BEST PRACTICE

39

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Consensus on antithrombotic medicines
Atrial fibrillation
TIA
Angina

bpac nz
better medicine

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Infant mental health and child protection

Contributed by: Dr Denise Guy – Child Psychiatrist, Incredible Families Charitable Trust

This is the third article in our series on vulnerable children and young people in New Zealand. This article aims to provide primary care professionals with an understanding of infant mental health, with particular reference to the needs of very young children who may come to the attention of Child Youth and Family

Many infants in New Zealand are taken into state care each year

Early neglect, abuse and parental stress have significant long-term mental health effects for infants and young children. Early assessment and intervention offers the potential for improved outcomes.

In the 12 months from June 2009, 62,543 babies were born in New Zealand. During this time, 166 babies and 502 children aged less than two years came into State care.[1] In 2008 3,456 children aged under two years were found to be physically, emotionally or sexually abused or neglected. An unknown but even larger number of infants will be growing up in less than satisfactory environments. On average 63 children aged under two years are admitted to hospital each year as a result of serious abuse.

Defining infant mental health

The age range used when addressing infant mental health is from birth to a child's fourth birthday.

"Infant mental health is the developing capacity of the child from birth to three to experience, regulate and express emotions; form close and secure interpersonal relationships; and explore the environment and learn – all in the context of family, community and cultural expectations for young children"[2]

Infants can have mental health problems

As adults, we find it uncomfortable to think of babies and toddlers having mental health difficulties and disorders, but they do; and there is a considerable body of knowledge and research in the discipline of infant mental health that is pertinent to assessment and intervention.

It is a myth to assume infants are immune to the impact of problematic care and trauma or to assume that their immaturity in some way constitutes resilience.

Early relationships are critical for an infant's social, emotional and cognitive development. Experiences antenatally and in the first years are pivotal in establishing

the building blocks for ongoing development and may impede or promote development. In recent years the science around genetics, epigenetics and neurobiology highlights the processes of nature via nurture such that nearly all of the elements of early human development are affected by the early caregiver environment, family, culture and community.

Every parent begins with the best of parenting intentions, but for some, "good intent" is not enough. The first months and early years of care giving are critical for a child's development and this is often the time when parents have the highest motivation to "get it right"' with their child. Potentially it is the most opportune time to engage families with multiple difficulties.

It is important to identify those infants and families for whom particular needs and risks contribute to vulnerability.

Adversity, stress and relationships

What looks like a social situation is actually a neurochemical situation

Infants who come to the attention of Child, Youth and Family have generally experienced complex trauma within their care giving environment. They may have had prolonged exposure to trauma (parents who withdraw, are emotionally unavailable or neglect to provide adequate care), experienced multiple traumatic events over time (domestic violence and physical abuse) or experienced different traumatic events at the same time.

Complex trauma has a profound effect on physical, emotional, behavioural and cognitive development. It causes major disruptions in attachment and relationship development. It changes the architecture of the brain and the way it functions potentially resulting in a significantly smaller brain.[3]

Care that is chronically or unpredictably traumatic is experienced by infants as severe stress. Their stress response system (the hypothalamic-pituitary-adrenal [HPA] axis) is over-used. Infants have a highly reactive adrenocortical response to stressors and those responses are regulated within the relationship interactions with their parents/caregivers. The cortisol response is gradually reduced or dampened during an infant's first year, provided they have adequate care. A parent, who is both the source of the stress and unable to respond to regulate the stress, leaves an infant uncontained and overwhelmed. Over time, the infant's HPA axis resets towards a hyper- or hypo-responsive pattern.

Given their age and development, infants have limited behavioural and emotional ways to express their stress – through fight, flight or freezing. All these responses are seen when we observe the infant – caregiver relationship while undertaking an assessment.

Over time it becomes more difficult for young children who have been exposed to trauma to manage normal developmental tasks and their adaptations become more inflexible.

Infants with mental health concerns may:

- Fail to achieve milestones – delayed toilet training, delayed language
- Struggle to master the challenges of regulating their emotions and impulses – prolonged and frequent temper tantrums, severe and persistent separation anxiety
- Be unable to negotiate peer relationships and appropriately play
- Struggle to problem solve
- Struggle to have trust in caregivers – becoming very controlling of them.

The prospective Dunedin and Christchurch Longitudinal Studies and the Adverse Childhood Experiences (ACE) Study (retrospective) have confirmed that adverse childhood experiences are linked to poorer physical, cognitive and mental health outcomes and psychopathology later in adolescence (and continuing into adulthood).

Vulnerable infants and families

It is important to be supportive of parents and caregivers in their desire to provide appropriate care for their very young children. It is also important to acknowledge openly that for some parents and caregivers this is going to be more difficult and at times additional support and intervention will be helpful.

The attributes that create vulnerabilities to abuse and neglect are well established with accumulating factors increasing the risks for an infant. Multiple factors are associated with an inability to provide adequate care for a child.

The factors that should be considered are:

- Current stressors – poverty, illness, parental conflict, family violence, loss and death. Poverty increases an infants' exposure to multiple difficulties and disproportionately affects Māori and Pacific peoples.
- Maternal or paternal mental health disorders – particularly bipolar affective disorder, persistent depression, alcohol and substance abuse and personality disorder.
- Adverse parental childhood experience – e.g. physical abuse, sexual abuse, neglect, being in foster care, exposure to severe family violence or significant loss and death.
- Teenage parents – difficulties include lack of adequate antenatal care, poor nutrition, negative responses from their families, high levels of depression and stress. Teen parents express less positive and more negative emotions with their infants and support more punitive care giving behaviour, particularly from the second half of the first year.
- Problematic pregnancy or birth – contributing to a parent being withdrawn, hostile or ambivalent about their baby.
- Social isolation – unsupported, abandoned by family or separated from family, or disconnected / alienated from a cultural community.
- Parent criminal history
- Developmentally disabled parents

There is some evidence that caregiving capacity is most disrupted for parents who have been sexually abused in childhood.[4]

In various ways these different factors impede the adult's capacity to read their infant's social and emotional cues and respond appropriately to them or manage their own emotional state - frightening or traumatising the infant.

It is also important to think about the difficulties an infant may have that further complicate a parent's care giving.

These include infants who are:

- Premature, of low birth weight or have medical problems
- Have physical or developmental disabilities
- Are temperamentally "difficult"
- Are physiologically irritable, sensitive to touch, cry a lot or are persistently difficult to console, feed or settle to sleep

Some babies are irritable and difficult to settle as a consequence of the antenatal in-utero environment, e.g. being exposed to high levels of maternal cortisol in the context of domestic violence.

In different ways these infants challenge the capacity of all parents and caregivers to accurately read their cues and support their development.

Recognising symptoms associated with trauma and stress

Given the accumulating evidence around long-term effects of adversity and complex trauma on the developing infant, primary care practitioners need to proactively identify those families with high needs who require extra time for an integrated care approach.

Infants and toddlers cannot advocate for themselves or give a coherent history so observations are essential in addition to eliciting the relevant information from a parent or caregiver.

Infants have relatively limited emotional and behavioural responses. Having eliminated underlying medical causes for distress, it is critical that the health practitioner explore problematic relationships and the potential for mental health disorders. Infant mental health problems are typically complex, requiring time to explore and a recognition that infants function within family relationships. A "whole person" approach is actually a "whole family system" approach with the child's experience kept central.

The most frequent concerns raised by parents or caregivers about infants are:

- Increased aggression and disruptive behaviour
- Sleep difficulties
- Increased separation anxiety

Think carefully about these presentations as all these symptoms may be related to trauma and stress. For example, irritability, tantrums and aggressive behaviour in a toddler may signal depression, anxiety or a traumatic stress reaction. Co-morbidity with problematic care is likely as are significant mental health, alcohol and drug and personality difficulties in one or both parents/caregivers.

What might you hear and need to take notice of:

- A parent who does not feel bonded to their infant
- A parent who fears they may hurt their infant
- A parent who holds a distorted perception or representation of their infant. All parents have negative feelings towards their children at times, however, distortions of perception should be considered when they persist or are developmentally inappropriate such as "he's exactly like my abusive father", [infant of 3 months]; "she hates me" "she's really manipulative", "he's going to end up in jail" [2 year old].
- A parent who feels their toddler is in control – "the boss" of them

What might you observe and need to take notice of:

- Limited or no observations of shared joy in the relationship
- A parent who frightens the infant
- A parent who seems frightened of their infant
- A parent who shows hostility, constant criticism or more worryingly, active rejection
- A parent who is withdrawn, uninvolved, passively rejects, does not respond or is perhaps dissociating, which is highly distressing for an infant
- An infant who is expected to care for the parent, to make them feel better
- An infant who seems perpetually anxious and on edge (hyper-reactive - fight state) and easily becomes dysregulated (e.g. aggressive or whinging and clinging) with minimal apparent triggers
- An infant who appears psychologically numb and shut-down (hypo-reactive - flight state)
- An infant who is aggressive, shaming and coercive of their parent

It is useful to observe interactions when an infant is distressed, hurt or upset. At these times of stress, a child is dysregulated and developmentally requires the care giver to provide care that soothes at both an emotional/ behavioural level and at a physiological level.

When implementing current screening and review for domestic violence, adult mental health and alcohol and other drug use, you should integrate questions about the emotional, social and cognitive development of infants. Remember to ask about experiences of significant loss and death – these tend to preoccupy parents and impede care giving.

Interventions

When the decision is made to place an infant or young child in care (extended family, foster placement) the provision of a different and potentially consistent, empathically responsive carer is a key intervention, irrespective of longer term plans that may include a return home. However, there are considerable challenges for foster parents and traumatised, neglected children in developing new relationships that will potentially support healthy social, emotional and cognitive development.

There are evidence based interventions for supporting foster parents to develop nurturing relationships in this age group.[5] It is appropriate to make referrals to Child and Adolescent Mental Health Services (CAMHS) or Infant Mental Health Services (where they are available) for assessment and intervention when problems persist within the placement beyond three to four months.

Interventions for infants at risk

There are well developed and researched interventions available:

- Assess and intervene (may involve referral) with parental mental health problems and refer for additional intervention around the parent-infant relationship.
- Both maternal and paternal depression are common in these early child rearing years and parental depression has long term effects on children's cognitive, emotional and behavioural development. Just treating a parent will not improve the outcome for children; intervention also needs to address the relationship.[6, 7]
- Refer infants who show significant social, emotional and behavioural problems such as:
  - Persistent aggression
  - Listless, depressed, apathetic infants
  - Failure to thrive (require paediatric review first)
  - Self-regulatory problems as a consequence of disturbed caregiving relationships which may be evidenced in sleep or eating difficulties, prolonged tantrums and self harm
- Refer families where parents identify they are fearful of abusing their child, do not feel bonded, dislike their child or may fear repeating abuse they experienced as children.
- Refer infants exposed to complex trauma:
  - If symptoms have lasted longer than three months and are interfering with functioning
  - If the parent/caregiver is traumatised or compromised (e.g. depression, alcohol abuse] in their ability to look after the child
  - If the trauma involved loss of a parent or significant caregiver

Consider referral to organisations that provide:

- Interventions that decrease social isolation and value connections with parents – e.g. playgroups, playcentre, Kohanga Reo, Pacific Island early childhood centres, kindergartens and other early childhood education services.
- Concrete assistance and advocacy to ensure families living in financial difficulty are able to access resources to assist with parenting and parental relationships – e.g. WINZ, budgeting advice, relationship services and community toy libraries
- Specialised Infant mental health services – in New Zealand these are not yet established in all DHB's but CAMHS are expected to offer assessment and intervention from birth and to work with child health, adult mental health, education and child protection.
- Evidence based parenting programmes including Incredible Years Parenting Programme, Triple P, Mellow Parenting (available in Counties Manukau DHB)
- Community/NGO Early Intervention Programmes including Ministry of Social Development funded home visiting programmes for vulnerable families (e.g. Family First, Early Start, PAFT with Ahuru Mowai).

