% in the 40-69 year age group; 17.6% and 49.2% in the 70-79 year age group; and 23.3% and 32.7% in the ≥80 year age group. These results show that glycaemic control was similar for all age groups up to 80 years and that greater proportions of the oldest people had satisfactory HbA_{1c} levels compared with younger people.

Other Evidence

Index

The American Diabetes Association (ADA) position statement (2002) states that HbA_{1c}, which reflects a mean glycaemia over the preceding 2-3 months, is the marker of choice for the assessment of risk for the development of microvascular complications, as well as for monitoring glycaemic control. HbA_{1c} testing should be performed routinely in all people with diabetes. In the absence of well-controlled studies that suggest a definite testing protocol, expert opinion recommends HbA_{1c} testing at least twice a year in people who have stable glycaemic control and more frequently (quarterly assessment) in people whose therapy has changed or who are not meeting glycaemic goals. The ADA recommends an HbA_{1c} of less than 7% as a goal for people with diabetes and that an HbA_{1c} of more than 8% requires further action. Measurement of HbA_{1c} should take into consideration conditions that lower haemoglobin levels, such as end stage renal disease and anaemia, especially in elderly people who are at high risk of anaemia due to malnutrition (Chen et al, 2001).

The question of whether achievement of strict metabolic control is of benefit in elderly people has still not been answered. The UKPDS 34 (1998) (mean follow-up 10 years) recruited people with newly diagnosed Type 2 diabetes up to age 65 and the VACSDM study (1995) (mean follow-up 27 months) included people up to age 69, however neither have published information on this subgroup.

Treatment targets for HbA_{1c} may need to be adjusted in elderly (especially the frail elderly) people with diabetes and in individuals with reduced life expectancy. The *Veteran Health Administration (VHA) Guideline* (1997) recommend that HbA_{1c} should be individualised and primarily based on both life expectancy and the presence or absence of microvascular complications.

The guideline recommends:

- ≤ 7.0% (≤ 1% above high normal range) if life span is 15 years or more, in the absence of microvascular complications, or 10 years or more in the presence of early to moderate microvascular disease;
- ≤ 8.0% (≤ 2.0% above high normal range) if life span is 5-15 years in the absence of microvascular disease, or is 5-10 years in the presence of microvascular disease, and
- ≤ 9.0% (≤ 3.0% above high normal range) if life span is less than 5 years, with or without macrovascular disease.

For the purposes of applying this recommendation, life expectancy is derived from the observed mortality rates of a population, adjusted for the reduced life expectancy of people with diabetes. A means of estimating life expectancy for men and women with Type 2 diabetes has been generated from a computer model, incorporating data from the Framingham Study (Eastman et al, 1997).

Other factors which should be taken into consideration in setting the HbA_{1c} target include predisposition to hypoglycaemia and coexisting comorbidities.

Blood pressure

Index

Isolated systolic hypertension (ISH) is frequent in the elderly and increases the difficulty in achieving the general blood pressure target for people with Type 2 diabetes

NHMRC Gradeable Evidence

The *National Evidence Based Guidelines for Diagnosis and Management of Hypertension* (Jerums et al, 2002a), recommend blood pressure measurement at every clinic visit or at least every 6 months in normotensive people with Type 2 diabetes and at least every 3 months in people with hypertension and Type 2 diabetes. Blood pressure should be measured with a mercury sphygmomanometer. The use of Ambulatory Blood Pressure Monitoring (ABPM) is only recommended if there is suspected 'office hypertension', resistance to antihypertensive therapy, or developing nephropathy.

The Guideline (Jerums et al, 2002a) highlights that hypertension in people with Type 2 diabetes is associated with a greater cardiovascular risk than equivalent blood pressure levels in people without diabetes, and that cardiovascular mortality and morbidity are closely related to the degree of reduction in blood pressure. Therefore hypertension in people with Type 2 diabetes should be intensively treated in order to prevent or attenuate macrovascular and microvascular complications.

The Guideline (Jerums et al 2002a) recommends a target blood pressure for anti-hypertensive therapy in people with Type 2 diabetes of <130/85mmHg, and <125/75mmHg for people who have proteinuria of >1g/day. The frequent occurrence of ISH in elderly people (>60-65 years) may make it difficult to achieve the systolic

blood pressure target of <130mmHg and a more realistic target may be a systolic blood pressure of <140mmHg. Franklin et al (1999) showed that commonly older people have a rise in systolic blood pressure and a fall in diastolic pressure. This increase in pulse pressure may be an independent factor in the development of vascular events.

The outcomes of interventions to lower blood pressure in the elderly is reviewed in the next section.

Lipids

Index

Lipid abnormalities are common and are strong predictors of cardiovascular events in elderly people with Type 2 diabetes

NHMRC Gradeable Evidence

Lipid abnormalities are common in people with Type 2 diabetes, specifically diabetes-related elevated triglycerides and reduced High Density Lipids (HDL) cholesterol, as well as similar changes in the general population – elevated total and Low Density Lipids (LDL) cholesterol. These abnormalities are a major contributor to the increase in CVD seen in people with Type 2 diabetes (Best et al, 2002).

These findings apply to people of different age groups, including elderly people with Type 2 diabetes. Barrett-Connor and colleagues (1982) found that the prevalence for hypertriglyceridaemia (>2.1mmol/L) was 35% in 191 men with diabetes aged 50-79 years of age, compared with 12% in 747 non-diabetic men ($p<0.001$). For 122 women with diabetes, the prevalence was 21% compared with 8% in 1032 controls ($p<0.001$). The overall prevalence of elevated total cholesterol was similar in diabetic and non-diabetic people. Total cholesterol was ≥6.5mmol/L in 15% of men and 28% of women with diabetes compared with 12% and 25% of controls (p=NS).

Cowie et al (1994) reported that Type 2 diabetes was associated with a pattern of dyslipidaemia, including lower HDL cholesterol, higher triglycerides and total cholesterol from the Second NHANES, which included 720 people with Type 2 diabetes (mean age 56.8 years) and 3,547 without diabetes (mean age 41.8 years). A worse lipid profile of mean cholesterol, triglycerides, and HDL cholesterol was generally apparent in people with Type 2 diabetes compared with nondiabetics. Separate analysis of Caucasian people aged 65-74 years showed dyslipidaemia in people with diabetes compared with those without diabetes. This is evidenced by triglyceride levels of 2.1 vs 1.6mmol/L in men, 2.1 vs 1.7mmol/L in women; total cholesterol levels of 5.9 vs 5.7mmol/L in men and 6.3 vs 6.3mmol/L in women; LDL cholesterol levels of 4.1 vs 3.9mmol/L in men and 4.2 vs 4.1mmol/L in women; and HDL cholesterol levels of 1.1 vs 1.2mmol/L in men and 1.3 vs 1.4mmol/L in women in people with diabetes compared with nondiabetics.

Measurement of total cholesterol, triglycerides and HDL cholesterol levels and calculation of LDL cholesterol should be performed in people with Type 2 diabetes, preferably following a 10 to 12 hour overnight fast. Due to the increased prevalence

of CVD in the elderly population, it is necessary to check lipid profiles annually in elderly people with a normal lipid profile, or more frequently (every 3-6 months) in those elderly people with an abnormal lipid profile, or if they are receiving treatment with lipid-lowering agents (Best et al, 2002).

Total cholesterol and LDL cholesterol levels are strong predictors of CVD risk and mortality in Type 2 diabetes. The treatment targets should be LDL cholesterol <2.5 mmol/L and triglyceride <2.0 mmol/L. People with Type 2 diabetes whose control is unsatisfactory should have their diabetes control improved as a means of improving the lipid profile before considering lipid modifying therapy. The effects of lipid modifying agents on CVD in Type 2 diabetes are clearly stated in the *National Evidence Based Guidelines for the Management of Lipid Abnormalities in Type 2 Diabetes* (Best et al, 2002).

The benefits of lipid lowering in elderly people with diabetes is reviewed in the next Section

Renal function

Index

Albuminuria predicts cardiovascular events and mortality and renal disease in elderly people with Type 2 diabetes

NHMRC Gradeable Evidence

Renal disease is a strong predictor of cardiovascular morbidity and mortality in people with Type 2 diabetes (Jerums et al, 2002b). The excess mortality is largely confined to people with proteinuria, predisposing them to premature cardiovascular death. However, microalbuminuria in elderly people with Type 2 diabetes, is also linked to CVD and total mortality, and the development of renal disease (proteinuria).

Mogensen et al (1984) assessed mortality in 76 elderly people with Type 2 diabetes (mean age ≥60 years) and microalbuminuria (albumin concentration 30-140ug/min), compared with 75 people with diabetes and urinary albumin <15ug/min, 53 with urinary albumin 16-29ug/min, and 29 with urinary albumin >140ug/min. During 9.5 years follow-up, the group with albumin 30-140ug/min was more likely to develop clinically detectable proteinuria (>400ug/min) than were the groups with lower urinary albumin concentrations. In addition, mortality was closely linked to urinary albumin concentration: mortality of 37% was observed in the group with urinary albumin <15ug/min during the follow-up, 76% in the group of 16-29ug/min, and 148% in the group with 30-140ug/min, but there was no further increase (105%) in the group with >140ug/min. These findings show that microalbuminuria in elderly people with Type 2 diabetes is predictive of clinical proteinuria and increased mortality.

Persistent microalbuminuria in people with Type 2 diabetes indicates an approximately 2-4 fold increase in the risk of developing a cardiovascular event compared with people without microalbuminuria. Schmitz and Vaeth (1988) performed a similar study to investigate the impact of microalbuminuria on mortality

in 503 people (mean age 65.8 years) with Type 2 diabetes during 10-years of follow-up. Urine albumin concentration (UAC) was classified into four categories: ≤15 ug/ml (n=328), ≤40ug/ml (n=88), ≤200ug/ml (n=62) and ≥200ug/ml (n=25). During follow-up 265 participants died, 58% of deaths were caused by CVD or stroke, and 3% by uraemia. Age (RR 1.07) and UAC had a highly significant influence on survival ($p<0.00005$ for both variables). The RR of UAC ≤40ug/ml was 1.53 (p=0.007), UAC ≤200ug/mi was 2.28 (p=0.000002), and UAC >200ug/ml was 1.82 (p=0.02) compared with a UAC of ≤15ug/ml. Diabetes duration (RR 1.36, p=0.0002), age at onset (RR 1.07**,** p=0.004), and serum creatinine (RR 1.81, p=0.004) were also significant predictive factors. Increased UAC was also associated with retinopathy (p=0.01).

Gerstein et al (2000) reported the prevalence of microalbuminuria in people with diabetes (mean age 65.4 years) and without diabetes (mean age 66.1 years) in the Heart Outcomes Prevention Evaluation (HOPE) Study. Microalbuminuria was expressed as the Albuminuria-to-Creatinine Ratio (ACR) and was defined as an ACR ≥2mg/mmol. Of the patient group, 32.2% of those with diabetes and 14.7% the nondiabetic participants had microalbuminuria. Age (Odds Ratio (OR), 95% CI 1.32, 1.24-1.40), waist-to-hip ratio (OR 1.10, 1.04-1.16), diabetes (OR 2.66, 2.36-2.99), smoking (OR 1.53, 1.30-1.81), hypertension (OR 1.52, 1.34-1.71), and vascular disease (1.44, 1.24-1.68) were independent determinants of microalbuminuria in all participants.

Pharmacological therapy can improve outcomes in elderly people with Type 2 diabetes and microalbuminuria. The MICRO-HOPE Study (2000) assessed the effects of Ramipril 10mg/d compared with placebo, on cardiovascular events and overt nephropathy over 4.5 years in 3577 people (mean age 65.4 years) with Type 2 diabetes, 32% of whom had microalbuminuria, and 56% of whom were hypertensive. All baseline characteristics were comparable between groups. At 4 years, the rate of the combined primary outcome of MI, stroke, or cardiovascular death was significantly lower in the Ramipril group than in the placebo group (RR reduction of 25% [CI 12-36], p=0.0004). One hundred and seventeen participants (7%) in the Ramipril group and 149 (8%) in the placebo group developed overt nephropathy (p=0.027). During follow-up, 20% of participants with baseline microalbuminuria and 2% without baseline microalbuminuria developed overt nephropathy. Moreover, Ramipril led to a lower ACR than placebo at 1 year and the end of the study (p=0.001, p=0.02, respectively). Ramipril reduced the risk of a combined microvascular outcome of overt nephropathy, dialysis, or laser therapy by 16% (1-29, p=0.036). The study concluded that Ramipril presented a vasculoprotective and renoprotective effect for elderly people with diabetes.

The goal in assessing people with diabetes for albuminuria is to identify those who might benefit from treatment to reduce morbidity and premature mortality. Incipient diabetic renal disease (microalbuminuria) is defined as Albumin Excretion Rate (AER) in the range of 20-200µg/min (30-300mg/24hours) with a urine test for proteinuria remaining negative, while overt diabetic renal disease is defined by persistent AER exceeding 200µg/min (300mg/24hours) and a positive urine test for proteinuria (Jerums et al, 2002b).

Assessment for albuminuria can be performed by timed urinary AER (24-hour or overnight collection) or by ACR. ACR should be measured on the first void morning

urine sample. The gender specific microalbuminuria cut-off values for ACR of ≥2.5mg/mmol in males and ≥3.5mg/mmol in females are equivalent to an AER of 20µg/min. The diagnosis of microalbuminuria should be in at least two urine samples. Assessment should be performed at least annually in all people with Type 2 diabetes from the time of diagnosis. For people with micro- or macroalbuminuria, the measurement interval should be every 3-months (Jerums et al, 2002b).

Elevated serum creatinine levels are a late sign of impaired renal function. Levels should be measured at least annually in all people with Type 2 diabetes, supplemented by measurement of glomerular filtration rate if creatinine levels are elevated (Jerums et al, 2002b). This is particularly important in theses elderly women whose creatinine clearance may be reduced despite serum creatinine levels as low as 40-50µM.

Eye examination

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Duration of diabetes and diabetes control significantly affect the risk of developing retinopathy

NHMRC Gradeable Evidence

Diabetic retinopathy (DR) is common in older people with Type 2 diabetes. In 1997 the NHMRC stated that the prevalence of DR among diabetic clinic patients varied from 35% to 49%, and overall DR was found in 1.1% to 2.2% of older Australian population samples.

Nathan et al (1986) reported a prevalence of retinopathy of 25% in 185 older people aged 55-75 years with Type 2 diabetes, most had background retinopathy, and most (95%) had both eyes affected. In contrast, only 2.4% of 48 age-matched controls without diabetes had retinopathy ($p<0.005$). Duration of diabetes and diabetes control measured by HbA_{1c} were the two major predictors of retinopathy. People with a duration of diabetes >10 years had a 4-fold higher prevalence than those with a duration <10 years (53% vs 12%, $p<0.001$). The mean HbA_{1c} was 9.6% and 8.3% in people with or without retinopathy, respectively ($p<0.001$).

Cahill et al (1997) reported the prevalence of DR in 150 elderly people aged 70-92 years with diabetes diagnosed after the age of 70 years and found that 14% had some form of DR and 6.6% had vision threatening DR or previously treated vision threatening DR. The mean duration of diabetes in those with DR was longer than in those without DR (5.0 v 3.5 years, $p=0.007$). However, there was no significant difference in HbA_{1c} levels, or in the proportion of HbA_{1c} above or below 7.0% between people with or without DR. People with DR were more likely to be treated with insulin (14% vs 2%, $p<0.05$) and fewer were treated with diet alone (33% vs 45%).

Phillipov and colleagues (1995) surveyed 888 people (mean age 58 years) with diabetes for the prevalence of NPDR and PDR. DR was present in 20.5%, 18.1% with

NPDR and 2.4% with PDR. People with DR had longer diabetes duration than those without DR (9.2 v 4.0 years, p=0.001).

In the Blue Mountains Eye Study (Mitchell et al, 1998), diabetes was found in 7% (256) of 3,654 people aged ≥49 years. The prevalence of DR was 2.3%, including 1.7% in people younger than 60 years of age, 2.4% in people 60-69 years of age, 2.7% in people 70-79 years of age, and 2.3% in people 80 years of age or older. Four people had signs of PDR, while 78 had signs of NPDR. In 39 people with newly diagnosed Type 2 diabetes, the retinopathy prevalence was 15.8%. After adjusting for age, gender, and the duration since diagnosis of diabetes, mean fasting blood glucose was significantly higher in people with moderate to severe DR compared to those with mild or no DR (odds ratio 1.05, CI 1.00-1.10).

The NHMRC (1997) established standards for eye examination, including a regular visual acuity assessment and eye examination at the time of diagnosis using a test with adequate sensitivity. If NPDR or PDR are found, appropriate actions should be taken as shown in Table 1.

Table 1: Categories of DR and required action (adapted from NHMRC, 1997)

NPDR or PDR	**Action**
No retinopathy	Review examination every two years
Minimal NPDR (isolated microanurysms)	Review examination at least yearly
Mild NPDR	Refer to ophthalmologist
Moderate or severe NPDR	Refer to ophthalmologist as soon as possible
PDR or macular edema	Refer urgently to ophthalmologist for laser treatment

There is a lack of relevant studies regarding the treatment of DR in elderly people with diabetes.

Foot assessment

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Elderly people with Type 2 diabetes are at increased risk of ulcer and amputation

NHMRC Gradeable Evidence

The *Evidence Based Guidelines for Type 2 Diabetes, Identification and Management of Diabetic Foot Disease* (Campbell et al, 2002) highlights that people with diabetes are more likely to have an amputation than those without diabetes. This risk is 3-fold higher for people aged 45-74 years and 7-fold higher for people aged over 75 years. Almost all amputations are preceded by an ulcer. Peripheral neuropathy, with or without Peripheral Vascular Disease (PVD), is considered a major underlying risk factor for the development of a foot ulcer in people with diabetes. People with neuropathy, peripheral vascular disease or foot deformity are recognised as being at risk of diabetic foot problems. People with foot deformity and neuropathy or PVD, previous ulcer or previous amputation are at high risk of foot ulcer or amputation.

Campbell et al (2002) concluded that performing foot risk assessments should include:

- Inquiring about previous history of ulcers, amputation and lower extremity arterial disease;
- Visual inspection of nails, web spaces and feet for ulcers, calluses and foot deformities;
- Assessment for loss of protective sensation using the 10g Semmes-Weinstein monofilament;
- Assessment for PVD by palpating pedal pulses, and
- Inspection of foot wea.r

The 10g monofilament is considered equivalent to, or better than, other simple tests of neuropathy, and is clinically reliable and practical. Testing of ankle jerks alone is of little value, since they are frequently absent in the elderly population.

Routine foot assessment should be performed at least once a year in people who have had no foot problems found previously, and every 3 to 6 months in people with at risk feet but without a current active problem (Campbell et al, 2002).

There are little data on whether diabetic neuropathy can be reversed by improving glycaemic control in people with Type 2 diabetes. In a one-year intervention, 34 elderly Swedish people with Type 2 diabetes (mean age 75.2 years) were randomised to treatment with insulin or sulphonylureas (Tovi et al, 1998). Neuropathy was present in 56% of people at entry to the study and did not alter over one year despite a reduction in HbA_{1c} from 9.2 ± 1.4% to 7.3 ± 1.1% ($p<0.001$) in the insulin-treated group (n=18). The sulphonylurea-treated group (n=16) had an initial HbA_{1c} of 9.1±1.2% which did not change significantly throughout the study period. The one-year duration of the study could be inadequate to detect any significant change in neuropathy.

Cognitive function

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Diabetes is associated with a decline in cognitive function

Cognitive impairment describes a broad spectrum, ranging from preclinical and mild impairment to more profound dementia, and severe Alzheimer's disease. It is highly prevalent among elderly people with diabetes. In addition, other common medical conditions such as depression, hypertension, and vascular problems, may effect cognition. The clinical implications of cognitive impairment in the elderly are often not considered, although even mild levels of impairment will have a direct impact on the individuals' diabetes self-management, quality of life, level of independence and carer support needs (Gregg EW, 2002b; Gregg et al, 2000a).

Some studies have shown a relationship between diabetes and cognitive decline. A large prospective study of 9,679 community-dwelling elderly women aged 65-99 years has reported that diabetes was associated with both poorer cognitive

performance at baseline and rapid decline over 6 years (Gregg et al, 2000a). Seven percent of participants had diabetes with a mean duration of 10.2 years. Three tests including Digit Symbol, Trail B and m-Mini Mental State Examination (m-MMSE) were used to assess cognitive function. Depression was defined as a Geriatric Depression Score of 6 or higher. Women with diabetes were more likely to have visual impairment, hypertension, CVD, stroke or fair to poor health status, compared with women without diabetes. Women with diabetes had poorer scores on all 3 tests compared with women without diabetes at both baseline and follow-up in the Digit Symbol and Trail B tests ($p<0.001$) and m-MMSE ($p=0.03$). Their cognitive decline over time was also greater on the Digit Symbol test ($p=0.01$) and m-MMSE ($p=0.03$). Duration of diabetes was associated with increased cognitive impairment and major cognitive decline on the Digit Symbol and Trail B tests but not the m-MMSE (p for trend <0.01 for each). Women with more than 15 years of diabetes had a 57% to 114% greater risk of major cognitive decline compared with women without diabetes.

Two studies found that diabetes was associated with increased risk of dementia and Alzheimer's disease in the elderly. Ott et al (1999) studied 6,370 elderly people (mean age 70 years) without dementia at entry, and followed them up to 2.1 years in a prospective cohort study. At baseline, 692 people had diabetes, of which 390 were controlled by diet alone, 232 were treated with OHAs and 70 with insulin. People with diabetes were more likely to have a history of hypertension and stroke, compared with people without diabetes (both $p<0.001$). During the follow-up, 126 people developed dementia, 89 were diagnosed with Alzheimer's disease, 18 were classified with vascular dementia, and 19 had another type of dementia. People that developed dementia had a higher diabetes prevalence (27.0% vs. 10.5%, $p=0.005$) and were older than those who were nondemented (80.6+/-7.7 vs. 68.6+/-8.6 years). Diabetes increased the risk of dementia and the age and sex-adjusted relative risk was 1.9 (95% CI 1.3-2.8), with the highest risk in insulin-treated people, 4.3 (95% CI 1.6-11.8), and the lowest risk in people managed by diet-alone, 1.3 (95% CI 0.7-2.3). Diabetes also increased the risk of Alzheimer's disease with a RR of 1.9 (95% CI 1.2-3.1), RR 1.8 (95% CI 1.1-3.0) for people without CVD, and 3.0 (95% CI 1.0-9.3) for people with CVD.

Leibson et al (1997) followed 1455 people aged 45 to 99 years with Type 2 diabetes for 15 years in a prospective study. During the follow-up, 101 people became demented, and of these 77 were diagnosed with Alzheimer's disease. The incidence of dementia and Alzheimer's disease increased with age in the 45-89 year age group, but not in 90-99 year age group, and age-specific rates of dementia were higher for men than for women. The risk of dementia for people with diabetes was 1.66 (95% CI 1.3-2.1) times higher than for people without diabetes. The association between diabetes and dementia did not depend on age ($p=0.59$). The risk of Alzheimer's disease was also increased for people with diabetes, RR of 2.3 (95% CI 1.6-3.3) for men, and of 1.3 (0.9-2.0) for women, reaching significance only in men ($p=0.008$). No significant effect of diabetes duration for either dementia or Alzheimer's disease was observed in this study.

Failure to identify cognitive impairment in elderly people with diabetes may lead to failure to achieve adequate diabetes care and support and suboptimal treatment and management plans. In order to effectively manage elderly people with diabetes, prioritise their needs, and implement an individualised diabetes care plan, routine

assessment of cognitive function is now considered an important part of the clinical assessment. The MMSE is widely used in clinical practice for screening cognitive function (Sinclair et al, 2000; Sinclair et al, 1997; Croxson et al, 1995; Gregg et al, 2000a).

A systematic review (Tombaugh et al, 1992) showed that in approximately 70% of the studies which assessed a wide variety of subjects, ranging from cognitively intact community residents to those with severe cognitive impairment with different types of dementing illnesses, a MMSE score of less than 23 was associated with the diagnosis of dementia in at least 79% of the studies. All studies with a mean MMSE score of 15 or less for the demented people report relatively high levels of sensitivity (80-100%), while the two studies with a mean MMSE score greater than 20 for the impaired group reported low levels of sensitivity (44% and 57%). This might suggest that high levels of sensitivity increase as cognitive impairment increases. Most studies reported moderate to high levels of specificity (70-100%). The MMSE was highly correlated with other cognitive screening tests, as well as neuropsychological tests measuring intelligence and memory, and Activities of Daily Living (ADL). The MMSE scores were affected by some demographic factors; age, educational levels, and cultural background, but not gender. A systematic review of 16 longitudinal studies using test-retest intervals ranging from 1 month to 3 years has shown that MMSE scores for dementia decline over time, generally fell between 2 and 5 points per year. Recommendations were made based on this systematic review for the use of the MMSE. The MMSE should not be served as the sole criterion for diagnosing dementia, however, the MMSE scores and its cut-off points may be used to define the severity of cognitive impairment. In addition, the MMSE should not be used clinically unless the person has at least a grade eight education.
[1]

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[1] The MMSE consists of a variety of questions, has a maximum score of 30 points, and usually can be administrated in 5-10 minutes. The questions represent different cognitive functions: orientation to time (5 points); orientation to place (5 points); registration of three words (3 points); attention and calculation (5 points); recall of three words (3 points); language (8 points) and visual construction (1 point). The MMSE score is the total number of correct answers and has been used to classify the severity of cognitive impairment: 24-30 indicating no cognitive impairment; 18-23 mild cognitive impairment; 0-17 severe cognitive impairment

NHMRC Gradeable Evidence table for Assessments and Targets

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Barrett-Connor et al, 1982	Case-control	III	Lipid abnormalities in diabetes
Best et al, 2002	Systematic review	I	Lipid Guidelines for Type 2 Diabetes
Bruce et al, 2000	Cross-sectional	III	Glycaemic control
Cahill et al, 1997	Cross-sectional	III	Prevalence of diabetic retinopathy
Cowie et al, 1994	Cross-sectional	III	Lipid abnormalities in diabetes
Campbell et al, 2002	Systematic review	I	Foot Disease Guidelines for Type 2 Diabetes
Franklin et al, 1999	Cohort	II	Relationship between systolic hypertension, pulse pressure and vascular events
Gerstein et al, 2000	Case-control	III	Prevalence of albuminuria
Jerums et al, 2002a	Systematic review	I	Hypertension Guidelines for Type 2 Diabetes
Jerums et al, 2002b	Systematic review	I	Renal Disease Guidelines for Type 2 Diabetes
Leibson et al, 1997	Cohort	III	Diabetes and dementia
Mitchell et al, 1998	Cross-sectional	III	Prevalence of diabetic retinopathy
Mogensen CE, 1984	Case-control	III	Microalbuminuria and mortality
Nathan et al, 1986	Cross-sectional	III	Prevalence of retinopathy
NHMRC, 1997	Systematic Review	I	Management of Diabetic Retinopathy Guidelines
Ott et al, 1999	Cohort	III	Diabetes and dementia
Phillipov et al, 1995	Cohort	III	Prevalence of DR
Schmitz and Vaeth, 1988	Cohort	II	UAC and mortality
Shorr et al, 2000	Cross-sectional	III	Glycaemic control
Tombaugh et al, 1992	Systematic review	I	The validity and reliability of the MMSE
Tovi et al, 1998	RCT	II	Effect of insulin treatment on diabetic neuropathy

Barrett-Connor E, Grundy SM, Holdbrook MJ. Plasma lipids and diabetes mellitus in an adult community. Am J Epidemiol 1982;115:657-63

Best J, Colagiuri S, Malouf N, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Lipid Abnormalities. Draft. Diabetes Australia. Canberra, 2002

Bruce DG, Davis WA, Davis TME. Glycaemic control in older subjects with Type 2 diabetes mellitus in the Fremantle Diabetes Study. J Am Geriatric Soc 2000;48:1449-53

Cahill M, Halley A, Godd M, O'Meara N, Firth R, Mooney D, Acheson RW. Prevalence of diabetic retinopathy in patients with diabetes mellitus diagnosed after the age of 70 years. Br J Ophthalmol 1997;81:218-222

Campbell L, Smith L, Colagiuri S, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Diabetic Foot Disease. Draft. Diabetes Australia. Canberra, 2002

Cowie CC, Howard BV, Harris MI. Serum lipoproteins in African Americans and Whites with non-insulin-dependent diabetes in the US population. Circulation 1994;90:1185-93

Franklin SS, Kahn SS, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. Circulation 1999;100:354-60

Gerstein HC, Mann JFE, Pogue J, Dinneen SF, Halle J-P, Hoogwere B, Joyce C, Rashkow A, Young J, Zinman B, Yusuf S. Prevalence and determinants of microalbuminuria in high-risk diabetic and nondiabetic patients in the Heart Outcomes Prevention Evaluation Study. Diabetes Care 2000;23(Suppl 1):B35-9

Gregg EW. Complications of diabetes in elderly people. Underappreciated problems include cognitive decline and physical disability. BMJ 2002b;325:916-7

Jerums G, Colagiuri S, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Hypertension. Draft. Diabetes Australia. Canberra, 2002a

Jerums G, Smith T, Colagiuri S, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Renal Disease. Draft. Diabetes Australia. Canberra, 2002b

Leibson CL, Rocca WA, Hanson VA, Cha R, Kokmen E, O'Brien PC, Pulumbo PJ. Risk of dementia among persons with diabetes mellitus: a population-based cohort study. Am J Epidemiol 1997;145:301-8

Mitchell P, Smith W, Wang JJ, Attebo K. Prevalence of diabetic retinopathy in an older community. Ophthalmology 1998;105: 406-11

Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Eng J Med 1984;310:356-60

Nathan DM, Singer DE, Godine JE, Harrington CH, Perlmuter LC. Retinopathy in older Type II diabetics. Association with glucose control. Diabetes 1986;35:797-801

National Health Medical Research Council. Management of diabetic retinopathy. NHMRC. Canberra, 1997

Ott A Stolk RP, van Harskamp F, Pols HAP, Hofman A, Breteler MMB. Diabetes mellitus and the risk of dementia: The Rotterdam Study. Neurology 1999;53:1937-42

Phillipov G, Alimat A, Phillips PJ, Drew AC. Screening for diabetic retinopathy. Med J Australia 1995;162:518-20

Schmitz A, Vaeth M. Microabluminuria: A major risk factor in non-insulin-dependent diabetes. A 10-year follow-up study of 503 patients. Diabet Med 1988;5:126-34

Shorr RI, Franse LV, Resnick HE, Di Bari M, Johnson KC, .Pahor, M. Glycaemic control of older adults with Type 2 diabetes: Findings from the Third National Health and Nutrition Examination Survey, 1988-1994. J Am Geriatric Soc 2000;48:264-7

Tovi J, Engfeldt P. Well-being and symptoms in elderly Type 2 diabetes patients with poor metabolic control: effect of insulin treatment. Practical Diabetes International 1998; 15(3): 73-77

Tombaugh TN, McIntyre NJ. The Mini-Mental State Examination: A comprehensive review. J Am Geriatric Soc 1992;40:922-35

Assessments and Targets – Other References

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Abraira C, Colwell JA, Nuttall FQ, Sawin CT, Nagel NJ, Comstock JP, Emanuele NV, Levin SR, Henderson W, Lee HS. VACSDM Group. Veterans Affairs Cooperative Study on glycemic control and complications in Type II diabetes (VA CSDM). Results of the feasibility trial. Diabetes Care 1995;18:1113-23

American Diabetes Association. Tests of glycaemia in diabetes. Position Statement. Diabetes Care 2002;25(Suppl 1):S74-7

Binns CW (Ed). National Health and Medical Research Council Dietary Guidelines for Older Australians, Canberra: NHMRC, 1999

Chen CCH, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42

Colagiuri S, Colagiuri R, Ward J. National Diabetes Strategy and Implementation Plan. Diabetes Australia, Canberra, 1998

Rosenstock J. Management of Type 2 diabetes mellitus in the elderly. Special considerations. Drugs and Aging 2001;18:31-44

UKPDS 34. Effect of intensive blood-glucose control with Metformin on complications in overweight patients with Type 2 diabetes. Lancet 1998;352:854-65

Veteran Health Administration. Clinical Guidelines for Management of Patients with Diabetes Mellitus. Department of Veterans Affairs, United States of America. Washington DC. 1997

2.3 Special Treatments

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Are there special treatments/managements that should be encouraged or discouraged in elderly people with diabetes?

Answer

Yes. Metabolic changes associated with ageing may result in changes in:
- specific nutritional requirements
- precautions for and efficacy of physical activity
- effectiveness of and responses to medications

Why

- Undernutrition is common in the elderly and may be more important than dietary composition when formulating a nutrition plan for elderly people with diabetes
  NHMRC Evidence Level III

- The composition of the diet influences glycaemic control and lipid levels in elderly people with diabetes
  NHMRC Evidence Level II – III-2

- Nutrition education improves metabolic outcomes in elderly people with diabetes
  NHMRC Evidence Level III

- Low to moderate intensity exercise in elderly people with diabetes improves fitness and reduces cardiovascular disease risk factors
  NHMRC Evidence Level II

- High-intensity resistance training is effective in improving glycaemic control and muscle strength in elderly people with diabetes
  NHMRC Evidence Level II

- Moderate alcohol intake (1-2 standard drinks/day) is associated with a reduction in risk of coronary heart disease morbidity and mortality
  NHMRC Evidence Level III

- Smoking increases the risk of macrovascular disease in people with diabetes
  NHMRC Evidence Level II

Diabetes Control:

- Glycaemic control can be effectively improved in elderly people with Type 2 diabetes with a variety of antidiabetic medications used singulary or in combination
  NHMRC Evidence Level II – III-2

- Hypoglycaemia is the major risk associated with antidiabetic therapy in the elderly
  NHMRC Evidence Level II - IV

- Lactic acidosis is a rare side effect of Metformin therapy
  NHMRC Evidence Level III-2

- Poor adherence to diabetes medication is a problem in the elderly
  NHMRC Evidence Level III-2

Hypertension:

- Treatment of hypertension in the elderly is associated with reduced cardiovascular events
  NHMRC Evidence Level II – III-2

- Treatment of isolated systolic hypertension in elderly people with Type 2 diabetes improves cardiovascular outcomes
  NHMRC Evidence Level II

Lipids:

- Statins which lower lipids reduce cardiovascular events in elderly people
  NHMRC Evidence Level II

Aspirin:

- Aspirin is effective in the prevention of acute myocardial infarction in people with diabetes, but is associated with increased gastrointestinal bleeding in the elderly
  NHMRC Evidence Level II

Recommendations

- Elderly people with diabetes should have initial and routine nutrition assessments and be encouraged to follow the *NHMRC Dietary Guidelines for Older Australians*. In addition, attention to the intake and distribution of carbohydrate is important

- Weight loss in elderly people is not recommended unless they are at least 20% overweight

- Elderly people with diabetes should be encouraged to follow the *National Physical Activity Guidelines for Australians* which recommend 30 minutes of physical activity each day (aerobic exercise and/or strength training). Prescription of exercise in the frail elderly should be tailored to the individual

- Alcohol intake in elderly people who are current drinkers is recommended not to exceed one standard drink in women or two standard drinks per day

- Smoking cessation is recommended for all people with diabetes, including the elderly

- The choice of hypoglycaemic agent for an elderly person with diabetes should take into account comorbidities, contraindications and potential side effects, especially hypoglycaemia with long acting sulphonylureas and insulin

- A range of antihypertensive agents can be used to control blood pressure in elderly people with diabetes

- Lipid lowering therapy should be considered in elderly people, especially in those who have had a previous vascular event

Nutrition

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Background

Nutrition intervention is an integral component of diabetes management. Since many factors may affect nutritional status in elderly people with diabetes, nutrition intervention can be particularly challenging. These factors include co-existing illness and polypharmacy, cognitive dysfunction, age-related decline in taste perception, poor prior eating habits, impaired swallowing, impaired food shopping capabilities or food preparation skills, poorly fitting dental prosthesis, limited finances, poor motivation and a lack of sufficient education (Binns, 1999). In addition, the elderly may also develop nutritional deficiencies due to impairments in nutrition absorption associated with the use of certain medications. When recommending a nutrition intervention plan these factors should be taken into account to achieve overall better diabetes management.

