

The WXYZ of cardiodiab risk

Early recognition of the risk factors for cardiovascular disease and diabetes enables control of the progression of these factors by lifestyle changes (weight loss and increased physical activity) and/or medication.

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In Australia we have accepted the importance of the ABCs of diabetes care (controlling glycosylated haemoglobin [A_{1c}], blood pressure [B] and cholesterol [C], quitting smoking [s] and taking salicylates [s]) when managing patients with diabetes. This article considers the risk factors for cardiovascular disease and diabetes, introducing the mnemonic WXYZ. It is important to recognise these cardiodiab risk factors and respond to them since their progression can be controlled by lifestyle changes, medication or both. As the post-World War II baby boomers move into their 60s and, for women, their size 16 clothes, the metabolic syndrome and 'diabesity' will become more and more common.

The mnemonic WXYZ

The main cardiovascular disease and diabetes risk factors are represented by the mnemonic WXYZ, where:

- W = the weight/waist factor, especially in women
- X = the metabolic problems (syndrome X, or metabolic syndrome) associated with central overweight
- Y = why a particular person develops the metabolic syndrome
- Z = sleep apnoea, not getting enough zzz's.

A case study of a woman in her forties is used in this article to discuss each of these cardiodiab risk factors in detail.

IN SUMMARY

- **W** – each year our weight and waist get bigger, both as individuals and as a population. There are many factors but the 'big two' are high energy food and low energy lifestyle.
- **X** – syndrome X, or the metabolic syndrome, has three core components: overweight/waist, cardiovascular risk and abnormal glucose metabolism. Lifestyle change (eating less and walking more) can reverse, stop or slow the progression of these. Cardioprotective medications such as ACE inhibitors, statins or a low dose aspirin may be necessary depending on an individual's cardiovascular risk.
- **Y** – why people develop the metabolic syndrome is usually a consequence of the 'f' words (forty, family and fat). The modifiable risk factor (fatness) should be focused on sooner rather than later, but avoid 'blaming the victim' for his or her problem.
- **Z** – sleep apnoea, or not getting enough zzz's, often occurs with the other risk factors for cardiovascular diseases and diabetes, and may worsen both the W and X factors. Night-time sleep disturbance can worsen the metabolic profile and daytime tiredness can reduce motivation and capacity for lifestyle change.

continued

Table 1. Factors in increasing weight and waist measurements²

The ‘big two’

- Eating more
- Walking less

Possible other factors

- Not enough sleep
- Climate control
- Less smoking
- Prenatal effects
- Fat equals fecund
- A little older
- More medications
- Pollution
- Mature mums
- Like marrying like

W – the weight/waist factor
Wendy

Wendy presents to you concerned about her weight. She had her 45th birthday last week and found that none of her party clothes fitted her. She is now size 16, a size she says she would have thought ‘gross’ when she was younger. She weighs 69 kg and her waist circumference is 90 cm. Looking back, she can track a steady weight gain from her trim size 10 and 50 kg when she was married 20 years ago. She no longer likes looking in the mirror, buying clothes or going out, and she has started wearing loose fitting dark clothes. She is very upset and would like your help.

Weight gain

Wendy is not alone. Australian women aged between 20 and 50 years are gaining about 0.6 kg each year, partly because they are getting older and partly because Australians of all ages are getting fatter (Figure 1).¹ Australian men are also getting heavier, gaining about 0.4 kg per year. This is

the W factor for cardiometabolic risk, and is assessed by waist circumference (>88 cm for women; >102 cm for men).

The obvious explanation for weight gain is the ‘big two’ of high energy food and low energy lifestyle – fast foods, television and computers, for example. While it is true that we live in an environment disposing towards obesity, where healthy lifestyle choices are the hard choices, there may be other systematic factors that also lead to weight gain. The most plausible alternatives, which are summarised in Table 1, are:²

- smoking less and sleeping less seem to predispose to weight gain – the QUIT campaign has been a great public health success but the price may have been a fatter Australia; also, we try to cram as much as we can into a day and compared to 1960 we now sleep 1.5 hours less each night
- heating and air conditioning in homes and workplaces have reduced the need for body energy expenditure to keep warm or cool
- heavier people tend to have more children and, as overweight has a strong genetic component in our society, overweight people tend to have overweight children
- some groups of people are fatter than others, such as older people and certain ethnic groups
- women are delaying having children, and older mothers seem to have fatter children
- people tend to be attracted to those who are like them, so a fat person is likely to marry another fat person, possibly amplifying increases in obesity from other causes (particularly genetics and the tendency of heavier people having more children)
- people are now exposed to more chemicals (pharmaceuticals and industrial/agricultural chemicals – many of the latter of which become environmental pollutants), and some of these can lead to weight gain.

