Diabetes and mental illness

Challenges and practical progress

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Severe mental illnesses are associated with premature death and accelerated cardiometabolic disease. Diabetes contributes substantially to the health burden in severe mental illness, with glycaemic, lipid and hypertension control often below the targets accepted as standard of care. Treatment disparities and unmet health needs are common and contribute to poorer health outcomes.

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Severe mental illnesses, such as severe depression, schizophrenia and bipolar disorder, are associated with death 20 to 25 years prematurely, mostly attributable to cardiovascular disease and diabetes.[1,2] Diabetes rates are substantially higher in patients with severe mental illness, compounding physical disease burden and comorbidities.[3] This excess disease burden has been termed a 'scandal of premature mortality that contravenes international conventions for the "right to health".'[4] Treatment disparities exist between those patients with and those without mental illness and many opportunities to prevent diabetes are missed in patients with mental illness.

Key points

- **Diabetes and prediabetes are common in patients with severe mental illness.**
- **Screening for diabetes with measurement of fasting glucose levels and/or HbA_{1c} should be undertaken every six months in people with severe mental illness. If weight gain occurs in this group, lifestyle strategies to prevent diabetes should be undertaken, with support and follow up.**
- **People with severe mental illness and diabetes should be considered as a 'special needs' group, requiring longer, more frequent appointments, and regular follow up with medical and allied health professionals.**
- **Assumptions should not be made about a patient's healthy behaviour literacy, access to healthy food and food preparation facilities, and knowledge and skill sets necessary to prepare healthy meals. People with severe mental illness and diabetes may require supported training in these areas.**
- **Disparities in diabetes health service delivery are well documented. Addressing these disparities is necessary to ameliorate the premature morbidity and mortality experienced by people with severe mental illness.**

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Medications commonly used to treat severe mental illness*

Antipsychotics

First generation

Chloropromazine
Fluphenazine
Haloperidol
Perphenazine
Thioridazine

Second generation

Amisulpride
Aripiprazole
Clozapine
Olanzapine
Quetiapine
Risperidone
Ziprasidone

Antidepressants

Tricyclics

Amitriptyline
Amoxapine
Doxepin
Imipramine
Nortriptyline
Trimipramine

SSRI/SNRI

Citalopram
Escitalopram
Fluoxetine
Paroxetine
Sertraline
Venlafaxine

Mood stabilisers

Anticonvulsants

Lamotrigine
Sodium valproate
Topiramate
Valproic acid

Others

Lithium carbonate

* Reproduced with permission from Blanchard E, Samaras K. Diabetes Management 2014; 4: 339-353.[5]

Abbreviations: SNRI = serotonin and noradrenaline reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Medications used in severe mental illness and their impact on diabetes risk

Patients with severe mental illness are typically treated with long-term psychological interventions and medications, which can be generally categorised into antipsychotics, mood stabilisers and antidepressants (Box).[5]

Antipsychotics are classified as either first or second generation, distinguished by risk of causing severe motor adverse effects (i.e. tardive dyskinesia, dystonia and extrapyramidal symptoms). Both generations of antipsychotic are associated with weight gain, obesity and metabolic complications,[6] which contribute to disease risk. A treatment objective for clinicians engaged in the care of people with severe mental illness is to actively prevent, detect and intervene in these adverse metabolic complications.

Antipsychotics: diabetes and metabolic risk

Antipsychotic use is associated with a two- to fivefold higher incidence of diabetes, as well as high rates of undiagnosed diabetes (5 to 14%) and prediabetes (33 to 53%).[7-10]

Higher rates of diabetes in patients taking antipsychotic medications are related to the weight gain associated with their use, although recent studies have suggested weight-independent effects on beta cells.[5] Tables 1 and 2 show the relative impact of different antipsychotics on weight gain and diabetes risk, which occur even in childhood.[5,11,12] A recent study in children and youths found a threefold higher diabetes incidence in those taking antipsychotics, compared with those taking antidepressants, evident within 12 months of medication initiation.[10] However, the study was likely to have underestimated diabetes risk, because there was no routine glucose screening and diabetes was ascertained by use of glucose-lowering medications.[13]