The goals of nutrition therapy in elderly people with diabetes are to:

- Provide adequate energy and nutrition intake;
- Maintain blood glucose within the target range;
- Facilitate effective management of coexisting morbidities;
- Prevent, delay, or treat nutrition-related complications;
- Promote quality of life, safety, and overall well being, and
- Meet cultural needs.

A thorough nutritional assessment by a qualified dietitian is the first step in implementing nutrition intervention. Teaching elderly people about nutrition and diabetes self-care should be multifaceted, and easy to follow and understand. Nutritional interventions should take into account the individual's ability to shop and prepare food i.e. elderly men may require active cooking education. It may be useful to have a mixture of group and individual sessions.

Undernutrition is common in the elderly and may be more important than dietary composition when formulating a nutrition plan for elderly people with diabetes

NHMRC Gradeable Evidence

Nutritional status, according to the Mini Nutrition Assessment (MNA), of 80 elderly nursing home residents (mean age 84 years) was assessed by Saletti et al (1999). The majority had multiple medical problems, such as congestive heart failure (6%), chronic obstructive lung disease (5%), hypertension (10%), Type 2 diabetes (9%), joint disorders (8%) and others (24%). The assessment included BMI, Mid-Arm Circumference (MAC), Calf Circumference (CC) and weight. MNA scores <17 indicated malnutrition, 17 to 23.5 at risk of malnutrition, and >24 well nourished. The mean MNA score was 22.2 ±3.0. Overall, 3% were malnourished, 62% were at risk of malnutrition, and 35% were well nourished. The mean BMI was 22.7±0.5 kg/m^2. One third of subjects had BMI <20 and 64% had BMI ≤23 kg/m^2. MNA correlated with BMI, r=0.58 ($p<0.0001$), MAC, r=0.46 ($p<0.0001$), and CC, r=0.29 ($p<0.01$). Two thirds of subjects were identified as having suspected or confirmed

malnutrition. Unless an elderly individual is more than 20% overweight, weight loss interventions should not be implemented.

Horwath and Worsley (1991) undertook a study comparing the dietary characteristics of elderly people (≥65 years) with diabetes (n=151) and without diabetes (n=2,044) and found that 64% of people with diabetes reported following a diabetic diet, although only 6% were consuming a high carbohydrate diet (≥50% energy intake). In comparison to nondiabetic individuals, people with diabetes had a lower intake of refined carbohydrate ($p<0.001$) and a higher protein intake ($p<0.0001$). There were no differences in intake of complex carbohydrate, fibre, or total or saturated fat between the two groups.

In a 16-week cohort study (Coulston et al, 1990), 18 people with Type 2 diabetes (mean age 78 years) from two residential care facilities, were monitored for glycaemic control on a diabetic diet and a regular diet (4 weeks on diabetic diet before and after an 8-week regular diet). All participants had good glycaemic control (FPG 7.0±0.6mmol/L) at entry into the study. Compared with the diabetic diet, the regular diet had more energy intake ($p<0.05$), more carbohydrate, fat, monounsaturated and polyunsaturated fatty acid intake (all $p<0.05$). There was a small mean increase in FPG of 0.6mmol/L in the regular diet period ($p<0.05$ vs diabetic) but HbA_{1c} did not change significantly. Plasma triglycerides and cholesterol levels tended to increase during the regular diet period, but these changes were not significant and body weight remained stable. These results indicate that short-term substitution of regular diet for diabetic diet did not result in marked changes in metabolic control in elderly people with diabetes.

Other Evidence

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Malnutrition is a frequent and serious problem in the elderly, and it has been associated with adverse outcomes (Chen et al, 2001). Weight loss per unit of time is believed to be a major indicator of malnutrition in the elderly, and the most accepted definition for clinically important weight loss has been a weight loss in the order of 5% over a 6-12 month period.

Assessment of the nutritional status of the elderly is important for integrating nutrition into the overall diabetes management plan. The assessment should include (VHA, 1997):

- Current height/weight and BMI;
- Nutritional history: usual food intake and pattern of intake; energy and macronutrient composition; weight history (especially in the proceeding 6 months), appetite, and digestion problems; alcohol intake; use of vitamin, mineral, or nutrient supplements;
- Exercise pattern: type of activity, frequency, and duration;
- Psychosocial and economic issues: living situation, cooking facilities, ability to obtain and prepare food, finances, educational background, employment, ethnic or religious beliefs and considerations, literacy, family support, need for food assistance, if applicable;
- Frequency and severity of hypoglycaemia, and
- Measurement of serum albumin, haemoglobin

The nutritional assessment should be initially performed when the integrated diabetes management plan is made. Given the higher risk of malnutrition in the elderly, especially those living in an institutional setting, nutritional status should be assessed regularly.

The composition of the diet influences glycaemic control and lipid levels in elderly people with diabetes

NHMRC Gradeable Evidence

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High carbohydrate diets

The effects of variations in dietary carbohydrate and the reciprocal changes in fat intake on glycaemic control and lipid profile were assessed in 9 elderly people aged 52-71 (mean age 63 years) with diabetes (Coulston et al, 1987). One diet contained 20% protein, 20% fat, and 60% carbohydrate, with 10% of total calories as sucrose, while the other diet comprised 20% protein, 40% fat, and 40% carbohydrate, with sucrose accounting for 3% of total calories. The two diets were consumed in random order over two 15-day periods. Mean FPG and fasting insulin levels were similar with both diets. The high carbohydrate diet resulted in higher daylong (8am to 4pm) mean postprandial plasma glucose levels (PPG) ($p<0.01$) and insulin concentrations, as well as increased mean 24-hour urine glucose excretion ($p< 0.02$). In addition, fasting and postprandial triglyceride levels were increased ($p<0.001$, $p<0.05$, respectively) and HDL-cholesterol level was reduced ($p<0.02$).

In another study Coulston et al (1989) compared diets containing either 40 or 60% carbohydrate with reciprocal changes in fat content from 40 to 20% (polyunsaturated/ saturated ratio 1.0-1.1), consumed in random order in a 6 week crossover design study of 8 people (mean age 66 years) with Type 2 diabetes treated with sulphonylureas or diet alone. The high-carbohydrate diet significantly increased plasma glucose levels between 0800 and 1600 hrs ($p<0.001$), although mean fasting glucose level was not different. Fasting triglyceride levels increased by 30% from about 1.9 to 2.4 mmol/L ($p<0.001$) after 1 week on the 60% carbohydrate diet and the hypertriglyceridaemia persisted over the 6-week period. Total cholesterol remained unchanged with both diets. These diets contained low amounts of fibre (14.3 and 18.1grams/day respectively) and, judging by the meal plans, high glycaemic index carbohydrates (e.g. cornflakes, banana, potato).

Garg et al (1992) assessed glycaemic control and lipid profile in 8 men (mean age 63 years) with Type 2 diabetes during a randomised dietary periods of 21 days. The high carbohydrate diet consisted of 60% carbohydrate (10% simple CHO), 25% fat and 15% protein; the low carbohydrate diet consisted of 35% carbohydrate, 50% fat (11% Saturated Fatty acid SFA, 32% Mono Unsaturated Fatty Acid (MUFA), 7% Poly Unsaturated Fatty Acid (PUFA) and 15% protein. On the high carbohydrate diet, fasting glucose levels were not different on the two diets, but glucose response to a meal tolerance test fell on the low carbohydrate diet ($p<0.05$) and did not change on the high carbohydrate diet. Mean triglyceride level was 3.25 mmol/L on the high carbohydrate diet and 2.55 mmol/L on the low carbohydrate diet ($p=0.002$). HDL cholesterol was 0.68 mmol/L on the high carbohydrate diet and 0.76 mmol/L on the low carbohydrate diet ($p=0.013$). Total cholesterol and LDL cholesterol were not significantly different between the two diets.

Low glycaemic index diets

Wolever et al (1992) used a randomised controlled crossover design to assess the effects of a low Glycaemic Index (GI) diet on glucose and lipid metabolism in 15 people (mean age 67 years) with Type 2 diabetes. Over a 2-week period, reducing the GI of a high carbohydrate

diet (59% of total energy), high fibre (24g/1,000kcal) diet from 87 to 60, significantly lowered fructosamine (3.28 mmol/L in high GI diet v 3.17 mmol/L in low GI diet, $p<0.05$) and total cholesterol levels (5.9 v 5.5 mmol/L, $p<0.02$), but triglycerides levels were similar.

All food was provided for 20 people (mean age 67 years) with Type 2 diabetes, in a randomised crossover study by Jarvi et al (1999). Over 24 day periods on a low GI (57) diet (55% energy as carbohydrate, 27% fat, 18% protein, 38g/day fibre) compared with a high GI (83) diet (54% carbohydrate, 29% fat, 18% protein, 34g/day fibre), baseline fructosamine level of 353µmol/L fell to 347µmol/L on the low GI diet, but rose to 356µmol/L on the high GI diet ($p=0.05$ for change on low GI diet v high GI diet). On both diets total, LDL and HDL cholesterol and triglycerides fell significantly and the differences between the low and high GI diets were relatively small compared with these changes. Total cholesterol at baseline was 5.79mmol/L and fell to 4.23mmol/L on the low GI diet v 4.46mmol/L on the high GI diet ($p<0.01$ for both changes, $p=0.002$ for low v high GI). LDL cholesterol fell from 4.03 to 2.87mmol/L on the low GI diet v 3.13mmol/L on the high GI diet ($p<0.01$ for both changes, $p=0.003$ for low v high GI). Improvement in triglycerides was similar on both diets, from 1.80mmol/L at baseline to 1.25mmol/L on low GI v 1.22mmol/L on high GI ($p<0.001$ for both changes). HDL cholesterol reduction was also similar on both diets, from 1.06mmol/L at baseline to 0.88mmol/L on low GI v 0.87mmol/L on high GI ($p<0.01$ for both changes).

Sucrose Index

The study with the largest variation in sucrose intake was performed by Abraira and Derler (1988). Dietary intake was closely regulated, as the 18 people (mean age 61.4 years) with Type 2 diabetes were hospitalised for the 40 days of the study duration. None was taking hypoglycaemic medication at the time of the study. After a baseline period, subjects were randomised to diets of similar composition (50% of energy as carbohydrate, 35% fat, 15% protein), but with either 220g sucrose or 3g sucrose daily. There was no difference in glycaemic control or in total, LDL and HDL cholesterol or triglycerides between the two groups.

An Australian study by Cooper et al (1988) compared daily supplements of 28g sucrose with 30g starch and saccharin (isocaloric and equal sweetness with sucrose) over 6 week periods in 17 people (mean age 62.4 years) with Type 2 diabetes on oral hypoglycaemic therapy, using a randomised crossover design. The addition of sucrose had no effect on fasting glucose or on total, LDL and HDL cholesterol or on triglycerides.

Similarly, another Australian study with randomised crossover design (Colagiuri et al, 1998) showed that the addition of sucrose (45g/day, 9% of total daily energy) or an equivalent sweetening quantity of aspartame to the usual diet (43% carbohydrate, 39% fat, 18% protein, 29g/day fibre) of 9 people (mean age 65.9 years) with Type 2 diabetes on diet alone or sulphonylurea therapy, had no deleterious effects on glycaemic control or lipid levels (total cholesterol, HDL cholesterol or triglycerides) over a 6 week period.

Bantle et al (1993) also used a randomised crossover study to assess the effect of dietary sucrose on glycaemia and the lipid profile in 12 people (mean age 62 years) with Type 2 diabetes, on diet alone, oral hypoglycaemic therapy or insulin. The substitution of starch with sucrose (19% of total energy in the diet compared with 3% in the control diet) in standard diabetic diets (55% carbohydrate, 30% fat and 15% protein) had no adverse effect on fasting glucose, total, LDL and HDL cholesterol or on triglycerides over 4 weeks.

Diets high in monounsaturated fatty acids

The largest and longest of these studies was the outpatient-based study by Garg et al (1994), which was a four –centre randomised crossover study in 42 people aged 35-78 years (mean age 58±10 years) with Type 2 diabetes on sulphonylurea treatment. All food was supplied for the diets, which consisted of 55% total energy as carbohydrate, 30% fat (10% MUFA), 15% protein, 15g/4,200 kJ fibre for the high carbohydrate diet and 40% carbohydrate, 45% fat (25% MUFA), 15% protein, 11g/4,200 kJ fibre for the high MUFA diet. After 6 weeks, fasting glucose, glycosylated Hb and body weight did not differ significantly on the two diets. Mean fasting triglyceride level was 2.19mmol/L on the high carbohydrate diet and 1.75mmol/L on the high MUFA diet ($p<0.0001$). Total, LDL and HDL cholesterol did not differ significantly between the two diets. Day-long plasma glucose was increased by 12% ($p<0.0001$) and day long triglycerides by 10% ($p=0.03$) on the high carbohydrate diet. A subgroup of 21 people continued the diet they received for a further 8 weeks, and the differences in glucose and lipid metabolism were sustained for the total of 14 weeks.

One study evaluated the effects on lipid metabolism of a high MUFA diet compared with high carbohydrate diet, during hypocaloric, weight loss therapy. Low et al (1996) studied 8 people with Type 2 diabetes assigned to a high carbohydrate diet (70% total energy as carbohydrate, 35% simple carbohydrate, 10% fat, 20% protein) and 9 people assigned to a high MUFA diet (10% carbohydrate, 70% fat, 49% MUFA, 20% protein). Energy intake was set for 6 weeks at a 50% deficit, based on prediet weight maintenance requirements, followed by 4 weeks at weight maintenance requirements, during a period of refeeding. Mean weight loss was similar in the two groups (8.3kg on the high carbohydrate diet vs 7.3kg on the high MUFA diet). Mean fasting glucose fell from 12.6 to 8.0mmol/L on the high MUFA diet, compared with 11.2 to 8.8mmol/L on the high carbohydrate diet ($p<0.05$ for high MUFA vs high carbohydrate). Total cholesterol fell from 5.0 to 3.9mmol/L on the high MUFA diet, compared with 4.4 to 4.0mmol/L on the high carbohydrate diet ($p<0.05$ for high MUFA vs high carbohydrate). Triglyceride levels fell from 3.2 to 1.4mmol/L on the high MUFA diet, compared with 2.7 to 2.2mmol/L on the high carbohydrate diet ($p<0.05$ for high MUFA vs high carbohydrate). LDL cholesterol and HDL cholesterol levels did not change significantly on either diet.

In contrast, Craig et al (1998) studied the effects of a disease-specific formula diet (reduced carbohydrate, modified fat higher in monounsaturated fat) compared with a standard high carbohydrate formula diet in a randomised controlled trial of 34 enterally-fed long-term care residents aged 52 to 100 years (mean age 81 years) with Type 2 diabetes. Twenty seven of the 34 participants completed the 12-week study. FPG and capillary glucose (fingerstick) values tended to be lower in the disease-specific formula group, but were not significantly different from the standard formula group. The lipid profile was similar in both groups except HDL-cholesterol was higher at 12 weeks in the disease-specific group ($p=0.038$). The amount of insulin administered was consistently less than before initiation of the formula in the disease-specific formula group, in contrast with increased insulin requirements in the standard formula group. This study did not show any significant difference in the metabolic profile of people receiving the disease-specific formulae.

Diets high in polyunsaturated fatty acids (PUFA) or saturated fatty acids (SFA) Index

An Australian crossover study in 10 men (mean age 61.0±12.1 years) with Type 2 diabetes, treated with diet alone or sulphonylurea therapy, included an arm with high SFA intake, as well as a high carbohydrate diet arm consumed for periods of 2 weeks. High carbohydrate,

high fibre and high protein arms were also included (O'Dea et al, 1989). After two weeks on the high SFA diet (27% carbohydrate, 55% fat, PUFA/SFA ratio 0.26, 18% protein, 14g/day fibre) mean fasting glucose rose from 9.0 to 11.4 mmol/L ($p<0.05$), but rose only from 8.7 to 8.8mmol/L on the high carbohydrate diet (63% carbohydrate, 12% fat, PUFA/SFA ratio 0.71, 25% protein, 20g/day fibre). With high SFA, total cholesterol changed from 5.44 to 5.74 mmol/L vs 4.85 to 4.74mmol/L with high carbohydrate; with high SFA, LDL cholesterol changed from 3.95 to 4.24mmol/L vs 4.85 to 4.74mmol/L with high carbohydrate. With high SFA, triglycerides changed from 1.53 to 1.60mmol/L vs 1.53 to 1.36mmol/L with high carbohydrate; with high SFA, HDL cholesterol did not change from 1.08mmol/L, but changed from 0.95 to 0.92mmol/L with high carbohydrate. None of these changes was statistically significant.

Diets high in fibre

Comparing the high carbohydrate (65% of total energy), high fibre (45g/day) arm with the high carbohydrate (63%), low fibre (20g/day) arm of the study of 10 men with mean age of 61 years by O'Dea et al (1989), mean fasting glucose fell from the baseline level of 9.9 to 8.2mmol/L ($p<0.01$) with high fibre, but rose from 8.7 to 8.8mmol/L on the low fibre diet. Total cholesterol fell from 5.17 to 4.32mmol/L ($p<0.001$) with high fibre, but only from 4.85 to 4.74mmol/L with low fibre; LDL cholesterol fell from 3.32 to 2.59mmol/L ($p<0.001$) with high fibre and from 3.58 to 3.51mmol/L with low fibre. Triglycerides and HDL cholesterol did not change significantly with either diet.

Chandalia et al (2000) used a randomised crossover design in 13 people (mean age 61 years) with Type 2 diabetes, treated with diet alone or sulphonylurea therapy, to compare high carbohydrate (55% of total energy) diets with 24g/day fibre (8g soluble/16g insoluble) vs 50g/day fibre (25g soluble/25g insoluble). After 6 weeks on the high fibre diet mean fasting glucose was 7.2mmol/L vs 7.9 mmol/L on the moderate fibre diet ($p=0.04$). Total cholesterol was 5.07mmol/L on high fibre vs 5.43mmol/L on moderate fibre diet ($p=0.02$); LDL cholesterol was 3.44mmol/L on high fibre vs 3.67mmol/L on moderate fibre diet ($p=0.11$). Triglycerides were 2.08mmol/L on high fibre vs 2.31mmol/L on moderate fibre diet ($p=0.02$); HDL cholesterol was 0.72mmol/L on high fibre vs 0.75mmol/L on moderate fibre diet ($p=0.80$).

Other Evidence

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The variable results of the above data do not provide definitive information to formulate specific agreed nutrition recommendations for elderly people with diabetes. Therefore nutrition recommendations for elderly people with diabetes should be extrapolated from nutrition recommendations for elderly people without diabetes proposed in the *Dietary Guidelines for Older Australians* (Binns, 1999). Similar to recommendations for the general population, older adults are advised to consume a diet high in vegetables, fruit, cereals, breads and pasta; low in saturated fat and salt; and consume sugar in moderation. In contrast to the general population, older adults are advised to increase fluid intake, consume an increased amount of protein (1-1.25g protein/kg/day) and foods high in calcium. These latter recommendations acknowledge the common occurrence of dehydration in the elderly (ABS, 1998), a decreased efficiency of dietary protein ultilisation in the elderly (Campbell et al, 1994), and the increased prevalence of osteoporosis in the elderly, resulting in osteoperotic fractures (Geelhoed, 1994). For older adults, with established Type 2 diabetes, the NHMRC guidelines also suggest consumption of foods with a low glycaemic index, as they are associated with improvements in glycaemic control (Binns, 1999).

It is important to emphasise that weight loss is not always necessary in elderly people, as many are not obese and some may even be underweight, particularly those who live in residential or supported care settings. Caution should therefore be taken when prescribing weight loss in elderly people as weight reduction is not recommended in elderly persons over the age of 70 years unless they are at least 20% overweight (Ruoff et al, 1993).

Nutrition education improves metabolic outcomes in elderly people with diabetes

NHMRC Gradeable Evidence

In order to evaluate the impact of a nutrition intervention on blood glucose and lipoprotein levels, 98 elderly people (≥65 years) with Type 2 diabetes were randomly assigned to either the intervention group or the control group for at least 1 year (Miller et al, 2002). The intervention included 10 weekly group sessions, each session lasting 1.5 to 2 hours, led by the same registered dietitian. Participants were encouraged to monitor food intake, were assessed for their eating patterns in relation to dietary goals, and were taught how to use the carbohydrate counting method for meal planning. Program staff reviewed food intake records weekly and written feedback was provided. No nutrition or diabetes-related information was given to participants in the control group. The experimental group had significant improvements in FPG (-0.07 v –1.04mmol/l, $p<0.05$) and HbA_{1c} (0 v -0.5%, $p<0.01$) when compared with the control group, and 35.9% in the experimental group compared with 26.1% in the control group had optimal total cholesterol values at posttest (<5.18mmol/l, $p=0.03$). The BMI of the two groups was not significantly different at baseline and was not recorded at the study follow-up. These results demonstrate that nutrition education can improve metabolic outcomes among elderly people with diabetes over a 12-month period.

Franz et al (1995) compared two levels of medical nutrition therapy on metabolic control and clinical outcomes in 179 people with Type 2 diabetes (aged 38-76 years) in a 6-month randomised controlled trial. The first therapy was administered according to Practice Guideline Nutrition Care (PGNC) and the second according to Basic Nutrition Care (BNC). The BNC group had only one visit with a dietitian, while the PGNC group included an initial visit with a dietitian followed by two visits during the first 6 weeks of the study period. At 6 months, PGNC resulted in a significant reduction in FPG ($p<0.001$) and HbA_{1c} levels ($p<0.001$) and BNC resulted in a significant reduction in HbA_{1c} ($p<0.001$). Weight loss occurred in both groups ($p<0.001$ for PGC, $p<0.01$ for BC). In this study both groups benefited from the nutrition intervention but the intensity of the intervention did not determine outcomes.

Exercise

Index

Background

Physical activity is an important part of diabetes management in the elderly. Exercising regularly has several benefits for elderly people with diabetes, including improved insulin sensitivity and cardiovascular fitness, as well as improvement in bone density, muscle mass, arterial compliance and energy metabolism. These are all important factors for elderly people

to maintain their independence, quality of life and sense of well-being (Mazzeo and Tanaka, 2001).

The benefits of exercise in elderly non-diabetic people has been widely documented and is well recognised for its role in improving and maintaining coordination, balance, muscle strength and mobility, thereby preventing falls in the elderly and their major repercussions such as hip fractures.

The prevalence of atherosclerosis, CVD and Coronary Artery Disease (including myocardial infarcts and arrhythmia's) in the elderly, increases their risks associated with physical activity (Rosenstock, 2001). Exercise-induced injuries such as muscle strain, falls, and fractures are also a concern in the elderly, especially injury that might occur without awareness in people with peripheral neuropathy.

Little evidence exists about the effects of exercise in elderly people with diabetes. In younger populations (50-65 years) without diabetes, low and high intensity home-based exercise programs have been found to improve fitness (King et al, 1991).

Low to moderate intensity exercise in elderly people with diabetes improves fitness and reduces cardiovascular disease risk factors

NHMRC Gradeable Evidence

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A 3-month study conducted in Switzerland showed that cardiovascular risk profile was significantly changed by a regular exercise program (50-70% VO_{2max} for 30-45 minutes 3 times per week) among people with Type 2 diabetes (Lehmann et al, 1995). Sixteen participants (aged 42 to 79 years) were assigned to the exercise program while 13 age- and gender-matched participants with the same duration of diabetes and a similar degree of physical activity served as the control group. Both groups maintained their regular diet and medications. After 3 months in the intervention group, plasma triglycerides decreased by 20% from 2.81 to 2.24mmol/L ($p<0.05$), while HDL cholesterol increased by 23% from 1.15 to 1.35 ($p<0.001$); and total cholesterol did not change. Improvements were also observed in diastolic and systolic blood pressure and resting heart rate ($p< 0.001$, $p< 0.05$, and $p< 0.001$, respectively). Body weight did not change during the study in either group, but there was a significant reduction in waist-hip circumference ratio from 0.96 to 0.92 ($p<0.001$) and percent body fat from 35.3% to 33.0% ($p<0.001$) in the intervention group. In contrast, there were no significant changes in FBG, HbA_{1c} and fasting insulin levels. Changes in the intervention group occurred regardless of intensity of exercise, and there was no change in any parameters in the control group. This study demonstrates that improvements in physical fitness by regular physical exercise, as part of a treatment program for people with Type 2 diabetes, significantly improves their cardiovascular risk profile.

Similar findings were noted in a 26-week exercise program, in which 25 obese people (mean age 63 years) with Type 2 diabetes were instructed in an aerobic training program 3 times per week for 50 minutes at 60-80% VO_{2max} compared with 26 people with Type 2 diabetes who served as a control group (Ligtenberg et al, 1997). The exercise regimen consisted of 6 weeks of exercise under supervision; a further 6 weeks at home according to personalised training advice, and a further 14 weeks at home without any encouragement. After 6 weeks, VO_{2max}

increased significantly in the training group ($p<0.01$) and lipid profile was also improved compared with the control group ($p<0.01 – 0.05$). These differences were sustained for the whole 26 weeks ($p<0.001$). Weight, waist circumference and waist-hip ratio were unchanged in both groups during the study.

A case-control study of 18 elderly people (mean age 67.5 years) with diabetes assessed the effects of 12 months of weight bearing exercise in two groups with statistically similar baseline characteristics (Caplan et al, 1995). The 8 participants in the intervention group met for 1 hour twice a week for an exercise class that consisted of a warm-up and low impact exercise for 20-25 min, followed by 10 minutes of ball games for fun and hand-eye coordination, floor work for strength and flexibility and 10 minutes of relaxation. There was an increase in the mean percent change in lumbar spine bone mineral concentration and life satisfaction index in the intervention group compared with controls ($p=0.015$ and $p=0.046$, respectively). In addition, there was a reduction in body mass index and weight in the intervention group ($p=0.031$ and $p=0.036$, respectively). There was no significant difference between the two groups in HbA_{1c}.

High-intensity resistance training is effective in improving glycaemic control and muscle strength in elderly people with diabetes

NHMRC Gradeable Evidence

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Dunstan et al (2002) examined the effect of a high-intensity resistance training program in 36 elderly people (aged 60-80 years) with Type 2 diabetes who were randomly assigned to either high-intensity resistance training plus moderate weight loss group (RT+WL) or flexibility exercise plus weight loss (WL) group in a 6 month study. All participants were placed on a healthy eating plan aimed at a moderate weight loss of 0.25kg/wk over the study period. People assigned to the resistance exercise group attended the exercise session 3 days per week. Resistance training consisted of a 5 minute warm-up and 5 minute cool-down period of low-intensity stationary cycling and 45 minutes of high-intensity resistance training. The goal was to achieve 75-80% of one-repetition maximum strength. The sessions of the control program (WL) were involved stationary cycling with no workload for 5 minutes, followed by a series of stretching exercises for 30 minutes. All sessions were supervised for correct technique and the appropriate amount of exercise. Baseline characteristics in regards to age, diabetes duration, BMI, body composition, BP, glucose and insulin, and serum lipids were comparable between the two groups. The RT+WL program was associated with significant reduction in HbA_{1c} at both 3 ($-0.6\pm0.7\%$, $p<0.01$) and 6 months ($-1.2\pm0.9\%$, $p<0.01$). The difference in HbA_{1c} between RT+WL and WL was -0.5% at 3 months ($p<0.05$) and -0.8% at 6 months ($p<0.05$). There were no differences between the groups for either plasma insulin and glucose during the study. A significant reduction in body weight was observed after 3 and 6 months in both groups (RT+WL: -1.8 kg, -2.5 kg; WL: -2.0 kg, -3.1 kg; respectively), fat mass also decreased in both groups (RT+WL: -2.4 kg, WL: -2.1 kg). Lean body mass increased in the RT+WL group, but decreased in the WL group ($+0.5\pm1.2$ kg vs. -0.4 ± 1.0 kg, $p<0.05$). The increase in upper and lower body strength was observed in the RT+WL group at 6 months (41.7%, 28.0%, respectively, both $p<0.01$). There were no changes in muscle strength in the WL group. After 6 months, both SBP and DBP were reduced in the RT+WL group (vs. baseline, both $p<0.05$), but no difference between two groups. Serum lipids were unchanged in both groups during the study. No major complications or injuries were reported

by the groups. The results indicate that supervised resistance training was effective in improving glycaemic control and muscle strength, and was safe and well tolerated by elderly people with diabetes.

Other Evidence

As much as half of the functional decline associated with ageing has been found to be a factor of disuse and therefore could be reversed by exercise aimed at improving fitness. In addition, exercise can prevent bone loss which predisposes to osteoperotic fractures, and can improve insulin sensitivity (NHMRC, 1994).

The *NHMRC Guidelines for Older Australians* reported positive outcomes of aerobic and strength training exercise in older adults which include a decreased risk of diabetes, hypertension, heart disease, osteoporosis and colon cancer. Increases in energy expenditure as a result of exercise result in increases in energy intake and improved physical and mental wellbeing (Binns, 1999).

Mazzeo and Tanaka (2001) suggest the use of heart rate as a common and objective standard to assess physical activity with a maximal heart rate of 55-70% corresponding to moderate intensity exercise. Compared with the higher intensities of exercise, moderate exercise is associated with a significantly lower rate of injury and results in better compliance and maintenance in older people. Recommendations for exercise in the elderly include a routine of gentle warm-up and stretching muscles, followed by a minimum of 30 minutes per day of moderate intensity exercise. Special attention should be paid to the feet with appropriate shoes being essential, and elderly people should check their feet for injury or blisters before and after exercise. The selection of type/mode of activity needs to be based on the participant's fitness level as well as their interests and available resources. Walking has become a popular choice of physical activity for elderly people because it does not require specific skills or special clothing or equipment.

Alcohol and Smoking

Index

Background

Alcohol intake is part of food habits and cultural practices in many societies within Australia. For people with diabetes, the same precautions apply regarding the use of alcohol as in the general population. Encouraging a healthy lifestyle (diet, exercise, smoking avoidance and ensuring a moderate alcohol intake) in elderly people with diabetes to improve their quality of life and well-being is an important part of management.

For any individual, excessive alcohol intake increases the health risks such as liver damage, brain damage and increased blood pressure. The adverse effects of alcohol intake are exacerbated in people with diabetes and may cause or worsen hypoglycaemia and diabetic neuropathy, and increase weight gain due to increases in energy intake. Heavy alcohol intake poses additional risks in elderly people with diabetes, including falls, depression, dementia, isolation, and impaired ability to self-care. Alcohol may also interact with a number of medications producing undesirable side effects (Bell, 1996; Criqui et al, 1999).

In contrast to the adverse effects of excessive alcohol intake, light-to-moderate (5-15g/day) alcohol intake is associated with a decreased risk of CHD, presumably due to the concomitant increase in plasma HDL cholesterol (ADA, 2002).

Smoking is a well-recognised risk factor for ill health for all individuals and increases the risk of diabetes complications. Smoking cessation is recommended in all elderly people with diabetes (ADA, 2002b).

Moderate alcohol intake (1-2 standard drinks/day) is associated with a reduction in risk of coronary heart disease morbidity and mortality

NHMRC Gradeable Evidence

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There are limited data on the impact of alcohol intake in people with diabetes, especially in the elderly population. An inverse association between moderate alcohol consumption and CHD has been observed in some studies (Tanasescu et al, 2001; Valmadrid et al, 1999).

The Wisconsin Epidemiologic Study of Diabetic Retinopathy, examined a population of 983 people with Type 2 diabetes aged 68.6 ±11.0 years (Valmadrid et al, 1999) They found a reduction in mortality from CHD among individuals consuming <2, 2 to 13 and ≥14g alcohol/day, compared with nondrinkers: 0.54 (CI 0.33-0.90), 0.44 (CI 0.23-0.84) and 0.21 (CI 0.09-0.48), respectively. The risk of death from CHD in former drinkers tended to be lower than that of non-drinkers, however this difference was not statistically significant. The CHD mortality rates for non-drinkers and former drinkers were 43.9 and 38.5 per 1000 person-years respectively, while the rates for those with alcohol intakes of <2, 2-13, and ≥14g/d were 25.3, 20.8, and 10.0 per 1,000 person-years respectively. Further adjustment for blood pressure, BMI, physical activity and diabetes duration did not change the association observed. These findings demonstrate that alcohol consumption of 1-2 standard drinks/ day (where 1 standard drink = 10g of alcohol) has a protective effect for CHD.

Tanasescu et al (2001) follow up 2,419 men (mean age 60 years) with reported diabetes for 8 years to investigate the incidence of CHD according to different alcohol intake categories. Of the group, 39% of men were non-drinkers, while 31% consumed ≤0.5 drinks/day, 20% between 0.5 and 2 drinks/day and only 10% consumed >2 drinks/day. During period, 150 new cases of CHD (81 nonfatal MI and 69 fatal MI) were reported. The age-adjusted RR across categories of alcohol consumption (<0.5, 0.5-2.0, and >2.0 drinks/day) was 0.76 (95%, CI 0.52-1.12), 0.64 (95%, CI 0.40-1.02) and 0.59 (95%, CI 0.32-1.09), respectively, as compared with non-drinkers (p for trend = 0.06). After adjusting for potential covariates this inverse association was stronger: 0.78 (95%, CI 0.52-1.15), 0.62 (95%, CI 0.40-1.00) and 0.48 (95%, CI 0.25-0.94) (p for trend = 0.03). The benefits of moderate consumption did not statistically differ by beverage type. This study concluded that moderate alcohol consumption was associated with lower risk of CHD in men with Type 2 diabetes.

The Physicians' Health Study examined 2,790 men (mean age > 60 years) with diabetes at baseline (Ajani et al, 2001). Reported risk reductions for CHD death were 1.11 (CI 0.66-1.89), 0.67 (CI 0.42-1.07) and 0.42 (CI 0.23-0.77) (p for trend = 0.002) corresponding to monthly alcohol levels (≥1 drink per month, but <1 drink per week), weekly (≥1 drink per

week, but <1 drink per day), and daily (≥1 drink per day) as compared with rarely/never drinkers. In a subsample of 510 people followed for CHD incidence, RR were 0.84 (CI 0.46-1.54), 0.75 (CI 0.45-1.26), 0.66 (95% CI 0.38-1.16) for the same categories of alcohol intake.

Scherr et al (1992) in another study in elderly people who did not have diabetes, supported the findings of these studies. The study found a significantly lower total and cardiovascular mortality for low (<28.4g) to moderate (≥28.4g) consumers of alcohol compared to nondrinkers. Three population based cohorts of men and women (aged 65 years or older) without diabetes were studied. The RR of low to moderate consumption of alcohol was 0.7 (95%, CI 0.6-0.8) in East Boston and 0.6 (95%, CI 0.5-0.8) in New Haven compared with non-drinkers. For cardiovascular mortality, the RR was 0.6 in East Boston and 0.5 in New Haven. No significant differences were found between non-consumers and consumers of alcohol in Iowa. Also, no significant associations between alcohol consumption and cancer mortality were found for any of the populations. These data suggest that the relationship between low to moderate alcohol consumption and reduced total and cardiovascular mortality found in middle age, also occurs in elderly populations.

Other Evidence

The effects of moderate alcohol intake include beneficial effects on insulin resistance, HDL cholesterol, platelet aggregation, and fibrinolysis (Bell, 1996). Due to the high risk of IHD in people with diabetes, the use of a moderate amount of alcohol should not be discouraged. However, this is not to suggest that current abstainers start drinking alcohol (Binns, 1999). The *NHMRC Dietary Guidelines for Older Australians* recommend an alcohol intake of one to no more than two standard drinks per day (Binns, 1999), where one standard drink is defined as 285ml of beer, 100ml of table wine, 60ml of port or fortified wine and 30ml of spirit or liqueur (Nutrition Australia, 2001). In order to reduce the risk of hypoglycaemia, alcohol should be consumed with carbohydrate (ADA, 2002).

Smoking increases the risk of macrovascular disease in people with diabetes

NHMRC Gradeable Evidence

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There is little information on smoking as a risk factor for complications specifically in elderly people with Type 2 diabetes.