Over the last 40 years our society has changed in many ways that make it more and more difficult to control the W factor.

X – metabolic problems
Wendy, three years later

Wendy is now 48 years old and presents for a health check as she is worried about her future health. She weighs 73 kg (height, 151 cm; BMI, 32 kg/m²) and has a waist circumference of 94 cm. Examination confirms the central overweight but is otherwise unremarkable:

- blood pressure, 140/90 mmHg
- total cholesterol, 6.2 mmol/L; HDL cholesterol, 0.8 mmol/L; triglycerides 2.8 mmol/L; LDL cholesterol, 4.0 mmol/L
- fasting plasma glucose, 6.7 mmol/L.

With the exception of her fasting plasma glucose level, these values are outside the National Heart Foundation target ranges (i.e. blood pressure, <130/80 mmHg; total cholesterol, <4.0 mmol/L; HDL cholesterol, >1.0 mmol/L, triglycerides <1.5 mmol/L, LDL cholesterol, <2.5 mmol/L).³

You explain that these features indicate that something should be done about her weight as otherwise her health is going to worsen.

The metabolic syndrome

Wendy has syndrome X – more often known these days as the metabolic syndrome. There are many definitions but all contain three components: overweight/waist (central obesity), cardiovascular risk and abnormal glucose metabolism (Table 2). Within these components, blood glucose, blood pressure, blood fats and prothrombosis are the most important in clinical practice because they can be treated.

The major feature of the metabolic syndrome is the progressive nature of the overweight and associated problems. Wendy’s fasting glucose is now in the impaired fasting glucose (prediabetes) range but has been rising for years (her

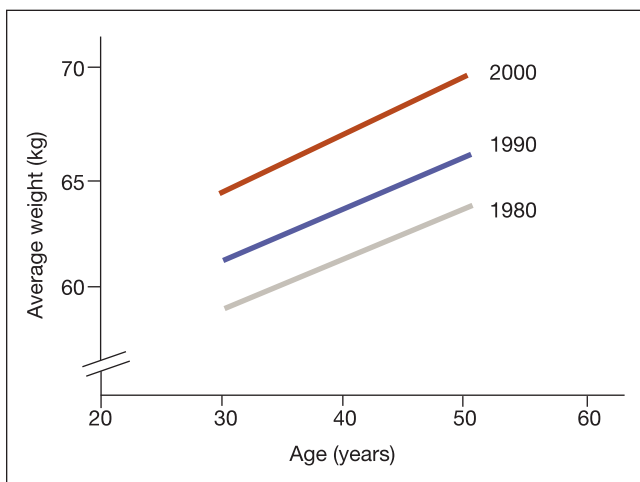
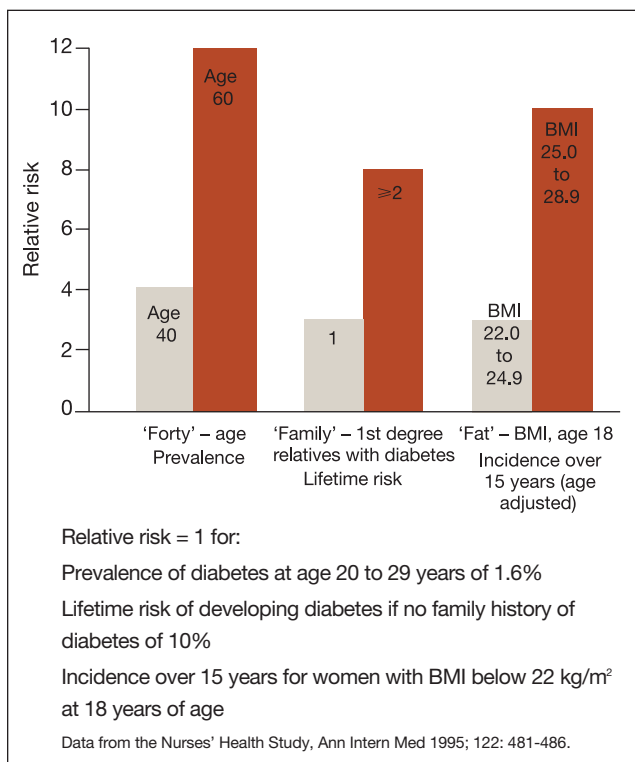