Table 1. Prevalence of preventable metabolic risk factors in severe mental illness*

Risk factor	Prevalence (%)	Relative risk
Obesity	75	1.5 to 2
Metabolic syndrome	54	2 to 3
Smoking	67	2 to 3
Hyperglycaemia	29	2 to 3
Hyperlipidaemia	33 to 50	≤5
Hypertension	54	2 to 3

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Regular diabetes screening is recommended internationally in all people prescribed antipsychotic drugs, regardless of age or duration of therapy, as part of global psychiatry initiatives to improve physical health in people with severe mental illness.[12,14]

All antipsychotics can cause weight gain. Quality longitudinal and controlled studies consistently show substantial weight gain occurs in 60% of treatment-naïve individuals within 10 to 16 weeks of commencing an antipsychotic for first-episode psychosis, with 60 to 100% affected after one to two years.[15] A three-month prospective study of treatment-naïve youth starting antipsychotics found significant weight gain, ranging from 4.4 kg in those taking aripiprazole to 8.5 kg in those taking olanzapine, compared with 0.2 kg weight gain in controls.[6] These findings were confirmed by others in a 12-month study of antipsychotic initiation in treatment-naïve people with first-episode psychosis, with clinically adverse weight gain (>7% of baseline) occurring in 86% of patients taking olanzapine, 65% of those taking quetiapine, 53% of those taking haloperidol and 37% of patients taking ziprasidone.[16]

Rapid onset of hyperlipidaemia and insulin resistance after antipsychotic initiation have also been documented, predicted by weight gain.[17,18]

Australian data show alarmingly high rates of overweight and obesity in youth receiving antipsychotics for a first episode of psychosis, affecting 55% of males and 42% of females after about eight months, with body mass index directly related to antipsychotic treatment duration.[19]

Antidepressants: diabetes and metabolic risk

Depression is common in people with diabetes, affecting at least one in three patients.[20,21] Diabetes prevalence is also higher in those with depression. The combination of diabetes and depression is associated with poorer health outcomes, translating to a 15-year reduction in life expectancy.[1]

Table 2. The weight-promoting effect and lipid and/or glucose metabolism dysfunction of antipsychotic medications used to treat severe mental illness*

Antipsychotic medication	Weight gain potential	Risk of glucose and/or lipid dysfunction
Chloropromazine	Substantial	High (with limited data)
Clozapine	Substantial	High
Olanzapine	Substantial	High
Paliperidone	Intermediate	Mild
Quetiapine	Intermediate	Moderate
Risperidone	Intermediate	Mild
Thioridazine	Intermediate	High (with limited data)
Amisulpride	Low	Mild
Aripiprazole	Low	Low
Fluphenazine	Low	Low (with limited data)
Haloperidol	Low	Low
Perphenazine	Low	Low
Ziprasidone	Low	Low

* Reproduced with permission from Blanchard E, Samaras K. Diabetes Management 2014; 4: 339-353.[5]
Originally adapted from Foley 2011[11] and De Hert 2012.[13]

Similar to psychosis, depression is associated with lifestyle choices that increase a patient's risk of developing diabetes, including smoking, higher caloric intake and sedentariness. However, the increased diabetes risk can not be attributed entirely to lifestyle factors. Several physiological changes are evident, including increased insulin resistance, activation of the hypothalamic–pituitary–adrenal axis and the sympathetic system, and elevated levels of inflammatory cytokines.[22]

Antidepressant medications generally fall into three categories, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) (Box),[5] and all are associated with weight gain and insulin resistance. A systematic literature review found associations between antidepressant use and diabetes.[23] Diabetes prevalence rates in patients receiving antidepressants are 40 to 100% higher than rates in controls; data from the UK General Practice Research Database of more than 165,000 people showed diabetes risk was increased by 80% with antidepressant use.[24] Diabetes risk appears to be similar in patients taking SSRIs and in those taking tricyclic antidepressants and is mitigated by short treatment duration.