Although the influence of diabetes itself on the risk of CVD is substantial, the classical risk factors, including smoking, are of major importance in determining the risk of CVD in people with diabetes. One of the largest population studies reporting the importance of CVD risk factors in people with Type 2 diabetes was the Multiple Risk Factor Intervention Trial (Stamler et al, 1993). This trial, which involved twelve years of follow-up in 347,978 men (aged 35-57 years) of whom 5,163 were taking medication for diabetes, confirmed an independent effect of diagnosed diabetes which increased the risk of the development of CVD three-fold (Stamler et al, 1993). In addition to this baseline risk attributable to diabetes *per se*, the risk of death from CVD was higher for men with diabetes compared with non-diabetic men at every age stratum, ethnic background and risk factor level including cholesterol, blood pressure and smoking. The effect of each individual risk factor was additive to the effect of diabetes, an increase in each risk factor increasing the absolute risk of CVD more steeply than in non-diabetic men (Stamler et al, 1993). In the United Kingdom

Prospective Diabetes Study (Turner et al, 1998) the standard risk factors of LDL cholesterol, HDL cholesterol (negatively correlated), hypertension and smoking were confirmed as risk factors for CHD, in addition to HbA_{1c}. The estimated hazards ratios for the upper third relative to the lower third of each risk factor group were 2.26 (CI 1.7-3.0) for LDL cholesterol, 0.55 (CI 0.41-0.73) for HDL cholesterol, 1.52 (CI 1.15 2.01) for HbA_{1c}, 1.82 (CI 1.34 - 2.47) for systolic blood pressure and 1.41 (CI 1.06 to 1.88) for smoking (Turner et al, 1998). In the Non-Insulin Dependent Diabetes Patient Outcomes Research Team (NIDDM PORT) study the standard CVD risk factors of age, hypertension, cigarette smoking and total/HDL cholesterol ratio were associated with prevalent CVD (Meigs et al, 1997). The Nurses' Health Study assessed the relationship between cigarette smoking and mortality in 7,401 women (mean age 62 years), 1,752 with Type 2 diabetes at baseline and 5,649 who developed diabetes during 20 years of follow-up (Al-Delaimy et al, 2001). Of the group, 724 deaths were reported during the period. After adjusting for age, history of high blood pressure and high cholesterol, and other cardiovascular risk factors, and compared with people who had never smoked, the RR of mortality was 1.31 (CI 1.11-1.55) for past smokers, 1.43 (CI 0.96-2.14) for current smokers of 1-14 cigarettes/day, 1.64 (CI 1.24-2.17) for current smokers of 15-34 cigarettes/day, and 2.19 (CI 1.32-3.65) for current smokers of ≥35 cigarettes/day (p for trend=0.0002). Women with Type 2 diabetes who had stopped smoking for ≥10 years had a mortality RR of 1.11 (CI 0.92-1.35) compared with women with diabetes who had never smoked.

In addition to the risk of CVD, smoking is an independent risk factor for the progression of a higher albumin excretion rate in people with Type 2 diabetes (Jerums et al, 2002).

There is little information available about the effects of smoking cessation on CVD risk, or the effectiveness of smoking cessation programs in achieving abstinence in people with Type 2 diabetes. In order to minimise the risk of CVD, all elderly people with diabetes should be encouraged to cease smoking.

Medications

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Background

Diet and exercise remain the cornerstone of management for Type 2 diabetes, with the aim of achieving and maintaining ideal body weight and reversing potentially damaging metabolic consequences of diabetes. In general, if an average of 3 months of diet and exercise intervention fail to achieve optimal glycaemic control, then pharmacological treatment should be commenced.

Pharmacological treatment, including oral medications and insulin, either alone or in combination, requires special consideration in the elderly. These include age-related physiological changes, overall health status and comorbidities, ability to self-care, and risk of drug interactions if the person is taking multiple medications. Few long-term studies have specifically involved older people and none have attempted to assess the benefits of pharmacological intervention in the frail elderly.

Regular assessment is required to identify the development of contraindications for oral therapies. Hypoglycaemia is one of the major side effects of concern in the elderly because it

may precipitate a serious event, such as myocardial infarction or stroke. Therefore, in the elderly avoiding hypoglycaemia and other adverse drug reactions is as important as achieving optimal glycaemic control.

Since hypertension and dyslipidaemia are risk factors for diabetes micro- and macrovascular complications which are common in the elderly, antihypertensive and lipid-lowering agents are part of diabetes management strategies. Similarly these agents should be used with consideration of their metabolic effects, interaction with other medications and side effects.

Glycaemic control

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Glycaemic control can be effectively improved in elderly people with Type 2 diabetes with a variety of antidiabetic medications used singly or in combination

NHMRC Gradeable Evidence

Metformin alone

Metformin is used extensively both as monotherapy and in combination with other antidiabetic agents and its effectiveness has been demonstrated in the elderly.

In a 24-week randomised double blind crossover study, Josephkutty and Potter (1990) compared the efficacy, metabolic control and side effects of Metformin and Tolbutamide in 20 elderly people (aged 65-94 years) with diabetes. All people who had FPG >8.0mmol/L or RBG >15.0mmol/L were randomly assigned to Metformin or Tolbutamide at an initial dose of 500 (1 tablet) –2000 (4 tablets) mg/day, depending on the previous treatment level; and dosage was increased gradually to a maximum of 6 tablets with the aim of achieving an FPG <8.0mmol/L and an HbA_{1c} <10%. A reduction in body weight was observed with Metformin (-2.0kg) compared with an increase with Tolbutamide (+ 1.6kg; p=0.001 for the difference). After 12 weeks, FPG changed from 8.0±2.1mmol/L to 9.1±2.8mmol/L in the Metformin group, while FPG was the same as before treatment, 8.3±2.8mmol/L in the Tolbutamide group. HbA_{1c} changed from 10.2% to 10.8% in the Metformin group, 10.1% to 10.0% in the Tolbutamide group. No differences were found between groups in FPG, HbA_{1c}, fasting insulin levels, urea, liver function, and cholesterol or triglyceride levels. Use of Metformin was associated with an increased incidence of gastrointestinal side effects, however these were only short term and did not prevent participants from completing the study. Therefore, the effects of Metformin and Tolbutamide were similar except for weight loss.

Sulphonylureas alone

Rosenstock et al (1993) compared the efficacy and safety of Glyburide and Glipizide in 139 people aged ≥65 years over 4 months. Seventy participants were randomly assigned to the Glyburide group and 69 to the Glipizide group. During a 4 to 8 week titration phase, doses were adjusted to obtain optimal glycaemic control (FPG <8.9mmol/L). The mean dose of Glyburide (8.5mg/d) was approximately half that of Glipizide (15.4mg/d) at the end of the maintenance period. Glyburide decreased mean FPG levels from 11.0mmol/L to 8.0mmol/L after 8 weeks (p≤0.001), while Glipizide decreased mean FPG levels from 10.6mmol/L to 8.3mmol/L (p≤0.001). Mean HbA_{1c} levels fell from 5.7% to 5.5% in the Glyburide group (p≤0.05), and 5.8% to 5.6% in the Glipizide group (p=NS) at the end of titration,n and there

was no change in HbA_{1c} during the maintenance period. There were 10 adverse events in the Glyburide group and 8 in the Glipizide group. Hypoglycaemia was noted in three people taking Glyburide and one taking Glipizide.

In a crossover trial (Brodows, 1992), 21 elderly people (mean age 70 years) with Type 2 diabetes were randomised into two groups to take Glyburide or Glipizide for 8 weeks in order to achieve a fasting plasma glucose <7.8mmol/L, or until a maximum dose of 20mg/day was reached. HbA_{1c} levels did not differ between the two groups at the end of the treatment period (6.06±0.18% in Glipizide vs. 6.12± 0.21% in Glyburide). Mean daily dose was 11.9mg in the Glipizide group, and 8.4mg in the Glyburide group. Overall, 7% of the home SMBG readings were <4.5 mmol/L in the Glipizide group, compared with 11% during Glyburide treatment.

The Diamicron MR Study Group (2000) reported the efficacy and safety of Diamicron MR and Diamicron in a double-blind 12-month randomised control trial of 800 people with Type 2 diabetes (310 were aged ≥ 65 years). Participants who were previously treated with diet for 3 months with or without oral antidiabetic drugs, were randomised to receive either once-daily Diamicron MR (30-120 mg/day) or twice daily Diamicron (80-320mg/d) (where 30mg of Diamicron MR = 80mg of Diamicron). Baseline characteristics were comparable between the two treatments groups and 45% of elderly people had impaired renal function (creatinine clearance 20-80ml/min). After 10 months, the difference between treatments was very small: 0.08% for HbA_{1c}, and 0.14mmol/L for FPG. Diamicron MR was as effective as Diamicron in terms of HbA_{1c} ($p<0.001$) and FPG ($p<0.001$). The glycaemic control in elderly people with impaired renal function was similar to that in the whole study population. During a 2-month period of switching from Diamicron to Diamicron MR, the glycaemic control remained stable and comparable between the groups. Few people experienced symptoms of hypoglycaemia, with no difference between the groups: 5.2% in Diamicron MR group and 4% in Diamicron group. Among 310 elderly people, 1.4% in Diamicron group and 1.2% in Diamicron group experienced hypoglycaemia. This study concluded that Diamicron MR given once daily, was at least as efficient as Diamicron, and can be safely administrated to elderly people.

Insulin

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The Veterans Affairs Cooperative Study (Abraira et al, 1995) in people with Type 2 diabetes was a feasibility trial to evaluate the impact of intensive treatment, including multiple daily insulin injections, on glycaemic control and complications. Seventy five people with a mean age of 60 years went through a 4-step plan in order to achieve HbA_{1c} levels as close to normal (5.1%) as possible and attempted to attain a normal mean FPG level of 4.4 -6.4mmol/L and preprandial glucose levels of <7.2mmol/L. The four steps were 1) bedtime insulin, 2) bedtime insulin plus daytime Glipizide, 3) twice daily insulin and 4) multiple daily insulin injections. The intensive group was compared with a control group of 78 people who received standard treatment of one or two injections of insulin daily aiming to avoid diabetes symptoms, excessive glycosuria, or overt hypoglycaemia. The mean duration of follow-up was 27 months. There were no significant differences in baseline characteristics between the two treatment arms. After 6 months, mean HbA_{1c} in the intensive group was at or below 7.3% and remained 2% lower than the control group for the duration of the study ($p <0.001$). FPG was reduced to close to the normal range from 3 months onward in the intensive group and changed little in the control group ($p<0.0001$). The daily mean insulin doses increased in both groups but were significantly higher in the intensive group ($p<0.001$). At the end of the first year, 85% were in step 1 or 2 and 15% in step 3 or 4. Most of the decrease in HbA_{1c} occurred with a single dose of bedtime intermediate insulin. The addition of Glipizide resulted in an additional small fall in HbA_{1c}. Since the aim of this study was to further lower HbA_{1c}, the

majority went on to to receive two or more doses of insulin by the end of the study. The incidence of mild or moderate hypoglycaemia was higher in the intensive therapy group (16.5/patient year) compared with standard therapy (1.5/patient year) ($p<0.001$).

Birkeland et al (1996) evaluated the efficacy of insulin or Glibenclamide treatment in achieving an HbA_{1c} of 7.5% in 36 people (mean age 59 years) with Type 2 diabetes in a randomised controlled trial over a 42-month period. Insulin treatment resulted in a reduction in mean HbA_{1c} levels from 9.1% to 8.2% ($p<0.05$) after 42 months. In contrast, Glibenclamide treatment resulted in an increase in HbA_{1c} levels from 8.5% to 10.2%. 11 out of 18 people in the Glibenclamide treatment group had to be switched to insulin treatment due to increasing hyperglycaemia ($HbA_{1c}>10\%$). Mean body weight increased by 7.2kg in the subjects allocated to insulin during the study period. Insulin was more effective than Glibenclamide treatment in controlling hyperglycaemia and once glycaemia improved, it did not deteriorate over 42 months in the insulin treated group.

Wolffenbuttel et al (1996) compared three different insulin regimens in 95 elderly people (mean age 68 years) with poorly controlled Type 2 diabetes despite diet and maximal dose of oral hypoglycaemic agents (15mg Glibenclamide, or in 29 people, Glibenclamide plus Metformin) over a six-month period. The first group received a twice-daily injection of premixed insulin (Mixtard 30/70). The second group received a combination of NPH insulin administered at bedtime with Glibenclamide during the day. The third group received a combination of NPH insulin before breakfast with Glibenclamide during the day, but if bedtime blood glucose levels exceeded 10mmol/L, a second injection of NPH insulin before dinner was added. After six months, FPG of the whole study population decreased from 14.1mmol/L to 8.3mmol/L ($p<0.001$) and HbA_{1c} fell from 11.0% to 8.3% ($p< 0.001$). Subjects in the twice-daily insulin group were more likely to achieve HbA_{1c} <8.0%, but they also had the highest insulin dose among all groups. One-third of subjects starting with one insulin injection daily needed a second injection to achieve better glycaemic control. Moderate weight gain was observed in all 3 groups (all $p<0.05$ vs baseline value). One episode of severe hypoglycaemia was observed during the study period. Combined insulin and sulphonylurea was almost 20% more expensive than twice-daily insulin.

Coscelli et al (1992) evaluated the safety and efficacy of self-mixed insulin and pre-mixed insulin in 64 elderly people (mean age 67) with Type 2 diabetes. Participants were randomly assigned to self-mixed insulin or pre-mixed insulin for 8 weeks, then crossed over for a further 8 weeks. There were no differences in glycaemic control or the number of hypoglycaemic episodes. However, there was a reduction in accuracy in the self-mixed insulin group ($p<0.001$) and an increase in errors and increased difficulty preparing insulin in the self-mixed insulin group ($p<0.002$, $p<0.001$, respectively).

A pseudo- randomised controlled trial assessed the effectiveness of daily injections of insulin in 22 elderly people with diabetes aged 50-88 (mean 67 years) compared with a control population continuing oral hypoglycaemic therapy (Tindall et al, 1988). Participants were initially allocated to insulin therapy or control group according to FBG values, and then those allocated to insulin therapy were randomised to receive Humulin Zn insulin or Neulente insulin. After 6 months of follow up, there was a reduction in HbA_{1c} with both Humulin Zn insulin (from 13.2% to 10.6%) and Neulente insulin (from 13.1% to 11.2%) ($p<0.02$ for both). However, postprandial blood glucose decreased only in participants taking Neulente insulin ($p<0.02$). There was a similar reduction in both HbA_{1c} and postprandial glucose values in the control group at 2 months ($p<0.05$ and $p<0.01$, respectively), but after 6 months

this only remained significant for the postprandial blood glucose ($p<0.001$). The majority of patients on insulin reported a daily injection of insulin more convenient than remembering to take tablets. These results demonstrate that a daily injection of insulin was sufficient to reduce both HbA_{1c} and postprandial blood glucose levels over 6 months in elderly people with Type 2 diabetes.

Insulin therapy has also been associated with improved treatment satisfaction. A study by Tovi and Engfeldt (1998) randomised 35 elderly people (mean age 75) with Type 2 diabetes to insulin therapy or treatment with sulphonylurea for one year, in order to assess the effects of improved metabolic control on patient well-being and diabetes symptoms. A reduction in HbA_{1c} (from 9.3% to 7.2% at 6 months, to 7.3% at 12 months) and FBG (from 13.8mmol/L to 9.0mmol/L at 6 months, to 9.8mmol/L at 12 months) was observed in the insulin treated group after 6 and 12 months ($p<0.001$ for all) compared with no change for those on sulphonylurea therapy. In addition, in the insulin treated group, there was an increase in satisfaction with treatment ($p<0.05$) and no change in the number of hypoglycaemic episodes at 12 months compared with baseline. However, significant weight gain was noted in the insulin group ($p<0.01$) compared with weight loss in the sulphonylurea group ($p<0.05$) at 12 months. There were no differences between groups or within groups (at 12 months compared with baseline) for well-being scores or symptom reduction.

Reza et al (2002) also assessed the effects of insulin therapy on patient well being, treatment satisfaction and mood, and carer strain in 40 subjects aged >65 years. All participants had poor glycaemic control (HbA_{1c} 13.2±2.0%) at baseline. Insulin treated participants received either twice daily isophane or premixed soluble/isophane insulin, while control participants were treated with Gliclazide, Metformin and Acarbose. There was an increase in SF36 scores for emotional, physical, mental health and vitality domains, following 4 weeks of insulin treatment ($p<0.05$, $p<0.05$, $p<0.05$, $p<0.001$, respectively), in combination with an increase in diabetes treatment satisfaction scores at 4 and 12 weeks of follow up ($p<0.01$ for both). In addition, insulin therapy resulted in a reduction in the perceived hyperglycaemia score, depression scores and carer strain at 4 weeks ($p<0.05$ for all) and at 12 weeks ($p<0.05$, $p<0.01$, p=NS, respectively).

Other non-gradeable studies indicate that several factors should be considered when prescribing insulin therapy in elderly people (Davis and Brown, 1999; Ruoff, 1993; Kreinhofer et al, 1988). These include, reduced awareness of symptoms of hypoglycaemia, altered drug ultilisation and drug interactions, comorbidities, functional impairment, nutritional issues and age-related learning characteristics. The initial insulin dose should be small and it should be remembered that learning to inject insulin is challenging for the elderly. Errors may occur due to decreasing dexterity, poor eyesight, ignorance, forgetfulness, not understanding the reasons for insulin injections and their relationship to foods and being unable to evaluate the risk of hypoglycaemia.

Combination therapy Index

Many combinations of antidiabetic medications have been used in people with diabetes, including the elderly.

In a 4-month study (Calle-Pascual et al, 1995), 35 people with Type 2 diabetes on sulphonylurea treatment were allocated to three treatment groups. Group A (mean age 67.8 years) with HbA_{1c} of 9.1±1.6% received 0.3 IU/kg of protracted Zn-insulin at 10-11pm, Group B (mean age 64.3 years) with HbA_{1c} of 9.2±1.6% received sulphonylurea plus

Metformin 850 mg/d, and Group C (mean age 64.3 years) with HbA_{1c} of 9.5±2.4% received sulphonylurea plus Acarbose 300mg/day. HbA_{1c} decreased significantly in the three groups (Group A: 9.1±1.6% vs. 7.3±0.6%; Group B: 9.2±1.6% vs. 7.5±1.4%; Group C: 9.5±2.4% vs. 8.6±1.9%) (all $p < 0.05$; A and B v C, $p < 0.05$; A v B, p=ns). Body weight increased in the insulin group and decreased in the other two groups (A: +1.8±2.9%; B: -1.2±1.9%; C: -0.6±1.6%; A v B and A v C, $p<0.05$; B v C, p=ns). Blood pressure decreased significantly in the Metformin group. HDL cholesterol increased ($p<0.05$) and triglyceride levels decreased ($p<0.05$) in the insulin group. The study concluded that sulphonylurea combined with either insulin or Metformin results in better glycaemic control than Acarbose plus sulphonylurea. Metformin combined with sulphonylurea offered the additional advantages of control of blood pressure and body weight.

The effects of increasing sulphonylurea dosages or adding Metformin in poorly controlled (HbA_{1c} > 9%) elderly people (> 70 years) with Type 2 diabetes was evaluated by Gregorio et al (1999) in an 18-month study. Eighty five participants were randomly assigned to increasing doses of sulphonylurea (Glibenclamide 7.5 to 12.5-15mg/day or Gliclazide 120 to 200-240mg/day), while in 89 subjects, Metformin (850-1700mg/d) was added to the sulphonylurea. Similar improvements in glycaemic control were observed over a 3-month period. In the sulphonylurea treated group FPG decreased from 14.2mmol/L to 9.9mmol/L and HbA_{1c} fell from 10.3% to 8.7%. In the sulphonylurea plus Metformin group FPG decreased from 14.6mmol/L to 9.1mmol/L and HbA_{1c} fell from 10.3% to 8.8% ($p < 0.0005$ for all results). In addition, LDL cholesterol decreased ($p<0.05$) and HDL cholesterol increased ($p<0.02$) in the Metformin group. No changes in liver or renal function and no serious adverse effects were observed. Fasting lactate concentrations were unchanged in the Metformin treated group.

The effects of substituting maximal sulphonylurea medication with a single injection of human zinc insulin taken either at bedtime or in the morning was studied in a group of elderly people (mean age 77 years) with Type 2 diabetes by Niskanen et al (1992) in a randomised, placebo controlled prospective crossover study of eight months duration in people who were poorly controlled (mean diurnal glucose 17.4±0.9mmol/L and HbA_{1c} 11.8±0.7%) on oral hypoglycaemic agents. After two-month treatment with either bedtime (BTI) or morning insulin (MI), low dose Glibenclamide (GL 3.5mg/d) was given for an additional two months. Both insulin regimes decreased mean diurnal blood glucose (from 17.4±0.9mmol/L to 9.2±1.2mmol/L in MI+GL group, to 10.5±1.1mmol/L in BTI+GL group) and HbA_{1c} values (from 11.8±0.7% to 8.5±0.5% in MI+GL group, to 10.5±1.1% in BTI+GL group) to a similar extent (vs. baseline, $p< 0.01$ - 0.05), but with a lower daily insulin dose with bedtime insulin (0.30IU/kg) compared with morning insulin (0.39IU/kg; $p< 0.01$). A further improvement in metabolic control was observed in both groups after the introduction of low dose Glibenclamide. The mean reduction in HbA_{1c} levels was 1.4% in people on bedtime insulin and 0.7% in the group on morning insulin ($p < 0.01$ and 0.05, respectively).

Quatraro et al (1991) studied the introduction of Gliclazide in 70 elderly people with diabetes poorly controlled on insulin alone. More than half (64%) had a reduction in glucose and HbA_{1c} ($p< 0.01$), but weight did not change. These results were maintained after a five-year follow-up period. A small incidence of hypoglycaemic episodes occurred, but the frequency was not significantly higher than that occurring during the previous insulin treatment, and was ameliorated by reducing the insulin dose.

α-glucosidase inhibitors

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The effectiveness and safety of Acarbose in the treatment of 1,027 older people (mean age 64 years) with Type 2 diabetes was studied by Scorpiglione et al (1999). The study population was assigned to three different groups according to the physician's clinical judgement - group A (n=283) Acarbose considered as an elective treatment, group B (n=250) Acarbose considered to be of uncertain benefit and group C (n=494) Acarbose deemed not to be appropriate. In group B, people were randomised either to continue their standard treatment (n=124) or to add Acarbose 100mg, 3 times daily (n=126) for one year. After one year, mean HbA_{1c} was 0.3% lower in the Acarbose group compared with the control group (p=0.07). The number of participants with HbA_{1c} below 8% increased from 31% to 44% in the Acarbose group and from 40% to 45% in the control group (p=0.058). There was a small reduction in post-prandial glycaemia in the Acarbose group (p=0.04 v control) but no difference in FPG levels. When assessed in relation to baseline HbA_{1c} levels, mean benefit of Acarbose was 0.14% in people with HbA_{1c} levels <8%, 0.28 % in those with values between 8.0% and 9.9% and 0.65% in those with values > 10 %. The study concluded that the benefits of Acarbose in an unselected population were significant but of marginal clinical relevance.

In a 2-year, placebo-controlled, double-blind study, 74 people aged 40 to 80 years insufficiently controlled by diet alone were randomized to receive Acarbose (100mg 3 times daily) or placebo (Hasche et al, 1999). Subjects requiring additional antidiabetic agents were classified as "non-responders". The main variables were comparable between the two groups at baseline except HbA_{1c} levels, which were higher in the Acarbose group than in the placebo group (p=0.04). The mean HbA_{1c} values showed similar reduction over the first 20 weeks in both groups. After this point, HbA_{1c} fell gradually throughout the study period, reaching a final value of 6.8±1.7% in the Acarbose group, while a final HbA_{1c} value of 7.4±1.0% was observed in the placebo group (p=0.024). The mean reduction in 2hour postprandial glucose was greater in the Acarbose group than in the placebo group, however this was not significant (p=0.11). During the study, 20 people (acarbose: 3 v placebo: 17) received additional antidiabetic agents giving a response rate of 89% in the Acarbose group and 47% in the placebo group (p=0.0005). Overall, adverse events were reported in 32 people (acarbose: 19; placebo: 13), with flatulence being the most common event.

In a 12-week placebo-controlled study (Willms and Ruge, 1999), 89 people with inadequately controlled Type 2 diabetes were randomised to receive Acarbose (100mg 3 times daily), Metformin (850mg twice daily), or placebo in addition to their sulphonylurea therapy to compare the efficacy and safety of Acarbose and Metformin. HbA_{1c} decreased in all three groups after 12 weeks. The decrease was greater in the two groups receiving active therapy compared with placebo, Acarbose -2.4%; Metformin -2.5 %; and placebo -1.3%, and differences between both active therapies and placebo were significant (Acarbose v placebo, p<0.01; Metformin v placebo, p <0.004). No significant difference in HbA_{1c} was seen between Acarbose and Metformin. Reduction in body weight over the treatment period was seen in all three groups and was greatest in the Acarbose group (Acarbose 3.5 kg, Metformin 1.0 kg, placebo 1.4 kg). There were no significant differences in the incidence of gastrointestinal side effects between the three groups and all regimens were generally well tolerated.

Other agents

Thiazolidinediones and Repaglinide are available in Australia, but they are not currently available through the Pharmaceutical Benefits Scheme. Their use in elderly people with diabetes has not yet been specifically evaluated. Some characteristics of these agents may

make them an attractive option for some elderly people. A recent published post-hoc analysis (Kreider and Heise, 2002) described the efficacy and safety of Rosiglitazone in elderly people (>/=70 years) with Type 2 diabetes. Eight RCTs, lasting from 12 to 52 weeks, were included in this analysis. A total of 3,127 people were randomised to Rosiglitazone 4 or 8mg/d (<70 years, n=2099; >/=70 years, n=427) or placebo (<70 years, n=497, >/=70 years, n=104). Elderly people had a longer duration of diabetes and more comorbid diseases than younger people, but the mean HbA1c and FPG were comparable between treatment groups and age groups at baseline. In both age groups, Rosiglitazone (4 or 8mg/d) reduced HbA1c and FPG compared with baseline and placebo at week 26, and no difference between age groups. Rosiglitazone was well tolerated in younger people, as well as in older people. Oedema was more common with Rosiglitazone than placebo in younger (4.3% vs. 2.4% and older (9.1% vs. 0.0%) people. Hypoglycaemic episodes occurred in <1% of people on Rosiglitazone in both age groups. Two people in the <70 year age group discontinued Rosiglitazone because of hypoglycaemia.

Hypoglycaemia is the major risk associated with antidiabetic therapy in the elderly

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A 4-year cohort study investigated the incidence and risk factors for serious hypoglycaemia in an older population (mean age 78±7 years) treated with insulin or sulphonylurea (SU) (Shorr et al, 1997a). The study identified 586 people with a first episode of serious hypoglycaemia (defined as hospitalization, emergency department admission, or death associated with hypoglycaemic symptoms and a concomitant blood glucose level of less than 2.8 mmol/L) during 33,048 person-years of insulin or SU use. The overall incidence of serious hypoglycaemia was 1.81 (CI 1.67 – 1.95) per 100 person-years of hypoglycaemic agents use; 1.23 (CI 1.08 – 1.38) in SU users, 2.76 (CI 2.47 – 3.06) in insulin users, and 3.38 (CI 1.50 – 5.26) among users of both. Recent hospital discharge was the strongest predictor of subsequent hypoglycaemia in older people with diabetes. The rate of serious hypoglycaemia in the first 30 days after discharge from hospital was 6.51 (CI 5.24 – 7.77) per 100 person-years. Compared with people aged 65-70 years, people aged 80 or over had a higher RR of developing hypoglycaemia (RR 1.8, CI 1.4 – 2.3). People using 5 or more concomitant medications, and people who were new to hypoglycaemic drug therapy, were also at higher risk of hypoglycaemia (RR 1.3, CI 1.1 – 1.5; RR 1.4, CI 1.0 – 1.9; respectively). Based on these findings, risk factors for severe hypoglycaemia were recent hospital admission, advanced age (> 80 years), and a large number of concomitant medications.

Glibenclamide can cause severe and prolonged hypoglycaemia (blood glucose <2.8 mmol/L) in elderly people with Type 2 diabetes. Sonnenblick and Shilo (1986) reported that 13 people with a mean age of 76 years who were taking Glibenclamide, developed severe prolonged hypoglycaemia that lasted longer than 12 hours, despite treatment with periodic injections of hypertonic glucose. In two people, hypoglycaemia continued for more than 60 hours despite continuous infusions of 5 or 10% glucose. All of these people were older than 68 years, and contributing factors included renal failure and congestive heart failure.

Tessier et al (1994) compared the frequency of hypoglycaemic events of Glibenclamide and Gliclazide in 22 elderly people with Type 2 diabetes. Glycaemic control was equivalent and HbA_{1c} similar at 6 months (Glibenclamide 7.4±0.2%; Gliclazide 7.9±0.5%). Hypoglycaemic events were significantly more frequent with Glibenclamide than with Gliclazide: 17 v 4 ($p<0.01$).

Shorr et al (1996) reported on 255 people with a first episode of serious hypoglycaemia during 20,715 person-years of sulphonylurea use. The crude rate (per 1000 person-years) of serious hypoglycaemia was highest in Glyburide users, 16.6 (95% CI 13.2-19.9) and lowest among users of Tolbutamide - 3.5 (95% CI 1.2-5.9). Glipizide users had an intermediate rate of hypoglycaemia - 8.6 (95% CI 5.2-12.0).

Burge et al (1998) dtudied the risk of developing sulphonylurea-induced hypoglycaemia in 52 elderly people (mean age 65 years) with Type 2 diabetes. Subjects were randomly assigned to Glyburide or Glipizide. Each person participated in three 23-hour fasting studies after the sequential administration of one week of placebo, one week of 10mg and one week of 20mg of the assigned sulphonylurea. No hypoglycaemia (defined as plasma glucose <3.3mmol/L) was observed during 156 fasting studies. Plasma glucose level decreased to 4.0mmol/L for a 20mg dose of Glyburide compared with 8.3mmol/L for placebo and to 5.8mmol/L for a 20mg dose of Glipizide, compared with 8.7mmol/L for placebo.

Holstein et al (2001) examined the incidence of severe hypoglycaemia in people with Type 2 diabetes (mean age 79 years). Hypoglycaemia was defined as the requirement for intravenous glucose or glucagon injection, and blood glucose value of <2.8mmol/L. Of the 145 episodes of severe hypoglycaemia, 100 episodes involved insulin therapy and 45 with sulphonylurea therapy. Glimepiride induced fewer episodes than Glibenclamide (6 vs. 38 episodes respectively), and one episode occurred with a combination of the two agents. The incidence of severe hypoglycaemia was 0.86/1,000 person-years for Glimepiride and 5.6/1,000 person-years for Glibenclamide. Forty five people who experienced hypoglycaemia had an average age of 79 years (CI 75.2-82.6) and marked comorbidities, 62% had a creatinine clearance of <60 ml/min; 36% had cardiac failure and 29% had CHD. In addition, this group was found to have HbA_{1c} value of 5.4% (CI 5.1-5.7), indicating that their diabetes was well controlled.

Summary

Hypoglycaemia is the most common and serious side effect associated with the use of sulphonylurea and insulin, and might precipitate stroke, MI, injury and death. Hypoglycaemia is considerably more common with treatment with a long-acting sulphonylurea such as Glibenclamide (Glyburide) than Gliclazide. The possibility of hypoglycaemia should be considered when prescribing antidiabetic medications in the elderly, and they should be carefully monitored for the occurrence of hypoglycaemia after commencing antidiabetic therapy.

Lactic acidosis is a rare side effect of Metformin therapy

NHMRC Gradeable Evidence

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Lactic acidosis is a life-threatening condition characterised by low arterial pH (<7.35) and elevated arterial lactate levels (>5.0mEq/L). Although rare it is the most serious side effect of Metformin.

Selby et al (1999) investigated the change in HbA_{1c} at 6 months after starting Metformin (up to 2,550mg daily), and hospitalisation rates for lactic acidosis among 9,875 people during a 20-month period. Of the group, 81% had baseline HbA_{1c} ≥8.5%. People starting Metformin had significantly lower HbA_{1c} 6 months later ($p<0.0001$). Compared with those aged <50years, older people were more likely to achieve a significant reduction in HbA_{1c} - OR 1.92 [CI 1.49-2.46] and 3.08 [CI 2.13-4.43] for people 50-69 years and ≥ 70 years, respectively. Of the group, 1.3% had serum creatinine >1.5mg/dl at baseline, and they were more likely to have Metformin stopped (hazard ratio: 2.45 [CI 1.79-3.35]). During 4,502 person-years on Metformin, only one probable case of Metformin-related lactic acidosis was identified.

Chalmers et al (1992) studied 70 people (mean age 63±9.9 years) with Type 2 diabetes treated with Metformin (45 as monotherapy and 25 in combination with a sulphonylurea) over a mean of 5 years. All participants had normal renal and hepatic function before commencement of Metformin. Older participants (>65 years) had a significantly higher serum urea and creatinine concentration ($p<0.001$) than younger participants (≤65 years), but were still within the reference range. There were no differences on blood lactate and plasma Metformin between older and younger participants, and no correlation between plasma Metformin or blood lactate and age was found. During the 3-month study period, 3 people

(one had PVD, one was taking non-steroidal-anti-inflammatory agents, and one was aged 70 years) developed renal impairment with raised serum creatinine since starting Metformin therapy, confirming the need to regularly monitor renal function in the elderly.

Davis et al (2001) recruited 272 people (mean age 66 years) with diabetes from the Fremantle Diabetes Study to assess the association between Metformin therapy and fasting plasma lactate. Of the 272 people, 182 (67%) were taking Metformin with a mean dose of 1.5g/day. HbA_{1c} was higher among people taking Metformin (7.6%) than those who were not taking Metformin (6.8%) ($p<0.001$). Fasting plasma lactate was higher (1.86mmol/L v 1.58mmol/L, $p<0.001$) in people taking Metformin, and more than one third of the total sample had a raised fasting plasma lactate concentration (>2.0mmol/L). In a regression analysis, plasma glucose and BMI were two strong positive determinants of the fasting plasma lactate ($p<0.001$). After adjusting for both plasma glucose and BMI, the difference between the mean plasma lactate fell from 0.28mmol/L to 0.16mmol/L This study showed that Metformin therapy was associated with an increase in the fasting plasma lactate concentration in elderly people with Type 2 diabetes, but levels generally remained below those commonly associated with lactic acidosis.

Despite the rare occurrence of lactic acidosis, several clinical conditions seem to predispose to its development and there is evidence that these are often overlooked. In a retrospective cohort study, 204 people who received at least one dose of Metformin during 263 inpatient admissions (some were admitted more than once), were investigated for the risks of lactic acidosis with Metformin therapy (Calabrese et al, 2002). Renal dysfunction (specifically serum creatinine ≥1.5mg/ml in males and ≥1.4mg/ml in females), CHF requiring pharmacological treatment, acute or chronic metabolic acidosis and using intravascular iodinated contrast were classified as absolute contraindications to Metformin use, while age ≥80 years, clinical or laboratory evidence of hepatic disease, presence of any condition associated with hypoxemia, chronic obstructive pulmonary disease, acute MI, or dehydration) were determined as precautionary conditions. The results showed that despite the presence of an absolute contraindication or a precautionary condition, the prevalence of continuing Metformin therapy was 75% for elevated serum creatinine, 100% in people aged ≥ 80 years, 42% in people with elevated aspartate aminotransferase or alanine aminotransferase, and 11% in people with chronic obstructive pulmonary disease.

Poor adherence to diabetes medication is a problem in elderly people

In elderly people with comorbidities and polypharmacy, impaired cognitive function, or those with low socio-economic status, adherence to diabetes medications might be a problem. Poor adherence can be a major obstacle to achieving optimal glycaemic control in the elderly.