Further resources:

www.imhaanz.org.nz

The website of the New Zealand Affiliate of the World Association of infant mental health where you will find contact details for the regional infant mental health groups that cover most of New Zealand. These groups, generally comprised of health and early childhood education professionals, are an information source for Infant Mental Health resources in the area.

www.mothersmatter.co.nz

The website of the Postnatal Depression Family-Whānau New Zealand Trust for health professionals and families which is focused on New Zealanders, covers a spectrum of mental health difficulties and up to date medicine information.

www.developingchild.harvard.edu

The National Scientific Council on the Developing Child (NSCDC) is a multi-disciplinary collaboration comprising leading scholars in neuroscience, early childhood development, health and economics. Publications are regularly revised, concise and designed to integrate the science of what is known with what needs to be done.

www.zerotothree.com

This American non-profit organisation informs, trains and supports professionals, policymakers and parents in their efforts to improve the lives of infants and toddlers. The website has numerous resources for parents, caregivers and health professionals.

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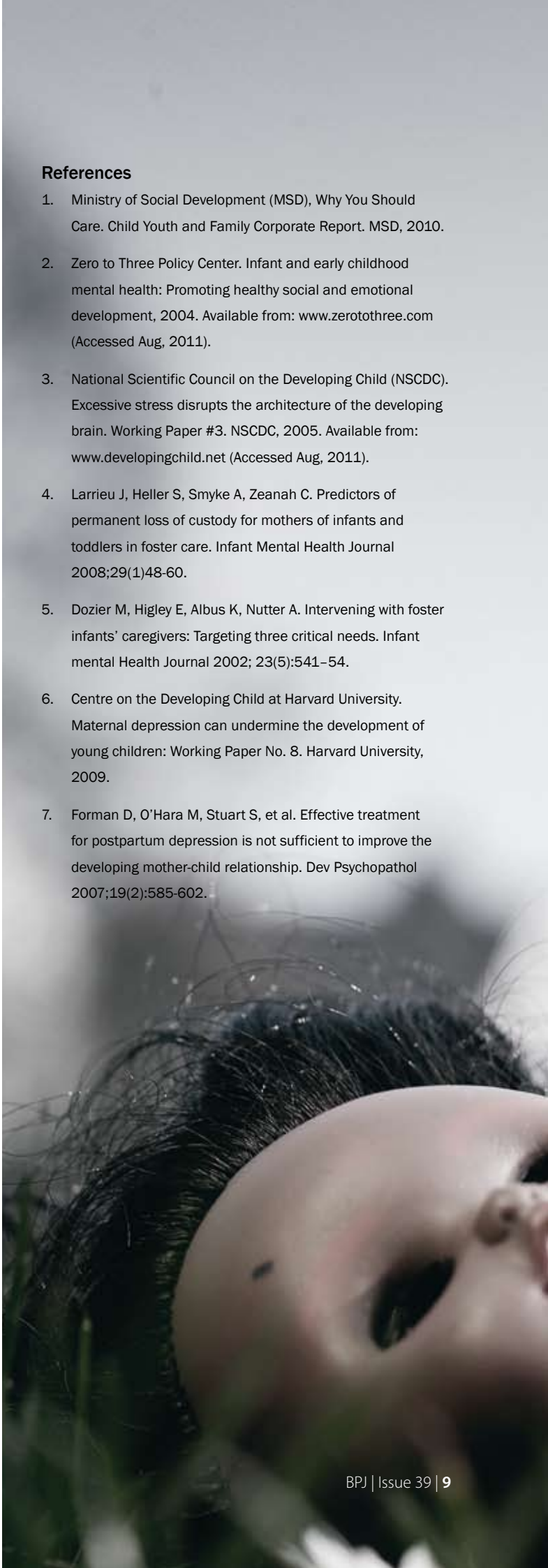
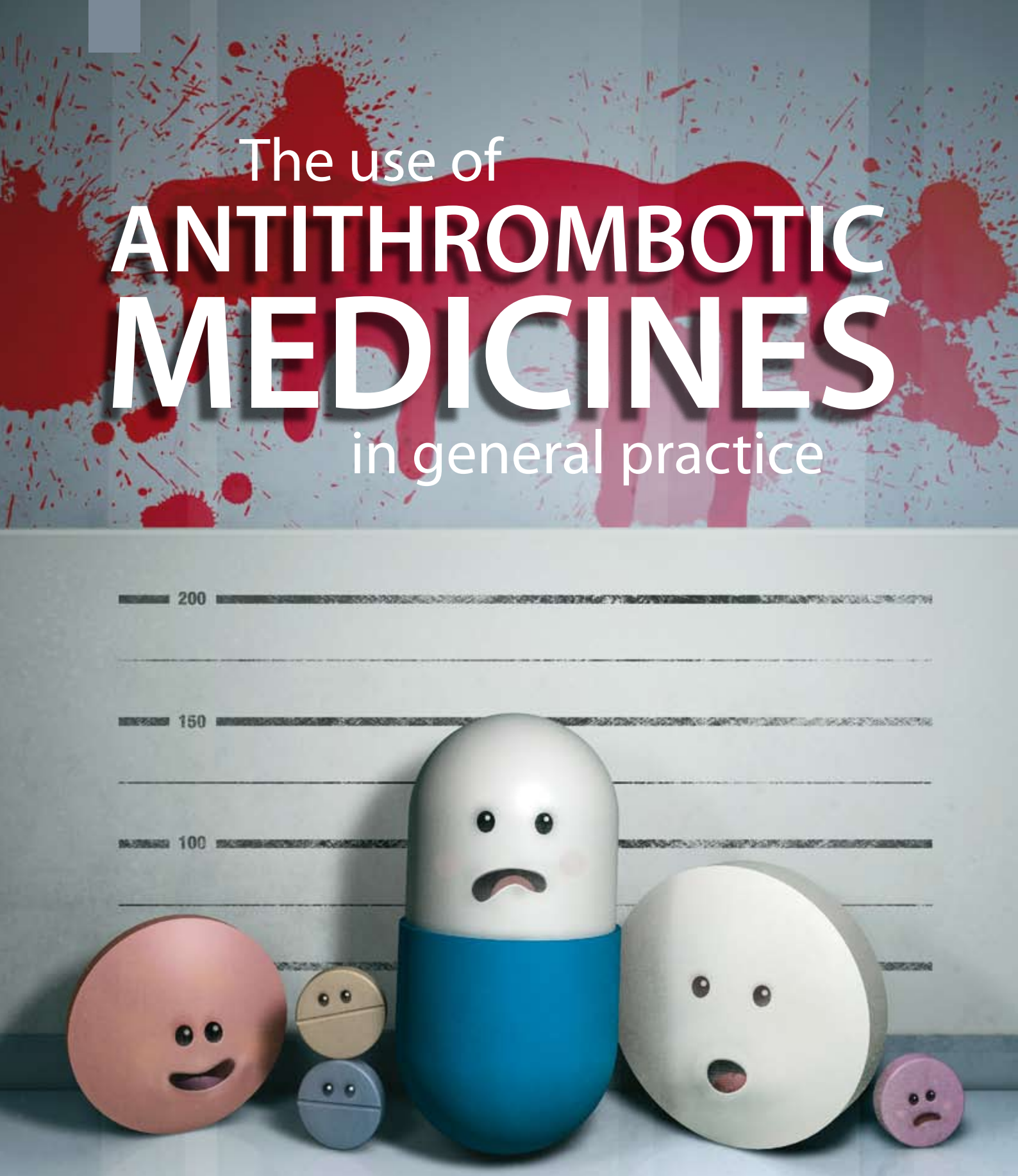


The use of ANTITHROMBOTIC MEDICINES in general practice



A CONSENSUS STATEMENT

In July 2011, a consensus forum was held in Wellington to discuss the use of antithrombotic medicines in general practice. This was attended by representatives from primary care, secondary care, bpac[nz], PHARMAC and the New Zealand Guidelines Group.

The conditions discussed were:

- Primary and secondary prevention of cardiovascular disease (including ischaemic stroke)
- Treatment after haemorrhagic stroke
- Prevention from thromboembolic events in patients with prosthetic heart valves or with haemodynamically significant valvular disease
- Venous thromboembolism (VTE) prophylaxis (post-surgery and for long haul travel) and treatment

The antithrombotic medicines associated with these conditions are: aspirin, clopidogrel, warfarin, dipyridamole and dabigatran (all fully funded with no restrictions on prescribing), enoxaparin and rivaroxaban (funded under Special Authority restriction).

This consensus statement represents the opinions of the experts involved, and although based on trial evidence, also reflects clinical practice. The advice given may therefore differ from some current guidelines.

Forum Participants:

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Primary prevention of cardiovascular disease including stroke–people without atrial fibrillation

Consensus

The role of aspirin for primary prevention of cardiovascular disease (CVD), including stroke, is controversial. Current evidence does not justify the routine use of low-dose aspirin, for the primary prevention of CVD in apparently healthy individuals, because of the potential risk of serious bleeds and the lack of beneficial effect on mortality. However, patients at high CVD risk (defined in the New Zealand Cardiovascular Guidelines as a cardiovascular risk of more than 15%) may benefit from aspirin.[1]

Primary prevention of cardiovascular disease including stroke – people without atrial fibrillation:

Medicine	Dose	Duration	Comments
Aspirin	100 mg daily	Lifelong	Cardiovascular risk > 15% only Individual assessment required

Evidence

Current evidence does not recommend the routine use of aspirin for the primary prevention of cardiovascular disease. Most guidelines continue to recommend aspirin for primary prevention in patients who are at increased CVD risk (e.g. >15%), however, individual assessment is required as recent evidence does not support routine use of aspirin in patients with risk factors such as diabetes and hypertension.

The Antithrombotic Trialist's (ATT) Collaboration was a key meta-analysis of primary prevention studies and showed a 0.06% reduction only in absolute risk with the use of aspirin.[2] There was no significant difference in cardiovascular mortality rate and the authors concluded that the benefit of using aspirin for primary prevention in low risk populations was very small. This and other similar evidence changed the way clinicians viewed the use of aspirin for primary prevention.[2, 3, 4]

This view has been reinforced in recent publications. Calculations from the ATT data have shown that the number needed to be treated (NNT) with aspirin for one year to prevent one cardiovascular event was 1666.[5] Updated meta-analyses have now included a total of nine primary prevention trials. Similar conclusions have been reached in these studies:

- Although aspirin reduced the risk of total cardiovascular events and non-fatal myocardial infarction, there was no significant reduction in the incidence of stroke, total coronary heart disease, cardiovascular mortality and all cause mortality.[6]
- If 1,000 people were treated with aspirin for five years, 2.9 major cardiovascular events would be prevented but aspirin would cause 2.8 major bleeds.[7]

The evidence of benefit of aspirin for primary prevention of stroke in people who have diabetes is also inconclusive, with several trials showing no benefit from the use of aspirin in these people.[8, 9, 10]

There is evidence that statins should be used as first-line treatment for primary prevention in people who have moderate to high CVD risk.[11] The addition of aspirin for these people appears to give no further benefit because the increased risk of bleeding offsets any improvement in cardiac morbidity.[2]

Primary prevention of stroke – people with atrial fibrillation

Consensus

Anticoagulation is recommended for the primary prevention of stroke in people with non-valvular atrial fibrillation (AF) who are at moderate or high risk of stroke. Both stroke and bleeding risk should be considered when making the decision to anticoagulate, using assessment tools such as $CHADS_2$ and HAS-BLED (see "Stroke risk assessment tools" over page).[12, 13] Co-morbidities, monitoring requirements and patient preference should also be considered when determining whether anticoagulation is suitable for a patient.

Once the decision to anticoagulate has been made, the next decision is which oral anticoagulant to use, i.e. warfarin or dabigatran.

Treatment of other modifiable risk factors such as hypertension, dyslipidaemia and smoking should also be initiated for all patients with AF.

For further information on choosing between dabigatran and warfarin, see "The use of dabigatran in general practice", BPJ 38 (Sep, 2011).