Figure 1 (above). The increase in the average weight of Australian women aged 20 to 50 years from 1980 to 2000.¹

Figure 2 (right). The 'f' words (forty, family and fat) and diabetes risk. Data from the Nurses' Health Study showing the relative risks of diabetes increase progressively with increasing age over 40 years, having one and two or more first degree relatives with diabetes, and increasing BMI at age 18 years.⁹



fasting glucose level of 6.2 mmol/L is lower than that required to diagnose diabetes [≥ 7.0 mmol/L] but higher than the normal reference range [< 6.1 mmol/L]). Based on the progression of glycaemia seen in the Diabetes Prevention Program,⁴ Wendy's blood glucose level started rising in her twenties and will continue to rise into the diabetic range as she gets older. Similarly, her blood pressure and blood fats are clearly abnormally high now but have also been progressively increasing.

Epidemiological studies show that there is a continuum of cardiovascular risk with risk progressively increasing with increasing blood glucose, blood pressure and blood fat levels, even in the so-called normal range. Twenty years ago, Wendy's fasting glucose level was 3.0 mmol/L, her blood pressure was 110/70 mmHg and her blood fat levels were well within target values. Now they are not particularly abnormal for her age but they are much higher than when she was younger (and healthier). They are also likely to progress

unless Wendy is able to make lifestyle changes and/or you are able to control the risk factors with medication.

If Wendy cannot change her lifestyle by eating less and walking more⁵ or if her blood glucose, pressure and fats are still not on target, medication might help. The Diabetes Prevention Program showed that metformin could reduce the progression from prediabetes to diabetes by one-third and the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) study showed that rosi-glitazone could do much the same.^{4,6} However, in Australia, neither metformin nor rosiglitazone is available on the PBS to prevent diabetes. If you were to consider prescribing metformin or rosiglitazone (Avandia), or the combined rosiglitazone and metformin preparation (Avandamet), on a private script it would be wise to warn Wendy about the side effects of these medications (gastro-intestinal upset with metformin, fluid retention with rosiglitazone). She should

also be asked to sign an informed consent form for off label use if you do prescribe either of these medications.

Table 2. Features of the metabolic syndrome

Central obesity

- Increased BMI
- Increased waist circumference
- Increased waist-hip ratio

Cardiovascular risk

- Increased blood pressure
- Abnormal triglycerides, HDL cholesterol
- Prothrombosis
- Microalbuminuria

Abnormal glucose metabolism

- Impaired fasting glycaemia, impaired glucose tolerance or diabetes
- Insulin resistance

continued

Wendy’s cardiovascular risk is considerable (10% over the next five years) because of her age, hypertension and dyslipidaemia, and her prediabetes would increase this further.

Irrespective of her other risk factors, Wendy might be wise to take an antihypertensive medication (such as an ACE inhibitor) and, when her hypertension is controlled, an antithrombotic medication (such as low dose aspirin). If prescribing aspirin, some doctors would consider testing for *Helicobacter pylori* and eradi-

cating it if present to reduce the future risk of gastrointestinal haemorrhage.

Given Wendy’s hypertension (blood pressure, 152/96 mmHg) and dyslipidaemia (total cholesterol, 6.2 mmol/L; HDL cholesterol, 0.8 mmol/L), she is eligible for a PBS subsidy for cholesterol lowering therapy (statins) according to the criteria introduced in October 2006 for patients with hypertension (i.e. total cholesterol >6.5 mmol/L or total cholesterol >5.5 mmol/L and HDL cholesterol <1 mmol/L).⁷

It is not current practice to prescribe the full ‘type 2 tablet’ (metformin, ACE inhibitor, statin and aspirin)⁸ for people like Wendy with the metabolic syndrome. Three of the components seem appropriate in Wendy’s case – ACE inhibitor, aspirin and a statin; metformin may be indicated in the near future.