Pullar et al (1988) compared compliance with prescribed tablets in 179 people with Type 2 diabetes (mean age 64 years) who were randomly allocated to take 2mg Phenobarbital once daily (OD, n=59), or 2mg twice daily (BD, n=60) or 2mg three times daily (TID, n=60) for 28 days. Phenobarbital was used as the indicator because it had little inter-individual and even less intra-individual variation in its pharmacokinetics in adults, and there was a good linear relationship between dose and steady plasma concentration. Inadequate compliance was defined as evidence of missing some study tablets, a value for compliance by tablet count <85%, or a phenobarbital level/dose ratio (LDR) <85% of the age-related lowest values of normal volunteers (<10.1 for those >50 years). Participants had two interviews during the study: one at baseline, in which the physician recorded all medications taken and the person's level of compliance. The second interview was conducted after 28 days, and each person was asked whether they had taken all the study tablets and all their diabetic agents. Phenobarbital concentration was also measured. People in three groups were comparable in their mean age, degree of diabetes control (good, moderate and poor), and physicians' impression of their compliance. When inadequate compliance was assessed by a tablets count, there was no difference found between the three groups (2 in OD vs. 4 in BD vs. 4 in TID, $p>0.05$). Twenty people in OD group, 24 in BD group and 33 in TID group had LDRs <85% of the lowest value of normal volunteers ($p<0.05$). In addition, the mean LDR in TID group was significantly lower than in OD group ($p<0.01$) or in BD group ($p<0.05$). Mean compliance by tablet count was 100.4+/-9.3%, 95.3+/-14.5%, and 95.2+/-10.0% for OD, BD, and TID group, respectively (OD vs. BD, $p<0.05$; OD vs. TID, $p<0.05$). In conclusion, compliance rates with the once daily and twice daily regimens were highest and similar. Both were better than a three-time-daily regimen.

Depression is common among people with chronic medical illness, especially with diabetes. Ciechanowski et al (2000) found that there was an association between severe depressive symptoms and poorer adherence to diet and medication, and functional impairment in diabetic subjects. Three hundred and sixty seven people with diabetes (both Type 1 and Type 2) were divided into three groups according to depressive symptom severity tertiles (based on HSCL-90-R depression subscale scores): low <0.5 (n=119), medium 0.5-1.0 (n=119), or high >1.0 (n=121). People with higher depressive symptom severity tertile were more likely to be younger (high vs. low, 59.0 vs. 63.5 years, $p=0.01$), have a higher diabetes knowledge score (high vs. low, 78.2 vs. 68.2, $p<0.001$; medium vs. low, 74.8 vs. 68.2, $p=0.01$), and had one or more diabetes complications (high vs. low, 62% vs. 37%, $p<0.001$; medium vs. low, 55% vs. 37%, $p=0.01$). In terms of diabetes self-care, depressive symptom severity was significantly associated with worse adherence to OHA regimen (defined as the percentage of days of nonadherence to OHA therapy, high vs. low: 14.9% vs. 7.1%, $p<0.05$), as well as with less adherence to dietary advice of diet type and amount (high and medium vs. low, $p<0.001$). A nonsignificant increase in HbA_{1c} level (7.9±1.5% vs. 7.6±1.4% vs 7.4±1.4%) was also observed. Depressive symptom severity had a significant impact on physical (high vs. low, $p<0.001$; medium vs. low, $p<0.001$) and mental function (high vs. low, $p=0.006$; high vs. medium, $p<0.001$).

In a retrospective cohort study, Donnan et al (2002) examined the patterns and predictors of adherence in people with Type 2 diabetes receiving a single oral hypoglycaemic agent. Of the 2,920 subjects (mean age 68 years) identified during a 3-year period, adequate adherence (≥90%) was only found in 31% (CI 28-33%) of those on sulphonylurea, and 34% (CI 30-38%) of those on Metformin. Those with better adherence tended to be younger and have a shorter duration of diabetes. There were linear trends of poorer adherence with increasing daily number of tablets for both sulphonylurea (p=0.001) and Metformin (p=0.074). In addition, there were highly significant trends of decreasing adherence with the number of co-medications for sulphonylurea alone after adjustment for other factors (p=0.0001).

Poor adherence to diabetes medication can be reduced by calendar blister packs. Simmons et al (2000) conducted an 8-month randomised controlled double-blind study to assess the impact of the use of calendar blister packs on glycaemic control in 68 people (mean age 58 years) with poor glycaemic control (HbA_{1c} >9%). The calendar blister pack group (n=36) received a special kit including the medication within a calendar blister pack in a labeled box and instructions on how to take the medication. The control group (n=32) received the same packaging but with the medication contained within the usual containers. The two groups were well matched for age, sex, ethnicity and HbA_{1c}. After 8 months, HbA_{1c} was reduced by 0.95±0.22% in the calendar blister pack group and 0.15±0.25% in the control group (p=0.026). The new packaging was found to be useful by 77% of those with calendar blister packs and 27% of the control group (p<0.001).

Blood Pressure

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Background

The potential benefits of antihypertensive treatment in people with Type 2 diabetes have been reviewed in the *National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus, Diagnosis and Management of Hypertension*. Modification of lifestyle factors such as obesity, physical inactivity, excessive dietary sodium and/or alcohol intake should be addressed before starting antihypertensive therapy. A number of studies (Syst-Eur, 1999; HOT, 1998; NORDIL, 2000; CAPPP, 2001 STOP Hypertension-2, 1999; ALLHAT, 2000; UKPDS 38, 1998; UKPDS 39, 1998) have examined the effects of a variety of antihypertensive agents on outcomes in middle-aged people with diabetes and concluded that in those with uncomplicated hypertension, ACE inhibitors, angiotensin receptor blockers (ARB), β-blockers and diuretics can be used as initial therapy. ACE inhibitors and ARB should be used to treat people with diabetic renal disease because of their antiproteinuric effect. In order to achieve target blood pressure, combinations of antihypertensive agents are often required.

Isolated systolic hypertension (ISH) is a frequently presented hypertension pattern in the elderly (Jerums et al, 2002). ISH is defined as a systolic blood pressure ≥140mmHg and diastolic blood pressure <90mmHg (WHO-ISH, 1999). When deciding on treatment of hypertension in the elderly, ISH should be taken into consideration.

Treatment of hypertension in the elderly is associated with reduced cardiovascular events

The PROGRESS study (2001) examined the effects of a blood-pressure-lowering in 6,105 people (mean age 64±10 years) with a history of stroke or transient ischaemic attack. Subjects were randomly assigned to active treatment (n=3,051) or placebo (n=3,054). Active treatment involved the ACE inhibitor Perindopril 4mg daily with the addition of the diuretic Indapamide 2.5mg daily. Thirteen percent of participants in the active group and 12% in the placebo group had diabetes. The mean blood pressure of all participants was 147/86mmHg; and among those classified as hypertensive, the mean was 159/94mmHg and among those classified as non-hypertensive, the mean was 136/79mmHg. The primary outcome was fatal or nonfatal stroke, with a mean duration of follow-up of 3.9 years. Ten percent in the active group and 14% in the placebo group had a stroke (RR reduction 28% [CI 17-38%], $p<0.0001$). Active treatment also reduced the risk of total major vascular events (26% [CI 16-34]). Blood pressure was reduced by an overall average of 9.0/4.0mmHg among those on active treatment compared with those on placebo. In addition, when compared with placebo, active combination therapy achieved greater reduction in blood pressure (12.3/5.0mmHg) than single-drug therapy (4.9/2.8mmHg) and combination therapy reduced stroke risk by 43% (CI 30-54), while single therapy produced no significant reduction in the risk of stroke.

In the SCOPE study (SCOPE Study Investigators, 2002), 4,964 people (aged 70-89 years) with mild hypertension (SBP 160-179mmHg and/or DBP 90-99mmHg) were randomised to receive either angiotensin 1-receptor blocker Candesartan Cilexetil or placebo. The primary endpoint was major cardiovascular events defined as a combined endpoint of cardiovascular death, non-fatal MI and non-fatal stroke. The secondary endpoints focused on the effects on cognitive function and dementia, total mortality, cardiovascular mortality, MI, stroke, renal function, hospitalisation and quality of life. There was a 28% reduction ($p=0.041$) in non-fatal strokes in elderly people treated with Candesartan Cilexetil compared with placeb,o and a non-significant trend to reduced risk (11% risk reduction, $p=0.19$) of major cardiovascular events in the active treatment group. Lowering blood pressure was associated with maintained cognitive function, as measured by the MMSE. Candesartan Cilexetil was well tolerated in elderly people.

Dahlof et al (1991) reported the effects of active treatment (three β-blockers and one diuretic) and placebo on the frequency of cardiovascular events among 1,627 elderly hypertensive people (aged 70-84 years) with SBP 180-230mmHg and/or DBP 90-120mmHg. Eight hundred and twelve people were randomly allocated to active treatment and 815 to placebo, and were followed up for 65 months. Primary endpoints were stroke, MI, and other cardiovascular death. A 19.5/8.1mmHg difference in blood pressure between treatment groups was observed. Active treatment had significantly fewer primary endpoints (58 v 94, $p=0.0031$), lower morbidity and mortality from stroke (29 v 53, $p=0.0081$), and lower total mortality compared with the placebo (36 v 63, $p=0.0079$).

Two recent studies have reported that ACE inhibitors exert additional beneficial effects and slow the decline in physical function. Participants in a retrospective cohort study (Gambassi et al, 2000) had CHF and were taking either an ACE inhibitor (n=4911) or Digoxin (n=14890). 22% of Digoxin users and 27% of ACE inhibitor users had diabetes. The study compared outcomes of ACE inhibitors and Digoxin on 1-year mortality, morbidity and physical function (measured by ADL) among older people with a mean age of 85 years. The overall mortality rate among ACE inhibitor recipients was 10% less than that of Digoxin users (relative rate, 0.89, CI 0.83-0.95). The rate of physical function decline was greatly

reduced among ACE inhibitor users (RR 0.74; CI 0.69-0.80). This effect was consistent and independent of background comorbidity and baseline ADL level. Subjects who used ACE inhibitors also tended to have a slightly reduced rate of hospitalization.

In another 3-year cohort study (Onder et al, 2002), 641 older women (mean age 78.9 years) who had hypertension but not CHF were assigned to four groups: continuous users of ACE inhibitors (n=61), intermittent users of ACE inhibitors (n=133), continuous/intermittent users of other antihypertensive drugs (n=301), or never drug users (n=146). There were no significant differences across the four groups for baseline knee extensor muscle strength and walking speed. Mean 3-year decline in muscle strength in continuous users of ACE inhibitors (-1.0kg) was significantly lower than that of either continuous/intermittent users of other antihypertensive drugs (-3.7kg, p=0.016) or never drug users (-3.9kg, p=0.026), but did not differ from that of intermittent users of ACE inhibitors (-3.0kg, p=0.096). Mean 3-year decline in walking speed among continuous users of ACE inhibitors was significantly lower than that in all other groups (all $p< 0.05$). After adjustments for occurrence of stroke, congestive heart failure, and MI, these results remained unchanged, suggesting that positive effects on muscle strength were independent of cardiovascular events.

The question of increased risk of hypoglycaemia has been raised with two potentially useful classes of antihypertensives: β-blockers and ACE inhibitors. Two studies have reported that the use of ACE inhibitors was associated with increased insulin sensitivity in people with diabetes, which may precipitate severe hypoglycaemia. In a case-controlled study (Herings et al, 1995), 94 people (58% aged 60 to ≥ 75 years) with diabetes (70 on insulin, 24 on OHA) admitted to hospital for hypoglycaemia were compared to 654 people who acted as controls. With adjustment for potential confounding factors, hypoglycaemia was significantly associated with current use of ACE inhibitors (OR 2.8 CI [1.4-5.7]) and was 2.5 times more frequent among insulin users than among OHA users (OR 2.8 CI [1.2-6.4]).

Similarly, Morris et al (1997) reported that ACE inhibitor use was associated with an increased risk of admission to hospital for severe hypoglycaemia. In this case-controlled study of 6,649 people with diabetes taking insulin or OHA, 64 people (mean age 60 years) who had been admitted to hospital with hypoglycaemia were identified and 440 subjects selected from the same cohort served as controls. In the unadjusted analysis, ACE inhibitor use was associated with an increased risk of admission for hypoglycaemia, OR 3.2 (1.2-8.3, p= 0.023). In contrast, use of beta-blockers (OR 0.9 [0.3-3.3], p=0.88) and calcium antagonists (OR 1.7 [0.2-2.1], p=0.54) did not significantly affect the risk of hypoglycaemia. There was no difference in glycaemic control, serum creatinine, or the use of cardiovascular drugs between case and control groups. After adjusting for treatment, hospital care, loop diuretic use, and diabetes duration, the risk of admission for users of ACE inhibitors was still significant, with an OR of 4.3 (1.2-16.0) (p= 0.028).

In contrast, a large cohort study reported that specific antihypertensive agent therapy had little impact on the risk of hypoglycaemia in older people with diabetes (Shorr et al, 1997b). Of 13,559 elderly people with diabetes (8,368 on sulphonylurea, 5,171 on insulin), 598 people (mean age 78 years) with an episode of serious hypoglycaemia were identified during the study period. The relative risk of serious hypoglycaemia among users of antihypertensive agents ranged from 1.26 (nonselective β-blockers) to 0.80 (thiazide diuretics) compared with people not prescribed antihypertensive agents. When compared with users of nonselective β-blockers, the adjusted RR of serious hypoglycaemia ranged from 0.58 (selective β-blockers)

to 0.93 (ACE inhibitors). Although nonselective β-blockers were associated with the highest rate of hypoglycaemia, none of the findings were statistically significant.

Treatment of isolated systolic hypertension in elderly people with Type 2 diabetes improves cardiovascular outcomes

NHMRC Gradeable Evidence

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A variety of antihyptensive agents have been shown to be beneficial in improving outcomes in people with ISH. In the Systolic Hypertension in the Elderly Program (SHEP) Study (Curb et al, 1996), 4,736 elderly people with ISH including 583 with diabetes were randomised to active treatment based on a low dose of the diuretic Chlorthalidone, or to placebo. The 5-year major CVD rate was reduced by 34% with active treatment compared, with the placebo. Absolute RR with active treatment compared with the placebo was twice as great for diabetic v nondiabetic people (101/1,000 v 51/1,000).

Given the possible deleterious metabolic consequences of thiazide diuretics, Emeriau et al (2001) conducted a double-blind, randomised 12-week study in 524 people including 128 with ISH (mean age 72.4 years). Participants were randomly assigned to three parallel groups: Indapamide SR 1.5mg (n=178), Amlodipine 5mg (n=175) and Hydrochlorothiazide 25mg (n=171). There were no significant differences between treatment groups at randomisation. The mean decreases in SBP/DBP were similar in the three groups: -22.7/-11.8 mmHg for Indapamide SR 1.5mg, -22.2/-10.7 mmHg for Amlodipine 5mg, and –19.4/-10.8 mmHg for Hydrochlorothiazide 25mg, respectively ($p<0.001$). In the ISH subgroup, Indapamide SR 1.5mg demonstrated a trend to greater efficacy than Hydrochlorothiazide 25mg in reducing SBP, but this reduction was not significant (-24.7 vs –18.5 mmHg, $p=0.117$), a similar reduction was observed with Amlodipine 5mg (-23 mmHg,). The blood pressure normalisation rate (defined as DBP ≤90mmHg in the whole population, and SBP ≤160mmHg in people with ISH) was relatively high for Indapamide SR 1.5mg (75.3%), when compared with Amlodipine (66.9%) and Hydrochlorothiazide (67.3%), especially in the ISH subgroup, 84.2% vs 80.0% for Amlodipine, vs 71.4% for Hydrochlorothiazide. From a metabolic point of view, changes observed with Indapamide SR 1.5mg and Hydrochlorothiazide 25mg were mild, and mainly involved serum potassium (serum potassium 3.4-3.0mmol/L was observed in 10.1% for Indapamide SR 1.5mg and 8.2% for Hydrochlorothiazide 25mg; <3.0mmol/L in 0.6% and 2.3%, respectively) with no drug-related ECG abnormalities or uric acid levels. MMSE scores showed no impairment of cognitive function with any treatment.

Calcium channel blockers (CCBs) are effective as monotherapy in elderly people with ISH. The SystEur Study (Tuomilehto et al, 1999) compared outcomes of Nitrendipine compared with placebo in 4,695 elderly people (10.5% had diabetes) with ISH (SBP of 160-219 mmHg and DBP ≤ 95mmHg). After 2-year Nitrendipine reduced overall mortality by 55%. Among people receiving Nitrendipine, reductions in overall mortality, mortality from CVD, and all cardiovascular events were significantly greater in the diabetic group than in the nondiabetic group ($p=0.04$, $p=0.02$, and $p=0.01$, respectively).

The Swedish Trial in Old Patients with Hypertension-2 (STOP HT-2) study compared conventional antihypertensive therapy (β-blockers or diuretics) and newer therapies (ACE

inhibitors or CCBs) in 6,614 people aged 70-84 with ISH, 719 of whom had diabetes (Hansson et al, 1999). The older and newer medications achieved similar prevention of cardiovascular mortality and major events. In the subgroup of people with diabetes, there were no differences in the incidence of primary endpoints between treatment groups (conventional therapy vs. ACE inhibitor vs. CCBs).

The use of CCBs in the treatment of hypertension in people with diabetes has been controversial and this issue is reviewed in the National Evidence Based Guidelines for Diagnosis and Management of Hypertension. Studies on CCBs in diabetic hypertensive people have provided conflicting results. In systolic hypertension dihydropyridine CCB outcomes were similar to older treatments and in diastolic hypertension nondihydropyridine CCB was also as effective as older treatments. However a worse outcome in risk of MI has been reported in one study (Estacio et al, 1998) and a worse risk of combined cardiovascular outcomes in another study with the use of dihydropyridine CCBs compared with ACE inhibitors (Tatti et al, 1998). Although controversy continues about these findings, because of these lingering doubts and the availability of suitable alternate agents, it is considered that CCBs should not be used as first line therapy in treating people with diabetes and hypertension, except possibly in those with systolic hypertension. More data are required to establish whether any possible differences in outcomes apply equally to the subclasses of CCBs.

Lipids

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Lipid lowering with statins reduces cardiovascular events in elderly people

NHMRC Gradeable Evidence

Statins and fibrates can prevent CHD in people with Type 2 diabetes. However, there is currently a scarcity of data in the elderly, especially with fibrates.

Lipid lowering therapy has been shown to effectively improve the lipid profile in elderly people with Type 2 diabetes. Twelve elderly people (mean age 72 years) with Type 2 diabetes participated in a double-blind, randomised cross-over study comparing Simvastatin 30mg/day and a placebo (Paolisso et al, 1991). After treatment of Simvastatin 30mg/day for 3 weeks, there were significant changes in lipid profile. Treatment with Simvastatin significantly reduced total cholesterol (7.9 v 5.3mmol/L, $p<0.001$), LDL cholesterol (7.2 v 4.3mmol/L), triglycerides (2.9 v 2.1mmol/L, $p<0.01$), and increased HDL cholesterol (0.9 v 0.6mmol/L) compared with the placebo group.

The Cholesterol and Recurrent Events (CARE) trial (Goldberg et al, 1998), ia a 5-year trial that compared the effect of Pravastatin (40mg/d) and placebo in 4,159 people aged 21-75 years, including 586 (14.1%) people (mean age 61 years) with clinically diagnosed Type 2 diabetes. The group with diabetes had slightly, but significantly lower, mean LDL cholesterol and HDL cholesterol, and higher mean triglyceride levels than the nondiabetic group at baseline (all $p<0.001$). Treatment with Pravastatin (40mg/d) over 5 years had similar effects on plasma lipid concentration in the people with diabetes as in the nondiabetic groups. Pravastatin reduced total cholesterol of 5.33mmol/L by 19% and LDL cholesterol of 3.52mmol/L by 27% in the diabetic group, and by 20% and 28% in the nondiabetic group, respectively. Mean triglyceride levels fell by 13% and mean HDL cholesterol of 0.97mmol/L rose by 4% in the diabetic group. In the nondiabetic group triglyceride levels fell by 14% and HDL cholesterol rose by 5%. In the placebo group, people with diabetes suffered more recurrent coronary events, including CHD death, nonfatal MI, CABG and PTCA, than did the nondiabetic group (37% vs. 25%, $p<0.001$). Stroke occurred in 8% of diabetic and 3% of nondiabetic people in the placebo group ($p<0.001$). Pravastatin treatment reduced the absolute risk of coronary events for the diabetes group and nondiabetic group by 8.1% and 5.2%; and the RR by 25% ($p=0.05$) and 23% ($p<0.001$), respectively. Pravastatin reduced the RR for revascularisation procedures by 32% ($p=0.04$) in the diabetic group.

The LIPID (Long-term Intervention with Pravastatin in Ischaemic Disease, 1998) study compared the effect of Pravastatin 40mg daily with a placebo in 9,014 subjects who were 31-75 years of age (39% were aged ≥65 years) over an average of 6.1 years. All subjects had a history of MI or unstable angina and a baseline plasma total cholesterol level of 4.0 to 7.0mmol/L. Of the group, 782 subjects (9%) had diabetes at entry. Death from CHD occurred in 6.4% of the subjects in the Pravastatin group and 8.3% of the placebo group, a relative reduction of risk of 24% (CI 12-35, $p<0.001$). Overall mortality was 22% lower (CI 13-31) in the Pravastatin group (11%) than in the placebo group (14.1%, $p<0.001$). Mortality from cardiovascular causes was 25% (CI 13-35) lower in the Pravastatin group (7.3% vs. 9.6%, $p<0.001$). Pravastatin therapy reduced mortality from CHD and overall mortality in subjects who had a broad range of initial total cholesterol levels.

In the LIPID trial (2002), among 7882 people alive (mean age 62 years) after 6 years, 7680 had 2 years of open-label Pravastatin 40mg/d treatment extended follow-up. The mean cholesterol concentration in people originally on placebo fell significantly to match those originally on Pravastatin over 2 years. Average total cholesterol was 4.54mmol/L and average LDL cholesterol was 2.66mmol/L for Pravastatin people; and was 4.50mmol/L and 2.63mmol/L, respectively for placebo people. Similarly, there were no significant differences in HDL cholesterol or triglyceride levels between groups during extended follow-up. However, people originally on Pravastatin had a lower risk of death from all causes (5.6% vs. 6.8%, $p=0.029$), CHD death (2.8% vs. 3.6%, $p=0.026$), and CHD death or nonfatal MI (4.5% vs. 5.2%, $p=0.08$). Over the total 8-year period, all-cause mortality was 717 (15.9%) in the group originally assigned Pravastatin and 888 (19.7%) in the group originally assigned placebo, CHD mortality was 395 (8.8%) versus 510 (11.3%), MI was 435 (9.6%) versus 570 (12.7%, all $p<0.0001$), and stroke was 224 (5.0%) versus 272 (6.0%, $p=0.015$). In the subgroup analyses, there was a relative risk reduction of 20% (CI 1-35) in CHD events among people aged ≥70 years during the whole study period.

The Prospective Pravastatin Pooling Project Group (Sacks et al, 2000) has examined the combined results of the CARE and LIPID studies which included 1,368 people with diabetes and 13,137 people without diabetes. The 17% risk reduction in combined coronary death and

non-fatal MI in people with diabetes was not significant, whereas the reduction in all coronary endpoints of 25% was (p<0.002).

The recently completed Heart Protection Study (HPS) was a primary and secondary prevention study of Simvastatin 40mg daily and anti-oxidant vitamin therapy (Vitamin E 600 mg, Vitamin C 250 mg, beta-carotene 20 mg daily) in a 2x2 factorial design (Heart Protection Study Collaborative Group, 2002a; Heart Protection Study Collaborative Group, 2002b). The study included 20,536 people aged 40-80 years with total cholesterol >3.5mmol/L and a substantial 5 year risk of death because of a past history of coronary disease or occlusive disease of non-coronary arteries, or diabetes or treated hypertension (Heart Protection Study Collaborative Group, 2002a). In the 10,269 people assigned to treatment with Simvastatin, the risk of a major vascular event (CHD, stroke, or revascularisation) was 19.8%, compared with 25.2% in the 10,267 people on placebo (24% relative risk reduction, p<0.00001). Of the 5,963 people with diabetes, 1,981 had had a previous CHD event. Overall, there was a highly significant 13% reduction in all cause mortality (14.9% v 12.9%, p< 0.0003) due to an 18% reduction in coronary death (p<0.0005). In the diabetic cohort, there was a 12% reduction in first major vascular event (p<0.05). The study failed to show any effect of antioxidant vitamin therapy for the whole cohort or any subcategories (Heart Protection Study Collaborative Group, 2002b).

Aspirin

Index

Aspirin is effective in the prevention of acute myocardial infarction in people with diabetes but is associated with increased gastrointestinal bleeding in the elderly

NHMRC Gradeable Evidence

The use of aspirin as an antiplatelet agent in people with Type 2 diabetes offers the potential to reduce the development of clinical macrovascular events.

In the Early Treatment Diabetic Retinopathy Study (ETDRS), 3,711 people with diabetes aged 18-70 (30% had Type 1 diabetes), approximately half of whom had a history of CVD, were randomly assigned to aspirin (2 x 325mg/day) or placebo, and followed for a mean of five years (ETDRS Investigators, 1992). The RR for fatal and non-fatal acute MI was 0.83 (99% CI 0.66-1.04, p=0.04) for the users of aspirin compared to placebo. The RR for all cause mortality in aspirin users was 0.91 (CI 0.75-1.11). Whilst MI was reduced by 18%, all vascular events were reduced by only 10% (RR 0.9 [CI 0.74-1.09]), due to a 17% (RR 1.17 [CI 0.79-1.74]) rise in strokes in the aspirin group (ETDRS Investigators, 1992).

In the Physicians Health Study, aspirin use at a dose of 325mg/every other day in physicians aged 40-84 years free of acute MI and CVD protected against the development of acute MI, especially in those with good adherence to therapy (Glynn et al, 1994). In the group, as a whole there was a 44% reduction in risk of MI (RR 0.56; CI 0.45-0.70) but no reduction in CVD mortality or all-cause mortality. Good adherers in the aspirin group had a 51% reduction in acute MI and 26% reduction in the risk of a first major cardiovascular event compared with the placebo group (Glynn et al, 1994). Poorer adherers to aspirin therapy were

less well protected (Glynn et al, 1994). In the subgroup of 533 men with diabetes, 4.0% of men on aspirin compared with 10.1% of men not on aspirin, had an MI.

The risk of gastrointestinal haemorrhage with aspirin use may be particularly high in the elderly population. In a randomised controlled trial in elderly Australians aged 70-90 years (diabetes not specified) (Silagy et al, 1993), low dose aspirin (100mg daily) was associated with clinical gastrointestinal bleeding in 3% of people receiving aspirin and none receiving placebo ($p<0.05$). The haemoglobin level fell 0.33g/dl in those on aspirin compared with 0.11g/dl in those taking placebo ($p <0.05$) during the twelve months of the study (Silagy et al, 1993). The authors emphasised the need to understand the risk benefit ratio for even low-dose aspirin use in elderly people.

NHMRC Gradeable Evidence table for Nutrition

Index

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Abraira and Derler, 1988	RCT	II	Added sucrose in diet
Bantle et al, 1993	RCT	II	Added sucrose in diet
Chandalia et al, 2000	RCT	II	Diets high in fibre
Colagiuri et al, 1989	RCT	II	Added sucrose in diet
Cooper et al, 1988	RCT	II	Added sucrose in diet
Coulston et al, 1987	RCT	II	High carbohydrate diet
Coulston et al, 1989	RCT	II	High carbohydrate diet
Coulston et al, 1990	Cohort	III-2	Dietary management
Craig et al, 1998	RCT	II	Reduced carbohydrate, modified-fat enteral formula
Franz et al, 1995	RCT	II	Medical nutrition therapy by dietitian
Garg et al, 1992	RCT	II	High vs low carbohydrate diet
Garg et al, 1994	RCT	II	Diets high in UFA or high carbohydrate
Horwath and Worsley, 1991	Case-control	III	Dietary habits of elderly
Jarvi et al, 1999	RCT	II	Low GI diet
Low et al, 1996	Case-control	III-2	Diets high in UFA
Miller et al, 2002	RCT	II	Nutrition education
O'Dea et al, 1989	Cohort	III-2	Diets high in fibre or SFA
Saletti et al, 1999	Cross-sectional	III	Nutritional status assessment
Wolever et al, 1992	RCT	II	Low GI diet

NHMRC Gradeable Evidence table for Exercise

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Caplan et al, 1995	Case-control	III-2	Exercise training and bone density
Dunstan et al, 2002	RCT	II	High-intensity resistance exercise and glycaemic control, body composition and muscle strength
Lehmann et al, 1995	Cohort	III-2	Physical training and reduced cardiovascular risk factors
Ligtenberg et al, 1997	RCT	II	Physical training and VO_2max

NHMRC Gradeable Evidence table for Alcohol and Smoking

Index

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Ajani et al , 2001	Case-control	III	Alcohol consumption and risk for CHD
AL-Delaimy et al, 2001	Cohort	II	Smoking and mortality
Jerums et al, 2002	Systematic review	I	Hypertension Guidelines for Type 2 diabetes
Meigs et al, 1997	Cohort	II	Smoking increases the risk of macrovascular disease
Scherr et al, 1992	Cohort	II	Risk of alcohol consumption on total and cardiovascular mortality
Stamler et al, 1993	Cohort	II	Smoking increases the risk of macrovascular disease
Valmadrid et al, 1999	Cohort	III	Alcohol consumption and risk for CHD
Tanasescu et al, 2001	Cohort	III	Alcohol consumption and risk for CHD
Turner et al, 1998	Cohort	II	Smoking increases the risk of macrovascular disease

NMHRC Gradeable Evidence table for Medications

Index

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Abraira et al, 1995	RCT	II	Combination of sulphonylurea and insulin
ALLHAT, 2000	RCT	II	Comparison of diuretics, α-blockers, CCB and ACEI on the incidence of cardiovascular disease
Birkeland et al, 1996	RCT	II	Insulin vs Glibenclamide
Brodown et al, 1992	RCT	II	Glyburide vs Glipizide
Burge et al, 1998	RCT	II	Sulphonylurea induced hypoglycaemia
Calabrese et al, 2002	Cohort	III-2	Risk of lactic acidosis with Metformin
Calle-Pascual et al, 1995	Cohort	III-2	Combination of sulphonylurea and insulin, Metformin, or acarbose
Chalmers et al, 1992	Cohort	III-2	Metformin monotherapy
Ciechanowski et al, 2000	Cohort	III	Depression and poor adherence to OHA therapy
Coscelli et al, 1992	RCT	II	Comparison of self-mixed and premixed insulin
Curb et al, 1996	RCT	II	Low dose diuretic vs placebo on cardiovascular risk
Dahlof et al, 1991	RCT	II	β-blockers or diuretics vs placebo on cardiovascular morbidity and mortality
Davis et al, 2001	Cohort	III	Metformin and raised fasting plasma lactate level
Diamicron MR Study Group, 2000	RCT	II	Diamicron MR vs Diamicron
Donnan et al, 2002	Cohort	III-2	Adherence to OHA
Emeriau et al, 2001	RCT	II	Diuretics vs CCBs and diuretics
Estacio et al, 1998	RCT	II	CCB vs ACE inhibitors
ETDRS Study Investigators, 1992	RCT	II	Aspirin vs placebo on cardiovascular events
Gambassi et al, 2000	Cohort	III-2	ACE inhibitors on physical function
Glynn et al, 1994	RCT	II	Aspirin in preventing MI
Goldberg et al, 1998	RCT	II	Pravastatin vs placebo on recurrent cardiovascular events
Gregorio et al, 1999	RCT	II	Maximum sulphonylurea alone vs sulphonylurea plus Metformin

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Hansson et al, 1998	RCT	II	Low dose aspirin vs placebo on cardiovascular events
Hansson et al, 1999	RCT	II	Comparing β-blockers or diuretics and ACE inhibitors or CCBs
Hansson et al, 2000	RCT	II	ACE inhibitors vs diuretic/β-blockers on cardiovascular morbidity and mortality
Hasche et al, 1999	RCT	II	Acarbose vs placebo
Herings et al, 1995	Case-control	III-2	ACE inhibitors and hypoglycaemia
Holstein et al, 2001	Cohort	III-2	Glimepiride vs Glibenclamide on hypoglycaemia
HOPE Study Investigators, 2000	RCT	II	Ramipril vs placebo on cardiovascular events
Josephkutty and Potter, 1990	RCT	II	Comparison of Metformin and Tolbutamide
Kreider and Heise, 2002	Systematic review	I	The efficacy and safety of rosiglitazone
LIPID Study Group, 1998	RCT	II	Pravastatin vs placebo on cardiovascular events
LIPID Study Group, 2002	RCT	II	Pravastatin on cardiovascular events
Morris et al, 1997	Case-control	III-2	ACE inhibitors and hypoglycaemia
MRC/BHF Heart Protection Study, 2002a	RCT	II	Simvastatin vs placebo on cardiovascular events
MRC/BHF Heart Protection Study, 2002b	RCT	II	Vitamin E, Vitamin C and β-carotene vs placebo on cardiovascular events
Niskanen et al, 1992	RCT	II	Sulphonylurea + insulin
Niskanen et al, 2001	RCT	II	ACE inhibitor vs diuretic/β-blocker on cardiovascular morbidity and mortality
Onder et al, 2002	Cohort	III-2	ACE inhibitors on physical function

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Paolisso et al, 1991	RCT	II	Simvastatin vs placebo on lipids
PROGRESS study, 2001	RCT	II	ACE inhibitors + diuretic vs placebo on stroke
Pullar et al, 1988	RCT	II	Compliance with prescribed medications
Quatraro et al, 1991	Cohort	III-2	Combination of sulphonylurea and insulin
Reza et al, 2002	Cohort	III-2	Insulin monotherapy
Rosenstock et al, 1993	RCT	II	Glyburide vs Glipizide
Sacks et al, 2000	RCT	II	Pravastatin vs placebo on CVD events
SCOPE study, 2002	RCT	II	Angiotensin receptor blocker vs placebo on hypertension
Scorpiglione et al, 1999	RCT	II	Acarbose
Selby et al, 1999	Cohort	III-2	Metformin
Shorr et al, 1996	Cohort	III-2	Sulphonylurea and hypoglycaemia
Shorr et al, 1997a	Cohort	III-2	Hypoglycaemia in persons using insulin and sulphonylurea
Shorr et al, 1997b	Cohort	III-2	Antihypertensive agents on hypoglycaemia
Silagy et al, 1993	RCT	II	Adverse effects of aspirin
Simmons et al, 2000	RCT	II	Medication packaging
Sonnenblick and Shilo, 1986	Case series	IV	Glibenclamide induced hypoglycaemia
Tatti et al, 1998	RCT	II	ACE inhibitors vs CCBs on CVD events
Tessier et al, 1994	RCT	II	Glibenclamide vs gliclazide
Tindall et al, 1988	RCT	II	Comparison of two insulin regimens
Tovi and Engfeldt, 1998	RCT	II	Effects of insulin treatment on well being and symptom control
Tuomilehto et al, 1999	RCT	II	CCBs vs placebo on total mortality, cardiovascular events
UKPDS 38, 1998	RCT	II	Tight BP control on micro- and macrovascular complications
UKPDS 39, 1998	RCT	II	Atenolol vs Captopril on micro- and macrovascular complications
WHO-ISH, 1999	Systematic review	I	Guidelines for the management of hypertension
Willms and Ruge, 1999	RCT	II	Comparison of Acarbose and Metformin
Wolffenbuttel et al, 1996	RCT	II	Effects of different insulin regimens

Abraira C, Colwell JA, Nuttall FQ, Sawin CT, Nagel NJ, Comstock JP, Emanuele NV, Levin SR, Henderson W, Lee HS. VA CSDM Group. Veterans Affairs Cooperative Study on glycemic control and complications in Type II diabetes (VA CSDM). Results of the feasibility trial. Diabetes Care 1995;18:1113-23

Abraira C, Derler J. Large variations of sucrose in constant carbohydrate diets in Type II diabetes. Am J Med 1988;84:193-9

Al-Delaimy WK, Willett WC, Manson JE, Speizer FE, Hu FB. Smoking and mortality among women with Type 2 diabetes. The Nurses' Health Study cohort. Diabetes Care 2001;24:2043-8

ALLHAT Collaborative Research Group. Major cardiovascular events in hypertensive patients randomised to doxazosin vs chlorthalidone. The Antihypertensive and Lipid-Lowering treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2000;283:1967-75

Ajani UA, Gaziano M, Lotufo PA, Liu S, Hennekens CH, Buring JE, Manson JE. Alcohol consumption and risk of coronary heart disease by diabetes status. Circulation 2001;102:500-5

Bantle JP, Swanson JE, Thomas W, Laine DC. Metabolic effects of dietary sucrose in type II diabetic subjects. Diabetes Care 1993;16:1301-5.