Assessment of stroke risk and management using $CHADS_2$ and CHA_2DS_2-VASc

	Medicine	Dose	Duration	Comments
$CHADS_2$ score ≥2	Anticoagulant – warfarin or dabigatran	Warfarin: dose to attain INR 2–3 Dabigatran: Aged under 80 years – 150 mg, twice daily, if creatinine clearance >30 mL/min Aged over 80 years* – 110 mg, twice daily, if creatinine clearance >30 mL/min	Lifelong	Creatinine clearance must be calculated if dabigatran considered Use dabigatran with caution if < 60kg or creatinine clearance 30–50 mL/min
$CHADS_2$ score <2	**Calculate CHA_2DS_2-VASc score**			
CHA_2DS_2-VASc score ≥ 2	Anticoagulant – warfarin or dabigatran	As above	Lifelong	Creatinine clearance must be calculated if dabigatran considered Use dabigatran with caution if < 60kg or creatinine clearance 30–50 mL/min
CHA_2DS_2-VASc score 1	Anticoagulant or aspirin (with preference for anticoagulation)			
CHA_2DS_2-VASc score 0	No treatment			

* There is some suggestion that a lower dose of dabigatran is appropriate for patients aged > 75 years, but at this stage no changes have been made to dosing recommendations in the medicine datasheet.

Stroke risk assessment tools

The risk of stroke in people with AF can be evaluated using a risk stratification tool such as $CHADS_2$ or the updated version, CHA_2DS_2-VASc, preferred by many clinicians. The updated tool puts greater emphasis on increasing age (≥75 years) and also incorporates additional risk factors for stroke – female gender, age group 65 – 75 years and a history of vascular disease, e.g. myocardial infarction, peripheral arterial disease.[14] Scores for each tool are calculated as follows:

$CHADS_2$	Score
Congestive heart failure	1
Hypertension	1
Age 75 years or older	1
Diabetes mellitus	1
Previous **S**troke or TIA	2
Maximum score	**6**

CHA_2DS_2-VASc	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA	2
Vascular disease (prior MI, peripheral vascular disease)	1
Age 65–75 years	1
Sex **c**ategory (i.e. female gender)	1
Maximum score	**9**

N.B. Maximum score is 9 as age is either allocated one or two points

If the $CHADS_2$ score is ≥ 2, the patient should be anticoagulated. If a patient has a $CHADS_2$ score of less than 2, CHA_2DS_2-VASc can be used to further evaluate risk and to guide treatment choice.

A patient with a CHA_2DS_2-VASc score of 0 is truly low risk and does not need anticoagulation and may not even need aspirin. Anticoagulation is recommended for people with a CHA_2DS_2-VASc score ≥ 1.

Aspirin may be considered as an option for patients with AF who are unsuitable for anticoagulation, e.g. patients with severe liver disease, recent history of gastrointestinal bleeding.

HAS-BLED

This tool can be used to calculate the risk of bleeding when considering anticoagulant use. A score of ≥ 3 indicates a patient who may be at high risk of bleeding complications.[13]

HAS-BLED Bleeding Risk Score[13]	Score
Hypertension (systolic blood pressure > 160 mm Hg)	1
Abnormal renal and liver function	1 point each
Stroke (past history)	1
Bleeding (previous history of bleeding or predisposition to bleeding)	1
Labile INRs (unstable, high or insufficient time within therapeutic range)	1
Elderly (> 65 years)	1
Drugs or alcohol (including concomitant use of aspirin, other antiplatelet agents and NSAIDs)	1 point each
Maximum score	**9**

For further information about HAS-BLED, see "The warfarin dilemma", BPJ 31 (Oct, 2010).

Secondary prevention of stroke* – people without atrial fibrillation

*for people where the initial event was non-haemorrhagic

Consensus

In a patient with a history of transient ischaemic attack (TIA) or stroke, who does not have AF, antiplatelet treatment for secondary prevention should be initiated (provided there are no contraindications). Although aspirin has been shown to be effective in the secondary prevention of non-embolic stroke, there is evidence that treatment with clopidogrel is slightly more effective than aspirin. The combination of aspirin and modified release dipyridamole is slightly more effective than aspirin alone and provides similar benefits to treatment with clopidogrel. However, clopidogrel monotherapy is simpler and usually better tolerated by patients.

Treatment of other modifiable risk factors such as hypertension, dyslipidaemia and smoking cessation should also be initiated for all patients.

The management of TIA and a minor stroke are largely the same and both should be regarded as a medical emergency. The highest risk of a stroke is within the first week (particularly in the first 48 hours) after a TIA. If a patient presents with signs and symptoms of a stroke which are still present after one hour, then this event should be regarded as a stoke as the majority of "true" TIAs resolve within one hour. The main difference in management is that all patients with stroke should be referred immediately to hospital for investigation prior to commencing antithrombotic treatment due to the possibility of intracerebral haemorrhage (ICH). Antiplatelet treatment should be initiated immediately (after resolution of symptoms) for patients with TIA to avoid delay prior to assessment as the risk of ICH is extremely low.

For further information see "Transient ischaemic attack" (Page 30)

Secondary prevention of stroke – people without atrial fibrillation

Medicine	Dose	Duration	Comments
First-line: Clopidogrel	Loading dose of 300 mg followed by 75 mg daily	Lifelong	Although evidence and consensus opinion favours clopidogrel monotherapy first line, combination treatment with aspirin and dipyridamole or aspirin monotherapy remain alternative first-line choices
Second-line: Aspirin + dipyridamole	Aspirin 100 mg and dipyridamole 150 mg* twice daily	Lifelong	Consider for patients who cannot tolerate clopidogrel
Third-line: Aspirin alone	Aspirin 100 mg	Lifelong	Consider for patients who cannot tolerate clopidogrel or dipyridamole

*The funded strength of dipyridamole in New Zealand is the 150 mg long-acting tablet, however, in the majority of clinical trials the dose used was 200 mg extended release capsules, twice daily.

Evidence

The Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE) trial found that clopidogrel significantly reduced the risk of the combined outcomes of ischaemic stroke, myocardial infarction or death in people with atherosclerotic cardiovascular disease.[15, 16] There was an approximately 9% reduction in relative risk of these events (N.B. figures for absolute risk were not reported). However, among the subgroup of people who had previous stroke, there was no significant difference in outcomes between aspirin or clopidogrel monotherapy (p value 0.26). The combination of aspirin and clopidogrel has not been shown to provide any greater benefit in preventing stroke and dual antiplatelet treatment significantly increases the risk of bleeding. This combination is, however, effective in acute coronary syndromes.[17, 18]

The Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) trial looked at the combination of modified-release dipyridamole with aspirin compared to clopidogrel. The results showed similar risks and benefits with each antiplatelet regimen.[19]

Evidence from the European/Australasian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT) found treatment with aspirin and dipyridamole, compared with aspirin monotherapy, resulted in a reduction in absolute risk of 1.0% per year.[20]

Secondary prevention of stroke* – people with atrial fibrillation

*For people where the initial event was non-haemorrhagic

Consensus

Oral anticoagulants have been shown in a number of randomised controlled trials to be effective in reducing stroke in people with AF. Individualised bleeding risk should be considered prior to anticoagulation.

In addition to oral anticoagulation treatment, a patient with a TIA or stroke, who has AF, should also be started on a statin and an antihypertensive (usually an ACE inhibitor) unless there are contraindications. Aspirin should only be used in the immediate post-stroke period before the establishment of effective anticoagulation or in patients who are unable to tolerate ongoing oral anticoagulation.

Secondary prevention of stroke – people with atrial fibrillation

Medicine	Dose	Duration	Comments
Anticoagulant – warfarin or dabigatran	Warfarin: dose to attain INR 2–3 Dabigatran: Aged under 80 years – 150 mg, twice daily, if creatinine clearance > 30 mL/min Aged over 80 years – 110 mg, twice daily, if creatinine clearance > 30 mL/min	Lifelong	Stop aspirin and clopidogrel Creatinine clearance must be calculated if dabigatran considered Use dabigatran with caution if weight < 60kg or creatinine clearance 30–50 mL/min

Evidence

There is evidence that oral anticoagulation with warfarin reduces stroke risk more effectively than aspirin in people with AF.[21, 22] If oral anticoagulation is contraindicated, not indicated or is declined by the patient, aspirin should be prescribed, as it reduces the risk of stroke compared to placebo.

Evidence for the effectiveness of dabigatran in the secondary prevention of stroke in patients with non-valvular AF comes from the RE-LY trial.[23]

See "The use of dabigatran in general practice", BPJ 38 (Sep, 2011), for further discussion of the RE-LY trial.

In the Birmingham Atrial Fibrillation Treatment of the Aged Study (BAFTA), which included people with AF aged over 75 years, the risk of a primary endpoint (stroke, intracranial haemorrhage or arterial embolism) was significantly lower with warfarin (1.8%) compared with aspirin (3.8%), and there was no evidence that warfarin caused more bleeding complications than aspirin.[24]

Secondary prevention after haemorrhagic stroke

Consensus

Patients with a suspected haemorrhagic stroke should be referred immediately to hospital (do not give aspirin) and decisions on treatment will be made in hospital after appropriate imaging has been completed.

In a general practice setting, decisions on treatment for patients who have a history of intracranial haemorrhage (ICH) may be difficult. Treatment choices are not straightforward, e.g., in a patient who has a history of ICH, who subsequently develops AF. The decision regarding medicines in these patients will depend on the individual patient circumstances, the site of the ICH, the underlying pathology, and co-morbidities. The care of these patients requires discussion with, and usually referral to, secondary care. Accurate documentation of the history of ICH must be available to guide treatment decisions.

Patients who do not have a documented history of ICH, but who may recall a problem or have information in their patient notes that may raise suspicion of a past ICH need to have this history clarified – this role will generally fall to the primary care team.

Secondary prevention of acute coronary syndrome*

*Acute coronary syndrome includes ST and non-ST elevation mycoardial infarction and unstable angina

Consensus

Early combination treatment with dual antiplatelet medicines is highly effective in patients with acute coronary syndromes. Treatment choice depends on the type and outcome of the event, the time since it occurred and the stability of the patient.

Evidence

In patients with acute coronary syndrome without ST-segment elevation, combined treatment with clopidogrel and aspirin gave a 20% reduction in relative risk of MI, stroke and cardiovascular death.[25]

Clopidogrel and aspirin should be used in combination for patients who have had angioplasty, insertion of a bare metal or a drug-eluting stent. The duration of treatment is usually 12 months except if a bare metal stent is used, where treatment is required for a minimum of six months, as outlined in the table over the page.

If aspirin is not tolerated, clopidogrel can be used as monotherapy.[25] Allergy or intolerance to both aspirin and clopidogrel is rarely seen, however, aspirin desensitisation therapy is available in some clinics around the country.

Secondary prevention of acute coronary syndrome

Scenario	Medicine	Dose	Duration	Comments
After acute event: no stent	Aspirin and clopidogrel	Aspirin 100 mg daily and clopidogrel 300 mg loading dose followed by 75 mg daily	12 months	After 12 months stop clopidogrel
After acute event: bare metal stent	Aspirin and clopidogrel	Aspirin 100 mg daily and clopidogrel 300 mg loading dose followed by 75 mg daily	12 months (do not stop treatment in first 6 months)	After 12 months stop clopidogrel
After acute event: drug eluting stent	Aspirin and clopidogrel	Aspirin 100 mg daily and clopidogrel 300 mg loading dose followed by 75 mg daily	12 months (do not stop treatment in this period)	After 12 months stop clopidogrel
After acute cardiac event: patients with indications for anticoagulation, e.g. AF	Aspirin and warfarin	Aspirin 100 mg daily and warfarin – dose to attain INR 2-3	Lifelong anticoagulation Aspirin for 6-12 months or lifelong if high CVD risk and lower bleeding risk	Warfarin is the preferred anticoagulant for these patients* Clopidogrel may also be given for 6–12 weeks although there is an increased risk of bleeding
After acute cardiac event: patients with a mechanical heart valve	Warfarin and aspirin	Warfarin – dose to attain INR 2.5-3.0 for aortic valve prosthesis, 3.0–3.5 for mitral valve prosthesis Aspirin 100 mg daily and in selected patients, clopidogrel 300 mg loading dose followed by 75 mg daily	Lifelong anticoagulation Aspirin for 6-12 months or lifelong if high CVD risk and lower bleeding risk Clopidogrel for 2–12 weeks depending on the use of stents and bleeding risk	Warfarin is the preferred anticoagulant for these patients* The risk of bleeding is substantially increased in patients taking warfarin, aspirin and clopidogrel and this combination should be used in consultation with a cardiologist
High risk patients: multiple events in more than one vascular territory, e.g. MI and stroke	Aspirin and clopidogrel	Aspirin 100 mg daily and clopidogrel 300 mg loading dose followed by 75 mg daily	Lifelong	Treatment for these high risk patients often requires secondary care input
Stable patients: no acute cardiac event in past 12 months†	Aspirin	If the event was cardiac: aspirin 100 mg daily	Lifelong	

N.B. Table excludes the immediate use of 300 mg aspirin used in the acute treatment of ACS

* Warfarin is preferred to dabigatran in these patients because:

- There is a possible increase in the risk of MI with dabigatran use
- Dabigatran is not currently indicated for use in patients with prosthetic valves or haemodynamically significant valvular disease

† In all stable patients >12 months post ACS, the combination of aspirin and anticoagulation is not usually required, but may be appropriate in selected high risk patients. Consultation with a cardiologist is recommended.