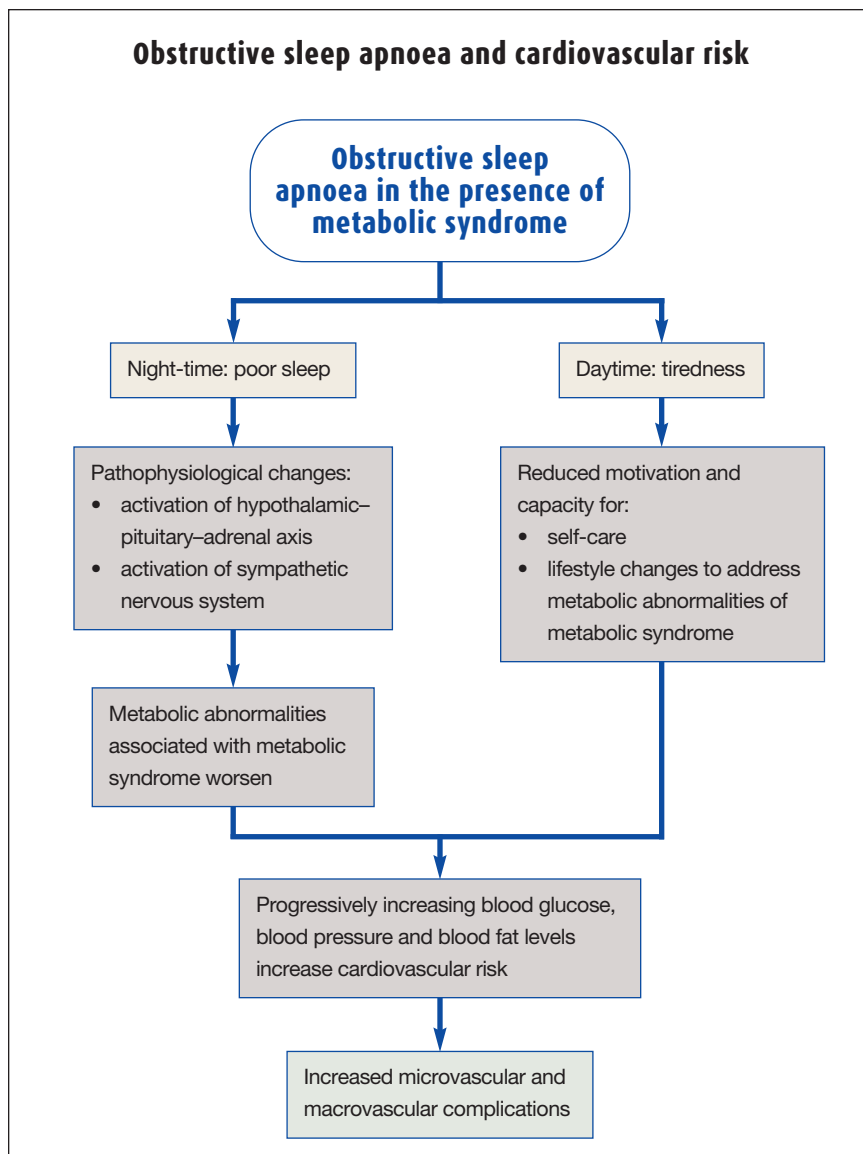
Y – why me?

Wendy might be asking you or herself why she has the metabolic syndrome. In Australia, the ‘f’ words account for most cases of metabolic syndrome and its components:

- forty – age over 40 years
- family – history of type 2 diabetes in a first degree relative (father, mother, sibling, offspring)
- fat – overweight/waist.

When asked, most doctors will identify fatness as a major risk factor, and possibly also family; however, we may struggle to identify age as another major risk factor. This may lead us to feel that those with diabetes are responsible for their own diabetes, a possible extreme view being ‘they are lazy gluttons who are suffering from their self-indulgence’. It is true that age and genes are fixed and that fatness is, to some degree, under the individual’s control but most of the 60% of our population who are fat do not get diabetes, and many people who do get diabetes are no fatter than the rest of us. We should focus on the modifiable risk factor (fatness) sooner rather than later, and avoid ‘blaming the victim’ for his or her problem.