Birkeland KI, Rishaug H, Hanssen KE, Vaaler S. NIDDM: a rapid progressive disease. Results from a long-term, randomized, comparative study of insulin or sulphonylurea treatment. Diabetologia 1996;39:1629-33

Brodows RG. Benefits and risks with Glyburide and Glipizide in elderly NIDDM patients. Diabetes Care 1992;15:75-80

Burge MR, Schmitz-Fiorentino K, Fischette C, Qualls CR, Schade DS. A prospective trial of risk factors for sulfonylurea-induced hypoglycemia in type 2 diabetes mellitus. JAMA 1998;279:137-43

Calabrese AT, Coley KC, DaPos SV, Swanson D, Rao RH. Evaluation of prescribing practices: Risk of lactic acidosis with Metformin therapy. Arch Intern Med 2002; 162:434-7

Calle-Pascual AL, Garcia-Honduvilla J, Martin-Alvarez PJ, Vara E, Calle JR, Munguira ME, Maranes JP. Comparison between acarbose, Metformin, and insulin treatment in Type 2 diabetic patients with secondary failure to sulphonylurea treatment. Diabete Metabolisme 1995;21:256-60

Caplan GA, Colagiuri R, Lord SR, Colagiuri S, Ward JA. Exercise in older people with Type 2 diabetes maintains bone density despite weight loss. Australian Journal on Ageing, 1995; 14 (2): 71-75

Chalmers J, Brown JRF, McBain AM, Campbell IW. Metformin: is its use contraindicated in the elderly? Practical Diabetes 1992; 9: 51-3

Chandalia M, Garg A, Lutjohann DVB, K., Grundy S, Brinkley L. Beneficial effects of high dietary fiber intake in patients with Type 2 diabetes mellitus. N Eng J Med 2000;342

Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes. Impact of depressive symptoms on adherence, function, and costs. Arch Intern Med 2000;160:3278-85

Colagiuri S, Miller JJ, Edwards RA. Metabolic effects of adding sucrose and aspartame to the diet of subjects with noninsulin-dependent diabetes mellitus. Am J Clin Nutr 1989;50:474-8

Cooper PL, Wahlqvist ML, Simpson RW. Sucrose versus saccharin as an added sweetener in non-insulin-dependent diabetes: short-and medium-term metabolic effects. Diabet Med 1988;5:676-80

Coscelli C, Calabrese G, Fedele D, Pisu E, Calderini C, Bistoni S, Lapolla A, Mauri MG, Rossi A, Zappella A. Use of premixed insulin among the elderly. Reduction of errors in patient preparation of mixtures. Diabetes Care 1992; 15 (11): 1628-1630

Coulston AM, Hollenbeck CB, Swislocki ALM, Chen Y-DI, Reaven GM. Deleterious metabolic effects of high-carbohydrate, sucrose containing diets in patients with non-insulin-dependent diabetes mellitus. Am J Med 1987;82:213-20

Coulston AM, Hollenbeck CB, Swislocki ALM, Reaven GM. Persistence of hypertriglyceridemic effect of low-fat high-carbohydrate diets in NIDDM patients. Diabetes Care 1989;12:94-101

Coulston AM, Mandelbaum D, Reaven GM. Dietary management of nursing home residents with non-insulin-dependent diabetes mellitus. Am J Clin Nutr 1990;51:67-71

Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, Camel G, Davis BR, Frost PH, Gonzalez N, Guthrie G, Oberman A, Rutan G, Stamler J. for the Systolic Hypertension in the Elderly Program Cooperative Research Group. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. JAMA 1996;276:1886-92

Craig LD, Nicholson S, Silverstone FA, Kennedy RD. Use of a reduced-carbohydrate, modified-fat enteral for improving metabolic control and clinical outcomes in long-term care residents with Type 2 diabetes: results of a pilot trial. Nutrition 1998;14:529-34

Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Webster P-O. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). Lancet 1991;338:1281-5

Davis TME, Jackson D, Davis WA, Bruce DG, Chubb P. The relationship between Metformin therapy and the fasting plasma lactate in Type2 diabetes: The Fremantle Diabetes Study. Br J Clin Pharmacol 2001;52:137-44

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Diamicron MR Study Group, Drouin P. Diamicron MR once daily is effective and well tolerated in Type 2 diabetes. A double-blind, randomised, multinational study. J Diabetes Complications 2000;14:185-91

Donnan PT, MacDonald TM, Morrist AD. Adherence to prescribed oral hypoglycaemic medication in a population of patients with Type 2 diabetes: a retrospective cohort study. Diabet Med 2002;19:279-84

Dunstan DW, Daly RM, Owen N, Jolley D, de Courten M, Shaw J, Zimmet P. High-intensity resistance training improves glycaemic control in older patients with Type 2 diabetes. Diabetes Care 2002;25:1729-36

Emeriau JP. Knauf H. Pujadas JO. Calvo-Gomez C. Abate G. Leonetti G. Chastang C. European Study Investigators. A comparison of indapamide SR 1.5mg with both amlodipine 5mg and hydrochlorothiazide 25mg in elderly hypertensive patients: a randomised double-blind controlled study. J Hypertens 2001;19:343-50

Estacio RO, Schrier RW. Antihypertensive therapy in Type 2 diabetes: implications of the Appropriate Blood Pressure Control in Diabetes (ABCD) trial. Am J Cardiol 1998;82:9R-14R

ETDRS Investigators. Early Treatment Diabetic Retinopathy Study Investigators. Aspirin effects on mortality and morbidity in people with diabetes mellitus. Early Treatment Diabetic Retinopathy Study Report 14. JAMA 1992;268:1292-300.

Franz MJ, Monk A, Barry B, McClain K, Weaver T, Cooper N, Upham P, Bergenstal R, Mazze RS. Effectiveness of medical nutrition therapy provided by dietitians in the management of non-insulin-dependent diabetes mellitus: a randomized, controlled clinical trial. J Am Diet Assoc 1995;95:1009-17

Gambassi G, Lapane KL, Sgadari A, Carbonin P, Gatsonis C, Lipsitz LA, Mor V, Bernabei R, The SAGE Study Group. Effects of angiotensin-converting enzyme inhibitors and digoxin on health outcomes of very old patients with heart failure. Arch Intern Med 2000;160:53-60

Garg A, Grundy SM, Unger RH. Comparison of effects of high and low carbohydrate diets on plasma lipoproteins and insulin sensitivity in patients with mild NIDDM. Diabetes 1992;41:1278-85

Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen Y-DI, Gundy SM, Huet BA, Reaven GM. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA 1994;271:1421-8

Glynn RJ, Buring JE, Manson JE, LaMotte F, Hennekens CH. Adherence to aspirin in the prevention of myocardial infarction. The Physician's Health Study. Arch Intern Med 1994;154:2649-57

Goldberg RB, Mellies MJ, Sacks FM, Moye LA, Howard BV, Howard WJ, Davis BR, Cole TG, Pfeffer MA, Braunwald E. Cardiovascular events and their reduction with Pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels. Subgroup analysis in the Cholesterol and Recurrent Events (CARE) Trial. Circulation 1998;98:2513-9

Gregorio F, Ambrosit F, Manfrini S, Velussi M, Carle F, Testa R, Merante D, Filipponi P. Poorly controlled elderly type 2 diabetic patients: the effects of increasing sulphonylurea dosages or adding Metformin. Diabet Med 1999;16:1016-24

Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Ménard J, Rahn KH, Wedel H, Westerling S, for The HOT Study Group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: Principal results of The Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998;351:1755-62.

Hansson L, Lindholm L, Ekbom T, Dahlof B, Lanke J, Schersten B, Wester P-O, Hedner T, de Faire U. The STOP-Hypertension-2 Study group. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 Study. Lancet 1999;354:1751-6

Hansson L, Hedner T, Lund-Johansen P, Kjeldsen SE, Lindholm LH, Syvertsen JO, Lanke J, de Faires U, Dahlof B, Karlberg BE, for the NORDIL study group. Randomised trial of effects of calcium channel antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study. Lancet 2000;356:359-65.

Hasche H, Mertes G, Burns C, Englert R, Genthner P, Heim D, Heyen P, Mahla G, Schmidt C, Schulze-Schleppinghof B, Steger-Johannsen G. Effects of Acarbose treatment in Type 2 diabetic patients under dietary training: A multicentre, double-blind, placebo-controlled, 2-year study. Diab Nurt Metab 1999;12:277-85

Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with Simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002a;360:7-22

Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20 536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002b;360:23-33

Herings RMC, de Boer A, Stricker BHC, Leufkens HGM, Porsius A. Hypoglycaemia associated with use of inhibitors of angiotensin converting enzyme. Lancet 1995;345:1195-8

Holstein A, Plaschke A, Egberts E-H. Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with Glimepiride versus Glibenclamide . Diabetes Metab Res Rev 2001;17:467-73

HOPE Study Investigators. Effects of ramipril on cardiovascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Lancet 2000;355:253-9

Horwath CC, Worsley A. Dietary habits of elderly persons with diabetes. J Am Diet Assoc 1991;91:553-7

Jarvi AE, Karlstrom BE, Granfeldt YE, Bjorck IE, Asp NL, Vessby BOH. Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low-glycemic index diet in Type 2 diabetic patients. Diabetes Care 1999;22:10-8.

Jerums G, Colagiuri S, Hepburn A, Colagiuri R. Evidence Based Guidelines for Type 2 Diabetes: Hypertension. Draft. Diabetes Australia. Canberra, 2002

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Josephkutty S and Potter JM. Comparison of Tolbutamide and Metformin in elderly diabetic patients. Diabet Med 1990;7: 510-4

Kreider M, Heise M. Rosiglitazone in the management of older patients with Type 2 diabetes mellitus. Int J Clin Pract 2002;56:538-41

Lehmann R, Vokac A, Niedermann K, Agosti K, Spinas GA. Loss of abdominal fat and improvement of the cardiovascular risk profile by regular moderate exercise training in patients with NIDDM. Diabetologia 1995;38:1313-9

Ligtenberg PC, Hoekstra JBL, Bol E, Zonderland ML, Erkelens DW. Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. Clin Sci 1997;93:127-35

Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with Pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998;339:1349-57

Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Long-term effectiveness and safety of Pravastatin in 9014 patients with coronary heart disease and average cholesterol concentration: the LIPID trial follow-up. Lancet 2002;359:1379-87

Low CC, Grossman EB, Gumbiner B. Potentiation of effects of weight loss by monounsaturated fatty acids in obese NIDDM patients. Diabetes 1996;45:569-75.

Meigs JB, Singer DE, Sullivan LM, Dukes KA, D'Agostino RB, Nathan DM, Wagner EH, Kaplan SH, Greenfield S. Metabolic control and prevalent cardiovascular disease in non-insulin-dependent diabetes mellitus (NIDDM): The NIDDM Patient Outcomes Research Team. Am J Med 1997;102:38-47

Miller CK, Edwards L, Kissling G, Sanville L. Nutrition education improves metabolic outcomes among older adults with diabetes mellitus: Results from a randomized controlled trial. Prev Med 2002;34:252-9

Morris AD, Boyle DIR, McMahon AD, Pearce H, Evans JMM, Newton RW, Jung RT, MacDonald TM, The DARTS/MEMO Collaboration. ACE inhibitors use is associated with hospitalization for severe hypoglycaemia in patients with diabetes. Diabetes Care 1997;20:1363-7

Niskanen L, Lahti J, Uusitupa M. Morning or bed-time insulin with or without Glibenclamide in elderly Type 2 diabetic patients unresponsive to oral antidiabetic agents. Diabetes Res Clin Pract 1992;18:185-90

Niskanen L, Hedner T, Hansson L, Lanke J, Niklason A. Reduced cardiovascular morbidity and mortality in hypertensive diabetic patients on first-line therapy with an ACE inhibitor compared with a diuretic/beta blocker-based treatment regimen: a subanalysis of the Captopril Prevention Project (CAPPP). Diabetes Care 2001;24: 2091-6.

O'Dea K, Traiandes K, Irealnd P, Niall M, Sadler J, Hopper J, DeLuise M. The effects of diet differing in fat, carbohydrate and fibre on carbohydrate and lipid metabolism in Type II diabetes. Journal of the American Dietetic Association 1989;89:1076-86.

Onder G, Penninx BWJH, Balkrishnan R, Fried LP, Chaves PHM, Williamson J, Carter C, Di Bari M, Guralnik JM, Pahor M. Relation between use of angiotensin-converting enzyme

inhibitors and muscle strength and physical function in older women: an observational study. Lancet 2002;359:926-30

Paolisso G, Sgambato S, De Riu S, Gambardella A, Verza M, Varricchio M, D'Onofrio F. Simvastatin reduces plasma lipid levels and improves insulin action in elderly, non-insulin dependent diabetics. Eur J Clin Pharmacol 1991;40:27-31

PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet 2001;358:1033-41

Pullar T, Birtwell AJ, Wiles PG, Hay A, Feely MP. Use of a pharmacologic indicator to compare compliance with tablets prescribed to be taken once, twice, or three time daily. Clin Pharmacol Ther 1988;44:540-5

Quatraro A,Consoli G, Minei A, Pinto D, Ceriello A, Varricchio M, Giugliano D. The combined insulin and sulfonylurea therapy in diabetes of elderly people. Arch Gerontol Geriatr 1991;13:245-54

Reza M, Taylor CD, Towse K, Ward JD, Hendra TJ. Insulin improves well-being for selected elderly Type 2 diabetic subjects. Diabetes Research and Clinical Practice 2002; 55: 201-207.

Rosenstock JB, Corrao PJ, Goldberg RB, Kilo C. Diabetes control in the elderly: A randomized comparative study of Glyburide versus Glipizide in non-insulin-dependent diabetes mellitus. Clin Ther 1993;15:1031-40

Sacks FM, Tonkin AM, Shepherd J, Braunwald E, Cobbe S, Hawkins M, Keech A, Packard C, Simes J, Byington R, Furberg CD. The Prospective Pravastatin Pooling Project Group. Effect of Pravastatin on coronary disease events in subgroups defined by coronary risk factors. The Prospective Pravastatin Pooling Project. Circulation 2000;102:1893-1900

Scherr PA, LaCroix AZ, Wallace RB, Berkman L, Curb JD, Cornoi-Huntley J, Evans DA, Hennekens CH. Light to moderate alcohol consumption and mortality in the elderly. Journal of the American Geriatric Society 1992; 40: 651-657.

SCOPE Study Investigators. Reducing hypertension in the elderly leads to a significant reduction in the incidence of stroke (Abstract). The meeting of the International Society of Hypertension and the European Society of Hypertension. Prague. 2002

Scorpiglione N, Belfiglio M, Carinci F, Cavaliere D, De Curtis A, Franciosi M, Mari E, Sacco M, Tognoni G, Nicolucci A. The effectiveness, safety and epidemiology of the use of Acarbose in the treatment of patients with type 2 diabetes mellitus. A model of medicine-based evidence. Eur J Clin Pharmacol 1999;55:239-49

Selby JV, Ettinger B, Swain BE, Brown JB. First 20 months' experience with use of Metformin for Type 2 diabetes in a large health maintenance organisation. Diabetes Care 1999;22:38-42

Shorr RI, Ray WA, Daugherty JR, Griffin MR. Individual sulphonylurea and serious hypoglycaemia in older people. J Am Geriatr Soc 1996;44:751-5

Shorr RI, Daugherty WA, Griffin MR. Incidence and risk factors for serious hypoglycaemia in older persons using insulin or sulphonylureas. Arch Intern Med 1997;157:1681-6

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Shorr RI, Ray WA, Daugherty JR, Griffin MR. Antihypertensive agents and the risk of serious hypoglycaemia in older persons using insulin or sulphonylureas. JAMA 1997;278:40-3

Silagy CA, McNeil JJ, Donnan GA, Tonkin AM, Worsam B, Campion K. Adverse effects of low-dose aspirin in a healthy elderly population. Clin Pharmacol Ther 1993;54:84-9.

Simmons D, Upjohn M, Gamble GD. Can medication packaging improve glycaemic control and blood pressure in Type 2 Diabetes? Results form a randomised controlled trial. Diabetes Care 2000;23:153-6

Sonnenblick M, Shilo S. Glibenclamide induced prolonged hypoglycemia. Age Aging 1986;15:185-9

Stamler J, Vaccaro O, Neaton JD, Wentworth D. For the Multiple Risk Factor Intervention Trial Research Group. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993;16:434-44

Tanasescu M, Hu FB, Willett WC, Stampfer MJ, Rimm EB. Alcohol consumption and risk of coronary heart disease among men with Type 2 diabetes mellitus. J Am Coll Cardio 2001;38:1836-42

Tessier D, Dawson K, Tetrault JP, Bravo G, Meneilly GS. Glibenclamide vs Gliclazide in Type 2 diabetes of the elderly. Diabet Med 1994;11:974-80

Tindall H, Bodansky HJ, Stickland M, Wales JK. A strategy for selection of elderly Type 2 diabetic patients for insulin therapy, and a comparison of two insulin preparations. Diabetic Medicine 1988; 5: 533-536.

Tovi J and Engfeldt P. Well-being and symptoms in elderly Type 2 diabetes patients with poor metabolic control: effect of insulin treatment. Practical Diabetes International 1998; 15 (3): 73-77.

Tuomilehto J, Rastenyte D, Birkenhager WH, Thijs L, Antikainen R, Bulpitt CJ, Fletcher AE, Forette F, Goldhaber A, Palatini P, Sarti C, Fargard R. Systolic Hypertension in Europe Trial Investigators. Effects of calcium-channel blockade in older patients with diabetes and systolic hypertension. N Engl J Med 1999:340:677-84

Turner RC, Millns H, Neil HAW, Stratton IM, Manley SE, Matthews DR, Holman RR, for the United Kingdom Prospective Diabetes Study. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus (UKPDS 23). BMJ 1998;316:823-8

UKPDS 38. The UK Prospective Diabetes Study 38. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UK Prospective Diabetes Study Group. Br Med J 1998;317:703-13

UKPDS 39. Efficacy of Atenolol and Captopril in reducing risk of macrovascular and microvascular complications in Type 2 diabetes: UK Prospective Diabetes Study Group. Br Med J 1998;317:713-20

Valmadrid CT, Klein R, Moss SE, Klein BEK, Cruickshanks KJ. Alcohol intake and the risk of coronary heart disease mortality in persons with older-onset diabetes mellitus. JAMA 1999;282:239-46

WHO-ISH (World Health Organization - International Society of Hypertension) Guidelines Subcommittee. 1999 World Health Organization - International Society of Hypertension guidelines for the management of hypertension. J Hypertens 1999;17:151-83

Willms B, Ruge D. Comparison of Acarbose and Metformin in patients with Type 2 diabetes mellitus insufficiently controlled with diet and sulphonylureas: a randomized, placebo-controlled study. Diabet Med 1999: 16:755-61

Wolever TMS, Jenkins DJA, Vuksan V, Jenkins AL, Buckley GC, Wong GS. Beneficial effect of a low glycaemic index diet in Type 2 diabetes. Diabet Med 1992;9:451-8.

Wolffenbuttel BHR, Sels J-PJE, Rondas-Colbers GJWM, Menheere PPCA, Nieuwenhuijen Kruseman AC. Comparison of different insulin regimens in elderly patients with NIDDM. Diabetes Care 1996;19(12):1326-32

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Special Treatments – Other References

Australian Bureau of Statistics. National Nutrition Survey; selected highlights. Canberra: Australian Government Publishing Service, 1998.

American Diabetes Association. Diabetes mellitus and exercise. Position Statement. Diabetes Care 2001;24 (Suppl 1):S51-5

American Diabetes Association. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. Position Statement. Diabetes Care 2002;25(Suppl 1):S50-60

American Diabetes Association. Smoking and diabetes. Diabetes Care 2002;25(Suppl 1):S80-1

Bell DSH. Alcohol and the NIDDM patient. Diabetes Care 1996; 19 (5): 509-513.

Binns CW (Ed). National Health and Medical Research Dietary Guidelines for Older Australians, Canberra: NHMRC, 1999.

Brand Miller J. The importance of glycaemic index in diabetes. American Journal of Nutrition 1994; 59 (Suppl): 747S-752S.

Campbell W, Crim M, Dallal G, Young V, Evans W. Increased protein requirements in elderly people: new data and retrospective reassessments. American Journal of Clinical Nutrition 1994; 60: 501-509.

Chen CC-H, Schilling LS, Lyder CH. A concept analysis of malnutrition in the elderly. J Adv Nurs 2001;36:131-42

Cirqui MH and Golomb BA. Should patients with diabetes drink to their health? JAMA; 282 (3): 279-280.

Davis SN and Brown JB. Insulin Use in the Elderly. Journal of Geriatric Drug Therapy 1999; 12: 61-81.

Geelhoed EA, Criddle A, Prince RL. The epidemiology of osteoperotic fracture and its causative factors. Clin Biochem Review 1994; 15: 173-178.

King AC, Haskell WL, Taylor CB, Kraemer HC, DeBusk RF. Group- vs home-based exercise training in healthy older men and women. A community-based clinical trial. JAMA 1991;266:1535-42

Kreinhofer M, Aufseesser-Stein M, Assal JP. Insulin injections: mistakes and errors made by patients and/or health care providers. Diabetes Research and Clinical Practice 1988; 4 (Suppl 1): 35-40.

Mazzeo RS, Tanaka H. Exercise prescription for the elderly. Current recommendations. Sports Med 2001;31:809-18

National Health and Medical Research Council. 1994a. Exercise and the Older Person. Series on Clinical Management Problems in the Elderly No2. Canberra: Australian Government Publishing Service.

National Health and Medical Research Council. 1994b Medication for the Older Person. Series on Clinical Management Problems in the Elderly No 7. Canberra: Australian Government Publishing Service.

Nutrition Australia 2001. I have heard that drinking red wine lowers the risk of heart disease. Is that correct? www.nutritionaustralia.org/Food_Facts/FAQ/red_wine_and_heart_disease_faq.asp, accessed on 20th July 2002.

Patrono C. Aspirin as an antiplatelet drug. N Engl J Med 1994;330:1287-94.

Rosenstock J, Management of Type 2 diabetes mellitus in the elderly. Special considerations. Drug and Aging 2001;18:31-44

Ruoff G. The management of non-insulin-dependent diabetes mellitus in the elderly. J Fam Pract 1993;36:329-35

The Diabetes Mellitus Working Group. Veterans Health Administration Clinical Guidelines for Management of Patients with Diabetes Mellitus. Washington DC, 1997

UKPDS 34. Effect of intensive blood-glucose control with Metformin on complications in overweight patients with type 2 diabetes. The Lancet 1998;352 :854-65

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2.4 Barriers to Health Care and Education

Index

What are the barriers to diabetes education and health care in elderly people with diabetes?

Answer

There are a number of age related barriers to diabetes education and health care in elderly people with diabetes

Why

- Comorbidities are frequent and may adversely affect diabetes management
  Evidence Level III
- Social and financial disadvantage can impact on access to diabetes care requirements
  Evidence Level III
- Impaired cognition is common among elderly people with diabetes and has a negative impact on diabetes self-management
  Evidence Level III
- Reduced physical ability may be a barrier to diabetes education and associated self-management in elderly people
  Evidence Level III
- The loss of special senses can affect access to health care and adherence to diabetes self care recommendations
  Evidence Level III
- Diabetes is associated with a decline in cognitive function and depression in elderly people
  Evidence Level III

Recommendations

- Special attention should be given to ensuring that elderly people with diabetes and their carers receive diabetes education, and have access to general and specialist health services required for optimal diabetes care
- Models and systems of care should be structured to ensure that elderly people with diabetes receive recognised standards of diabetes care and appropriate assessments
- Diabetes education for elderly people with diabetes should be individualised and should be specifically designed to address barriers which are common in the elderly - visual, hearing and cognitive impairment, depression, reduced mobility and manual dexterity, and social and financial problems
- Professional training and continuing education programs should be available for health professionals caring for elderly people with diabetes
- Government and community health and social services for the aged should ensure that their staff have at least basic training in the special needs of elderly people with diabetes

Background – Barriers to Health Care and Education Index

Type 2 diabetes is a major clinical problem in the elderly population. Therapeutic options such as physical activity, nutrition and medications are available to facilitate achieving optimal glycaemic control in elderly people with diabetes. However, elderly people frequently have special circumstances that may impact adversely on efforts to optimise control. Barriers to diabetes care are largely attributable to personal characteristics or health system issues. Where diabetes is under treated or inadequately managed due to such barriers elderly people may experience increased morbidity, disability and premature mortality (Sinclair and Barnett, 1993).

There are many generally recognised barriers to self-care education and adherence to self-care recommendations for people with diabetes (Zigbor and Simmons, 2001). In the elderly, there may be multiple additional factors that impair the capacity of the individual to understand and/or carry out adequate and appropriate self-care. These factors may include comorbidities, physical disability, polypharmacy, alteration of the senses, poverty, social isolation, a decline in cognitive function and depression, which can complicate diabetes management, exacerbate the impact of diabetes and the level of disability experienced.

Lack of adherence to medical recommendations may also lead to under treatment and under management (Hampson et al, 1995). An assumed lack of willingness to comply may be in fact due to previous experience of an adverse event, limited mobility, level of inconvenience, or deficits in functional, cognitive, physical and social abilities necessary to ensure adherence to a recommended diabetes care plan. The prescribing of multiple medications for existing comorbidities and diabetes and other non-prescription medications make costs prohibitive to many elderly people with diabetes and significantly influences compliance rates to medication regimens.

1. Comorbidities

Elderly people with diabetes often have preexisting chronic, physical and/or mental illness, and they may be taking many medications for these problems. These conditions limit physical capability, and some medications adversely affect either the physical or mental status of elderly people, and impact significantly on diabetes care.

2. Social situation

Social isolation such as loss of a spouse, living alone, and lack of family support directly affects motivation for optimal diabetes control in the elderly. According to Reed and Mooradian (1990), socioeconomic status also plays a significant role in diabetes care. A number of other reports suggest that elderly people who are living in poverty, have limited education, or have limited access to transportation are less likely to receive diabetes education, visit a diabetes specialist, have an eye examination, follow diet/exercise regimens, or to do home glucose monitoring.

3. Mental status and learning/memory capacity

Cognitive impairment, depression and dementia are common in the elderly. Communication difficulties such as dysphasia and dysarthria from cerebrovascular or neurological disease, and visual and hearing impairment or loss may cause failure to recognise diabetes care needs and poor understanding of educational content. In addition, dementia and depression may result in reduced self-care ability and loss of motivation to carry out self-care. Another

consequence of memory dysfunction is poorer recall of medication changes and this can affect optimal diabetes management (British Diabetic Association, 1999).

4. Physical ability

Decreased physical activity and dexterity due to age-related reduced muscle strength and chronic diseases such as arthritis which limit joint mobility and Parkinson's disease, prevent elderly people from shopping, preparing meals and even feeding themselves, as well as taking medications. It is almost impossible for the homebound elderly to have access to diabetes education. Lack of mobility may hinder access to health care in some elderly diabetic patients in nursing homes (Sherriff et al, 2000).

5. Loss of special senses

Alterations to taste and smell may affect food choice and, consequently, nutritional status. Hearing loss may lead to difficulty understanding instructions about diet, exercise and medications. Visual impairment may restrict ability to read printed educational material, medication labels or instructions on how to use blood glucose-testing devices.

All these age-related physiological changes and social factors can have a significant impact on diabetes care. In order to achieve optimal diabetes management in the elderly these factors need to be taken into consideration, especially in frail elderly people with special needs.

1. Comorbidities

Index

Comorbidities are frequent and may adversely affect diabetes management

NHMRC Gradeable Evidence

A cross sectional analysis of 1,002 women aged ≥65 years of age (mean 78.8 years), of whom 160 had diabetes, found an association between diabetes and an increased number of comorbidities (Volpato et al, 2002). Compared with their counterparts without diabetes, participants with diabetes were more likely to have a cardiovascular condition, severe peripheral nerve dysfunction, and visual impairment (all p values <0.01). After adjustment for age, the prevalence of CHD, CCF, peripheral arterial disease, hypertension and depression were related to the duration of the disease (all $p<0.05$). These results confirm that comorbidities are commonly associated with diabetes in elderly people and that the number of comorbidities increases with increasing duration of diabetes.

A 6-year follow-up study of 4,205 elderly people (mean age 76.4) assessed the impact of chronic conditions on the incidence of functional limitations in older adults (Dunlop et al, 2002). Arthritis, diabetes, prior CVD, incontinence, and impaired vision were significant predictors of the onset of moderate functional limitation after controlling for demographics. Prior moderate functional limitation, CVD and vision impairment predicted the onset of severe functional limitation. Based on these findings, the prevention of functional decline should target chronic conditions in older adults.

Other evidence

A non-systematic review, found that coexisting chronic medical problems such as CVD, arthritis, Parkinson's disease and dementia, exacerbate the impact of diabetes, thereby increasing the level of disability and adversely affecting diabetes management (Sinclair and Barnett, 1993).

2. Social Situation

Index

Social and financial disadvantage can impact on access to diabetes care requirements

NHMRC Gradeable Evidence

Self-monitoring blood glucose (SMBG) is an important component of diabetes management. A study assessing SMBG in 41,363 participants with Type 2 diabetes aged from 49-72 years (mean age 60.5), found that 60% reported practising SMBG less than current ADA recommendations (Karter et al, 2000). Significant independent predictors of nonadherence to ADA recommendations were belonging to an ethnic minority, having a lower education level, a reduced neighbourhood income level, difficulty communicating in English, and having higher out of pocket expenses for capillary blood test strips. These findings suggest an increased need for targeted, culturally sensitive health education in people with diabetes and assistance to reduce financial barriers to SMBG.

The importance of addressing these barriers is highlighted by studies that demonstrate that older people are capable of SMBG and benefit from education programs. A cross sectional study of 20 older people with diabetes (mean age 68 years) comparing SMBG with urine glucose testing on quality of life found no differences between the two groups (Gilden et al, 1990). The SMBG group reported no greater interference with quality of life and SMBG was not associated with greater difficulty in performance, record keeping or degree of embarrassment compared with the urine-testing group. In fact, people performing urine testing expressed a desire for SMBG ($p<0.01$) and had greater difficulty in record keeping ($p<0.05$ v SMBG group). This study demonstrates that SMBG did not interfere with quality of life, was easy to perform, was time saving, afforded better record keeping and was associated with a reduction in embarrassment.

Older people are also capable of responding to education programs. Gilden et al (1989) demonstrated improvements in diabetes knowledge, psychosocial functioning, and metabolic control in 48 older male diabetic patients (mean age 70) and their spouses over a 6-month period compared with 22 younger subjects (mean age 57) following a six-week diabetes education program. Older participants significantly increased their knowledge of diabetes ($p<0.05$) and the knowledge gain was correlated with an improvement in diet-related quality of life ($p<0.02$) and a reduction in stress ($p<0.05$), which was still evident after 6 months ($p<0.01$). In contrast, younger patients reported decreases in perceived quality of life ($p<0.05$). In addition, older participants with participating spouses compared with those without, demonstrated greater improvements in knowledge ($p<0.02$), an increase in family involvement ($p<0.05$), less stress ($p<0.02$), and improvements in metabolic control ($p<0.001$). The education program was also found to increase spouses' knowledge and perceived involvement in the care of their diabetic partners ($p<0.01$).

Other Evidence

A non-systematic review of external barriers to diabetes care in the general population found that socioeconomic mediators, such as education and income, play a significant role in the outcomes of people with diabetes due to their effect on access to health care and adherence to self-care recommendations (Zgibor and Songer, 2001). These findings would be expected to apply to the elderly, however, there is a lack of research into the effects of social factors on access to health care services and barriers to diabetes education, specific to elderly people.

The psychosocial needs of older adults may be affected by distance from family, financial status, level of independence, illness or death of a spouse, depression or the need to live in an extended care facility. In light of these factors, the ADEA (1999) highlighted the importance of developing a support system that provides encouragement, reinforcement and technical advice. Financial and transportation issues that act as barriers to accessing health care and purchasing equipment necessary for diabetes management, need to be assessed so that referral to appropriate community resources can be made.

In a non-systematic review of the psychosocial aspects affecting diabetes management in elderly patients, Holvey (1986) found that diabetes management imposes specific requirements that elderly patients view as an added burden. In particular she found that diet, exercise, self-monitoring of blood glucose levels, taking prescribed medications, and regular visits to the physician's office are difficult for elderly people to incorporate into their lives. Holvey also found that there has been little attention paid to teaching elderly people with diabetes how to integrate the disease into their lives and enhance their coping skills. She recommended that health professionals assess psychosocial barriers such as decline in health status, reduction in financial capacity, loss of spouse or friends and increasing cost and inaccessibility of services, faced by elderly people and consider these when formulating diabetes management care plans and educational interventions.

3. Mental Status and Learning/Memory Capacity

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Impaired cognition is common among elderly people with diabetes and has a negative impact on diabetes self-management

NHMRC Gradeable Evidence

Older people with Type 2 diabetes are likely to have greater deficits in processing complex verbal or nonverbal material than their non-diabetic counterparts (Reaven et al, 1990). In Reaven's case-controlled study, cognitive function including verbal intelligence, complex psychomotor skills, verbal learning and memory, and abstract reasoning were assessed in 29 people with Type 2 diabetes (mean age 69.8 years) and 30 nondiabetic controls (mean age 68 years). People with Type 2 diabetes had lower scores on cognitive measures of learning, abstract reasoning, and complex psychomotor functioning ($p<0.001$, $p=0.001$, $p=0.002$, respectively) compared with controls. The two measures of glycaemic control (HbA_{1c} and FPG) were highly correlated to cognitive function in the diabetic group ($r=0.79$, $p<0.01$), but not in the healthy control group. Among the diabetic participants, the higher the HbA_{1c} the

poorer the performance on measures of learning, reasoning, and complex psychomotor functioning,

U'Ren et al, (1990) in a study of 45 people aged 65-77 years, reported significant differences on eight of the thirteen cognitive function tests between diabetic participants and nondiabetic controls ($p<0.05$). On eleven tests classified as measures of attention, memory, and verbal learning functions, the diabetes group had significantly lower scores than did the control group ($p<0.01$-0.05).

Another study performed modified glucose tolerance tests and MMSE in 240 participants aged 75 years and over to ascertain whether diabetes in elderly people was associated with cognitive impairment (Croxson and Jagger, 1995). Participants with known diabetes were more likely to have a low MMSE compared with people without diabetes ($p<0.013$), and participants newly diagnosed with diabetes were also more likely to have a low MMSE compared with people without diabetes ($p<0.015$), but to a lesser extent than people with known diabetes.

Sinclair et al (2000) found that cognitive impairment is associated with changes in self-care behaviour and use of health services. This case-controlled study assessed cognitive function (MMSE ≤23 indicating cognitive impairment) in 396 elderly people with Type 2 diabetes and 393 nondiabetic controls. Seventy one percent of diabetic participants scored 24 or more on MMSE, compared to 88% of controls achieving a score of 24-30 ($p<0.0005$). The presence of diabetes was found to influence cognition test score ($p=0.005–$ 0.02). No relationship between HbA_{1c}, glucose, total cholesterol, HDL-cholesterol and triglycerides and cognitive test scores was observed. After adjusting for age and sex, diabetic participants with lower MMSE scores were less likely to undertake diabetes self-management ($p<0.001$) or to attend a diabetes specialist clinic ($p=0.03$). They were also more likely to have compromised physical function (lower ADL, $p<0.001$), and require more help with self-care ($p=0.001$).

Gregg et al (2000a) studied the relationship between diabetes and diabetes duration and cognitive decline in a 6-year cohort study of 9,679 community-dwelling elderly women aged 65-99 years. Seven percent of participants had diabetes with a mean duration of 10.2 years. Three tests including Digit Symbol, Trail B and m-MMSE were used to assess cognitive function. Depression was defined as a Geriatric Depression Score of ≥6. Women with diabetes were more likely to have visual impairment, hypertension, CVD, stroke and fair to poor health status compared with people without diabetes. People with diabetes had poorer scores on all 3 tests compared with people without diabetes at both baseline and follow-up: Digit Symbol and Trail B tests ($p<0.001$); m-MMSE ($p=0.03$), and they also had greater decline over time on Digit Symbol test ($p=0.01$) and m-MMSE ($p=0.03$). Duration of diabetes was associated with increased cognitive impairment and major cognitive decline on the Digit Symbol and Trail B tests, but not the M-MMSE (p for trend <0.01 for each). Women with more than 15 years of diabetes had a 57% to 114% greater risk of major cognitive decline compared with women without diabetes.