Prevention of thromboembolic events: post elective surgery

Consensus

Prophylaxis for the prevention of thromboembolic events post elective surgery is the responsibility of the surgeon, however, General Practitioners should be aware of the requirements and of the length of the post-operative course so that medicines are not continued (or discontinued) in error.

Prevention of thromboembolic events: post elective surgery

Medicine	Dose	Duration	Comments
Dabigatran*	220 mg (as 2 x 110 mg), once daily, if creatinine clearance > 50 mL/min 150 mg (as 2 x 75 mg), once daily, if creatinine clearance between 30-50 mL/min	Hip replacement: up to 35 days post- op Knee replacement: 10 days post-op	
Enoxaparin	40 mg sub cut, once daily	7-10 days	Dose reduced to 20 mg once daily in severe renal impairment (Creatinine clearance <30 mL/min)
Rivaroxaban*	10 mg tablet, once daily	Hip replacement: up to 5 weeks post- op Knee replacement: up to 2 weeks post-op	Special authority criteria apply Contraindicated in hepatic disease

*indicated for use after elective orthopaedic surgery

Prevention of thromboembolic events: prosthetic valves or haemodynamically significant valvular disease

Consensus

Warfarin is currently the only anticoagulant recommended for people with prosthetic heart valves or haemodynamically significant valvular disease (usually mitral valve stenosis). Dabigatran is currently not recommended for this indication. Anticoagulation treatment for these people will usually be initiated in secondary care. Aspirin is generally not effective for the prevention of thromboembolic events in these people although the risk of events is higher with no treatment.

Some patients may require combination treatment with warfarin and aspirin but guidelines differ in their recommendations regarding this.

Evidence

Patients with haemodynamically significant valvular heart disease or prosthetic valves were excluded from the RE-LY trial.[23] Patients with these conditions who are currently on warfarin must not be switched to dabigatran.

N.B. Patients who have valvular disease (excluding patients with severe mitral stenosis or prosthetic valves) but are in sinus rhythm do not usually require anticoagulation.

Prevention of thromboembolic events: prosthetic valves or haemodynamically significant valvular disease

Medicine	Dose	Duration	Comments
Warfarin	Warfarin – to attain INR of 2.5-3.5*	Lifelong	Dabigatran not indicated If high risk, aspirin may also be added

*The recommended INR range may vary depending on the type and location of the prosthetic valve

Prevention of thromboembolic events from long haul travel

Consensus

There is a risk of venous thromboembolism (VTE) during travel, particularly with longer flights (> four hours).

People at high risk of VTE include those with pro-thrombotic states (e.g. deficiencies of antithrombin III, protein C, protein S), a history of previous VTE, recent surgery or a significant medical illness. In these people consideration should be given to the use of: [26]

- Correctly fitted compression stockings which reduce the incidence of VTE by approximately 18 times in high risk people
- Prophylactic low molecular weight heparin (one injection on the day of travel). There is evidence to support the use of enoxaparin, although this medicine is not funded for this indication.

There is currently no evidence to support the use of dabigatran or rivaroxaban for VTE prophylaxis during travel. Aspirin is not adequate for prophylaxis and the risks of adverse effects (e.g. bleeding) outweigh the benefits of treatment. Routine use of prophylactic medicines for long haul travel is not necessary for people with no risk factors for VTE.

The following advice should be given to all people who are travelling long distances:[27]

- Sitting in an aisle seat provides more opportunity for movement. Also consider exercising leg muscles while seated and walking whenever possible.
- Ensure adequate hydration and avoid alcohol, particularly if combined with sedative medicines

Treatment of VTE

Treatment for VTE is increasingly initiated in the community with the availability of low molecular weight heparin (LMWH). LMWH is used until an INR level of 2–3 is attained for two consecutive days. Warfarin is used simultaneously, with the duration of treatment varying with individual circumstances.

Dabigatran is not currently indicated for use in the treatment of VTE.

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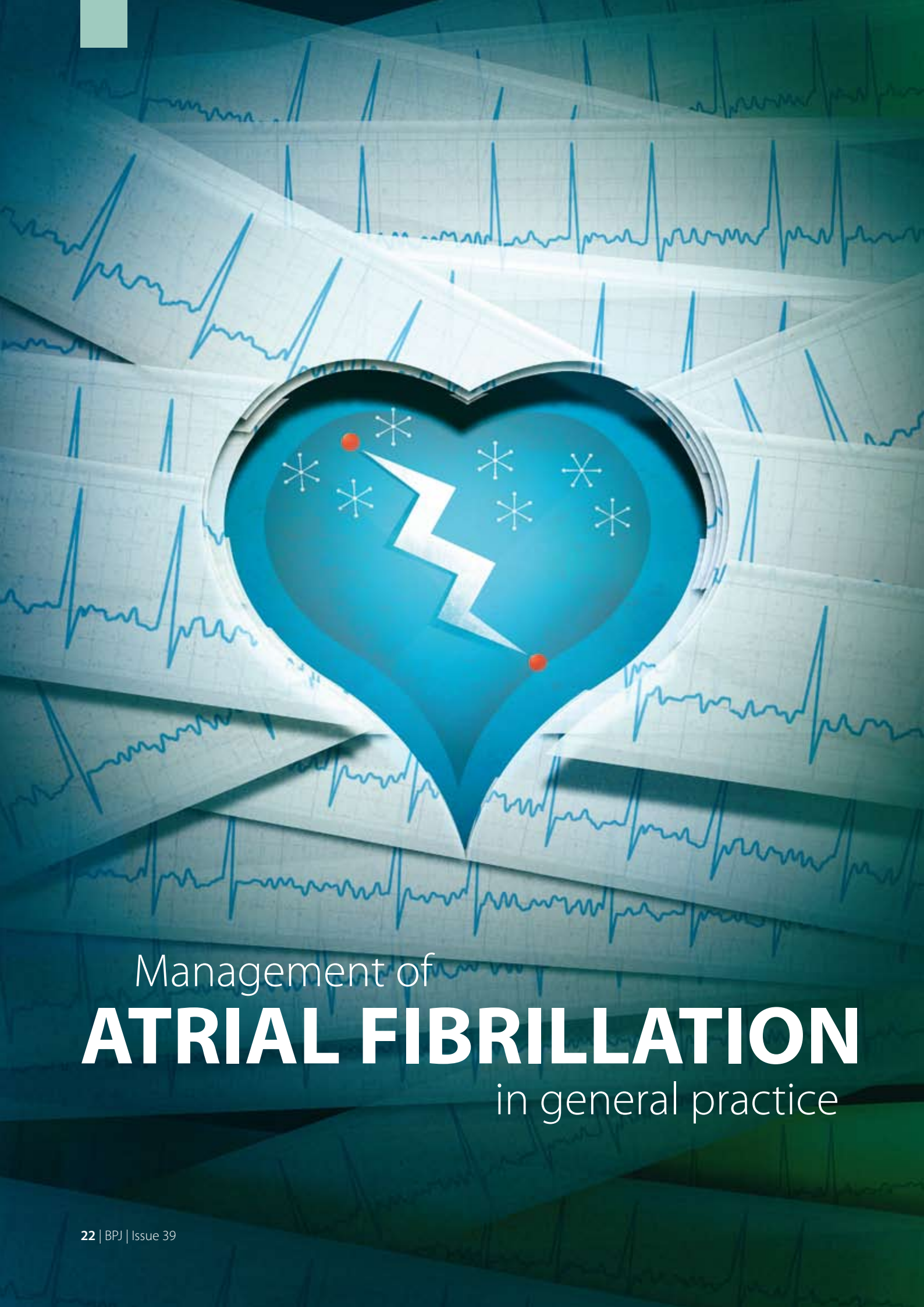


Management of ATRIAL FIBRILLATION in general practice

What is atrial fibrillation?

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in primary care. It is often diagnosed as an incidental finding during a routine medical check. The prevalence of AF increases with increasing age, particularly from age 50 years. The overall prevalence of AF is approximately 1%, increasing to approximately 10% in people aged ≥ 80 years.[1, 2] The presence of cardiovascular disease further increases the risk of AF. An understanding of the current management issues and treatment options available to patients with AF is therefore essential for primary care clinicians.

AF is a cardiac arrhythmia characterised by rapid irregular contractions of the atria and an irregular ventricular response. The main consequences of AF are a potential reduction in cardiac output and the formation of thrombus within the atria. Patients with AF can have significant symptoms that affect quality of life. The risk of stroke for a person with AF is up to five times that of a person without AF.[3] This risk can be significantly reduced with antithrombotic treatment, in high risk patients.

In people diagnosed with AF, there are two separate but equally important issues that must be considered. These are:

- Symptom management
- Assessment and management of thromboembolic risk

The aims of treatment of AF are to provide relief of symptoms (if present), to prevent thromboembolic complications and to prevent other serious complications such as heart failure. In the majority of patients with AF the most appropriate and effective treatment is to control the rate. Antithrombotic treatment should be initiated in patients who are considered to be at high risk of thromboembolic complications.[4, 5]

Key concepts

- Atrial fibrillation (AF) is often an incidental finding during a routine medical check - symptoms may or may not be present and the diagnosis of AF should be confirmed with ECG
- Most people presenting with new onset AF will not be haemodynamically compromised, however, urgent referral to secondary care for possible cardioversion is required for patients with significant symptoms or complications
- Symptom management consists of rate or rhythm control – the choice of treatment is guided by the type of AF and other factors such as age, the presence of co-morbidities, the presence or absence of symptoms and patient preference
- All patients for whom a rhythm control strategy is contemplated should be referred to a cardiologist
- Antithrombotic treatment can be determined after an assessment of stroke and bleeding risk – choice is also dependent on whether the AF is valvular (warfarin or aspirin) or non-valvular (warfarin, dabigatran or aspirin)

A stepwise approach to management is recommended

1. Confirm the diagnosis with ECG
2. Consider if urgent referral to secondary care is required
3. Determine the type of AF (e.g. persistent, paroxysmal or permanent)
4. Symptom management
5. Assess stroke risk to determine if antithrombotic treatment is required

Confirm the diagnosis

A comprehensive history should be taken, although not all patients with AF will be symptomatic. Typical symptoms include; palpitations, tachycardia, tiredness, weakness, dizziness, mild shortness of breath and reduced exercise capacity. Patients may also present with more severe symptoms including; significant shortness of breath, chest pains and fainting.

Check when the symptoms started, how often they occur and how long they last. Assess the severity of the symptoms and the presence of any associated features that may suggest an underlying cause (such as hyperthyroidism). Ask about any precipitating triggers such as exercise, alcohol or stress.

Examination should include assessment of: pulse (rate and rhythm); blood pressure, jugular venous pressure; heart sounds, e.g. for murmur; lungs, e.g. for signs of infection, heart failure, chronic obstructive pulmonary disease (COPD): and peripheral oedema.