Antidepressant use and incident diabetes was examined in the Diabetes Prevention Program, which found a two- to fourfold increased rate of incident diabetes in patients taking antidepressants who were randomised to the lifestyle intervention arm.[25] In contrast, those who were randomised to the lifestyle plus metformin arm had no increase in the rate of incident diabetes.[25] Pooled data from the Nurses' Health Study, Nurses' Health Study II and the Health Professionals Follow-up Study (>1.6 million person-year follow up) found an almost tripling in risk of incident diabetes in women taking antidepressants.[26]

There are little data to guide the choice of the best depression medication for people with diabetes, because people with diabetes are usually excluded from randomised trials. Counselling psychotherapy has proven efficacy in people with diabetes.[27] Further, the impact of different antidepressant medications on glucose control remains unclear. More studies are required.

Impact of severe mental illness on diabetes care

People with severe mental illness present several challenges for diabetes care and service delivery, which can be considered in several paradigms: psychiatric medication specific (discussed above), individual specific and service/system specific.

Individual-specific factors

It is important to consider how mental illness might reduce an individual's capability for diabetes self-care and diminish the effectiveness of interventions or glucose-lowering and risk factor management medications. The impact of sedentariness, lower quality diets and higher smoking rates should also be considered. Fewer than 30% of adults with schizophrenia undertake regular physical activity[28] and fewer than 25% of patients taking antipsychotic medication do the recommended 150 minutes of exercise per week.[29]

Our understanding of these 'lifestyle choices' is benefited by considering factors that may promote these choices including the sedating and appetite-promoting effects of antipsychotics, and the interrupted education and personal development and socioeconomic disadvantage experienced by many patients with mental illness. These factors not only diminish the efficacy of antidiabetic medications, but compromise an individual's capacity to adhere to appropriate diet, physical activity and weight advice. Considering an individual's unique situation and tailoring a lifestyle program that addresses their personal barriers to a healthier lifestyle will help. Common barriers include access to dietetic services and basic domestic management (e.g. managing on a limited budget, knowing where to purchase healthy food, how to select it, healthy cooking techniques). These barriers were addressed in the Keeping The Body In Mind Program, a lifestyle and life skills program developed by