Diabetes is associated with a decline in cognitive function and depression in elderly people

NHMRC Gradeable Evidence

In a prospective cohort study, 6,370 elderly people (mean age 70 years) without dementia at entry were followed up to 2.1 years (Ott el al, 1999). At baseline, 692 people had diabetes, of which 390 were controlled by diet alone, 232 used OHAs and 70 were treated with insulin. People with diabetes were more likely to have hypertension and stroke history, compared with people without diabetes (both $p<0.001$). During the follow-up, 126 people developed dementia, 89 were diagnosed with Alzheimer's disease, 18 were classified into vascular dementia, and 19 had another type of dementia. People developed dementia had a higher diabetes prevalence (27.0% vs. 10.5%, $p=0.005$) and were older than those who were nondemented (80.6+/-7.7 vs. 68.6+/-8.6 years). Diabetes increased the risk of dementia and the age- and sex-adjusted relative risk was 1.9 (95% CI 1.3-2.8), with the highest risk in insulin-treated people, 4.3 (95% CI 1.6-11.8), and the lowest risk in diet-alone people, 1.3 (95% CI 0.7-2.3). Diabetes also increased the risk of Alzheimer's disease with a RR of 1.9 (95% CI 1.2-3.1), RR 1.8 (95% CI 1.1-3.0) for people without CVD, and 3.0 (95% CI 1.0-9.3) for people with CVD.

Leibson et al recruited 1,455 people aged 45 to 99 years with adults onset diabetes mellitus (AODM) and followed them up for 15 years in a prospective study. During the follow-up, 101 people met criteria for dementia, and 77 of them were diagnosed with Alzheimer's disease. The incidence of dementia and Alzheimer's disease increased with age in people with AODM through 45 to 89 years, but not in 90-99 year age group, and age-specific rates of dementia were higher for men than for women. The risk of dementia for people with AODM was 1.66 (95% CI 1.3-2.1) times higher than for people without AODM. The association between diabetes and dementia did not depend on age ($p=0.59$). The risk of Alzheimer's disease was also increased for people with AODM, RR of 2.3 (95% CI 1.6-3.3) for men, and of 1.3 (0.9-2.0) for women, but it reached significance only in men ($p=0.008$). No significant effect of diabetes duration for either dementia or Alzheimer's disease was observed in the study.

When depression occurs in individuals with diabetes, it is associated with poor adherence to diet and the medication regimen, and decreased quality of life. Anderson et al (2001) conducted a systematic review to estimate the prevalence of clinically relevant depression in adults with diabetes. In this review, 18 controlled studies, which included a nondiabetic comparison group, were identified through Medline and PsycINFO database searches (including 5 studies involving 4,124 elderly people with a mean age of 63.0 to 74.2 years). Of these studies, 7 used clinician interviews and psychiatric diagnostic criteria to diagnose depression, and 11 used threshold scores on self-report depression symptom scales. After adjusting for type of diabetes, sex, and method of depression assessment, the odds of depression were twice as high in those with diabetes compared with the control subjects (OR 2.0, 95% CI 1.8-2.2, $p<0.0001$). Overall, the prevalence of depression in people with diabetes (both Type 1 and Type 2) ranged from 8.5% to 49.3%, and was between 11.0% and 13.6% in elderly people with diabetes. The depression scores were higher in people with diabetes than people without diabetes ($p<0.01$). The combined prevalence of depression was significantly higher in women with diabetes than in men with diabetes (28.2% vs. 18.0%, $p<0.0001$, OR 1.6, 95% CI 1.4-1.8). In addition, women were more likely to have a higher depression score than men ($p<0.01$). The results indicate that the presence of diabetes doubles the odds of comorbid depression.

Egede et al (2002) conducted a cross-sectional study using the data from the 1996 Medical Expenditure Panel Survey to compare the prevalence of clinically diagnosed comorbid depression in individuals with diabetes with that in a general population without diabetes.

The diagnosis of depression and diabetes were based on patients' self-report and then verified by contacting medical providers and pharmacies. Among 825 people with diabetes (type not stated), 85 had diagnosed depression. After adjusting for age, sex, race, marital status, poverty status, and comorbidity, people with diabetes were nearly twice as likely to have comorbid clinical depression than those without diabetes (OR 1.9, 95% CI 1.5-2.5). In those with diabetes and depression 71% were aged <65 years, while 29% were >65 years. These were more likely to be in poor physical health (68% vs. 45%, p=0.002) and poor mental health (31% vs. 13%, p=0.002) than nondepressed people with diabetes. With regard to health care cost, diabetic people with depression had higher expenditures for prescription medications than those without depression (US$1,392 vs. US$666, p<0.0001). In conclusion, clinical depression is prevalent in people with diabetes and is associated with higher health care expenditures.

Calcium channel blockers (CCB), β-blockers and ACE inhibitors are frequently prescribed for treatment of ischaemic heart disease and hypertension in the elderly. A study showed among diabetic subjects, new prescriptions of CCB and β-blockers were associated with two- to three-fold increased risk of subsequent diagnosed depression. 972 diabetic subjects (mean age 69.8 years) with newly diagnosed depression, of whom 23.3% were taking antidepressants and 972 age- and sex-matched diabetic controls without depression were recruited in this case-controlled study (Rathman et al, 1999). Overall, there were 28 people with a new prescription of β-blockers, 55 with CCB and 81 with ACE inhibitors during the 6 months prior to the study; in addition, 3 people were receiving both CCB and β-blockers. After adjusting covariates, newly diagnosed depression was significantly associated with a new prescription of β-blockers (OR 2.6, 95% CI 1.1-7.0) and CCB (OR 2.2, 95% CI 1.2-4.2), while no association was found for ACE inhibitors (OR 1.3, 95% CI 0.8-2.2), or β-blockers and CCB together (OR 0.4, 95% CI 0.02-0.8). The adjusted OR for depression associated with high exposure (estimated daily prescribed dosage above the median of cases and controls) to β-blockers (OR 4.5, 95% CI 1.2-29.5) or CCB (OR 4.3, 95% CI 1.7-13.5) was increased to four-fold when compared to non-users, while no association was found among low daily dosage users for both β-blockers (OR 1.5, 95% CI 0.4-5.6) and CCB (OR 1.2, 95% CI 0.5-2.8), compared to non-users. The median duration between first prescription and index date of depression was 83 days (range 4-172 days) for β-blockers users and 108 days (17-182 days) for CCB users.

Ciechanowski et al (2000) found that there was an association between severe depressive symptoms and poorer adherence to diet and medication, and functional impairment in diabetic subjects. 367 people with diabetes (both Type 1 and Type 2) were divided into three groups according to depressive symptom severity tertiles (based on HSCL-90-R depression subscale scores): low <0.5 (n=119), medium 0.5-1.0 (n=119), or high >1.0 (n=121). People with higher depressive symptom severity tertile were more likely to be younger (high vs. low, 59.0 vs. 63.5 years, p=0.01), have a higher diabetes knowledge score (high vs. low, 78.2 vs. 68.2, p<0.001; medium vs. low, 74.8 vs. 68.2, p=0.01), and had one or more diabetes complications (high vs. low, 62% vs. 37%, p<0.001; medium vs. low, 55% vs. 37%, p=0.01). In terms of diabetes self-care, depressive symptom severity was significantly associated with worse adherence to oral medications (defined as the percentage of days of nonadherence to oral therapy, high vs. low: 14.9% vs. 7.1%, p<0.05), as well as with less adherence to dietary advice of diet type and amount (high and medium vs. low, p<0.001). A nonsignificant increase in HbA_{1c} level (high vs. medium vs. low, 7.9±1.5% vs. 7.6±1.4% vs 7.4±1.4%) was also observed. Depressive symptom severity had a significant impact on physical (high vs.

low, p<0.001; medium vs. low, p<0.001) and mental function (high vs. low, p=0.006; high vs. medium, p<0.001).

Brown et al (2000) conducted a cross-sectional study of evaluating the quality of life associated with diabetes mellitus among 292 people (mean age 61.7 years) with a mean duration of diabetes of 20.9 years (both Type 1 and 2), of whom 87 were treated with diet alone or oral agents, while 205 were on insulin therapy. Overall, 218 people had one or more comorbidities which included diabetic retinopathy, neuropathy, nephropathy, depression, gastroparesis, cardiac disease, and diabetic-related extremity disease. The following factors were found to be associated with a significant decrease in diabetes-related quality of life: (1) the requirement of insulin (p=0.05); (2) the presence of depression (p=0.01), and a history of depression which was present in 74 people (25%); (3) the presence of retinopathy (p=0.03); and (4) the presence of any comorbid condition (p=0.01).

Other Evidence

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Age-related changes throughout the life cycle can affect the processing of information. Based on these, the ADEA Position Statement (1999) recommended a slow-paced stepwise method of teaching that uses memory aids as a means of overcoming some age-related barriers to diabetes education.

Similarly, it has been reported that people with Type 2 diabetes often show mild cognitive impairment, specifically related to memory and learning. Also more depression in people with Type 2 diabetes is associated with poor cognitive performance and poor memory function. Therefore, cognitive impairment may be a result of the increased rate of depression in the elderly, as opposed to being a function of cognitive decline itself. In light of this, controlling for depression is important when assessing cognitive function in elderly people with diabetes (Tun et al, 1990).

These findings are supported by a non-systematic review of cognitive impairment in elderly people with diabetes (Morley, 1990) confirming previous claims that suggest a specific impairment in memory retrieval, while learning ability is relatively unaffected. In light of this, it is recommended that memory dysfunction in the elderly not be used as a reason to reduce attempts to achieve optimal glycaemic control, rather a stimulus to increase the intensity of educational interventions in the elderly, with the aim of improving self-care abilities.

4. Physical Ability

Reduced physical ability may be a barrier to diabetes education and associated self-management in elderly people

NHMRC Gradeable Evidence

Diabetes has been shown to be associated with an increased incidence of physical disability in elderly people. Sinclair et al (1997) reported that compared with 106 age- and sex-matched nondiabetic participants, 109 elderly people (mean age 83 years) with diabetes had higher levels of arterial disease (82% vs 70%, p<0.05), foot ulceration (23% vs 9%, p<0.01),

dementia (45% vs 28%, p<0.01) and kidney failure (5% vs 0%, p<0.05). Moreover, people with diabetes were more likely to have moderate/severe cognitive impairment (p<0.001) and a higher level of dependency including activities of daily living (p<0.01). People with diabetes also had more hospital admissions in the previous year and an increased length of stay while in hospital (p<0.05) compared with nondiabetic controls.

A study of 1,030 elderly people (mean age 70 years) with diabetes, found a higher prevalence of inability to perform physical function tasks in both women and men, when compared with people without diabetes (n=5,558) (Gregg et al, 2000b). 32% of women and 15% of men reported disability on at least one of the three tasks compared with 14% of women and 8% of men without diabetes. Inability to perform all 3 tasks was reported in 9% of women and 7% of men with diabetes compared with 4% of women and 2% of men without diabetes. Among women, diabetes was also associated with slower walking speed, decreased extremity function and decreased balance. In contrast men with diabetes only performed poorly on walking speed. In addition, women with diabetes had an increased falls risk (OR 1.58, 1.21-2.08). Physical disability was highly associated with duration of diabetes in both women and men (p for trend <0.001).

Lord et al (1993) compared sensori-motor function in 25 elderly people (mean age 65) with diabetes and 40 age and sex matched non-diabetic controls who were living independently in the community. Sensori-motor function was assessed by touch threshold, vibration sense, proprioception, quadricep strength and body sway. Both male and female participants with diabetes performed worse in tests of body sway on firm and compliant surfaces than controls (p<0.001 for women and p<0.05 for men), after adjustment for weight and BMI. Female participants also performed poorly in tests of peripheral sensation (p<0.05 for touch threshold; p<0.01 for proprioception) and quadricep strength (p<0.05) compared with controls. In addition, age-related declines in sensori-motor function were greater in the diabetic group than in the control group (p<0.01-0.05). These results demonstrate that elderly people with diabetes have problems with stability and related sensori-motor function that may place them at increased risk of falls.

In a cohort study, Gregg et al (2002a) reported the incidence of disability among 8,344 elderly women, 6.3% of whom had diabetes. At baseline, women with diabetes had higher BMI and were more likely to have hypertension, CHD, stroke, arthritis, cognitive impairment, depression, and visual impairment (all p<0.01) compared with women without diabetes. Functional disability was defined as the onset of a reduction in the ability to perform one or more physical functional tasks including walking 0.25 mile, climbing 10 steps, doing housework, shopping and cooking meals. During a mean of 8.8-years of follow-up, the yearly incidence of any functional disability was 9.8% among women with diabetes and 4.8% among those without diabetes. The age-adjusted hazard rate ratio (HRR) of disability for any tasks associated with diabetes was 2.05 (1.77-2.37), and for specific tasks ranged from 2.12 (1.82-2.48) for heavy housework to 2.50 (2.05-3.04) for walking 0.25 mile. After adjustment for baseline confounders and comorbidities, HRR dropped to 1.42 (1.23-1.65) for any tasks, and ranged from 1.53 (1.31-1.80) for heavy housework to 1.98 (1.40-2.79) for cooking meals. No relationship was found between duration of diabetes and overall risk of disability. In addition, increased age, higher BMI, CHD, arthritis, and severe visual impairment were each independently associated with disability.

Volpato et al (2002) assessed the association between diabetes and disability in 1,002 elderly women (mean age 78.8 years) of whom 15.9% had diabetes with a mean duration of 13.4

years. The age-adjusted prevalence of physical disability was consistently higher in women with diabetes than their non diabetic counterparts: OR 1.85 (95% CI 1.12-3.06) for mobility ability (62.2% v 51.4%), which included walking 0.25 mile, climbing 10 stairs; OR 1.61 (95% CI 1.06-2.43) for activities of daily living ability (41.2% v 29.5%), which included bathing, transferring from bed to chair, using toilet, dressing, and eating; and OR 2.34 (95% CI 1.56-3.50) for severe walking limitation (39.7% v 22.0%). Moreover, they had lower total physical performance including walk speed, chair stand and balance test scores than women without diabetes ($p<0.001$). Peripheral arterial disease, peripheral nerve dysfunction and depression were the most important factors contributing to the association between diabetes and disability.

The role of chronic conditions, including diabetes, on changes in functional limitation over 6 years was examined among 4,205 elderly (mean age 76.4 years) white and black people (Dunlop et al, 2002). CVD and arthritis were the two most prevalent chronic conditions across gender and racial groups. Functional limitation was assessed by self-reported moderate (1-2 ADLs) to severe (≥3 ADLs) inability to perform ADL. The 2-year cumulative incidence rate was 7.4% for moderate, and 2.5% for severe functional limitation. The presence of chronic conditions increased the risk of developing functional limitation. During 6-year follow-up of people aged 70-79 years without chronic conditions at baseline, 6% reported moderate functional limitation, while 17% reported severe functional limitation. Among people with 3 or more conditions aged ≥80 years without chronic conditions at baseline, 22% reported moderate functional limitation, while 49% reported severe functional limitation. After controlling for demographics, arthritis, diabetes, prior cerebrovascular disease, incontinence, and impaired vision were significant predictors of the onset of moderate functional limitation and prior moderate functional limitation. CVD and visual impairment predicted the onset of severe functional limitation.

A study of 9249 women aged ≥ 67 years, of them, 629 (6.8%) had diabetes, found an increased risk of falling among women with diabetes, particularly among those using insulin (Schwartz et al, 2002). At baseline, women with diabetes were more likely to have a history of arthritis and fainting, peripheral neuropathy, and poor physical and cognitive performance compared with women without diabetes (all $p<0.05$). Furthermore, all these risk factors for falls tended to be more common among women using insulin. During an average of 7.2 years follow-up, falls were ascertained every 4 months by postcard. A total of 1640 women had a fall more than once a year. Diabetes was associated with an increased risk of falling more than once a year: age-adjusted OR was 1.68 (1.37-2.07) for non-insulin-treated diabetes, 2.78 (1.82-4.24) for insulin-treated diabetes. Women with diabetes were also at increased risk of falling more than twice a year, OR was 1.63 (1.22-2.18), and 2.55 (1.45-4.49), respectively. In addition, women with diabetes had more falls (3.1 vs. 2.4, $p<0.01$) than women without diabetes in the first 2 years. After adjusting for multiple factors for falls which included poor balance, arthritis, CVD, depression, poor vision, and use of medication for sleeplessness or anxiety, the association between diabetes and falling remained significant in insulin-treated women, OR 2.76 (1.52-5.01), but not in non-insulin-treated women, OR 1.18 (0.87-1.60).

Langa et al (2002) found that elderly people aged 70 to ≥90 years with diabetes received more weekly hours of informal caregiving than those without diabetes: 10.5h for people on diet alone, 10.1h for people taking OHA, and 14.4h for insulin users, compared to 6.1h for people without diabetes ($p<0.001$). These people also had an increased incidence of comorbid conditions ($p<0.001$) and increased difficulties with ADL or instrumental activities of daily living (eg cooking, grocery shopping, taking medication, using telephone) ($p<0.001$).

5. Loss of Special Senses

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The loss of special senses can affect access to health care and adherence to diabetes self care recommendations

NHMRC Gradeable Evidence

The limited amount of research into the impact of loss of special senses on access to health care and adherence to diabetes self-care recommendations has focused on visual loss.

A cohort study reported the incidence of disability among 8,344 elderly women, 6.3% of whom had diabetes (Gregg et al, 2002a). At baseline, women with diabetes had higher BMI and were more likely to have hypertension, CHD, stroke, arthritis, cognitive impairment, depression, and visual impairment (all $p<0.01$) compared with women without diabetes. However, no relationship was found between duration of diabetes and overall risk of disability. In contrast, factors found to be independently associated with disability were increased age, higher BMI, CHD, arthritis, and severe visual impairment.

Volpato et al (2002) assessed the association between diabetes and disability in 1,002 elderly women (mean age 78.8 years) of whom 15.9% had diabetes with a mean duration of 13.4 years. Researchers found that women with diabetes were more likely to have CVD, peripheral nerve dysfunction, visual impairment and depression.

A study assessing the role of chronic conditions, including diabetes, on changes in functional limitation over 6 years examined 4,205 elderly people (mean age 76.4 years) (Dunlop et al, 2002). After controlling for demographics, impaired vision was a significant predictor of the onset of moderate functional limitation and that in combination with prior moderate functional limitation. CVD and visual impairment also predicted the onset of severe functional limitation.

NHMRC Gradeable Evidence table for Barriers to Health Care and Education Index

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Anderson et al, 2001	Systematic review	I	The prevalence of depression in adults with diabetes
Brown et al, 2000	Cross-sectional	III	Quality of life and diabetes
Ciechanowski et al, 2000	Cohort	III	Depression and diabetes
Croxson and Jagger, 1995	Cross-sectional	III	Cognitive Impairment
Dunlop et al, 2002	Cohort	III	Physical disability and comorbidities
Egede et al, 2002	Cross-sectional	III	Depression and diabetes
Gilden et al, 1989	Cohort	III	Effects of a diabetes education program on knowledge and quality of life
Gilden et al, 1990	Cross-sectional	III	Comparison of SMBG and urine testing on quality of life
Gregg et al, 2000a	Cohort	III	Cognitive impairment
Gregg et al, 2000b	Cross-sectional	III	Physical disability and comorbidities
Gregg et al, 2002a	Cross-sectional	III	Physical disability and comorbidities
Karter et al, 2000	Cross-sectional	III	Disadvantaged social situation
Langa et al, 2002	Cross-sectional	III	Comorbidities
Leibson et al, 1997	Cohort	III	Diabetes increases the risk of dementia
Lord et al, 1993	Case-controlled	III	Comparison of sensori-motor function in people with and without diabetes
Ott et al, 1999	Cohort	III	Diabetes increases the risk of dementia
Rathmann et al, 1999	Cross-sectional	III	Cardiovascular drug prescription and risk of depression
Reaven et al, 1990	Case-control	III	Cognitive impairment

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Schwartz et al, 2002	Cohort	III	Diabetes increases risk of falls
Sinclair et al, 1997	Case-control	III	Physical disability and comorbidities
Sinclair et al, 2000	Case-control	III	Cognitive impairment
U'Ren et al, 1990	Case-control	III	Cognitive impairment
Volpato et al, 2002	Cross-sectional	III	Physical disability and comorbidities

Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes. Diabetes Care 2001;24:1069-78

Brown GC, Brown MM, Sharma S, Brown H, Gozum M, Denton P. Quality of life associated with diabetes mellitus in an adult population. J Diabetes Complications 2000;14:18-24

Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes. Impact of depressive symptoms on adherence, function, and costs. Arch Intern Med 2000;160:3278-85

Croxson SCM and Jagger C. Diabetes and cognitive impairment: a community-based study of elderly subjects. Age and Ageing 1995; 24: 421-424

Dunlop DD, Manheim LM, Sohn M-W, Liu X, Chang RW. Incidence of functional limitation in older adults: The impact of gender, race, and chronic conditions. Arch Phys Med Rehabil 2002;83:964-71

Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. Diabetes Care 2002;25:464-470

Gilden JL, Hendryx M, Casia C, Singh SP. The effectiveness of diabetes education programs for older patients and their spouses. Journal of American Geriatric Society 1989; 37: 1023-30

Gilden JL, Casia C, Hendryx M, Singh SP. Effects of self-monitoring of blood glucose on quality of life in elderly diabetic subjects. Journal of American Geriatric Society 1990; 38: 511-515

Gregg EW, Yaffe K, Cauley JA, Rolka DB, Blackwell TL, Narayan KMV, Cummings SR. Is diabetes associated with cognitive impairment and cognitive decline among older women? Arch Inter Med 2000a; 160:174-80

Gregg EW, Beckles GLA, Williamson DF, Leveille SG, Langlois JA, Engelgau MM, Narayan KMV. Diabetes and physical disability among older U.S. adults. Diabetes Care 2000b;23:1272-7

Gregg EW, Mangione CM, Cauley JA, Thompson TJ, Schwartz AV, Ensrud KE, Nevitt MC. Diabetes and incidence of functional disability in older women. Diabetes Care 2002a;25:61-7

Karter AJ, Ferrara A, Darbinian JA, Ackerson LM, Selby JV. Self-monitoring of blood glucose. Language and financial barriers in a managed care population with diabetes. Diabetes Care 2000; 23 (4):477- 483

Langa KM, Vijan S, Hayward RA, Chernew ME, Blaum CS, Kabeto MU, Weir DR, Katz SJ, Willis RJ, Fendrick AM. Informal caregiving for diabetes and diabetic complications among elderly Americans. Journal of Gerontology: Social Sciences 2002; 57B: S177-86

Leibson CL, Rocca WA, Hanson VA, Cha R, Kokmen E, O'Brien PC, Pulumbo PJ. Risk of dementia among persons with diabetes mellitus: a population-based cohort study. Am J Epidemiol 1997;145:301-8

Lord SR, Caplan GA, Colagiuri R, Colagiuri A, Ward JA. Sensori-motor function in older persons with diabetes. Diabetic Medicine 1993; 10: 614-618

Ott A Stolk RP, van Harskamp F, Pols HAP, Hofman A, Breteler MMB. Diabetes mellitus and the risk of dementia: The Rotterdam Study. Neurology 1999;53:1937-42

Rathmann W, Haastert B, Roseman JM, Giani G. Cardiovascular drug prescriptions and risk of depression in diabetic patients. J Clin Epidemiol 1999;52:1103-9

Reaven GM, Thompson LW, Nahum D, Haskins E. Relationship between hyperglycemia and cognitive function in older NIDDM patients. Diabetes Care 1990;13:16-21

Schwartz AV, Hillier TA, Sellmeyer DE, Resnick HE, Gregg E, Ensrud KE, Schreiner PJ, Margolis KL, Cauley JA, Nevitt MC, Black DM, Cummings SR. Older Women with diabetes have a higher risk of falls. A prospective study. Diabetes Care 2002;25:1749-54

Sinclair AJ, Allard I, Bayer A. Observations of diabetes care in long-term institutional settings with measures of cognitive function and dependency. Diabetes Care 1997;20:778-84

Sinclair AJ, Girling AJ, Bayer AJ. Cognitive dysfunction in older subjects with diabetes mellitus: impact on diabetes self-management and use of care services. Diabetes Res Clin Pract 2000;50:203-12

U'Ren RC, Riddle MC, Lezak MD, Bennington-Davis M. The mental efficiency of the elderly person with Type 2 diabetes mellitus. J Am Geriatr Soc 1990;38:505-10

Volpato S, Blaum C, Resnick H, Ferrucci L, Fried LP, Guralnik JM. Comorbidities and impairments explaining the association between diabetes and lower extremity disability. The Women's Health and Ageing Study. Diabetes Care 2002;25;678-83

Barriers to Health Care and Education – Other References

Active Australia. National Physical Activity Guidelines for Australians. Commonwealth Department of Health and Aged Care. Canberra, 1999

ADEA (1999). Special considerations for the education and management of older adults with diabetes. Position statement. Diabetes Educator 1999; 25 (6): 879-881

British Diabetic Association. Guidelines of practice for residents with diabetes in care homes. British Diabetic Association. London. 1999

Hampson SE, Glasgow RE and Foster LS Personal models of diabetes among older adults: relationship to self - management and other variables Diabetes Educator 1995 July - August; 21 (4): 300 - 7

Holvey SM. Psychosocial aspects in the care of elderly diabetic patients. The American Journal of Medicine 1986; 80 (Suppl 5A): 61-63

Morley JE. Psychosocial aspects of diabetes mellitus in older persons. American Geriatric Society 1990; 38: 605-606

Reed RL, Mooradian AD. Nutritional status and dietary management of elderly diabetic patients. Cli Geriatr Med 1990;6:883-901

Sherriff P, Allison J, Large M, Quinn C, Routledge A, Hall E, Broughton DL, Kelly WF. Out of sight- out of mind? Elderly patients with diabetes in nursing homes. Prac Diab Int 2000; 17 (3): 73-6

Sinclair AJ, Barnett AH. Special needs of elderly diabetic patients. BMJ 1993 July24; 306(6886): 1142-1143

Tun PA, Nathan DM, Perlmuter LC. Cognitive and affective disorders in elderly diabetics. Clin Geriatric Medicine 1990; 6: 731-746

Zigbor JC and Songer TJ. External barriers to diabetes care: addressing personal and health systems issues. Diabetes Spectrum 2001; 14: 23-33

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2.5A Hypoglycaemia

Index

Are there special considerations for elderly people with diabetes regarding recognition of hypoglycaemia?

Answer

Yes

Why

- Elderly people with diabetes experience impairment in glucose counterregulation and reduced awareness of hypoglycaemia
  Evidence Level III

- Knowledge of hypoglycaemia is inadequate in elderly people with diabetes especially those taking oral hypoglycaemic agents
  Evidence Level III

- Sulphonlylureas and insulin increase the risk of hypoglycaemia
  Evidence Level III

- Polypharmacy is a risk factor for hypoglycaemia
  Evidence Level III

Recommendations

- Reduced glucose counterregulation and awareness of hypoglycaemia with ageing, and overall health status, should be considered when making treatment plans. Increased blood glucose monitoring may be required to detect unrecognised hypoglycaemia in elderly people with diabetes

- Elderly people with diabetes and their carers should receive a specific individualised education about managing hypoglycaemia, with any change in medication, environment, cognitive or functional status

- When prescribing sulphonylurea and/or insulin treatment in elderly people with diabetes caution should be taken (including a review of current medication) because of the increased risk of hypoglycaemia

Background – Hypoglycaemia

Hypoglycaemia is a common and acute short-term complication of diabetes and is defined as a blood glucose level below the normal range, or a blood glucose level which is low enough to cause symptoms (ADEA and NSW Health Department, 1997).

Symptoms of hypoglycaemia have been classified into 2 categories (Walter, 1990):

- Adrenergic, associated with the release of counter-regulatory hormones: palpitations, anxiety, tremor, hunger, and sweating, and
- Neuroglycopaenic, resulting from cerebral glucose deficiency: headache, fatigue, impaired concentration, irritability, confusion, seizures, hemiplegia, and coma.

The blood glucose level at which these occur is not well defined but probably differs according to age and sex, the rate at which the blood glucose level falls, and whether any associated medical conditions such as liver disease or CVD are present (NHMRC, 1991).

Hypoglycaemia in the elderly can be a potentially serious hazard if it is undetected and untreated as it may result in transient cognitive impairment, fitting and ultimately unconsciousness. All people with diabetes treated with oral hypoglycaemic agents (especially sulphonylureas) or insulin are at risk. Exacerbation of risk occurs in people with impaired liver or renal function or with a long duration of diabetes that may contribute to decreased awareness of hypoglycaemia.

Hypoglycaemia may result from the use of excess medication, suboptimal medication management and administration, insufficient carbohydrate intake, missing or delaying meals, prolonged physical activity without extra carbohydrate, drinking alcohol without eating carbohydrate, or vomiting. There is also an increased risk associated with increasing age (Brown and Jackson, 1994). Other factors increasing the risk of hypoglycaemia in the elderly include polypharmacy and an increase in atypical, nonspecific and in some cases a lack of symptoms of hypoglycaemia (Walter, 1990).

Elderly people with diabetes experience impairment in glucose counterregulation and reduced awareness of hypoglycaemia

NHMRC Gradeable Evidence

Index

A cross-sectional study compared the glycaemic and neuroendocrine responses to hypoglycaemia between 23 healthy elderly people (aged 60-70 years) and 18 healthy young people (aged 21-31 years) (Marker et al, 1992). Hypoglycaemia was induced by 0.05U/kg of insulin, administered intravenously for 180 minutes. During the period of hypoglycaemia, absolute reduction in plasma glucose concentration was similar for both groups. However, the rate of glucose recovery was reduced from 42.7 ± 5.0 uM/min in the young to 29.4 ± 2.2uM/min in the elderly ($p<0.02$); and plasma glucagon levels were lower in the elderly. Plasma insulin concentration was higher in the elderly group ($p<0.01$ at 10min, $p< 0.05$ at 40minutes, respectively compared with the young group). Increments in plasma epinephrine were similar in both groups, and maximum increments in plasma norepinephrine, cortisol, and growth hormone concentrations did not differ between the two groups. These results demonstrate an age-associated impairment of glucose counter-regulation that can be attributed to decreased insulin clearance, reduced glucagon secretion, or both.

In the same study described above (Marker et al, 1992) a further 11 elderly participants were restudied following 1 year of a physical training exercise program. The aim was to determine if the differences found between elderly and young participants were influenced by the sedentary lifestyle of the elderly. Participants exercised for 30minutes, 3 times/week at moderate intensity for the first 6 months, which was gradually increased to 50minutes, 4-5

times/week at high intensity for the remaining 6 months. There was no effect of training on glucose recovery or neuroendocrine responses to hypoglycaemia in the elderly, indicating that the original findings were not the result of a sedentary lifestyle.

Meneilly et al (1994) reported that elderly people with Type 2 diabetes had impaired glucagon and growth hormone responses to hypoglycaemia compared with healthy elderly people without diabetes. Ten healthy elderly people without diabetes (mean age 74 years) and 10 healthy elderly people treated with diet or oral hypoglycaemic agents (mean age 72 years), underwent two hyper-insulinaemic glucose clamp studies (insulin infusion, 60mU/m^2/min). Glucose was maintained at 5mmol/L for 5 hours in the control study in comparison glucose was maintained at 5mmol/L for 1 hour, and then lowered to 4.4, 3.8, 3.3 and 2.8mmol/L in each subsequent hour in the hypoglycaemic study. At a glucose level of 2.8mmol/L, people with Type 2 diabetes had reduced increases of glucagon and growth hormone compared with healthy elderly people ($p<0.05$, $p<0.01$, respectively). People with diabetes also had a greater impairment on the simple and choice reaction time tests (measures of psychomotor coordination) ($p<0.001$, $p<0.01$, respectively) than their nondiabetic counterparts. Despite these findings no differences in symptom scores at any glucose level were found between groups. These findings indicate that elderly people with diabetes have altered release of counterregulatory hormones and greater impairment in psychomotor performance during hypoglycaemia.

Matyka et al (1997) assessed changes in neurohumoral responses, subjective awareness and choice reaction time during hypoglycaemia in a study of 7 healthy older men aged 65 ± 3 years and 7 healthy younger men aged 23 ± 2 years. Plasma glucose was lowered from 5 to 2.4mmol/L and restored by an infusion of 20% glucose. Hormonal responses were similar in the two groups, but symptoms began earlier in the younger men (3.6 ± 0.1mmol/L in the elderly group v 3.0 ± 0.2mmol/L, in the young group, $p=0.02$) and were more intense ($p=0.03$). Older men showed a much more marked deterioration in four-choice reaction time (a measure of psychomotor coordination) than younger men ($p=0.016$). The difference between glucose level for subjective awareness of hypoglycaemia and onset of cognitive impairment was lost in older men (0.0 ± 0.2 v 0.8 ± 0.1mmol/L, $p<0.007$). The researchers concluded that older men were prone to more severe cognitive impairment during hypoglycaemia than younger men and were less likely to experience prior warning symptoms when blood glucose fell. Older people may be at greater risk of developing neuroglycopaenia because the onset of hypoglycaemic warning symptoms did not precede the development of cognitive dysfunction.

In a retrospective study, Jaap et al (1998) found that of 132 elderly people (>70 years) treated with insulin, 102 people had experienced hypoglycaemia within the preceding 2 months. The most frequently reported symptoms of hypoglycaemia in elderly people were lightheadedness, unsteadiness, poor concentration, trembling and sweating, with a median number of hypoglycaemic episodes of 6 (range 2-24) in the last year. On further examination three separate groups of symptoms were identified. First, those related specifically to impairment of coordination and articulation; second, more general neuroglycopaenic symptoms (such as drowsiness or confusion) and third, autonomic symptoms (such as sweating and shivering). The frequency and identification of these symptoms found in this elderly population were different from those found in younger people treated with insulin, and neurological symptoms of hypoglycaemia were more commonly reported. The researchers concluded that health care professionals should be aware of the age-specific differences in hypoglycaemic symptoms and be careful of interpreting neurological symptoms of hypoglycaemia as features of cerebrovascular disease.

Other Evidence

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A non-systematic review of the causes of hypoglycaemia unawareness found that it is now widely recognised that some people with long standing diabetes lose their ability to secrete the major counterregulatory hormones, glucagon and epinepherine, and therefore fail to develop the hypoglycaemia-related autonomic warning symptoms (Hoeldtke and Boden, 1994). Elderly people may have a limited perception of autonomic symptoms of hypoglycaemia that are generated at an earlier stage in the development of hypoglycaemia. This limitation in the recognition of symptoms may partly be a consequence of inadequate education in elderly people with diabetes.

Knowledge of hypoglycaemia is inadequate in elderly people with diabetes especially those taking oral hypoglycaemic agents

NHMRC Gradeable Evidence

Three studies assessing knowledge of hypoglycaemia in elderly people with diabetes indicated that knowledge of symptoms of hypoglycaemia was inadequate. A study assessed knowledge of hypoglycaemia in 161 elderly people using insulin (n=78, mean age 73 years) or sulphonylurea (n=83, mean age 76 years) (Mutch and Dingwall-Fordyce, 1985). Of the group, 9% did not know any symptoms of hypoglycaemia, despite 52% reporting experiencing hypoglycaemia including symptoms of weakness, sweating, confusion, inability to concentrate, palpitations, speech disturbance and tingling lips. Comparison of people on insulin and sulphonylureas found that people on insulin had a significantly higher knowledge of specific symptoms ($p< 0.01$), and had higher general knowledge scores (6.8 v 5.2). Knowledge score decreased with age (7.7 in under 70 years age group v 6.1 in over 80 years age group), but was not related to sex, duration of diabetes or living alone. Limited recognition of hypoglycaemic symptoms may partly be a consequence of inadequate education in elderly people with diabetes. Relatives of people with diabetes have also been shown to lack knowledge of the symptoms of hypoglycaemia. In addition, 30% of relatives did not know an appropriate first aid treatment of hypoglycaemia. These findings demonstrate a poor and equivalent level of knowledge of hypoglycaemic symptoms and treatment between participants and their relatives.