AF can be associated with conditions such as:[6]

- Hypertension
- Cardiovascular disease
- Cerebrovascular disease
- Diabetes
- COPD
- Hyperthyroidism
- Excessive alcohol consumption
- Infection

Approximately one-third of the estimated 35,000 people in New Zealand with AF will be asymptomatic.[7] Consider routinely checking and documenting the rate and rhythm of the radial pulse in older patients, particularly those with cardiovascular disease or in patients who have any of the conditions listed previously.

ECG

If AF is suspected on the basis of patient history or found incidentally during physical examination, the patient should have an electrocardiogram (ECG) to confirm the diagnosis. An initial ECG may also show evidence of other abnormalities that could suggest a possible underlying cause of the AF such as an old myocardial infarction (MI) or left ventricular hypertrophy. Other conduction abnormalities may be present such as pre-excitation (short PR interval) or bundle branch block. Assessment of the QT interval may be required prior to initiation of some anti-arrhythmic medicines such as amiodarone, sotalol and disopyramide.[5]

It is useful to check the patient's notes to see if they have a history of arrhythmia and to make a comparison with previous ECGs if available.

Blood tests

Blood tests are indicated to rule out any underlying condition that may have triggered AF. Consider:

- TSH to exclude hyperthyroidism
- CBC to exclude conditions such as anaemia or infection
- Electrolytes to exclude underlying metabolic abnormalities
- Creatinine/eGFR to check renal function
- Glucose to exclude diabetes
- LFT e.g. prior to anticoagulation or if high alcohol intake
- INR if warfarin is to be initiated

Echocardiography

All patients with newly diagnosed AF should ideally be referred for transthoracic echocardiography. This provides information that is helpful in assessing thromboembolic risk, particularly in relation to left ventricular function.

Other investigations

Depending on the clinical situation, patients with AF may require referral for other investigations including:

- Chest x-ray, e.g. in cases where shortness of breath is a significant feature as heart failure may co-exist or there may be other lung pathology
- Holter monitoring, e.g. in patients with paroxysmal symptoms and to assess effectiveness of rate control, especially in asymptomatic patients as poorly controlled AF, in the absence of symptoms, can be detrimental to cardiac function.

Consider if urgent referral to secondary care is required

The majority of people presenting with symptoms consistent with new onset AF will not be haemodynamically compromised, however, urgent referral to secondary care for possible cardioversion is required if the patient has:[6]

- A pulse rate > 150 beats per minute or a systolic blood pressure of < 90 mmHg
- Chest pain, increasing shortness of breath, severe dizziness or loss of consciousness (includes patients with acute ischaemic changes on ECG)
- Any complications of AF such as TIA, stroke, acute ischaemia or acute heart failure

In most acutely symptomatic patients, AF will be of new onset, however, in some patients it may be difficult to determine whether the AF is actually of new onset or rather is newly identified. An underlying condition can also trigger AF and reversion to sinus rhythm may result from appropriate treatment of the underlying condition.

Referral to or discussion with a cardiologist is recommended if the patient has:[6]

- Probable paroxysmal AF (as this requires medicines not usually initiated in primary care such as amiodarone or sotalol)
- ECG abnormalities such as Wolff-Parkinson-White syndrome or prolonged QT interval
- Known or suspected valvular disease
- Ongoing symptoms despite appropriate rate control treatment

Determine the type of AF

AF is generally classified into three types, although this may require further investigations and cardiologist input to determine. Knowing the type helps to guide treatment decisions regarding rate or rhythm control.

The three types of AF are:

- **Paroxysmal AF** – characterised by recurrent episodes of AF that last less than seven days (although often less than 24 hours) and resolve spontaneously within that time. Rhythm control is the preferred treatment.
- **Persistent AF** – characterised by episodes of AF that last more than seven days and that has not spontaneously resolved within this time. Treatment is rate or rhythm control depending on the individual patient situation.
- **Permanent AF** – AF that has been present for more than one year and cardioversion has failed or not been attempted. Rate control is preferred.

Symptom management

Rate or rhythm control?

The choice between rate or rhythm control is guided by the type of AF and other factors such as age, the presence of co-morbidities, the presence or absence of symptoms and patient preference. Clinical trials have not shown any significant differences between rate or rhythm control with respect to rates of stroke and mortality. Improvements in quality of life are seen with both treatment approaches.[5]

Rate control is recommended for the majority of patients.[4, 7] It should be considered in particular for patients with:

- Asymptomatic AF
- Permanent AF

Any concerns about a strategy of rate control for a particular patient can be discussed with a cardiologist.

Rhythm control, which aims to restore and maintain sinus rhythm, should be considered for patients with:[4, 7]

- Paroxysmal AF
- Persistent AF and ongoing symptoms, any haemodynamic compromise, failure of rate control or persistent symptoms despite rate control
- Structural heart disease, e.g. severe left ventricular dysfunction or hypertrophic cardiomyopathy (AF is usually not well tolerated in these patients)

All patients for whom a rhythm control strategy is contemplated should be referred to a cardiologist.

Rate control medicines

The ventricular rate may be controlled using beta blockers, rate limiting calcium channel blockers (verapamil or diltiazem) or digoxin. The choice of a medicine for rate control in patients in primary care should be guided by the presence of co-morbidities and also by the level of activity of the patient. Table 1 lists first to fourth-line options for rate control. Medicines may be used singularly or in combination.

As a guide, target heart rate should be ≤ 80 beats per minute at rest and ≤ 115 beats per minute with moderate walking. A patient who is active is unlikely to achieve rate control with digoxin alone. Patients who achieve poor rate control on maximally tolerated first, second or third-line medicines used in combination, particularly with ongoing symptoms, should be referred to a cardiologist for consideration of additional treatment options. This may include amiodarone, AF ablation or AV node ablation with pacemaker implantation. Consultation with a cardiologist

Table 1: Rate control medicines used in atrial fibrillation[7]

<table>
<tr><th>Co-morbidity</th><th>First line</th><th>Second line</th><th>Third line</th><th>Fourth line</th></tr>
<tr><td>No heart disease</td><td rowspan="3">Beta-blockers* (not sotalol)</td><td rowspan="3">Calcium channel blockers**</td><td rowspan="3">Digoxin</td><td rowspan="4">Amiodarone
Ablation and pacing may be considered</td></tr>
<tr><td>Hypertension</td></tr>
<tr><td>Ischaemic heart disease</td></tr>
<tr><td>Congestive heart failure</td><td>Metoprolol or carvedilol</td><td>Digoxin</td><td>Diltiazem</td></tr>
<tr><td>COPD</td><td>Calcium channel blockers**</td><td>Beta- blockers* (provided no significant reversible bronchospasm)</td><td>Digoxin</td></tr>
</table>

*Beta-blockers including atenolol, carvedilol, metoprolol, nadolol and propranolol but not sotalol

**Rate limiting calcium channel blockers, i.e. diltiazem or verapamil only. Avoid using verapamil with beta-blockers

is also recommended if there is any uncertainty over which combinations of medicines to use.

Rhythm Control

All patients, for whom rhythm control is considered to be the most appropriate treatment option, should be referred to a cardiologist. Sinus rhythm can be restored using electrical or pharmacological cardioversion, e.g. with flecanide or amiodarone. AF may recur after electrical or pharmacological cardioversion therefore ongoing rhythm control with antiarrhythmic medicines will usually be required. A brief overview of some of the available options follows – for more detailed information refer to the European Society of Cardiology Guideline.[5]

Medicines that are commonly used to achieve or maintain rhythm control after restoration of sinus rhythm include:

- Beta blockers, e.g. metoprolol, atenolol
- Sotolol, a beta blocker with additional class III antiarrythmic activity
- Flecanide, a class I antiarrythmic agent
- Amiodarone, a class III antiarrythmic

These antiarrythmic medicines (excluding beta blockers such as metoprolol and atenolol) carry a small (1%) but important risk of proarrhythmia (aggravation of existing or increased risk of new arrhythmia) and should not be prescribed without consultation with a cardiologist.[5, 8]

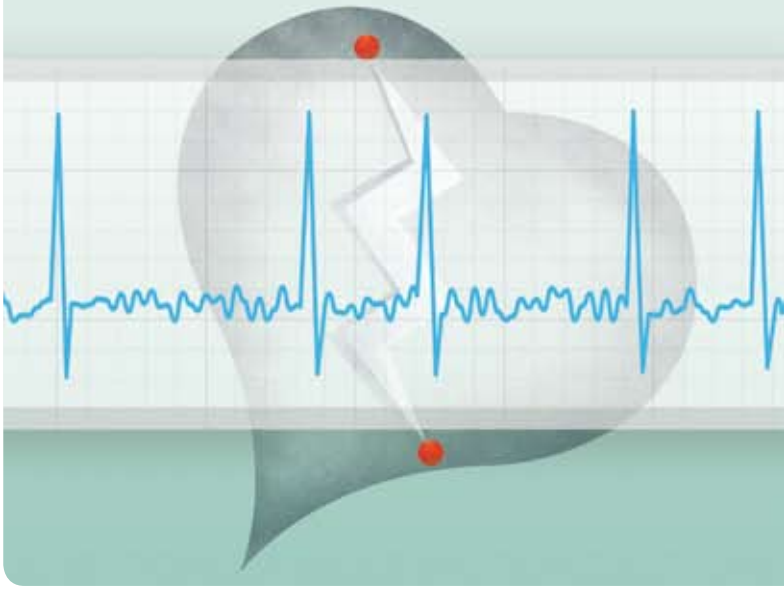
Treatment must be individualised with the risks and benefits fully explained to patients.

Radiofrequency ablation of AF is a new treatment option and may be considered in patients with significant limiting symptoms despite medical treatment or patients who wish to consider this treatment for lifestyle reasons.

Choosing rate or rhythm control

The following examples illustrate treatment choice between rate or rhythm control:

1. In a stable, older patient with few symptoms and a recent but unclear onset of AF, control of rate is the treatment of choice. Target heart rate should be ≤ 80 beats per minute at rest and ≤ 115 beats per minute with moderate walking.[7] Rate control medicines can be initiated in primary care.
2. In a younger patient with recurrent episodes of very symptomatic AF and a clear onset of symptoms, the preference is for rhythm control. Although spontaneous conversion to sinus rhythm may occur (up to 50% revert back within the first 24 hours),[8] the patient is likely to benefit from pharmacological or electrical cardioversion, ideally within 48 hours of the onset of symptoms. If cardioversion cannot be performed within 48 hours, the patient must be anticoagulated to facilitate this at a later date. Medicines such as metoprolol can be used to control the rate and relieve symptoms. Referral to secondary care is required for cardioversion whether pharmacological or electrical and also for advice about ongoing rhythm control.



Assess thromboembolic risk and stroke risk to determine appropriate antithrombotic treatment

AF is associated with a pro-thrombotic state and an approximately five-fold increase in stroke risk.[3] The presence or absence of a number of variables influences this risk (Table 2). The risk of stroke is the same regardless of whether the patient has paroxysmal or sustained (permanent or persistent) AF.

Bleeding risk should be estimated to help assess the risk-benefit ratio prior to choosing appropriate antithrombotic treatment.[9] Validated assessment tools such as $CHADS_2$, CHA_2DS_2-VASc and HAS-BLED are widely used to help guide treatment (Page 14).

If the $CHADS_2$ score is ≥ 2, the patient should be anticoagulated. If a patient has a $CHADS_2$ score of less than 2, consider using CHA_2DS_2-VASc to further evaluate risk and to guide treatment choice. Aspirin may be considered for patients with AF who are unsuitable for anticoagulation. Also consider co-morbidities, monitoring requirements and patient preference when determining whether anticoagulation is suitable.

Once the decision to anticoagulate has been made, the next decision is whether to use warfarin or dabigatran. All patients with haemodynamically significant valvular disease or a prosthetic valve should be anticoagulated with warfarin.

For further information about using dabigatran see "The use of dabigatran in general practice", BPJ 38 (Sept, 2011)

For further information about antithrombotic treatment in AF, see "Consensus statement" Page 10.