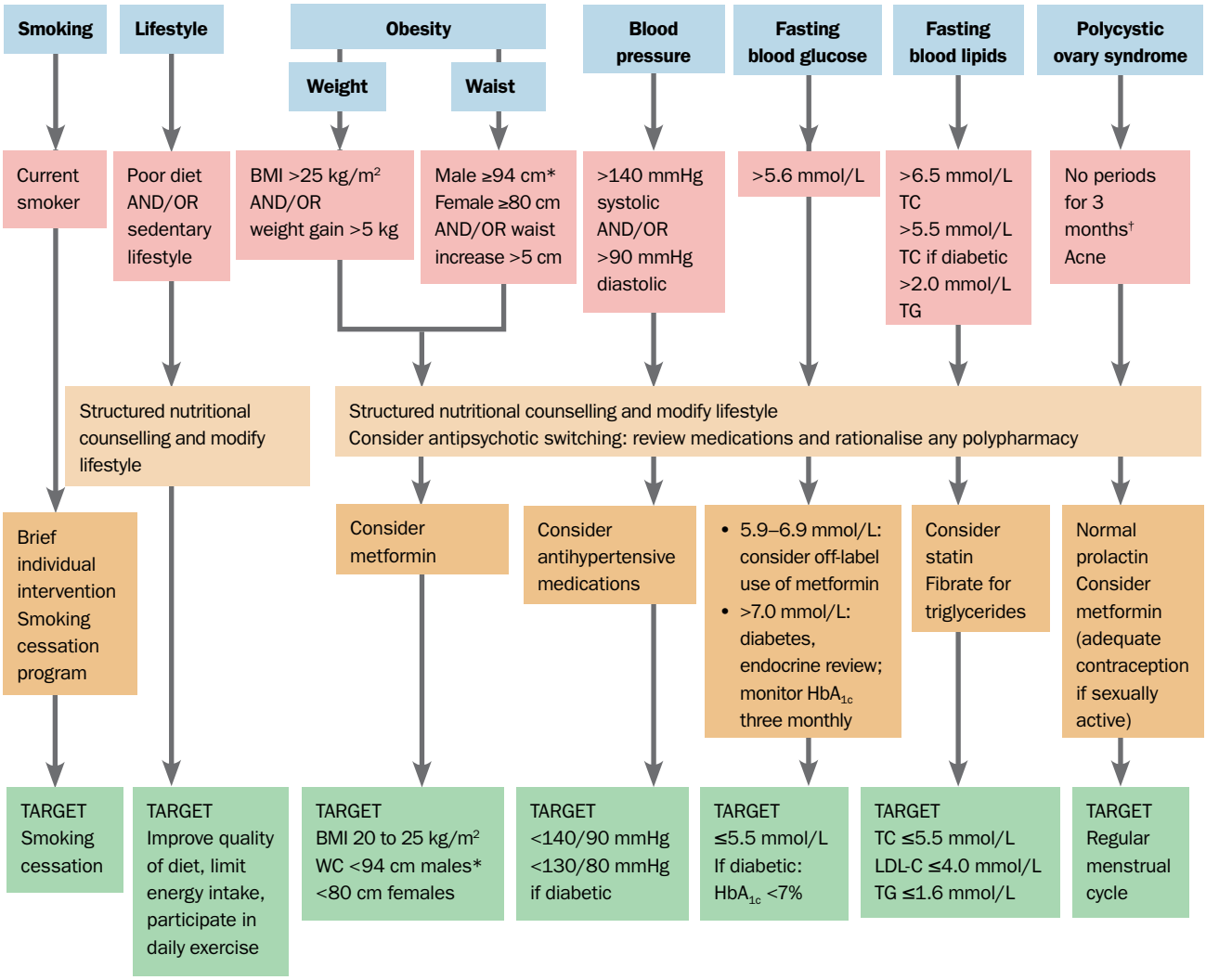

Figure. A positive cardiometabolic health intervention algorithm.

Reproduced with permission from Curtis J, Newall H, Samaras K. HETI 2011. http://www.heti.nsw.gov.au/cmalgorithm[30]

Abbreviations: BMI = body mass index; LDL-C = LDL cholesterol; TC = total cholesterol; TG = triglycerides; WC = waist circumference.
* For south Asians, Chinese, south and central Americans, recommended WC target <90 cm. †For premenopausal women.

the author and colleagues to prevent diabetes and obesity (discussed below).

For many patients taking antipsychotics, undertaking physical activity is challenging, because antipsychotics induce substantial or profound sedation, late wakening and fatigue and reduce incidental activity. Further, many people with severe mental illness experienced discomfort in busy, noisy environments, such as gyms or health facilities, and the lack of feeling safe for those with paranoia may make even a walk confronting. Identifying these factors is helpful in creating individualised strategies to overcome barriers to healthy lifestyle behaviours. The choice and dose of antipsychotic medication should be discussed with the psychiatry team to minimise sedating effects.

It is also of great importance to address active smoking with the patient. Smoking not only adversely affects cardiovascular risk, it worsens mood and contributes to depression. Advice and support for smoking cessation should be provided at each consultation for active smokers. All supports available should be utilised including the positive cardiometabolic health intervention algorithm (Figure).[30]

System-specific factors: health service access and service delivery disparities

Disparities in the delivery of health services to people with severe mental illness,[31] including less frequently achieved standard diabetes benchmarks,[32] less frequent prescription of blood pressure-lowering

History: smoking, exercise, diet, family history (diabetes, obesity, CVD), gestational diabetes, ethnicity, polycystic ovary syndrome.

Then at least three monthly

Examination: weight, BMI, WC, BP

Investigations: fasting blood glucose and lipids (TC, LDL-C, HDL-C and TG)

Vitamin D (twice a year)

Interventions:

Nutritional counselling: reduce take away and junk food, reduce energy intake to prevent weight gain, stop soft drinks and juices, increase fibre intake.

Physical activity: structured education-lifestyle intervention. Advise daily physical activity: e.g. 30 minutes of walking.