Thomson et al (1991) evaluated knowledge of hypoglycaemia in 45 elderly people (aged 61-82 years) with diabetes who were free of cognitive deficit. Of the 45 participants, 26 were receiving OHA's, and 19 were treated with insulin. Twenty three participants treated with OHA's and 6 participants treated with insulin had no knowledge of hypoglycaemia. Participants treated with insulin had higher knowledge scores than those treated with OHA's, demonstrated by an increased awareness of the possibility of hypoglycaemia (68% v 12%) ($p< 0.002$); and an increased knowledge of the correct treatment of hypoglycaemia (84% v 35%, $p< 0.03$). The most commonly recognised symptoms were weakness, unsteadiness, faintness and sleepiness.

Another study of 237 elderly people (mean age 65) with Type 2 diabetes treated with Glibenclamide (mean dose 6.7mg/day) found that three participants (1.3%) experienced one episode of severe hypoglycaemia each (Ratzmann and Schimke, 1995). Old age, maximum dose of Glibenclamide (15mg/day) and multiple comorbidities were identified as factors that

increased the incidence of hypoglycaemia. Furthermore, only 49% of all subjects had adequate knowledge about hypoglycaemia.

Sulphonlylureas and insulin increase the risk of hypoglycaemia

NHMRC Gradeable Evidence

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There is an increased incidence of hypoglycaemic episodes associated with use of sulphonylureas and/or insulin (Shorr et al, 1996; Shorr et al, 1997; Ben-Ami et al, 1999 a and b), especially with use of Glibenclamide (Van Staa et al, 1997).

Shorr et al (1996) reported that during 20,715 person-years of sulphonylurea use, 255 elderly people (mean age 78 years) had a first episode of serious hypoglycaemia, and the mean plasma glucose on presentation was 1.9 ± 0.5mmol/L. The majority presented with neuroglycopaenic symptoms, loss of consciousness (48%), lethargy (32%), syncope (7%), irrational behaviour (6%) and/or seizures (6%). The crude rate (per 1,000 person-years) of serious hypoglycaemia was highest in Glyburide (Glibenclamide) users - RR 16.6 (CI 13.2-19.9) and lowest among users of Tolbutamide - RR 3.5 (CI 1.2-5.9). There was a two-fold increase in the risk of hypoglycaemia among Glyburide (Glibenclamide) users compared with Glipizide users - RR 8.6 (CI 5.2-12.0). These results confirm that long-acting sulphonlyurea use was associated with the highest risk of hypoglycaemia.

In a 4 year cohort study Shorr et al (1997) aimed to determine the incidence and risk factors for developing serious hypoglycaemia among people aged 65 years or older (mean age 78) using sulphonylureas and/or insulin. Serious hypoglycaemia was defined as a hospitalisation, emergency department admission or death associated with hypoglycaemic symptoms and concomitant blood glucose of less than 2.8 mmol/L. The study identified 589 people with a first episode of serious hypoglycaemia during 33,048 person-years of insulin or sulphonylurea use. The overall RR of serious hypoglycaemia was 1.81 (CI 1.67- 1.95) per 100 person years of hypoglycaemic drug exposure. Specifically, RR was 1.23 (CI 2.47 – 3.06) among sulphonylurea users, 2.76 (CI 2.47- 3.06) among insulin users and 3.38 (CI 1.50 – 5.26) among users of both. Compared with people aged 65-70 years, people aged 80 or older had a higher RR (1.8) of developing hypoglycaemia (CI 1.4- 2.3; $p<0.05$). People using five or more concomitant medications and those new to hypoglycaemic drug therapy were also at higher risk of hypoglycaemia (RR 1.3, CI 1.1-1.5; RR 1.4, CI 1.0-1.9 respectively). These results demonstrate that elderly people, those using multiple medications, and those who are frequently hospitalised are at higher risk of drug-associated hypoglycaemia.

Van Staa et al (1997) retrospectively studied 33,243 people with diabetes treated with sulphonylureas to determine risk factors for hypoglycaemia. Participants were 20 years or older and had received at least one prescription for Glibenclamide, Gliclazide, Chlorpropamide, Glipizide or Tolbutamide. Of 34,052 person years of therapy, 605 cases of hypoglycaemia were identified, translating into an annual risk of 1.8%. Risk factors for hypoglycaemia identified included age greater than 65, RR 1.27 (CI 1.06-1.51), renal impairment, RR 3.5 (CI 1.95-6.47), polypharmacy, RR 1.84 (CI 1.55-2.17) and sulphonylurea type [Gliclazide v Glibenclamide RR 0.74 (CI 0.59-0.92) and Tolbutamide v Glibenclamide RR 0.75 (CI 0.58-0.97)]. These findings indicate that the rate of hypoglycaemia is higher for Glibenclamide than for other sulphonylureas, and that there is an increased risk of hypoglycaemia with increasing age, renal impairment and polypharmacy.

A retrospective analysis of 51 people (mean age 76 years) with Glibenclamide induced hypoglycaemic coma (GIHC) identified several risk factors (Ben-Ami et al, 1999a). Risk factors associated with GIHC included age >60 years, renal dysfunction, reduced calorie intake, infection, overdose, liver cirrhosis and metastatic liver disease. Factors found to explain the occurrence of GIHC in these people were their advanced age and prolonged duration of diabetes, which resulted in impaired counter-regulatory responses and the presence of concomitant risk factors for hypoglycaemia. Of 51 participants, 38 were found to have renal insufficiency. Use of Glibenclamide in these people may cause hypoglycaemia arising from the accumulation of biologically active metabolites, reduced renal gluconeogenesis and decreased caloric intake.

Drug-induced hypoglycaemic coma was examined in a 7-year retrospective cohort of 102 people (mean age 72 years) with Type 1 (10%) and Type 2 (90%) diabetes (Ben-Ami et al, 1999b). Of the 102 participants, drug-induced hypoglycaemic coma was the primary cause for hospitalisation. Medications examined were insulin alone, insulin and Glyburide, Glyburide alone, insulin and Metformin, and Glyburide and Metformin. Results demonstrated that drug-induced hypoglycaemic coma occurred mostly in people taking Glyburide (Glibenclamide), followed by insulin, Glyburide plus insulin, Glyburide plus Metformin and insulin plus Metformin. Contributing risk factors identified included age greater than 60 years (82.3% of the population), renal dysfunction, reduced energy intake (26.5% of the population had both renal dysfunction and reduced energy intake), infection and hypoglycaemia-potentiating medications such as beta-blockers (13.7% of the population).

Two studies failed to show any differences in incidence of hypoglycaemia between human and animal insulin (Colagiuri et al, 1992; Altman et al, 1998). Colagiuri et al (1992) conducted a study to assess the frequency and characteristics of hypoglycaemic episodes among 50 people aged 12-74 years (mean age 47 years) who reported a reduction of awareness of hypoglycaemia after changing treatment. Each person was treated in a double-blind manner for four 1-month periods, two with human insulin and two with porcine insulin, in random order. No significant differences in blood glucose concentrations were found between human insulin and porcine insulin treatment (mean 9.2± 1.5 v 9.3± 1.5mmol/L). The number of hypoglycaemic events per day associated with reduced or absent awareness was 0.25± 0.21 for human and 0.27± 0.21 for porcine insulin. The mean percentage of hypoglycaemic episodes associated with reduced or absent awareness was 64± 30% for human insulin and 69±31% for porcine insulin (p=0.82). The researchers concluded no significant differences between the insulin species with respect to glycaemic control or the frequency or severity of awareness of hypoglycaemia.

Altman et al (1998) assessed glycaemic control, frequency of hypoglycaemia and quality of life in 94 people with Type 1 diabetes who were switched from animal insulin to human insulin. All participants were randomly assigned either to continue their usual insulin (group A, mean age 58.1 years and maximum age 85 years, n=48) or convert to equivalent preparations of human insulin (group B, mean age 54.4 years and maximum age 92 years, n=46). There were no differences in duration of diabetes (20.8±1.4 vs. 19.6±1.6 years), HbA_{1c} value, and the length of previous insulin therapy. After 3 months of treatment, there were no differences in HbA_{1c} value (8.6±0.2 vs. 8.5±0.2%) and the frequency and intensity of hypoglycaemic episodes between the two groups. Quality of life assessed by a questionnaire was similar at baseline and after 3 months, but the anxiety level was significantly lower in group B (p=0.03) which might suggest that the fear of hypoglycaemia unawareness was not a

source of anxiety. The study concluded that elderly people with diabetes can safely be transferred to human insulin.

Other Evidence

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A nonsystematic review on avoiding hypoglycaemia in the elderly (Cryer, 1999) found that in people with Type 2 diabetes, the frequency of hypoglycaemia may increase with increasing duration of insulin therapy, and glucagon secretory responses may be reduced. Hypoglycaemia unawareness, as commonly occurs in elderly people, is the result of a reduction in the glycaemic threshold for hormonal and symptomatic responses to hypoglycaemia. Drug-induced hypoglycaemia, such as that found with use of Glibenclamide, occurs because hyperinsulinaemia is present but there is no glucagon response to counteract it. As a result, autonomic responses to falling glucose levels are reduced on subsequent occasions, resulting in reduced symptoms of, and impaired physiological defence against developing hypoglycaemia. This review also found that treatments that limit hepatic or renal glucose production or favour glucose utilisation may increase the risk of hypoglycaemia.

A non-systematic review of insulin use in the elderly reported that a reduced counterregulatory response and awareness to hypoglycaemia place the elderly at increased risk of morbidity and mortality from hypoglycaemia (Davis and Brown, 1999).

Polypharmacy is a risk factor for hypoglycaemia

NHMRC Gradeable Evidence

Due to an increase in concomitant disease in the elderly, there is a corresponding rise in multiple medication use. This polypharmacy has the potential to alter responsiveness to medications and increase the incidence of adverse effects among the elderly.

In a study assessing the risk of hypoglycaemia, van Staa et al (1997) reported that a diagnosis of hypoglycaemia during sulphonylurea therapy was recorded in 605 people over 34,052 person-years of sulphonylurea therapy. People aged ≥65 years experienced 427 cases of hypoglycaemia in 21,706 person-years of sulphonylurea therapy, which was equivalent to an annual risk of 2.0%, compared with 178 cases in 12,345 person-years and an annual risk of 1.4% for people aged less than 65 years. Following multivariate adjustment, polypharmacy was among the independent risk factors for hypoglycaemia with a relative risk of 1.84 (CI 1.55-2.17). People with polypharmacy (n=378) had a higher incidence of hypoglycaemia - 2.4%, compared with 1.2% in people without polypharmacy (n=218).

Malhortra et al (2001) studied 578 people (mean age 72.5 years) admitted to a medical emergency department during a 6-month period. The study population had an average number of 4.1 different medications prescribed and an average number of 5.9 tablets taken per day. Among all admissions, 83 (14.4%) were judged to be drug related. Among 39 admissions due to adverse drug reactions, hypoglycaemia induced by oral hypoglycaemic agents (type not specified) was the most common (30.8%). Other drugs commonly implicated were non-steroidal anti-inflammatory drugs. These findings demonstrate that many elderly admissions are commonly medication related, therefore educational interventions to reduce these are required.

NHMRC Gradeable Evidence table for Hypoglycaemia

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Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Altman et al, 1998	RCT	II	Incidence of hypoglycaemia in animal v human insulin treated subjects
Ben-Ami et al, 1999a	Retrospective Cohort	III	Glibenclamide induced hypoglycaemic coma
Ben-Ami et al, 1999b	Retrospective Cohort	III	Drug-induced hypoglycaemic coma
Colagiuri et al, 1992	RCT	II	Awareness of hypoglycaemia
Jaap et al, 1998	Retrospective cohort	III	Classification of hypoglycaemic symptoms
Malhotra et al, 2001	Cohort	III	Polypharmacy
Marker et al, 1992	Cross-sectional	III	Impaired glucose counterregulation
Matyka et al, 1997	Cross-sectional	III	Reduced awareness of hypoglycaemia
Meneilly et al, 1994	Cross-sectional	III	Impaired glucose counterregulation
Mutch, et al, 1985	Cross-sectional	III	Inadequate knowledge of hypoglycaemia
Ratzmann and Schimke, 1995	Cross-sectional	III	Inadequate knowledge of hypoglycaemia
Shorr et al, 1996	Cohort	III	Incidence of hypoglycaemia in people treated with sulphonylureas
Shorr et al, 1997	Cohort	III	Incidence and risk factors for hypoglycaemia
Thomson et al, 1991	Case-control	III	Inadequate knowledge of hypoglycaemia
Van Staa et al, 1997	Cohort	III	Polypharmacy

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Altman JJ, Feldman S, Bonnemaire M, Elian N, Squiban P and the Investigators of the Transfert Study. No increase of hypoglycaemia upon transfer of aged longstanding Type 1 diabetic patients to human insulin: a prospective study. Diabetes Metabolism 1998; 24: 419-423.

Ben-Ami H, Nagachandran P, Mendelson A, Edoute Y. Older patients are at particular risk of drug-induced hypoglycaemia. Glicenclamide induced hypoglycaemic coma in 51 older patients with Type 2 diabetes mellitus. J Am Gertiatr Soc 1999a; 47: 631-633.

Ben-Ami H, Nagachandran P, Mendelson A, Edoute Y. Drug-induced hypoglycaemic coma in 102 diabetic patients. Arch Intern Med 1999b; 159: 281-284.

Colagiuri S, Miller JJ, Petocz P. Double-blind crossover comparison of human and porcine insulins in patients reporting lack of hypoglycaemia awareness. Lancet 1992;339:1432-5

Jaap AJ, Jones GC, McCrimmon RJ, Deary IJ, Frier BM. Perceived symptoms of hypoglycaemia in elderly Type 2 diabetic patients treated with insulin. Diabet Med 1998; 15: 398-401.

Malhotra S, Karan RS, Pandhi P, Jain S. Drug related medical emergencies in the elderly: role of adverse drug reactions and non-compliance. Postgrad Med J 2001;77:703-7

Marker JC, Cryer PE, Clutter WE. Attenuated glucose recovery from hypoglycaemia in the elderly. Diabetes 1992;41:671-8

Matyka K, Evans M, Lomas J, Cranston I, Macdonald I, Amiel SA. Altered hierarchy of protective responses against severe hypoglycaemia in normal ageing in healthy men. Diabetes Care 1997;20:135-41

Meneilly GS, Cheung E, Tuokko H. Counterregulatory hormone responses to hypoglycaemia in the elderly patients with diabetes. Diabetes 1994;43:403-10

Mutch WJ, Dingwall-Fordyce I. Is it a hypo? Knowledge of the symptoms of hypoglycaemia in elderly diabetic people. Diabet Med 1985;2:54-6

Ratzmann KP and Schimke E. Incidence of severe hypoglycaemia in relation to metabolic control and patient knowledge. Med Klin 1995; 90 (10): 557-61.

Shorr RI, Ray WA, Daugherty JR, Griffin MR. Individual sulfonylureas and serious hypoglycaemia in older people. J Am Geriatr Soc 1996; 44: 751-755.

Shorr RI, Ray WA, Daugherty JR, Griffin MR. Incidence and risk factors for serious hypoglycaemia in older persons using insulin or sulfonylureas. Archives of Internal Medicine 1997; 157: 1681-1686.

Thomson FJ, Masson EA, Leeming JT, Boulton AJM. Lack of knowledge of symptoms of hypoglycaemia by elderly diabetic people. Age Ageing 1991;20:404-6

Van Staa T, Abenhaim L, Monette J. Risk factors for hypoglycaemia in users of sulphonylureas. Rates of hypoglycaemia in users of sulphonylureas. J Clin Epidemiol 1997;50:735-41

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Australian Diabetes Educators Association, NSW Health Department. A guide to diabetes education for health professionals. 1997.p 13

Brown DF, Jackson TW. Diabetes: 'Tight control' in a comprehensive treatment plan. Geriatrics 1994;49:24-36

Cryer PE. Unanswered questions on how to manage diabetes without risking hypoglycaemia. Hypoglycaemia is the limiting factor in the management of diabetes. Diabetes Metabolism Research Reviews 1999; 15: 42-46.

Davis SN and Brown JB. Insulin use in the elderly. Journal of Geriatric Drug Therapy 1999; 12: 61-81.

Hoeldtke RD and Boden G. Epinepherine secretion, hypoglycaemia unawareness, and diabetic autonomic neuropathy. Annals of Internal Medicine 1994; 120 (6): 512-517.

National Health and Medical Research Council Expert Panel on Diabetes. Series on diabetes no. 2. Hypoglycaemia and diabetes. Canberra: Australian Government Publishing Service, 1991

Walter RM Jr. Hypoglycaemia: Still a risk in the elderly. Geriatrics 1990;45:69-75

2.5B Hyperglycaemia

Index

Are there special considerations for elderly people with diabetes with regard to hyperglycaemia?

Answer

Yes

Why

- Hyperglycaemic hyperosmolar nonketotic coma is a serious and often fatal consequence of hyperglycaemia, and may be the first presentation of diabetes.
  Evidence Level III

- Mortality from hyperglycaemic hyperosmolar nonketotic coma increases with increasing age and increasing osmolarity
  Evidence Level III

Recommendation

The possibility of hyperosmolar hyperglycaemic nonketotic state should be considered in elderly people with extremely high blood glucose levels

Background – Hyperglycaemia

Persistent hyperglycaemia can cause short and long term diabetes complications, which ultimately result in a decreased quality of life and increased morbidity and early mortality in people with diabetes.

For clinical management purposes, hyperglycaemia is defined as a blood glucose level above 10mmol/L (ADEA and NSW Health Department, 1997). Hyperglycaemia is due to a relative, or absolute deficiency of insulin and may be caused by insufficient diabetic medication, emotional and/or physical stress and illness, infection, decreased physical activity, increased carbohydrate intake, or certain medications such as cortisone. Common symptoms of hyperglycaemia include excessive urination, thirst, tiredness, blurred vision, and recurrent infection.

Short term diabetes complications such as diabetic ketoacidosis (DKA) which predominantly occurs in people with Type 1 diabetes and hyperglycaemic hyperosmolar nonketotic coma (HHNC) which is more likely to occur in people with Type 2 diabetes, especially the elderly, are acute and life-threatening metabolic complications. Hyperosmolar nonketotic coma is a serious, often fatal emergency with a mortality rate ranging from 10% to 63%. At present about 50% of people with HHNC have not been diagnosed as having diabetes (Braaten, 1987). In contrast, persistent long-lasting hyperglycaemia, if untreated, can lead to chronic complications including diabetic retinopathy, diabetic renal disease, diabetic neuropathy, and cardiovascular and cerebrovascular disease.

HHNC is approximately one-tenth as common as diabetic ketoacidosis. Most people present with confusion, or in a coma. Some exhibit transient neurological deficits and others develop life-threatening neurological complications such as seizures or cerebral oedema. The hyperosmolar state may also predispose to critical events such as stroke, myocardial infarction or arterial insufficiency in the lower limbs, and renal dysfunction is common (Kennedy et al, 1999).

Symptoms of hyperglycaemia can present differently in elderly people with diabetes for three main reasons. First, there may be a reduction in the sensation of thirst and an increase in the renal glucose threshold as a consequence of normal ageing, therefore, polydipsia and polyuria may not be evident even when blood glucose levels are greater than 11.1 mmol/L (Terpstra and Terpstra, 1998). Second, the symptoms of hyperglycaemia may be masked by other conditions presenting similar symptoms, such as prostatism or urinary incontinence. Third, the common presentations of hyperglycaemia such as lethargy, blurred vision, skin or vaginal infections, poor wound healing and impaired cognition may be considered to be symptoms of old age. Symptoms of hyperglycaemia in elderly people with diabetes are often associated with symptoms of dehydration, such as dry skin, constipation, electrolyte imbalance, postural hypotension, increased occurrence of urinary tract infections and impaired cognition.

Hyperglycaemic hyperosmolar nonketotic coma is a serious and often fatal consequence of hyperglycaemia, and may be the first presentation of diabetes

NHMRC Gradeable Evidence

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Despite the significant impact HHNC has on morbidity and mortality rates in elderly people with diabetes, there is a paucity of evidence in the peer reviewed literature regarding the incidence and risk factors associated with this condition. Therefore, research including people outside the age range defined for the elderly population has been included in this review.

Predisposing factors for HHNC were identified in a case-controlled study of 135 people with HHNC and 135 age-matched diabetic controls (mean age 69.3 years) (Wachtel et al, 1987a). People with HHNC were more likely to be female (71% v 53%, p= 0.04), to be nursing home residents (28% v 15%, p= 0.02), to have newly diagnosed diabetes (32% v 7%), and to have a history of dementia (18% v 8%, p= 0.03), when compared with controls. People with HHNC were also more likely to have an acute infection, such as pneumonia or a urinary tract infection at the time of admission to hospital (39% v 19%, p=0.0005). Analysis of the participants found three independent predictors for the diabetic hyperosmolar state after adjustment for these variables: female gender, newly diagnosed diabetes, and acute infection.

Seki (1986) reported a case series of 12 people (mean age 51.3 years) with HHNC after cardiac operation. Only four were known to have diabetes. Polyuria was the first presenting symptom in 10 people (83.3%), followed by lethargy, confusion and restlessness. There was an average time lag of 6 days between the onset of polyuria and the diagnosis of HHNC. Diuretics were continued in 9 people despite the presence of polyuria. An elemental diet was used in 3 people, total parenteral nutrition in one, and another received a total dextrose infusion (50%) of 320 gm over 3 days. Therefore five people may have had a nutritional overload which might have caused dehydration. Overall mortality in this population was high (41.7%).

Pinies et al (1994) analysed the prognostic factors and outcome of HHNC in 132 elderly people with a mean age of 75 years during a 7-year period. Of 132 people, 64 (49%) had no previous history of diabetes. Dehydration was present in all people and 52% had severe dehydration. 83% had known precipitating factors, while no obvious precipitating factors were found in the remaining 17%. The mean plasma osmolarity was 380 ± 23mOsm/L and mean admission plasma glucose was 40.7 ± 13.6mmol/L. Infection (84%) was the most common precipitating factor, including respiratory, urinary tract and other site infections; followed by CVD (8%). In a multivariate regression analysis, osmolarity, sodium, urea, and glucose plasma levels were higher on admission in the most dehydrated states (all $p<0.01$). There was an association between the levels of dehydration and consciousness ($p<0.0001$). Of the total population, 22 people (16.9%) died. Non-survivors had a mean age of 79 years compared with 74 years for the survivors ($p<0.01$). Mortality was higher in people with CVD (acute MI or stroke) as a precipitating factor ($p<0.002$).

Hennis et al (1992) reported 7 people (4 of whom were aged over 60 years) with non-ketotic hyperglycaemia who developed focal seizures. Three people had newly diagnosed diabetes. Glucose levels varied from 17.8 to 55.1mmol/L and osmolarity was elevated in all cases (299.1 to 346.5 mOsm/L). None of the seven people had ketonuria. Four people had recurrent episodes of focal seizures when glucose levels were very high (>30 mmol/L). After insulin and intravenous fluid therapy was commenced, no further focal seizures occurred.

In another case series study, Popli et al (1990) reported 5 people (only one aged >60 years) with renal function impairment (mean serum creatinine 310 ± 107umol/L) who remained asymptomatic and alert on admission in spite of marked hyperglycaemia (45.8 to 92mmol/L).

Mortality from hyperglycaemic hyperosmolar nonketotic coma increases with increasing age and increasing osmolarity

NHMRC Gradeable Evidence

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Wachtel et al (1987b) retrospectively analysed the outcome of 135 people with HHNC and found that overall mortality was 17%. Non-survivors were older (77 v 67.7 years, $p=0.008$) and had significantly higher mean serum osmolarity and mean serum sodium (383 vs 358mOsm/L, $p<0.0001$; 148 vs 137.4mmol/L, $p<0.001$, respectively), compared with non-survivors. However, the mean glucose level was similar among survivors and non-survivors. The multiple regression model showed that age ($p<0.01$) and osmolarity ($p<0.01$) were two indicators of a greater risk of mortality. Mortality was 10% in those <75 years, 19% in those 75-84 years, 35% in those ≥85 years. Similarly, mortality was 7% when osmolarity was <350mOsm/L, 14% when osmolarity 350-374mOsm/L, 32% when osmolarity 375-399mOsm/L, and 37% when osmolarity >400mOsm/L. The presence of a chronic disease or an acute comorbid illness did not increase mortality.

NHMRC Gradeable Evidence table for Hyperglycaemia

Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Hennis et al, 1992	Case series	IV	HHNC
Pinies et al, 1994	Cohort	III	HHNC
Popli et al, 1990	Case series	IV	HHNC
Seki, 1986	Case series	IV	HHNC
Wachtel et al. 1987a	Case-control	III	HHNC
Wachtel et al, 1987b	Cohort	III	HHNC

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Hennis A, Corbin D, Fraser H. Focal seizures and non-ketotic hyperglycaemia. J Neurol, Neurosurgery and Psychiatry 1992;55:195-7

Pinies JA, Cairo G, Gaztambide S, Vazquez JA. Course and prognosis of 132 patients with diabetic non-ketotic hyperosmolar state. Diabete Metab 1994:20:43-8

Popli S, Leehey DJ, Daugirdas JT, Bansal VK, Ho DS, Hano JE, Ing TS. Asymtomatic, nonketotic, severe hyperglycaemia with hyponatremia. Arch Intern Med 1990;1501962-4

Seki S. Clinical features of hyperosmolar hyperglycaemic nonketotic diabetic coma associated with cardiac operations. J Thorac Cardiovasc Surg 1986;91:867-73

Wachtel TJ, Silliman RA, Lamberton P. Predisposing factors for the diabetic hyperosmolar state. Arch Intern Med 1987a; 147:499-501

Wachtel TJ, Silliman RA, Lamberton P. Prognostic factors in the diabetic hyperosmolar state. J Am Geriatr Soc 1987b; 35:737-41

Hyperglycaemia – Other References

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Australian Diabetes Educators Association, NSW Health Department. A guide to diabetes education for health professionals. 1997.p 15

Braaten JT. Hyperosmolar nonketotic diabetic coma: Diagnosis and management. Geriatrics 1987;42:83-92

Kennedy DD, Fletcher SN, Ghosh IR, Coakley JH, Monson JP, Hinds CJ. Reversible tetraplegia due to polyneuropathy in a diabetic patients with hyperosmolar nonketotic coma. Intens Care Med 1999;25:1437-9

Terpstra Tl and Terpstra TL. The elderly Type II diabetic: A treatment challenge. Geriatric Nursing 1998; 19(5): 253- 259.

2.6 Primary Prevention

Index

Are primary prevention strategies for Type 2 diabetes effective in the elderly?

Answer

Yes

Why

- Lifestyle factors are associated with increased risk of developing Type 2 diabetes in the elderly
  NHMRC Evidence Level III-2

- The development of Type 2 diabetes in the elderly can be prevented or delayed by lifestyle intervention
  NHMRC Evidence Level II

- Pharmacological therapy may prevent Type 2 diabetes in the elderly but is not as effective as lifestyle intervention
  NHMRC Evidence Level II

Recommendation

Elderly people should be encouraged to exercise regularly and to lose excessive weight in order to reduce their risk of developing Type 2 diabetes

Background – Primary Prevention

Worldwide, the prevalence of Type 2 diabetes is high and increasing. As the ageing population is growing, more elderly people are now developing diabetes. The recent AusDiab study (Dunstan et al, 2002) revealed that Type 2 diabetes affects 17.9% of the Australian population aged 65-74 years and 23.0% in people aged ≥75 years. Since diabetes is associated with a high risk for microvascular and macrovascular complications and with a high risk of premature death (de Vegt, 2001), and up to 10 out of every 100 people with IGT will develop diabetes per year (National Institute of Diabetes and Digestive and Kidney Disease, 2001), preventing diabetes is an important strategy to reduce the impact on individuals and society.

The evidence that obesity and physical inactivity increase the risk of Type 2 diabetes, and that the risk of developing Type 2 diabetes can be prevented by lifestyle and pharmacological intervention, have been reviewed in the National Evidence Based Guidelines for the Primary Prevention of Type 2 Diabetes (O'Dea et al, 2002). This section reviews the existing evidence with regard to the primary prevention of Type 2 diabetes in the elderly.

Lifestyle factors are associated with increased risk of developing Type 2 diabetes in the elderly

NHMRC Gradeable Evidence

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In the Physicians' Health Study, 21,272 male physicians (aged 40-84 years) were given specific questionnaires to assess their physical activity level (Manson et al, 1992). After an average of 5 years of follow-up, the age-adjusted incidence of Type 2 diabetes ranged from 369 cases per 100,000 person-years in men who participated in vigorous exercise less than once per week to 214 cases per 100,000 person-years in those exercising at least five times per week (p, trend < 0.001), and the age-adjusted RR for diabetes gradually fell with increasing frequency of exercise: 0.77 (CI 0.55-1.07) for once weekly, 0.62 (CI 0.46-0.82) for two to four times per week, and 0.58 (0.40-0.84) for five or more times per week (p, trend =0.0002). Vigorous exercise five or more times per week was associated with a 42% reduction in the age-adjusted risk of Type 2 diabetes compared with those who exercised less than once per week. This study concluded that exercise needs to be taken regularly for preventive effect.

Two US studies have examined the relationship between the glycaemic load of the diet and the risk of Type 2 diabetes. In these two studies, the glycaemic load of the diet was determined by averaging glycaemic index (GI). The dietary GI is an indicator of glucose response and insulin demand. Forty two thousand, seven hundred and fifty nine American men aged 40-75 years who were free of known Type 2 diabetes or CVD at baseline participated in a 6-year study (Salmeron et al, 1997a). The diet assessment was conducted using a semi-quantitative food frequency questionnaire. The average dietary glycaemic load was calculated for each participant. During 6-year follow-up, 523 participants had developed Type 2 diabetes. After adjustment for age, BMI, smoking, physical activity, family history of diabetes, total energy intake and consumption of alcohol and cereal fibre, the glycaemic load of the diet was found to be positively associated with risk of Type 2 diabetes. Comparing the highest and the lowest quintiles, the RR of diabetes was 1.37 (CI 1.02-1.83, p trend=0.03). The combination of a high glycaemic load and a low cereal fibre intake further increased the risk of diabetes (RR 2.17, CI 1.04-4.54) when compared with a low glycaemic load and high cereal fibre intake. Although the elderly population was included, the study did not have separate results of the relative risk of diabetes for the elderly subgroup.

In a similar study (Salmeron et al, 1997b), 65,173 American women aged 40-65 years of age and without known diabetes, heart disease or cancer completed a detailed dietary questionnaire in 1986. After 6 years of follow-up, there were 915 cases of Type 2 diabetes. After adjustment for the same variables as described above, the dietary glycaemic load was also found to relate to the risk of Type 2 diabetes. When comparing the highest quintile for glycaemic load to the lowest quintile, the RR was 1.37 (CI 1.09-1.71). Again, the combination of a high glycaemic load and a low cereal fibre intake further increased the risk of Type 2 diabetes (RR 2.50, CI 1.14-5.51).

The development of Type 2 diabetes in the elderly can be prevented or delayed by lifestyle intervention

NHMRC Gradeable Evidence

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A number of studies have reported that the development of Type 2 diabetes can be prevented or delayed by lifestyle modification but only the Diabetes Prevention Program study included a substantial number of people aged 60 years or older (20%) (Diabetes Prevention Program Research Group, 2002).

The Da Qing study (Pan et al, 1997) recruited 110,660 men and women with mean age 44 years from 33 health care clinics in the city of Da Qing, China and screened them for IGT and Type 2 diabetes. Five hundred and sevety seven subjects classified as having IGT were randomized to either one of three intervention groups: diet alone, exercise alone, diet plus exercise, or a control group. People in the intervention group were encouraged to increase the amount of their leisure physical activity and to consume a diet containing 50-65% carbohydrate, 10-15% protein and 25-30% fat aiming to maintain BMI <25kg/m^2. The type of exercise and intensity recommended depended on age, previous exercise pattern, and the existence of health problems. Follow-up evaluation examinations were conducted at 2-year intervals over a 6-year period to identify subjects who had developed Type 2 diabetes. After six years, the cumulative incidence of diabetes was 67.7% in the control group compared with only 43.8% in the diet group, 41.1% in the exercise group, and 46.0% in the diet plus exercise group (all $p< 0.05$). By a hazard analysis adjusted for differences in baseline BMI and fasting glucose, the diet, exercise and diet plus exercise interventions were associated with 31% ($p< 0.03$), 46% ($p< 0.0005$), and 42% ($p< 0.005$) reductions in risk of developing diabetes, respectively.

The Finnish Prevention Study provided evidence that Type 2 diabetes can be prevented by lifestyle changes in both men and women at high-risk of diabetes (Tuomilehto et al, 2001). Five hundred and twenty three overweight (mean BMI 31kg/m^2) subjects with IGT were randomly assigned to either the control or intervention group. The control group received general information about changes in lifestyle. The intervention group was given detailed information on diet and exercise modification including advice to undertake moderate exercise for 30 minutes per day. They were also informed about how to achieve a reduction in weight of 5% or more and a reduction in intake of total fat to <30% of energy, saturated fat to <10% of energy, and an increase in fibre intake to 15g/1000kcal. Subjects in the intervention group had a net weight loss of 3.5±5.5kg at the end of 2 years, compared with 0.8±4.4kg in the control group ($p< 0.001$). After an average 3.2-years of follow-up, the cumulative incidence of diabetes was significantly lower in the intervention groups than in the control group (11% vs 23%), representing a 58% reduction in the incidence of diabetes in the intervention group ($p< 0.001$).

The Diabetes Prevention Program also reported the effectiveness of lifestyle modification in people at high risk of developing Type 2 diabetes (Diabetes Prevention Program Research Group, 2002). In this study 20% of the population were ≥ 60 years of age. Three thousand, two hundred and thirty four participants with IGT were randomly assigned to either the lifestyle-modification group, control group, or treatment with Metformin. The goals of lifestyle intervention included engaging in physical activity of moderate intensity for at least 150 minutes per week; achieving at least 7% weight reduction with a low-caloric, low-fat

diet. During follow-up, the average weight loss was 5.6kg in the lifestyle intervention group, compared with 0.1kg in the control group ($p< 0.001$). After 2.8 years, the incidence of diabetes was 4.8, and 11.0 cases per 100 person-years in the lifestyle intervention and control groups, respectively. The lifestyle intervention reduced the incidence by 58% compared with the control ($p< 0.001$). Intensive lifestyle intervention was particularly effective in people aged 60 and older, reducing the development of diabetes by 71%, compared with 48%, 59% risk reduction in the 25-44 year age group and the 45-59 year age group, respectively.

One small study has also shown that IGT can be reduced by weight loss in older people. Thirty five obese men (mean age 60.0 years) determined by a high waist circumference and waist-hip ratio (WHR), were randomly assigned to a weight loss intervention group and another 15 obese men (mean age 62.0 years) to a control group. Fifty seven percent of men in the intervention group and 40% of men in the control group had IGT at baseline. The intervention group was provided with isocaloric American Heart Association step 1 diet for 3 months, then followed by a hypocaloric step 1 diet for 9 months, while the control group was only provided with isocaloric step 1 diet during 12 months. The intervention group lost a mean 9.0±2.0 kg ($p< 0.001$), resulting in an 8% reduction in waist circumference ($p< 0.001$), and a 2% reduction in WHR ($p< 0.01$), while these variables did not change in the control group. The prevalence of IGT decreased from 57% to 40% in the intervention group and increased in the control group from 40% to 67% (Colman et al, 1995).

Pharmacological therapy may prevent Type 2 diabetes in the elderly but is not as effective as lifestyle intervention

NHMRC Gradeable Evidence

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The greater benefit of weight loss and physical activity strongly suggests that lifestyle modification should be the first choice to prevent or delay diabetes. Drug therapy to prevent or delay diabetes appears to be less beneficial for several reasons. First, when directly compared with lifestyle modification, at least Metformin was considered less efficacious. Second, all glucose-lowering agents require monitoring, have been associated with some side effects and are contraindicated in some individuals. Third, none of the glucose-lowering agents have been studied regarding protection against CVD or have other clinical benefits for nondiabetic individuals (ADA, 2002).