Further reading

There are a number of guidelines available for the management of AF. The 2005 New Zealand guideline and the 2006 United Kingdom NICE guidelines are scheduled for review.[4, 7] The European Society of Cardiology Society Guidelines have recently been updated and are recommended reading.[5] With the recent introduction of dabigatran, further updates are expected.

Table 2: Risk factors for stroke and thromboembolism in non-valvular AF[5]

Major risk factors	Clinically relevant non-major risk factors
Previous stroke	Congestive heart failure or moderate to severe LV systolic dysfunction (e.g. LV ejection fraction ≤ 40%
TIA or systemic embolism	Hypertension, diabetes or vascular disease
Age ≥ 75 years	Age 65–74 years
	Female gender

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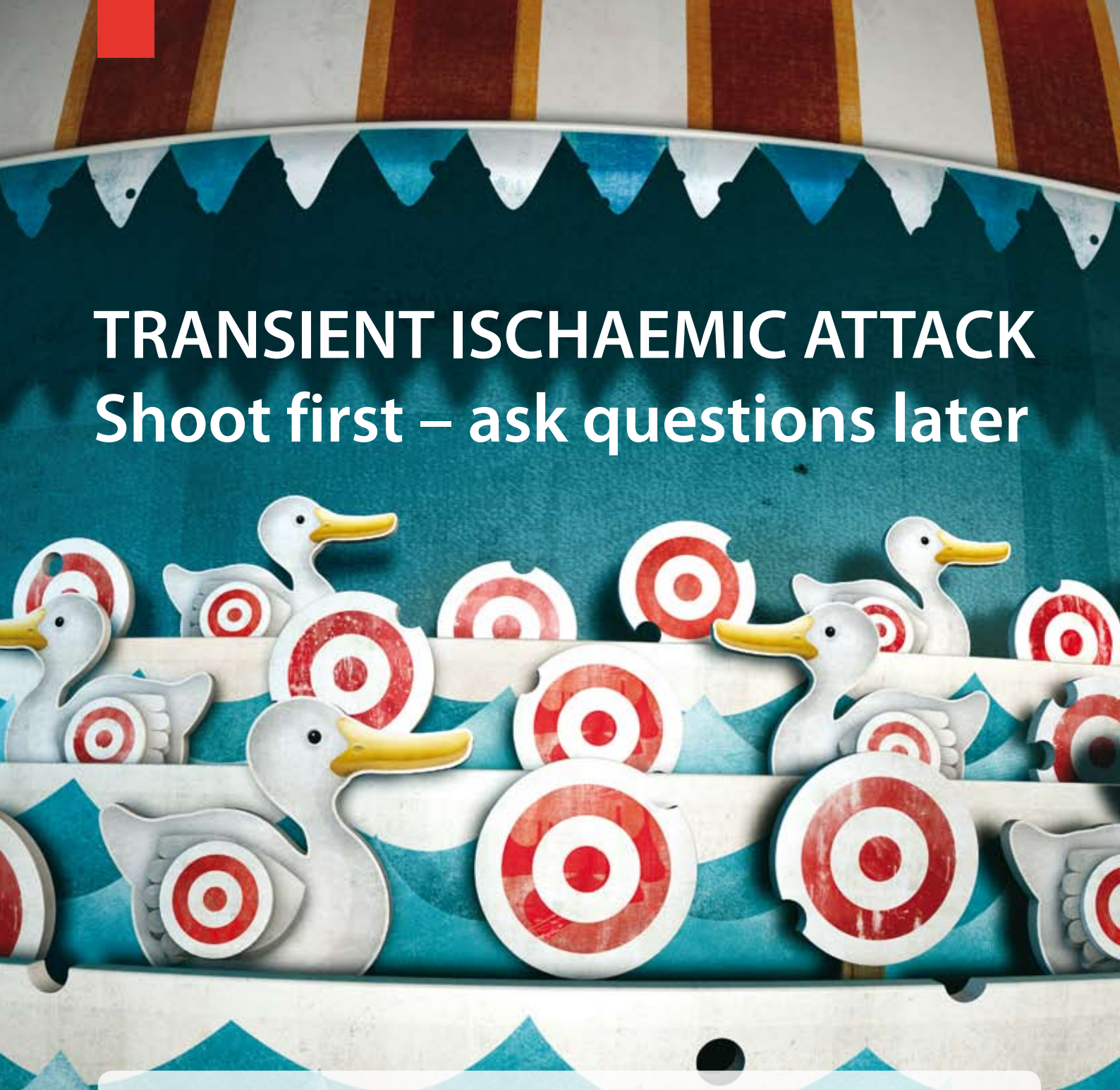
TRANSIENT ISCHAEMIC ATTACK
Shoot first – ask questions later



Key concepts

- A transient ischaemic attack (TIA) is a medical emergency due to the high risk that stroke will occur within the next 48 hours
- Aspirin, a statin and an antihypertensive medicine should be given to all patients immediately following a suspected TIA - if they are fully recovered and without contraindications
- All patients with a suspected TIA should have their risk of stroke assessed using the ABCD^2 tool, and then be referred to secondary care for urgent investigation and treatment (according to local protocols)
- As soon as a diagnosis of TIA is confirmed, risk factors should be assessed and a long-term, individualised secondary prevention plan implemented

Transient ischemic attack is a stroke warning

A transient ischaemic attack (TIA) is traditionally defined as a group of stroke symptoms which resolve within a 24 hour period. However, in practice, symptoms that last longer than one hour are likely to indicate a stroke. In New Zealand, approximately 8000 people per year experience a stroke and approximately one quarter of these people have a preceding (warning) TIA.[1] The risk of stroke is greatest in the first 48 hours following a TIA and some studies report the risk to be as high as 10% in the week following.[1, 2] A TIA is therefore a medical emergency.

Early diagnosis and intervention is important

If a TIA is rapidly diagnosed and appropriate interventions initiated, the risk of subsequent stroke can be significantly reduced. Prompt access to specialised stroke services can greatly enhance patient outcomes,[2, 3] although availability of these services is variable throughout New Zealand. Therefore it is important that primary care clinicians respond effectively and rapidly to manage a patient with a suspected TIA.

When to suspect TIA

Due to the high risk of stroke following a TIA, it is important that all people with a suspected TIA receive urgent treatment and referral for secondary care assessment. However, other conditions can mimic the symptoms of TIA and over diagnosis is frequent. It has been estimated that 50% to 80% of suspected TIA cases are subsequently confirmed.[1] A desire not to miss any cases must be balanced against the risk of an incorrect diagnosis, which can cause the patient anxiety and affect their ability to work, to drive, to travel in general or, in some cases, to qualify for medical insurance.

The best method of diagnosing TIA is an accurate description of the event provided by the patient, as soon as possible after it has occurred. If an observer was present then corroboration of detail is also useful. Brain imaging cannot be relied upon solely for diagnosis – although a positive finding may be confirmatory, negative imaging does not exclude TIA.

The difference between ischaemic stroke and TIA

The etiological difference between an ischaemic stroke and a TIA is that stroke causes brain damage, whereas a TIA does not – this is why the symptoms of a TIA resolve quickly. As brain imaging technology improves, neurologists are increasingly finding that TIAs lasting for longer than one hour are often associated with brain damage and are in fact strokes. This has led to the working definition of a TIA being changed to; stroke-like symptoms which resolve in less than one hour.

Both TIA and stroke are medical emergencies and the management of the two is largely the same. The crucial difference is that patients with stroke need to be referred to hospital immediately, in order to eliminate the possibility of intracranial haemorrhage (ICH), before antithrombotic treatment can begin. However, patients with TIA should be given aspirin, statin and antihypertensive treatment immediately after symptoms have resolved,[1, 2, 4] without waiting for secondary care assessment. This is because following resolution of symptoms, the chance of ICH is very small.

A diagnosis of TIA is more likely if the history includes:[1]

- Sudden and discernible onset of symptoms
- Neurological deficits maximal at onset
- Loss of function
- Rapid recovery (usually 30 – 60 minutes)

N.B. Progressive onset of symptoms, or a succession of muscular symptoms from one part of the body to another, is more likely to be due to epilepsy if it occurs over seconds to minutes, or a migraine if it occurs over a number of minutes.

TIA diagnosis

Typically, symptoms of TIA are "negative" and involve loss of localised neurological function (e.g. loss of sensation, vision or power). TIAs rarely cause "positive" symptoms such as pins and needles, limb movement or scintillating (bright, flashing, shimmering) visual disturbances. Symptoms of ataxia, vertigo, dysphagia (difficulty swallowing), dysarthia (difficulty articulating speech) and focal sensory symptoms may be consistent with TIA when combined with other typical symptoms. Hypoglycaemia should be excluded in all patients with sudden onset of neurological symptoms. Patients with a blood glucose < 3.5 mmol/L should be treated and then reassessed.[1] Table 1 outlines symptoms which are typical and atypical of TIA.

What do you do when you suspect TIA?

Step 1: Immediate empiric treatment to reduce stroke risk

Administer **aspirin**, **statin** and **antihypertensive** treatment immediately after symptoms have resolved – unless contraindicated (e.g. history of intracranial haemorrhage, anticoagulant treatment or hypotensive). Do not defer treatment until after secondary care assessment or brain imaging.[1]

Table 1: Diagnosis of TIA (adapted from Stroke Foundation of New Zealand, 2008)[1]

Symptoms typical of TIA	Symptoms atypical of TIA
Unilateral weakness of: Face Arm Leg	Generalised weakness or generalised sensory disturbances
Unilateral sensory disturbance	Reduced consciousness or reduced muscle tone resulting in falls
Dysphasia (speech deficit)	Light headedness
Hemianopia (blindness in one half of the visual field in one or both eyes)	Confusion – having excluded dysphasia
Transient monocular blindness (blindness in one eye)	Bilateral visual disturbances
	Incontinence
	Hypotension
	Amnesia
	Hypoglycaemia
	Focal epileptic seizures
	Anxiety or hyperventilation
	Isolated vertigo, nausea and ataxia
	Migraine aura without headache

The Early Use of Existing Preventive Strategies for Stroke (EXPRESS) trial of immediate, multiple pharmacotherapy after TIA demonstrated an 80% reduction in early recurrent stroke and improved patient outcomes, compared to less aggressive treatment.[2]

The first dose of aspirin should be between 150 and 300 mg (depending on whether the patient is already taking aspirin). This should then be reduced to 100 mg per day, prior to commencing long-term antithrombotic treatment.[5]

Aspirin is the only antiplatelet medicine with strong evidence for its effectiveness in the acute treatment of TIA. Two studies have shown that combination treatment of clopidogrel and aspirin, or dipyridamole and aspirin may also be effective in acute treatment following a TIA. However, more complete studies are required before medicines other than aspirin can be recommended.[5–7]

Antihypertensive treatment should be given unless the patient is hypotensive. An ACE inhibitor such as cilazapril (0.5 – 2.5 mg) is an appropriate choice. This treatment can be refined in response to blood pressure over the following weeks.

Unless the patient is already taking a statin (in which case their usual dose would be given), atorvastatin 80 mg can be given initially. Follow up testing of lipid levels may prompt a change in dose or statin.

A definitive plan for long-term secondary prevention can be made following a comprehensive evaluation of the patient.

Best Practice tip: Most practices will have aspirin available to give immediately. A prescription for an antihypertensive and a statin can be written and filled urgently at the closest pharmacy. General practitioners, especially rural or duty doctors, may consider carrying a TIA kit including aspirin, statin and an ACE inhibitor.

Haemorrhage risk

People using anticoagulant treatment, or with a documented history of intracranial haemorrhage or thunderclap occipital headache should not be given aspirin, and should be referred to hospital as soon as possible. Individual decisions on treatment will then be made once brain imaging procedures have been completed. In situations such as these, primary care has an important role to play in the recording and clarification of medical histories prior to admission.

Step 2: Assess stroke risk

Following TIA the risk of stroke is dangerously elevated. Assessment tools exist to help stratify this risk.