The Nurses’ Health Study followed a cohort of women for 14 years and monitored the development of components of the metabolic syndrome such as diabetes.⁹ As for many other chronic diseases, age emerged as a major risk factor with diabetes risk increasing 10-fold between the ages of 20 and 60 years (Figure 2). Not surprisingly genetic inheritance was also important, with the risk increasing twofold with one first degree relative (mother, father, sibling, offspring) and threefold



continued

Epworth sleepiness scale*

How likely are you to doze off or fall asleep in the situations described below, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you haven't done some of these things recently, try to work out how they would affect you.

Use the following scale to choose the most appropriate number for each situation:

- 0 = would never doze
- 1 = slight chance of dozing
- 2 = moderate chance of dozing
- 3 = high chance of dozing

Situation	Chance of dozing
Sitting and reading
Watching TV
Sitting inactive in a public place (e.g. a theatre or meeting)
As a passenger in a car for an hour without a break
Lying down to rest in the afternoon when circumstances permit
Sitting and talking to someone
Sitting quietly after a lunch without consuming alcohol
In a car, while stopped for a few minutes in traffic

Score:

- 0 to 10 Normal range
- 10 to 12 Borderline
- 12 to 24 Abnormal

* The Epworth sleepiness scale was developed by Dr Murray Johns, Melbourne (Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991; 14: 540-545).

with two or more who had developed diabetes. On top of these risk factors, increasing overweight further independently multiplied diabetes risk.

Wendy has two 'f' words (forty and fat) and is quite likely to have a family history as well. On questioning, Wendy says that her mother and her sister have type 2 diabetes, her father had gout and her sister's daughter developed gestational diabetes after ovulation induction because of infertility associated with polycystic ovary syndrome (another aspect of the metabolic syndrome).

Z - sleep apnoea Wendy's sleep problems

Wendy presents again, this time concerned about her sleeping. Her husband John is with her and tells you that he has moved into another bedroom because

Wendy's loud snoring is disturbing his sleep. Wendy is looking embarrassed and slightly annoyed. She says she can't help it and she doesn't think she sleeps well anyway. 'Even when I wake up, I'm tired. I'm so tired during the day that I drop off all the time. Once I went to sleep waiting for a traffic light to change and was woken up by the other cars beeping me!'

Sleep apnoea and lack of zzz's

Obstructive sleep apnoea is often associated with the other cardiometabolic factors and can predispose to increasing weight and waist and to worsening of the metabolic abnormalities associated with syndrome X. Night-time sleep disturbance can worsen the metabolic profile and daytime sleepiness reduces motivation and capacity for lifestyle change (see the flowchart on page 50).

Obstructive sleep apnoea can cause considerable disturbance to sleep, with activation of both the hypothalamic-pituitary-adrenal axis and the sympathetic response. Disturbed sleep can lead to daytime sleepiness, which does not help motivation to participate in active social activities or to adhere to a lifestyle prescription of eating less and walking more.⁵ The combination of nocturnal hormonal disturbance and daytime lethargy aggravates any innate tendency to weight/waist gain and to the associated adverse risk factor profile.

Neck circumference (more than 42 cm) or a high Epworth sleepiness score identifies patients who might warrant further investigation, such as a formal assessment at a sleep study centre. The Epworth sleepiness scale was developed to measure daytime sleepiness and has been shown to significantly distinguish normal subjects from patients with various conditions including obstructive sleep apnoea, narcolepsy and idiopathic hypersomnia.¹⁰ An example of the self-administered questionnaire is given in the box on this page.

Wendy is very likely to have obstructive sleep apnoea, which might respond to continuous positive airway pressure (CPAP). However, she might have a different or additional problem, which could be addressed by a chin splint, ENT surgery or other procedure.

If CPAP is indicated and is successful, the results can be dramatic, including weight and waist loss, decreases in blood glucose, blood pressure and blood fat levels, and increases in physical and mental functioning and wellbeing.

Conclusion

Early recognition of the risk factors for cardiovascular disease and diabetes enables control of the progression of these factors by lifestyle changes (weight loss and increased physical activity), medication or both. The mnemonic WXYZ provides a useful approach when considering these cardiometabolic risks. W represents

overweight/waist; X, syndrome X, or the metabolic syndrome; Y, why a patient develops X; and Z, the lack of sleep (zzz's) due to the obstructive sleep apnoea that often occurs with the other cardiometabolic risk factors and may worsen both the W and X factors. **MT**

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