Three diabetes prevention trials (Diabetes Prevention Program Research Group, 2002; Pan et al, 1997; Tuomilehto et al, 2001) used pharmacological therapy, and all reported a significant lowering of the incidence of diabetes. The Diabetes Prevention Program also included randomisation to treatment with Metformin and reported that Metformin was also effective in reducing the incidence of Type 2 diabetes. Participants assigned to the Metformin group were given 850mg twice a day plus standard lifestyle advice, while the control group received placebo and standard lifestyle advice. After 2.8 years of follow-up, Metformin reduced the incidence of diabetes by 31%, compared with the placebo ($p< 0.001$). Metformin was more effective in younger people, as illustrated by the incidence of diabetes i.e. 6.7%, 7.6%, and 9.6% in people aged 25-44, 45-59, and ≥ 60 years subgroups, respectively; and was more effective in people who were more overweight (BMI ≥ 35kg/m^2), incidence of diabetes was 8.8%, 7.6%, and 7.0% in BMI 22 to <30, 30 to < 35, and ≥ 35kg/m^2 subgroups, respectively. Gastrointestinal symptoms were 77.8 events/100 person-years in the Metformin group,

compared to 12.9, and 30.7 events/100 person-years in the lifestyle intervention and the control group, respectively (Diabetes Prevention Program Research Group, 2002). Therefore, in contrast to lifestyle intervention, which was most effective in the older age group, Metformin was least effective in the elderly.

Two other studies have examined other pharmacological agents in the prevention of Type 2 diabetes. The STOP-NIDDM study (ADA, 2002) recruited 1,429 people aged 40-70 years with IGT and were randomised in a double-blind fashion to receive either Acarbose or a placebo. After 3.3 years there was a 25% RR reduction in progression to diabetes in the Acarbose treated group. This effect was consistent among all age groups, BMI values and between both sexes.

NHMRC Gradeable Evidence table for Primary prevention

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Study – Author and Year	Study Design	Evidence Level	Focus/Themes of Study
Chiasson et al, 2002	RCT	II	Acarbose
Colman et al, 1995	RCT	II	Diet
Diabetes Prevention Program Research Group, 2002	RCT	II	Exercise, diet and Metformin
Manson et al, 1992	Cohort	II	Exercise
Pan et al, 1997	RCT	II	Exercise and diet
Salmeron et al, 1997a	Cohort	III-2	Dietary glycaemic load
Salmeron et al, 1997b	Cohort	III-2	Dietary glycaemic load
Tuomilehto et al, 2001	RCT	II	Exercise, diet

Primary Prevention
NHMRC Gradeable Evidence References

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Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M, STOP-NIDDM Trial Research Group. Acarbose for prevention of Type 2 diabetes mellitus: The STOP-NIDDM randomised trial. Lancet 2002;359:2072-7

Colman E, Katzel LI, Rogus E, Coon P, Muller D, Goldberg AP. Weight loss reduces abdominal fat and improves insulin action in middle-aged and older men with impaired glucose tolerance. Metabolism 1995;44:1502-8

Diabetes Prevention Program Research Group. Reduction in the incidence of Type 2 diabetes with lifestyle intervention or Metformin. N Eng J Med 2002;346:393-403

Manson JE, Nathan DM, Krolewski AS, Stampfer MJ, Willett WC, Hennekens CH. A Prospective study of exercise and incidence of diabetes among US male physicians. JAMA 1992;268:63-7

Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang H, Bennett PH, Howard BV. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537-44

Salmeron J, Alberto A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997a;20:545-50

Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997b;277:472-7

Tuomilehto JL, Lindstrom J, Eriksson JG, Valle TT, Hamalaninen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Louheranta A, Rastas M, Salminen VU, Uustipa M. Prevention of Type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Eng J Med 2001;344:1343-50

Primary Prevention - Other References

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De Vegt F, Dekker JM, Jager A, Hienkens E, Kostense PJ, Stehouwer CDA, Nijpels G, Bouter LM, Heine RJ. Relation of impaired fasting and postload glucose with incident Type 2 diabetes in a Dutch population: The Hoorn Study. JAMA 2001;285:2109-13

Dunstan DW, .Zimmet PZ, Welborn TA, De Courten MP, Cameron AJ, Sicree RA, Dwyer T, Colagiuri S, Jolley D, Knuman M, Atkins R, Shaw JE. The AusDiab Steering Committee. The rising prevalence of diabetes and impaired glucose tolerance. The Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care 2002;25:1-6

National Institutes of Diabetes and Digestive and Kidney Disease (NIDDKD). Diet and exercise dramatically delay Type 2 diabetes: diabetes medication Metformin also effective. August 2001; http:www.niddk.nih.gov

O'Dea K, Colagiuri S, Hepburn A, Colagiuri R. National Evidence Based Guidelines for Type 2 Diabetes: Primary Prevention. Diabetes Australia and NHMRC. Canberra, 2002

Section 3

Guideline Development Methods and Processes

1.0 Methods and Processes

Index

The methods and processes used in developing the *Guidelines for the Management and Care of Diabetes in the Elderly* were directly modeled on the National Evidence Based Guidelines for Type 2 Diabetes.

1.1 Defining the clinically relevant research questions

Over two face to face meetings, drawing on their own clinical experience using existing guidelines, and government reports which focussed on issues specific to diabetes and related disease areas and/or to the elderly, the Steering Committee identified a number of research questions to guide the literature searches. These questions centered attention on developing clinically relevant recommendations about aspects of care which may require different approaches in the elderly compared to younger adults with diabetes. They are:

1. Is case detection and diagnosis for Type 2 diabetes in the elderly worthwhile?

2. What clinical and laboratory assessments should be recommended for elderly people with diabetes and are there differences in treatment targets for the elderly?

3. Are there specific treatments/management's that should be encouraged or discouraged in elderly people with diabetes?

4. What are the barriers to diabetes education and health care in elderly people with diabetes?

5a. Are there special considerations for elderly people with diabetes with regard to loss of symptoms/early detection of hypoglycaemia?

5b. Are there special considerations for elderly people with diabetes with regard to hyperglycaemia?

6. Are primary prevention strategies for Type 2 diabetes effective in the elderly?

1.2 Searching the literature

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Prior to searching the peer reviewed medical press for evidence about diabetes in the elderly, efforts were directed at identifying issues of relevance to elderly people with diabetes from a number of sources.

1. Non - peer reviewed literature
An initial informal search for relevant government reports, position statements, and general background information relating to diabetes in the elderly was conducted. This search yielded a number of useful background references. Information sources explored included:

- Relevant professional organisations
- Commonwealth, State and Territory Health Departments
- Geriatric Departments of selected public hospitals
- Content experts and personal contacts of the Steering Committee

- Existing related guidelines
- The Internet

2. The peer – reviewed literature
A search strategy was developed using a breakdown of the research questions, as illustrated in Appendix 1, to assist identifying key words to focus the searches to identify the relevant articles.

Seven electronic databases were searched to identify relevant peer reviewed journal articles. As an example of the search strategy employed for the project, the MeSH terms and key words used in the Medline search is detailed in Appendix 1. All six research questions were searched on each database:

Medline	PsycINFO
Cochrane	ERIC
CINAHL	Sociological Abstracts
EMBASE	

3. Articles identified
A total of 2,168 potentially relevant journal articles (Medline: 120; EMBASE: 123; CINAHL: 13; PsycInfo: 4; Cochrane: 1768; ERIC: 68; Sociological Abstracts: 90) were found by systematically searching the electronic databases listed above.

1.3 Reviewing and grading the evidence

Index

The articles used to develop the recommendations were reviewed and graded according to the NHMRC Levels of Evidence criteria (NHMRC, 1999) as adapted for the Type 2 Diabetes Guidelines Project (Colagiuri et al, 2002). An electronic criterion based Diabetes Literature Review Program previously developed by the Australian Centre for Diabetes Strategies was used to standardise and assure consistent quality in grading the evidence. An example of a computerised review report for an intervention study is shown in Appendix 2.

All NHMRC gradeable articles reviewed were also evaluated for quality of evidence, strength and magnitude of effect, and relevance. An example of an Overall Assessment Report for both intervention, and diagnostic or risk factor studies is shown in Table 2 and the underpinning criteria used are detailed in Appendix 3. The results of these reviews were used to formulate the 'evidence statements' which support each recommendation.

For some questions, there was no available evidence. In this situation NHMRC non-gradeable information such as position statements, government reports, professional association policies and expert opinion were included as 'other evidence' to support the Consensus Statements.

Table 1. Levels of evidence criteria (NHMRC, 1999; NHMRC, 1997) Index

Intervention Studies		Prevalence, risk factors and diagnostic studies	
Levels		**Levels**	
I	Evidence obtained from a systematic review of all relevant randomised controlled trials	I[#]	Evidence obtained from a systematic review of all relevant population-based Studies
II	Evidence obtained from at least one properly-designed randomised controlled trial.	II[#]	Evidence obtained from a well-designed representative cohort study
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate Allocation or some other method).	III[#]	Evidence obtained from less well-designed, non representative cohort study or well-designed case-control study
III-2	Evidence obtained from comparative studies with concurrent controls and allocation, Non-randomised (cohort studies), case-control studies, or interrupted time series with a control group		
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group		
IV	Evidence obtained from case series, either post-test or pre-test and post-test	IV[#]	Evidence obtained from case series

[#] Studies with no intervention.

Table 2. Example of an Overall Assessment Report

Assessment Category	**Rating**			
	Value	Low	Medium	High
Level of evidence	II		✓	
Quality of evidence				✓
Strength/Magnitude of effect			✓	
Relevance			✓	

1.4 Sorting and culling the search yield

Index

Initially the Project Officer and Project Manager scanned the lists of titles generated by the electronic database searches and highlighted potentially relevant titles and obtained the abstracts from selected titles. The following criteria identified by the Project Team and agreed upon by the Steering Committee were used to ensure standardisation of this process:

1. Inclusion/Exclusion criteria

The criteria for the inclusion of studies in the literature review were:

- 1985 – present
- Humans aged 65 years and older
- Type 1 and 2 diabetes
- Primary focus on the English language literature

The criteria for the exclusion of studies from the literature review were:

- Studies involving laboratory research
- Population groups not relevant to Australia and New Zealand
- Studies of intervention not available in Australia

2. Culling by Content Experts

A one day face-to-face workshop of the three Content Experts, the Project Officer and the Project Manager was convened to cull the search yield and identify suitable articles for review. The search yield was sorted and culled according to i) the inclusion/exclusion criteria, ii) the clinical relevance and scientific merit of the research methods of each article e.g. as in the NHMRC Levels of Evidence (Table 1) and iii) the capacity of the article to address one or more of the research questions. This proved to be an efficient process and ensured the quality of the culling in that all articles were, in fact, triple culled.

In addition, to the articles identified by means of the electronic searches, the project officer hand searched the reference list at the end of each relevant article to identify additional articles that were not found by database searches, and a number of articles used in the NHMRC Type 2 Diabetes Guidelines were also identified as being relevant.

Where there were insufficient studies of an NHMRC gradeable standard to address a research question, the next best available evidence was included in the literature review as 'other evidence'.

As a result of these processes, a total of 237 relevant articles were identified and reviewed, 169 articles identified in this manner were used as NHMRC gradeable evidence and a further 68 were used as background information and 'other evidence'.

1.5 Formulating the recommendations

Index

Recommendations were formulated by synthesizing the available evidence or, in the absence of adequate scientific evidence, from expert consensus derived where possible from referable sources and labeled to indicate the nature of their source ie evidence or consensus.

Recommendations were formulated on the basis of their ability to:

- Address the clinical issues on which the research questions were based
- Do good and avoid harm
- Focus on feasible, accessible and acceptable treatment alternatives and management options

All recommendations were either made or reviewed by the Steering Committee.

References – Methods and Processes

Index

Colagiuri S, Zimmet P, Hepburn A, Colagiuri R. Evidence Based Guideline for Type 2 Diabetes: Case Detection and Diagnosis. Diabetes Australia and NHMRC. Canberra, 2002

NHMRC. National Health and Medical Research Council. Clinical practice guidelines for the management of diabetic retinopathy. Commonwealth of Australia, Canberra. 1997

NHMRC. National Health and Medical Research Council. Guidelines for preparing clinical practice guidelines toolkits series. How to use the evidence: assessment and application of scientific evidence. Commonwealth of Australia, Canberra. 1999

Appendix 1

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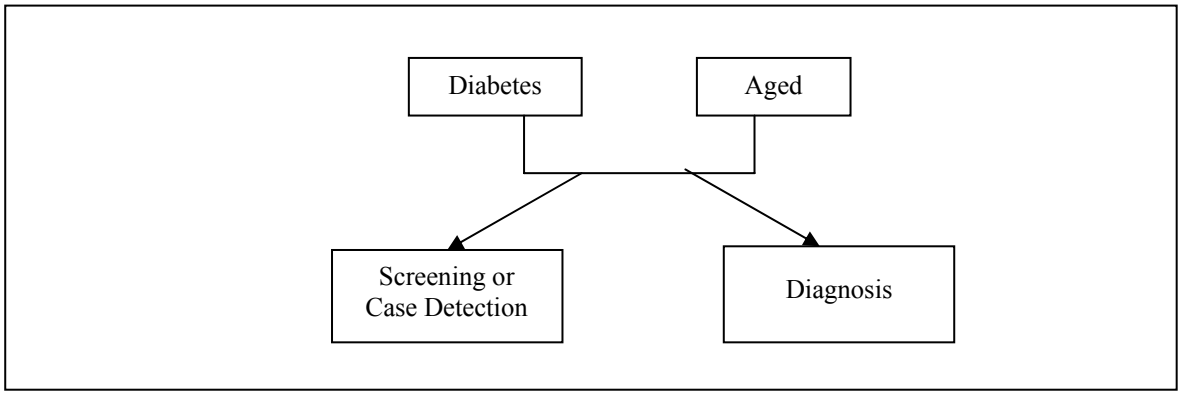
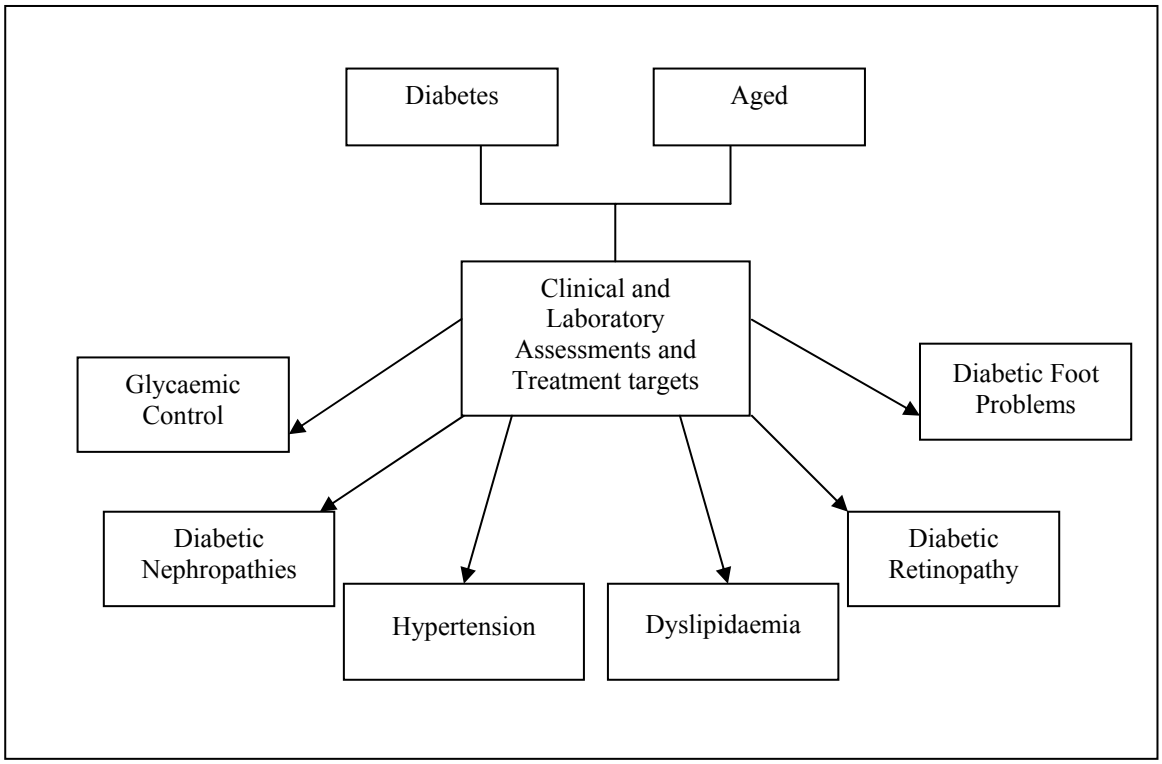
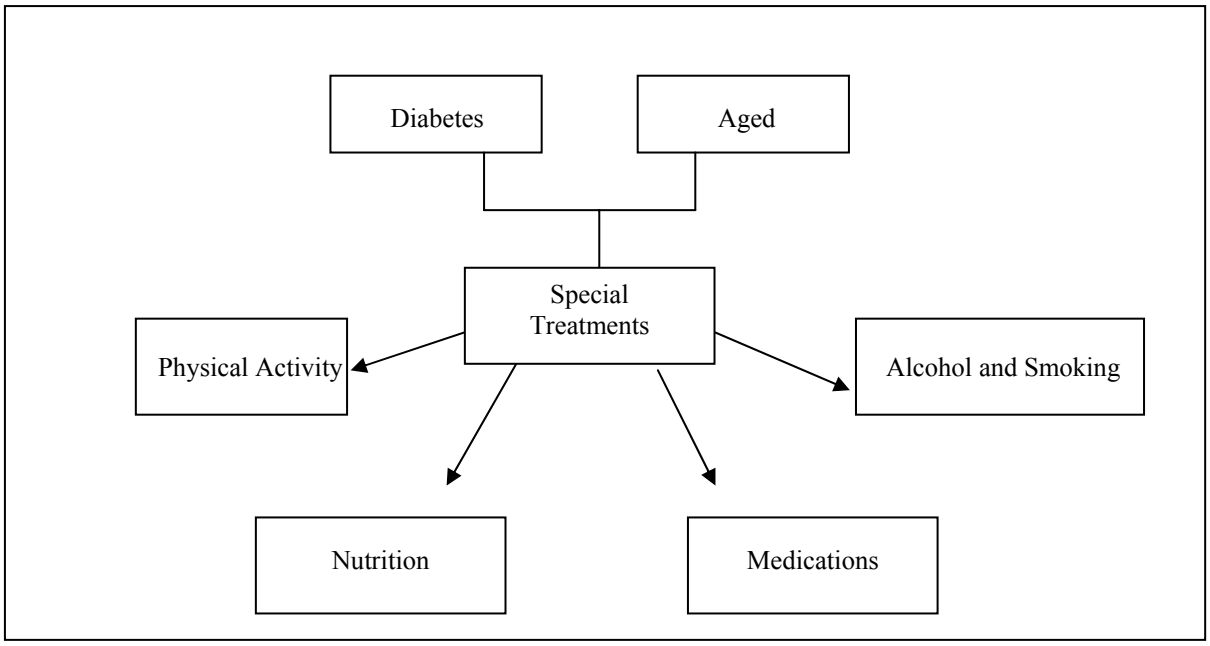
Research Question 1: Is **case detection** and **diagnosis** for **Type 2 diabetes** in the **elderly** worthwhile?



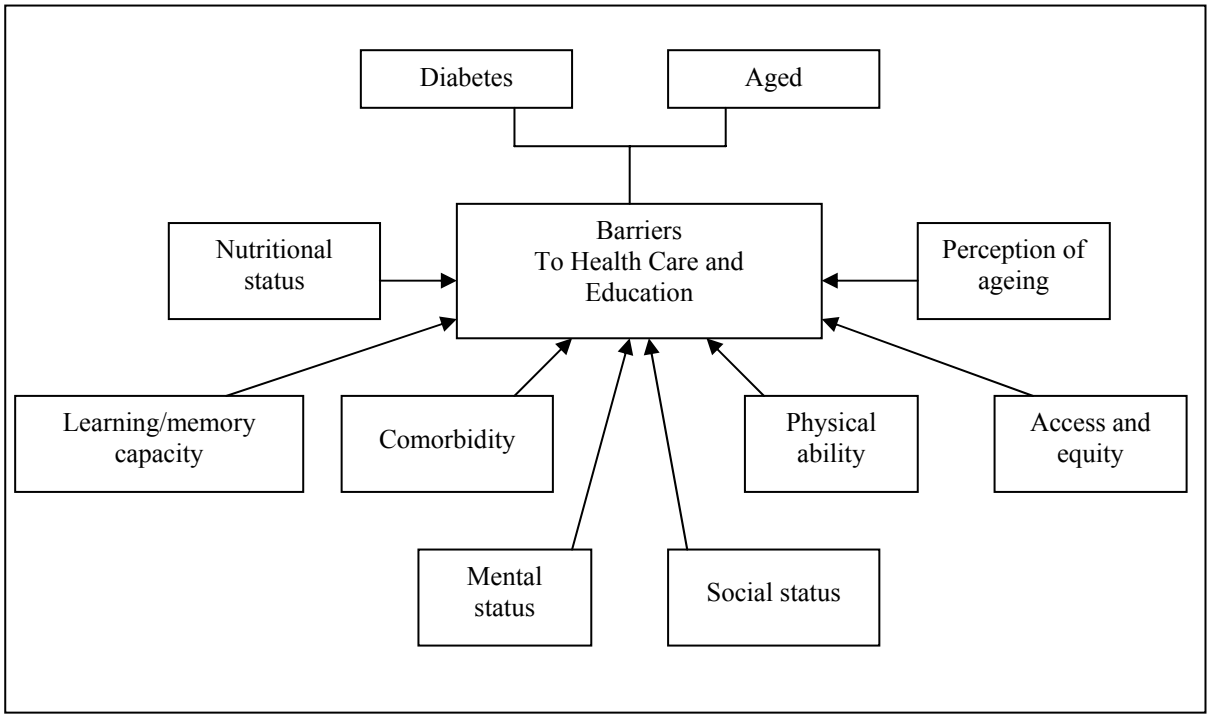
Research Question 2: What **clinical** and **laboratory assessments** should be recommended for **elderly people with diabetes** and are there differences in **treatment targets** for **the elderly?**



Research Question 3: Are there **special treatments/management's** that should be encouraged or discouraged in **elderly people with diabetes?**



Research Question 4: What are the **barriers to diabetes education and health care** in **elderly people with diabetes**?



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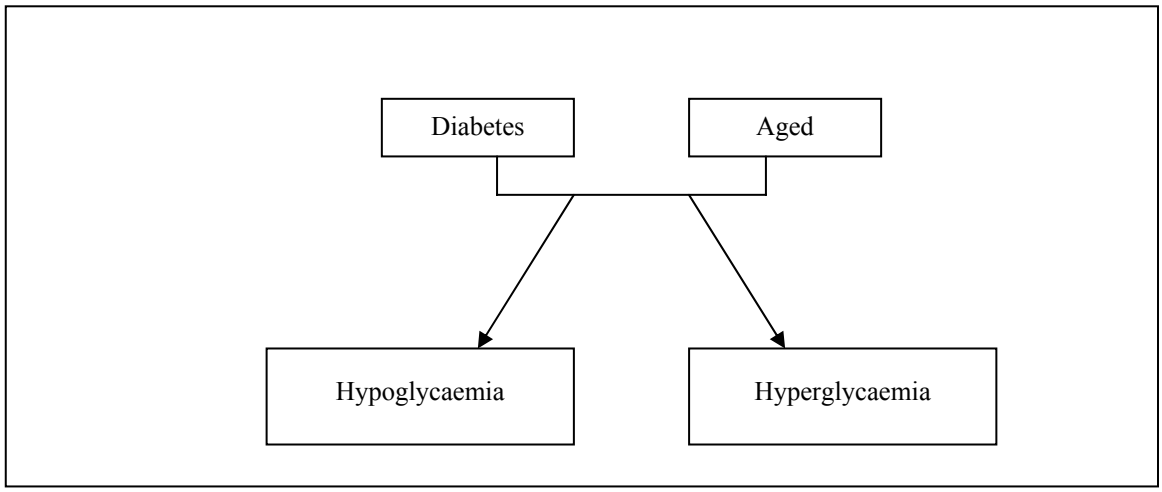
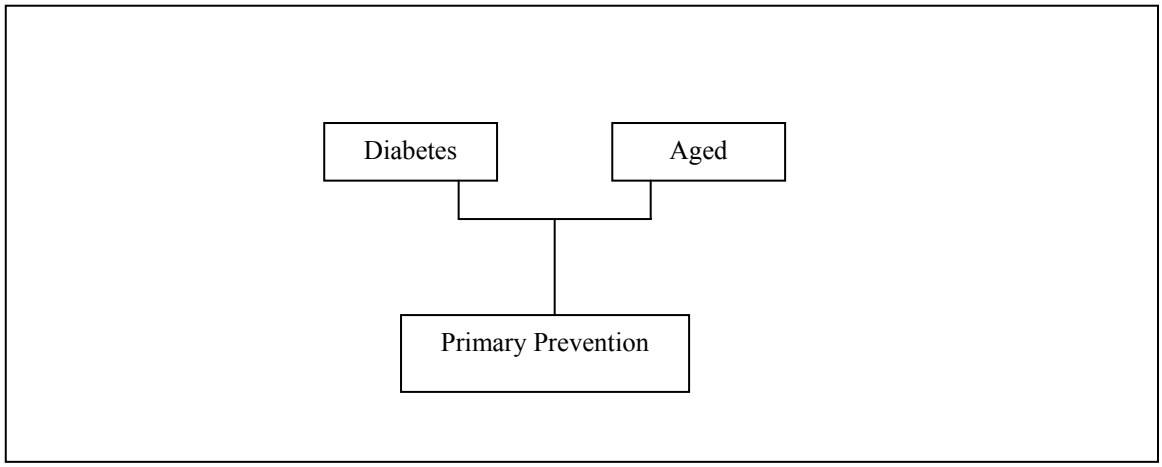
Research Question 5: Are there special considerations for **elderly people with diabetes** with regard to loss of symptoms/early detection of **hypoglycaemia/hyperglycaemia**?



Research Question 6: Are **primary prevention** strategies for Type 2 diabetes effective in the **elderly**?



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Research Questions	MeSH Terms/ Key words	No. Articles relevant
Q1. Is case detection and diagnosis for Type 2 diabetes in the elderly worthwhile?	Screening: exp diabetes mellitus/di,ep AND exp *aged/ AND exp mass screening/ M	0
	Diagnosis: exp diabetes mellitus/di AND exp *aged/ AND exp diagnosis/ M	2
Q2. What clinical and laboratory assessments should be recommended for elderly people with diabetes and are there differences in treatment targets for the elderly? - Glycaemic control - Blood pressure - Lipids - Renal function - Eye examination - Foot assessment	Glycaemic control: exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR exp clinical chemistry tests/ OR exp chemistry, clinical/ OR "laboratory techniques and procedures/) AND (exp hemoglobin A, glycosylated/ OR glycemic control.mp OR glycaemic control.mp) M	0
	exp diabetes mellitus/ AND exp *aged/ AND (exp hemoglobin A, glycosylated/ OR glycemic control.mp OR glycaemic control.mp) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0
	Lipids: exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR exp clinical chemistry tests/ OR exp chemistry, clinical/ OR "laboratory techniques and procedures/) AND (exp cholesterol/ OR exp triglycerides/ OR exp lipoproteins, HDL cholesterol/ OR exp lipoproteins, LDL cholesterol/) M	1
	exp diabetes mellitus/ AND exp *aged/ AND (exp cholesterol/ OR exp triglycerides/ OR exp lipoproteins, HDL cholesterol/ OR exp lipoproteins, LDL cholesterol/) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0

Research Questions	MeSH Terms/ Key words	No. Articles relevant
Q2. What clinical and laboratory assessments should be recommended for elderly people with diabetes and are there differences in treatment targets for the elderly? - Glycaemic control - Blood pressure - Lipids - Renal function - Eye examination - Foot assessment	Renal Function: exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR exp clinical chemistry tests/ OR exp chemistry, clinical/ OR "laboratory techniques and procedures/) AND (exp albuminuria/ OR exp proteinuria/ OR glomerular filtration rate/ OR kidney failure, chronic/) M	1
	exp diabetes mellitus/ AND exp *aged/ AND (exp diabetic nephropathies/ OR exp proteinuria/ OR exp kidney failure, chronic/) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0
	Blood pressure: exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR "laboratory techniques and procedures"/ OR exp physical examination/) AND (exp blood pressure/ OR exp blood pressure determination/) M	0
	exp diabetes mellitus/ AND exp *aged/ AND (exp blood pressure/ OR exp hypertension/) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0

Research Questions	MeSH Terms/ Key words	No. Articles relevant
	Eye Examination exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR exp physical examination/) AND [(exp retina/ OR retina.mp OR exp eye/ OR eye.mp) OR (exp macular degeneration/ OR exp diabetic retinopathy/ OR exp cataract/ OR exp glaucoma/)] M	0
	exp diabetes mellitus/ AND exp *aged/ AND (exp macular degeneration/ OR exp diabetic retinopathy/ OR exp cataract/ OR exp glaucoma/) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0
	Foot Assessment: exp diabetes mellitus/ AND exp *aged/ AND (exp diagnostic tests, routine/ OR exp physical examination/) AND (exp diabetic foot/ OR exp diabetic neuropathies/ OR monofilament.mp OR foot pulse.mp OR pedal pulse.mp OR foot assess.mp OR foot check.mp OR foot inspection.mp) M	1
	exp diabetes mellitus/ AND exp *aged/ AND (exp diabetic foot/ OR exp diabetic neuropathies/ OR exp foot ulcer/ OR exp gangrene/) AND (treatment.mp OR goals.mp OR outcomes.mp OR aims.mp OR targets.mp) M	0

Research Questions	MeSH Terms/ Key words	No. Articles relevant
Q3. Are there specific treatments/management's that should be encouraged or discouraged in elderly people with diabetes? - Nutrition - Physical Activity - Alcohol and Smoking - Medications	Nutrition: exp diabetes mellitus/ AND exp *aged/ AND (exp diabetic diet/ OR exp nutrition/ OR exp nutritional requirements/) M	8
	Medications: exp diabetes mellitus/ AND exp *aged/ AND (hypoglycemic agents/ OR insulin/ad,ae,aa,pk,ct,tu OR acarbose/ OR troglitazone.mp OR Metformin/ OR sulfonylurea compounds/) M	6
	exp diabetes mellitus/ AND exp *aged/ AND (exp exercise/ OR physical activities.mp OR lifestyle change.mp) M	15
	exp diabetes mellitus/ AND exp *aged/ AND (exp health behavior/ OR lifestyle change.mp OR exp diet/ OR exp nutrition/ OR exp alcohol drinking/ OR exp smoking/ OR exp substance-related disorders/) M	3
Q4. What are the barriers to diabetes education and health care in elderly people with diabetes? - Nutritional status - Comorbidities - Social situation - Perception of ageing - Learning/memory capacity - Mental state - Physical ability (dexterity etc) - Access and equity	exp diabetes mellitus/ AND exp *aged/ AND (exp health services accessibility/ OR barriers.mp) AND [exp comorbidity/ OR (exp diet/ OR exp nutrition/) OR (exp social isolation OR exp social alienation/ OR exp loneliness/ OR exp social support/) OR (attitude.mp OR perception.mp) OR (exp memory/ OR learning capacity.mp OR learning ability.mp) OR (exp cognition disorders/ OR exp dementia/ OR exp depression/) OR (exp activities of daily living/ OR exp movement/ OR exp disabled persons/) OR (access.mp OR equity.mp) M	0

Research Questions	MeSH Terms/ Key words	No. Articles relevant
Q5. Are there special considerations for elderly people with diabetes with regard to loss of symptoms/early detection of: - Hypoglycaemia - Hyperglycaemia	Hypoglycaemia: exp diabetes mellitus/ AND exp *aged/ AND (exp hypoglycaemia/ OR nocturnal hypoglycaemia.mp) AND (unawareness.mp OR exp awareness/) M exp diabetes mellitus/ AND exp *aged/ AND (exp hypoglycaemia/ OR nocturnal hypoglycaemia.mp) M Hyperglycaemia: exp diabetes mellitus/ AND exp *aged/ AND (exp hyperglycaemia/ OR exp hyperglycemic hyperosmolar nonketotic coma/) M	0 3 1
Q6. Are primary prevention strategies for Type 2 diabetes effective in the elderly?	exp diabetes mellitus/ AND exp *aged/ And exp primary prevention/ M	3

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Appendix 3

Study Assessment Criteria

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A. Prevalence, risk factor and diagnostic studies

Level of Evidence

I	Evidence obtained from a systematic review of all relevant population-based studies.
II	Evidence obtained from a well-designed population-based study or representative cohort study
III	Evidence obtained from less well-designed population study, non-representative cohort study or well-designed case-control study.
IV	Evidence obtained from case series.

Quality Criteria

Systematic reviews	Were the questions and methods clearly stated?
	Were comprehensive search methods described?
	Were explicit methods used to determine which studies were included in the review?
	Was the methodological quality of primary studies assessed?
	Was the selection and assessment of primary studies reproducible and free from bias?
	Were the differences in individual study results adequately explained?
	Were the results of primary studies combined appropriately?
	Were the reviewers' conclusions supported by data cited?
	Were sources of heterogeneity explored?
Population studies	Were the setting, population and selection criteria described?
	Were the subjects representative of the population?
	Was the study prospective, cross-sectional or retrospective?
	Were all clinically relevant outcomes reported?
	Were >80% of subjects accounted for in the results?
	Were the analyses appropriate?

Cohort studies	How were subjects selected for the cohort - comparison and control groups?
	Were the recruitment setting, diagnostic criteria, disease severity, co-morbidity and demographics documented?
	Was the study prospective, cross-sectional or retrospective?
	Was referral or diagnostic access bias avoided?
	Were the two groups comparable on demographic characteristics and clinical features?
	Were >80% of subjects entered accounted for in results and clinical status described?
	Were objective outcome criteria developed and used?
	Was follow-up complete and were there exclusions from the analysis?
Case-control studies	How were cases selected?
	How were controls selected?
	Was the definition of cases adequate?
	Are the two groups comparable on demographic characteristics and important potential confounders?
	Was ascertainment of exposure to the factor of interest blinded to case/control status?
	Were all selected subjects included in the analysis?

Strength and Magnitude

High:	A clinically important and statistically significant result was demonstrated.
Medium:	A statistically significant result was demonstrated but the effect is of small clinical significance or the confidence interval includes unimportant clinical effects.
Low:	The result is not statistically significant.

Relevance

Applicability to Australia
Acceptability to patient and professional
Feasibility of implementation (includes cost and access)
Appropriateness of measured outcomes

B. Intervention Studies

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Level of Evidence

I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test and post-test

Quality Criteria

Systematic reviews	Were the questions and methods clearly stated?
	Were comprehensive search methods described?
	Were explicit methods used to determine which studies were included in the review?
	Was the methodological quality of primary studies assessed?
	Was selection and assessment of primary studies reproducible and free from bias?
	Were differences in individual study results adequately explained?
	Were the results of primary studies combined appropriately?
	Were the reviewers' conclusions supported by data cited?
	Were sources of heterogeneity explored?
Randomised controlled trials	Were the setting and study subjects clearly described?
	Was assignment randomised and similar between groups documented?
	Was allocation to study groups adequately concealed from subjects, investigators and recruiters including blind assessment of outcome?
	Were all clinically relevant outcomes reported?
	Were >80% of subjects who entered the study accounted for at its conclusion?
	Were they analysed in the groups to which they were randomised (intention to treat)?
	Were both statistical and clinical significance considered?
Cohort studies	How were subjects selected for the cohort - comparison and control groups?
	Were the recruitment setting, diagnostic criteria, disease severity, co-morbidity and demographics documented?
	Was the referral pattern described?
	Was referral or diagnostic access bias avoided?

	Were the two groups comparable on demographic characteristics and clinical features?
	Were >80% of subjects entered accounted for in results and clinical status known?
	Were objective outcome criteria developed and used?
	Was outcome assessment blind?
	Was follow-up complete and were there exclusions from the analysis?
Case-control studies	How were cases selected?
	How were controls selected?
	Was the definition of cases adequate?
	Are the two groups comparable on demographic characteristics and important potential confounders?
	Was ascertainment of exposure to the factor of interest blinded to case/control status?
	Were all selected subjects included in the analysis?

Strength and Magnitude

High:	A clinically important and statistically significant result was demonstrated.
Medium:	A statistically significant result was demonstrated but the effect is of small clinical significance or the confidence interval includes unimportant clinical effects.
Low:	The result is not statistically significant.

Relevance

	Applicability to Australia
	Acceptability to patient and professional
	Feasibility of implementation (includes cost and access)
	Appropriateness of measured outcomes

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