Use your ABCD^2 risk tool

All patients presenting to primary care with suspected TIA should have an assessment of stroke risk using the ABCD^2 tool (Table 2).[1]

Table 2: ABCD^2 tool for stroke prediction following TIA[8]

	Risk factor	Points
A	Age: ≥ 60 years	1
B	Blood pressure: ≥ 140/90mm Hg	1
C	Clinical features:	
	unilateral weakness or	2
	speech impairment without weakness	1
D	Duration of symptoms:	
	≥ 60 minutes or	2
	10–59 minutes	1
D	Diabetes: Medication	1

The ABCD^2 tool is an aid only and it should not replace clinical decision making. Other factors which may place a patient in the high-risk category, but are not included in the ABCD^2 tool, are listed as follows.

High risk of stroke is indicated by:[5]

All people with an ABCD^2 score of **≥ 4**, or any of the following regardless of ABCD^2 score:

- Active TIA at presentation
- Crescendo TIAs
- Suspected TIA with atrial fibrillation
- Suspected TIA while taking anticoagulation treatment

Low risk of stroke is indicted by:[5]

All people with an ABCD^2 score of **≤ 3** or:

- People who present more than seven days after a suspected TIA

Step 3: Referral for assessment in secondary care

Referral for assessment is usually required in order to eliminate possible TIA mimics (e.g. subdural haematoma or brain tumour), to gain timely access to investigations and to assist in the development of a long-term treatment plan for secondary stroke prevention. The urgency of referral to secondary care is determined by the estimated risk of subsequent stroke occurring.[1] Patients with a TIA, who are already taking anticoagulants, should be referred to secondary care for immediate brain imaging. Some DHBs have protocols that allow for direct access of primary care to specialised investigations such as CT and carotid ultrasound for patients with high diagnostic certainty.

High risk

Patients judged to be at high risk for stroke require immediate referral for assessment including brain and possibly carotid imaging within 24 hours.[5] Referral processes from primary care are determined by the availability of specialist stroke services, which varies between regions.

 Contact your local DHB to find out how urgent TIA referrals are made in your area.

Low risk

Patients classified as low risk for stroke require brain and possibly carotid imaging within seven days. The need for referral is considered to be urgent, although, the risk of a stroke occurring within the next 48 hours is less than for people in the high-risk category.[1]

Secondary prevention and follow-up

All patients with a confirmed TIA require primary care follow-up (often in conjunction with secondary care) to establish an individual treatment plan for long-term stroke risk reduction. Results from secondary care assessment should be incorporated into this plan once they are known.

Routine investigations for patients without established risk factors would generally include; CBC, sodium and potassium, creatinine, eGFR, fasting lipids, CRP (to rule out vascular inflammation), glucose, ECG and INR if on warfarin.[1]

Modifiable risk factors

People who have had a TIA require individual strategies to modify identified risk factors. Where appropriate, interventions may include:[1]

- Smoking cessation advice and treatment
- A diet low in fat (especially saturated fat) and sodium, and high in fruit and vegetables
- A weight reduction programme
- Increasing the amount of regular exercise and activity
- Avoidance of excessive alcohol

Involving whānau in lifestyle changes can improve the success of any interventions. Māori or Pacific health providers can also provide support for achieving treatment goals.

Pharmacotherapy for secondary prevention

Long-term preventative treatment includes:[1]

- Antiplatelet treatment
- Anticoagulation (for people with atrial fibrillation)
- Blood pressure lowering treatment
- Cholesterol lowering treatment
- Nicotine replacement treatment or other smoking cessation aids

Antiplatelet treatment: Following a TIA, and provided the patient does not have atrial fibrillation (AF), commence antiplatelet treatment (if not taking an anticoagulant). Aspirin was previously considered the gold standard for secondary prevention of stroke, however, current recommendations, based on expert consensus are now:

1. Clopidogrel as first-line treatment – 300 mg loading dose, followed by 75 mg, per day
2. Aspirin (100 mg, per day) in combination with modified release dipyridamole (150 mg, twice daily) provides similar benefits to clopidogrel but has a higher incidence of adverse effects, therefore can be considered second-line treatment if intolerant to clopidogrel.[10]
3. Aspirin (100 mg, per day) alone is effective in the secondary prevention of stroke, however, it is marginally less effective than first or second-line treatments and is generally reserved for patients who are not able to tolerate clopidogrel or dipyridamole.[5]

Clopidogrel and aspirin in combination is not recommended for long-term secondary prevention after TIA or stroke, as any benefit in reduction of ischaemic events is outweighed by an increase in the risk of adverse effects, including bleeding.[5]

Anticoagulation treatment: For patients with a recent TIA and AF (i.e. high risk), anticoagulation treatment (warfarin or dabigatran) is substantially more effective than antiplatelet treatment and any risks are usually far

Carotid versus vertebrobasilar TIA

Carotid imaging is used in secondary care to diagnose carotid stenosis in patients with symptoms of carotid TIA (Table 3). Patients with severe stenosis of the carotid artery (if surgically fit and with a life-expectancy of at least two years) require urgent endarterectomy. In these cases the benefits outweigh the immediate risks of surgery.

Table 3: Symptoms of carotid and vertebrobasilar TIA[9]

Carotid TIA	Vertebrobasilar TIA
▪ Unilateral sensory and/or motor symptoms affecting the limbs and face ▪ Monocular transient blindness ▪ Dysphasia	▪ Bilateral sensory and/or motor symptoms affecting the limbs and face ▪ Cortical blindness ▪ Double vision ▪ Isolated hemianopia or quadrantanopia

outweighed by the benefits. Anticoagulation treatment should begin for all patients with TIA and AF as soon as brain imaging has excluded haemorrhage or another cause for the symptoms.[5] Aspirin should only be used in the acute period following the TIA before the establishment of effective anticoagulation. Anticoagulation treatment should not be given to patients with non-cardioembolic stroke (e.g. carotid stenosis) or TIA without AF.[4]

For further information see: "Consensus statement" (Page 10)

Blood pressure lowering treatment: Increased blood pressure is the major risk factor for all strokes. Lowering blood pressure decreases the likelihood of stroke following TIA. Following TIA all patients, unless hypotensive, and including those with AF, should receive blood pressure lowering treatment with a target of < 130/80 mm Hg. Currently, the strongest evidence of benefit is for the use of an ACE inhibitor, either alone, or in combination with a diuretic.[5]

Cholesterol lowering treatment: Statin treatment has been shown to marginally reduce the incidence of all stroke and to clearly reduce the incidence of ischaemic stroke in patients with a prior TIA.[5] Statin treatment should be considered for all patients following TIA, including those with AF. Randomised controlled trial evidence supports the use of atorvastatin 80 mg daily or simvastatin 40 mg daily.[11, 12] Atorvastatin 80 mg has been shown to reduce the risk of secondary stroke, as well as other cardiovascular events, compared with less intensive statin treatments. This option is recommended for patients with a fasting LDL >2.6 who are able to tolerate a high statin dose. Lower doses of artovastatin or simvastatin are appropriate for patients who have co-morbidities or are likely to experience adverse effects on high-dose statins. A life expectancy of at least two years is required for patients to gain significant stroke prevention benefit from statin treatment. Statins should not be used routinely for patients with intracerebral haemorrhage.[5]

Diabetes management

Glucose intolerance and diabetes are independent risk factors for stroke. Hyperglycaemia often occurs in the days immediately following TIA, therefore, once a patient has stabilised, an assessment of glucose tolerance should be made.[5]

Driving following TIA

People who have had a TIA should be restricted from driving for a period of:

- One month following a single TIA or;
- Three months following multiple TIAs that have been adequately investigated

Following a TIA, it is a requirement that vocational drivers have the cause of the event established and satisfactory treatment initiated. Vocational driving should be avoided for a period of at least six months. People who experience multiple TIAs should not return to vocational driving (although some exceptions may be granted).[13]

For further information on medicines used in TIA and stroke see: “Consensus statement” (Page 10)

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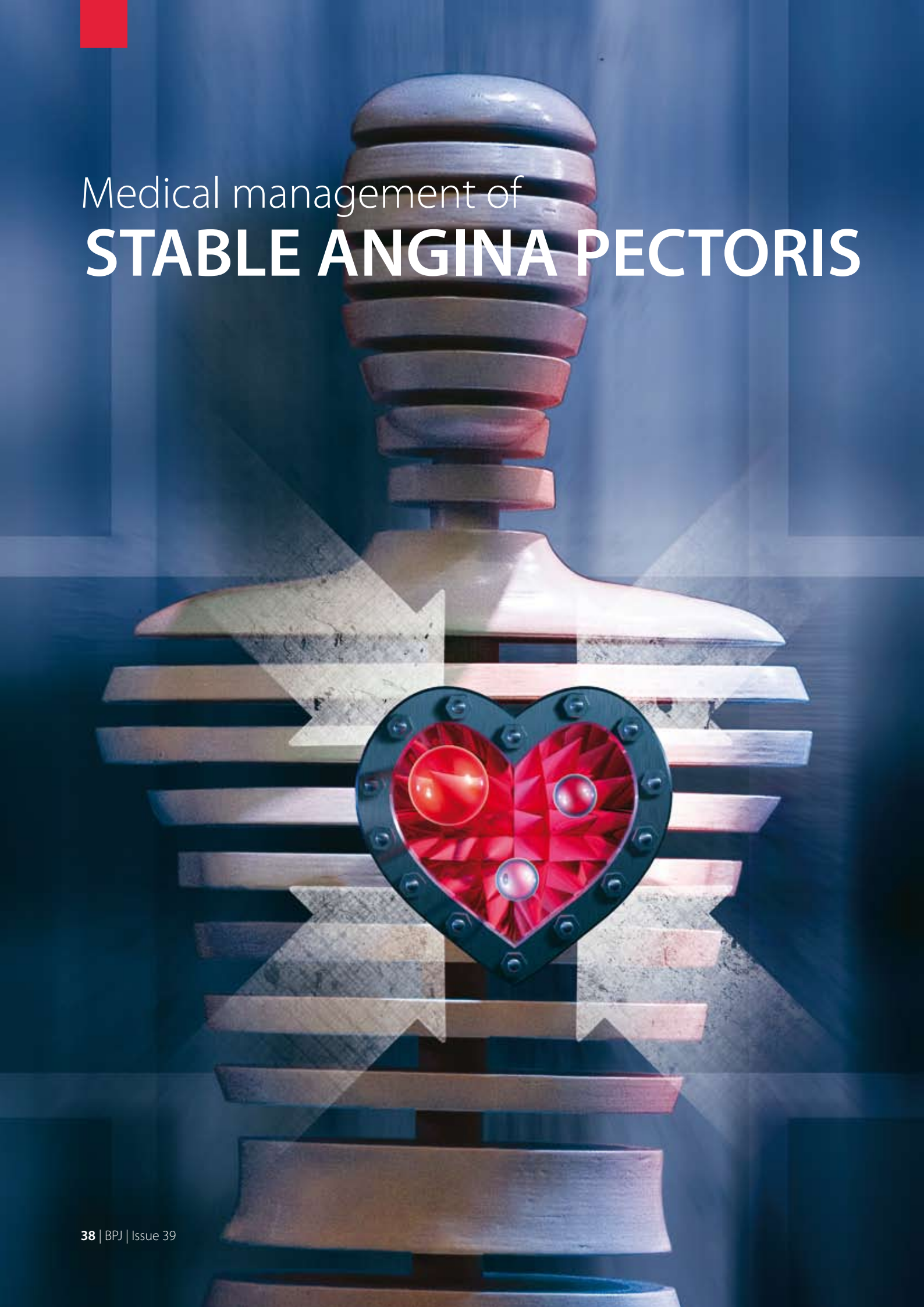
Medical management of

STABLE ANGINA PECTORIS



Defining angina

Angina is chest pain due to transient myocardial ischaemia, which usually occurs with physical activity or emotional stress, and is relieved by rest or sublingual nitroglycerin.[1,2] Angina is common, affecting 3.8% of people in New Zealand.[3] About half of patients with ischaemic heart disease initially present with symptoms consistent with a pattern of stable angina.[4]

Angina symptoms occur when there is insufficient blood supply to the heart at times of increased oxygen demand, e.g. exercise. This is most often due to coronary artery disease where atherosclerotic plaques in the coronary arteries cause narrowing of the lumen, reducing blood flow to the myocardium.[1]

Diagnosis of stable angina

Angina should be suspected in people presenting with tight, dull or heavy chest discomfort which is retrosternal or left-sided and may be radiating to the left arm, neck, jaw or back. The chest discomfort may also be associated with exertion or emotional stress and relieved within several minutes by rest. Women and older people are more likely to present with atypical symptoms of angina which include; breathlessness, nausea or belching.[1,2] Angina pain is not usually sharp or stabbing or influenced by respiration. Antacids and simple analgesia do not usually relieve the pain (also see "Other possible causes of chest pain", over page).[1,2]

A comprehensive history is required when angina is suspected as findings on physical examination and ECG are invariably normal even in patients presenting with acute coronary syndromes.