If unsuccessful after three months in reaching targets, then consider switching and medication interventions below

Switching: Consider switching to a more weight neutral medication. Review diagnosis and ensure ongoing need for all psychotropic medications.

Don't just SCREEN ➡ INTERVENE

for all patients in the

'red zone'

Screen cardiometabolic risk factors using screening tool; examine and investigate three monthly on all clients on psychotropic medications.

Note: additional considerations for those on mood stabilisers and clozapine not included here and need to be performed (e.g. medication plasma levels, thyroid function tests, urea, electrolytes and creatinine, echocardiogram, etc)

Always involve a GP and, where appropriate and possible, refer the patient to a specialist (e.g. dietitian, physician, diabetic clinic, exercise physiologist).

Note: Some drugs used in metabolic disease treatment are contraindicated in pregnancy (e.g. some antihypertensives and lipid-lowering drugs). If your patient on any metabolic medications is considering pregnancy, please discuss with their GP.

Specific pharmacological interventions:

Consider metformin if:

- impaired glucose
- Polycystic ovary syndrome
- obesity or rapid weight gain

Metformin therapy: start at 500 mg x half a tablet before breakfast and dinner for two weeks then increase to 500 mg twice daily. Dose can be increased to a maximum of 3 g daily, although as this is off label treatment, no adverse effects should be tolerated. If side effects of nausea, abdominal cramping, shift to after meal.

Lipid-lowering therapy: (use PBS guidelines)

Statin initiation doses for cholesterol lowering:

- simvastatin 10 mg nocte
- pravastatin 10 mg nocte
- atorvastatin 10 mg nocte
- rosuvastatin 10 mg nocte

Fibrate therapy for TG lowering:

- gemfibrozil 600 mg twice daily
- fenofibrate 145 mg mane

Antihypertensive therapy: multiple agents are available. Liaise with the GP who can monitor.

Vitamin D:

- <50 nmol/L: replenish stores: cholecalciferol 4000 IU daily for one month;
- maintenance: 1000 IU daily. Target >80 nmol/L.

Figure. A positive cardiometabolic health intervention algorithm continued.

Abbreviations: BP = blood pressure; BMI = body mass index; HDL-C = HDL cholesterol; LDL-C = LDL cholesterol; TC = total cholesterol; TG = triglycerides; WC = waist circumference.
For online access to this fact sheet, please visit http://www.heti.nsw.gov.au/cmalgorithm[30]

and lipid-lowering medications, and higher rates of suboptimal HbA_{1c},[32] lipid and blood pressure levels, are widespread.[33] Contributing factors to these disparities include:

- the impact of severe mental illness on a patient's capacity to follow advice (due to the sedating effects of medications, cognitive impacts on processing and memory, irregular attendance, non-engagement)
- the direct effects of antipsychotic and antidepressant medications that compromise glucose metabolism
- disparities in service delivery, which are often magnified in rural or remote locations
- lack of access to medical services, homelessness and poverty.

Another consideration is the documented lack of interdisciplinary collaboration and cohesiveness, which limits co-ordinated care of often complex health needs.

People with severe mental illness and diabetes are a vulnerable group, and in those perhaps less capable of managing complex diabetes self-care it is a potential double disability. The challenges of diet rigor, glucose monitoring, multiple medications, and hypoglycaemia detection and management should be considered in these patients, in addition to the stress for them of attending busy, noisy diabetes outpatient services.

In this regard, diabetes services to people with severe mental illness should more actively ensure care meets benchmarked standards. This may require 'above usual' clinical attention – that is, more frequent visits, reminder calls and ensuring patients see the same clinician every time. Diabetes care may require problem-solving and addressing barriers to better health that may include poverty and homelessness. For example, imagine the challenge of storing and administering insulin for a homeless person.

Table 3. Challenges for diabetes optimisation in people with severe mental illness and practical strategies to address them

Obstacle or challenge	Strategy
Attendance	• Phone or text message the patient the day before the scheduled appointment • Offer late morning or afternoon appointments (antipsychotics are major sedatives and create challenges for early waking)
Impaired information retention due to the sedating effects of medications	• Offer late morning or afternoon appointments, when the patient is less sedated • At each consultation, provide clear written advice on: – medication changes – physical activity goals – dietary changes and goals – next appointment data and time
Impaired or reduced motivation (due to illness and/or medication)	• Ensure information and education are provided when the patient is least sedated • Reinforce advice at each visit • Disappointment at failure is infectious, so keep it to yourself: use motivation and enthusiasm
Medication effects on promoting obesity and diabetes	• Collaborate with the prescribing psychiatrist and form a therapeutic alliance • Ask the psychiatrist: is this the best psychotropic medication(s) for my patient who also has diabetes and/or obesity?
Sedentariness due to the sedating effects of medications	• Offer individualised counselling with carer, family or case worker • Provide handouts with written and visual supports • Use visuals for portion control advice • Improve food literacy: – consider cooking classes – consider shopping and budget classes • Maintain follow up: learning may need reinforcement
Social exclusion and isolation	• Is your waiting room too noisy/busy/challenging for people who are depressed/anxious/paranoid/psychotic? • Is there a better place for challenged people to wait? • Recruit support from mental health case workers, friends, carers and allied health professionals
Financial restraint	• Check medications are being purchased • Check medications are appropriately subsidised, where possible • Is financial assistance needed? • Is housing assistance required? • If the patient lives in shared accommodation or is homeless, is there a safe place to keep medications? • Is there access to clean cooking spaces? • Is there access to healthy cheaper foods?

Pragmatic solutions and efficacy are required beyond usual practice guidelines.

Simple strategies to assist in addressing some of these special needs are listed in Table 3.

One immediate strategy to implement is longer appointment times, because people with severe mental illness not only have less knowledge about diabetes but also take longer to process information.[34] Memory deficits may require that education and management advice is repeated and supported by written or visual instructions to reinforce treatment, education and self-care instructions.

Further, many people experience their first episode of severe mental illness in youth or early adulthood, when life skills are usually being developed. Not only can school or tertiary education be abruptly interrupted by mental illness, so can life skills acquisition, compounded by social isolation and unemployment. Diabetes allied health professionals are aptly placed to address knowledge barriers to healthy eating patterns and physical activity.

Diabetes prevention in people with severe mental illness

Fundamental to diabetes prevention is early intervention to prevent weight gain when antipsychotic medications are commenced.[35,36] Numerous weight loss interventions have been shown to be efficacious in people with severe mental illness, recognising that weight loss may be initially slower, although net loss is comparable to that seen in the general population.[37] The Keeping the Body in Mind Intervention recently reported that the weight gain usually associated with antipsychotic initiation in youth with first-episode psychosis can be prevented by individualised lifestyle counselling.[37] This intervention was associated with 1.1 kg weight gain over 12 weeks compared with 7 kg weight gain in a matched control group.[37] These and other studies prove that it is worth putting in the effort for weight loss interventions in this group of patients. Metformin interventions have also shown weight and metabolic benefits.[38]

Thus, lifestyle interventions should be implemented in all individuals receiving antipsychotic therapy as a standard of care at the time of psychotropic medication initiation. Further, consideration of the addition of off-label metformin at the time of antipsychotic medication initiation has been recommended internationally by multiple authors.[39-41]

To further support cardiometabolic healthcare in people with severe mental illness, the author and colleagues have developed the positive cardiometabolic health algorithm[35,36] (Figure) adopted by NSW Health and adapted internationally into the National Institute for Health and Care Excellence (NICE) guidelines (guidelines CG155 [https://www.nice.org.uk/guidance/cg155] and CG178 [https://www.nice.org.uk/guidance/cg178]) for regular monitoring and support. This educational resource is to assist healthcare workers to identify and manage patients with cardiometabolic risk, highlighting action points, interventions and health targets.

Conclusion

People with severe mental illness experience shortened life expectancy and poor physical health and have unmet health needs. Cohesive and effective interdisciplinary collaboration, improved engagement with patients with severe mental illness and a measure of tenacity in never giving up on these patients and their needs will increase the likelihood of effectively improving health in people with severe mental illness and diabetes. Consider this our obligation and our privilege to assist. **ET**

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A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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