Key concepts

- All patients with suspected angina should be referred appropriately for diagnostic assessment including stress testing or similar further risk stratification, unless significant co-morbidities would preclude this.
- Results of this assessment will guide management, which may include revascularisation and pharmacological treatment, or pharmacological treatment alone
- While awaiting assessment, patients with suspected stable angina should be prescribed a sublingual nitrate and provided with an action plan for acute episodes of angina.
- Minimising the risk of future cardiovascular events is one of the most important aspects of the treatment of stable angina. This includes lifestyle modification and good control of other cardiovascular risk factors.
- An antiplatelet medicine, usually aspirin and a statin are appropriate for all patients with stable angina to prevent adverse cardiovascular events
- ACE inhibitors are appropriate for patients with co-existing conditions that would benefit from their use
- Beta-blockers are an appropriate first-line medical treatment to relieve the symptoms of angina. Calcium channel blockers or long-acting nitrates may be appropriate for those who do not tolerate or who have contraindications to beta-blockers.

All patients with suspected angina should be considered for referral for diagnostic assessment including stress testing or similar further risk stratification, unless significant co-morbidities preclude this.

Patients with pain at rest or on minimal exertion, or angina which seems to be progressing rapidly despite treatment, should be considered for referral to hospital as they may have unstable angina.[1]

Management of stable angina

The medical management of angina has two purposes; to prevent future myocardial infarction and death with vasculoprotective medicines and to reduce symptoms of angina with anti-ischaemic medicines. Further risk stratification is required with exercise tolerance testing or similar to identify patients who require angiography and possible revascularisation. Revascularisation is usually undertaken for symptomatic management of angina but also for prognostic benefit in a small subset of patients (e.g. those with left main coronary artery disease) identified at angiography (see Page 45 for further discussion of revascularisation).

Sublingual glyceryl trinitrate relieves acute anginal symptoms

Patients with newly diagnosed angina, or those with suspected angina waiting for further assessment, should be given a sublingual nitrate (either a spray or tablet) to use at the onset of angina. An angina action plan should be discussed with patients so they are aware of the appropriate actions to take if they experience chest pain.

Sublingual nitrates may also be used before activities that are known to bring on episodes of angina. Check first if a patient uses a phosphodiesterase (PDE5) inhibitor, e.g. sildenafil, as the concomitant use of this type of medicine with any form of nitrate is contraindicated.[5] If this combination cannot be avoided, most recommendations suggest withholding nitrate treatment for 24 hours after use of sildenafil and vardenafil and 48 hours after use of tadalafil.[6]

An example of an angina action plan can be found on the National Heart Foundation website (**www.heartfoundation.org.nz**). The plan contains the following instructions:

Other possible causes of chest pain[1]

Cardiac causes:	Non-cardiac causes:
Myocardial infarction – constant pain usually lasting more than 20 minutes. Nausea and vomiting may also be present	Oesophageal disorders, e.g. gastro-oesophageal reflux
Prinzmetal's angina – due to vasospasm. Pain is not precipitated by cardiac work and is associated with an unusual ECG	Musculoskeletal pain, e.g. costochondritis (swelling of a rib)
Unstable angina – increasingly frequent angina, angina at rest or prolonged episodes of severe angina	Psychological causes, e.g. panic attack, anxiety
Pericardial pain, e.g. pericarditis – pain influenced by breathing and change in posture	Pleural pain, e.g. infection, pulmonary embolism, tumour

- When an episode occurs, stop what you are doing and rest
- Use your glyceryl trinitrate spray (one puff) or one tablet (or as directed)
- Take a second dose five minutes after the first dose if the pain has not eased
- Call an ambulance if the pain has still not eased five minutes after the second dose or earlier if the pain is intensifying

Preventing future myocardial infarction and death

Reducing the risk of future cardiovascular events is the most important aspect of the treatment of stable angina. This is achieved by lifestyle modification, e.g. eating a healthy diet, smoking cessation and exercising regularly and good control of other cardiovascular risk factors, e.g. diabetes and hypertension – target blood pressure: <130/80 and target HbA_{1c}: 53 mmol/mol (see Page 54 for information on change of units).[7]

All patients with stable angina should be treated with aspirin and a statin, unless contraindicated.[1] ACE inhibitors are recommended for patients with co-existing conditions that would benefit from this treatment (Table 2).

All patients with stable angina should be taking aspirin or another antiplatelet medicine

All patients with stable angina should be taking aspirin 100 mg unless contraindicated, not tolerated or there is an indication for anticoagulation (e.g. patient also has atrial fibrillation). Evidence has shown that in people with cardiovascular disease, including those with stable angina, antiplatelet treatment leads to a significant reduction in serious vascular events, non-fatal myocardial infarction, non-fatal stroke and vascular mortality.[8]

Clopidogrel is an option for people who are intolerant of, or have contraindications to, aspirin. It is also used for 12 months in combination with aspirin for patients who have had percutaneous coronary intervention (PCI).[2]

See consensus statement on antithrombotic medicines (Page 10)

Table 2: Medicines to improve prognosis for stable angina (adapted from Abrams, 2005)[2]

Medicine	Indications	Comment
Aspirin	All patients, except those with aspirin allergy or intolerance. Clopidogrel may be considered as an alternative.	Dose: 100 mg daily
Statin	All patients, aiming to achieve LDL cholesterol of < 2 mmol/L and total cholesterol < 4 mmol/L	Dose: 40 mg simvastatin initially or switch to atorvastatin 40mg if targets not achieved.
ACE inhibitor	Patients with co-existing indications for ACE inhibitors; hypertension, diabetes, heart failure, asymptomatic left ventricular dysfunction or previous myocardial infarction	Uncertain usefulness in patients without co-existing indications for ACE inhibitors

All patients with stable angina should be taking a statin

All patients with stable angina should be taking a statin, unless contraindicated or not tolerated. Simvastatin 40 mg is recommended initially. If the treatment target is not achieved with this dose, switch to atorvastatin in preference to uptitrating simvastatin. High dose (80 mg) simvastatin has been associated with an increased incidence of rhabodomyolysis (see "Precautions with high-dose simvastatin" below).[9, 10] In clinical trials, statins reduced all-cause and coronary mortality, myocardial infarction, the need for coronary revascularisation and fatal or non-fatal stroke in patients with stable angina.[8]

ACE inhibitors are recommended for patients with coexisting indications for their use

There is conflicting evidence as to whether ACE inhibitors are of benefit in the treatment of stable angina. ACE inhibitors may not improve symptoms or long-term prognosis in people with stable angina, therefore they are only recommended for patients with co-existing conditions that would benefit from their use, e.g. hypertension, diabetes, heart failure, asymptomatic left ventricular dysfunction or previous myocardial infarction.[2]

Management of symptoms – beta-blockers, calcium channel blockers and nitrates

Beta blockers, calcium channel blockers and nitrates are used to manage the symptoms of angina (Table 3). While these medicines have been shown to reduce anginal symptoms, i.e. prolong the duration of exercise before the onset of angina and reduce the frequency of angina, none have been shown to prevent myocardial infarction or death in people being treated for chronic stable angina.[2, 12]

These medicines prevent attacks of angina by doing one or both of the following:[12]

- Decreasing myocardial oxygen consumption (by lowering heart rate, blood pressure, myocardial loading, or myocardial contractility)
- Increasing myocardial oxygen supply (by increasing coronary blood flow)

A beta-blocker is a suitable first-line regular treatment to reduce the symptoms of stable angina

Beta-blockers lessen anginal symptoms by reducing heart rate and myocardial contractility and decreasing

Precautions with high-dose simvastatin

Recently the United States Food and Drug Administration (FDA) recommended restricting the use of high-dose simvastatin (80 mg) because of the increased risk of myopathy. They advised that simvastatin 80 mg should only be prescribed for those already taking this dose for longer than 12 months with no signs of myopathy and that simvastatin 80 mg should not be started in newly diagnosed patients or in those already taking lower doses of simvastatin. Medsafe advises that high dose simvastatin should only be prescribed for patients who have not reached their target cholesterol level with a lower dose or with alternative medicines.[11]

See: "High dose simvastatin increases myopathy risk". Prescriber Update, Sept 2011. Available from: www.medsafe.govt.nz/profs/PUarticles.asp

See: "Simvastatin: risk associated with higher doses" BPJ 38 (Sept, 2011)

Table 3: Anti-anginal medicines (adapted from Abrams, 2005)[2]

Medicine	Dose	Adverse effects	Cautions
Beta-blockers			
Metoprolol tartrate	50–100 mg twice daily	Fatigue, shortness of breath, wheezing, weakness, dizziness, cold extremities	Caution with use in people with chronic obstructive pulmonary disease, diabetes, depression. Avoid in those with heart block
Metoprolol succinate	95–190 mg once daily		
Atenolol	25–100 mg once daily		
Calcium channel blockers			
Amlodipine	5–10 mg once daily	Headache, flushing, dizziness, oedema Verapamil may cause constipation	Verapamil and diltiazem should be used with caution in patients with low ejection fraction (< 30%) or with sinus or atrioventricular nodal dysfunction
Felodipine, sustained release	5–10 mg once daily		
Nifedipine, sustained release	30–90 mg once daily		
Verapamil, sustained release	120–240 mg once or twice daily		
Diltiazem, sustained release	120–360 mg once daily		
Nitrates			
Isosorbide mononitrate, long-acting formulations	40–120 mg once daily	Headache, dizziness, nausea, palpitations Tolerance is a major limiting factor	Contraindicated with phosphodiesterase (PDE5) inhibitors e.g. sildenafil
Nitroglycerin, patch	Initially one (5 mg/24 hour) patch daily. Maintenance: usually one (10 mg/24 hour) patch daily; may increase to two (10 mg/24 hour) patches daily. Used for no more than 12–14 hours per 24 hours		

Notes:

There is some evidence that the sudden withdrawal of a beta-blocker or a calcium channel blocker may cause an exacerbation of angina and therefore a gradual reduction of dose is preferable when either medicine needs to be stopped.[17]

Long-acting isosorbide mononitrate can be taken either in the morning or the evening, depending of the time of day that angina attacks usually occur.[18] Twice daily dosing of long-acting isosorbide mononitrate is not appropriate.[19]

blood pressure. This results in decreased myocardial oxygen demand.[12] They can be considered as the first-line treatment for reducing the symptoms of stable angina.

Beta-blockers have not specifically been shown to reduce the rate of coronary events or mortality in patients with stable angina, but there is evidence that they improve prognosis in those who have previously had a myocardial infarction or have heart failure.[2]

All beta-blockers appear to be equally effective in treating stable angina, however, cardioselective beta-blockers, such as metoprolol and atenolol, are preferred because they have advantages in terms of their adverse effect profile and precautions when compared with non-selective beta-blockers.[12, 13]

Calcium channel blockers are appropriate if beta-blockers are contraindicated or not tolerated

Calcium channel blockers can be considered second-line for treating the symptoms of angina if a beta-blocker is contraindicated or not tolerated. Calcium channel blockers have been shown to be equally effective as beta-blockers in the management of stable angina, i.e. studies have shown no difference in nitroglycerin use or exercise time and no evidence of a difference in total or cardiovascular mortality, or in risk of myocardial infarction or stroke.[13] The recently updated National Institute for Health and Clinical Excellence (NICE) guideline for the management of stable angina considers either a beta-blocker or a calcium channel blocker as appropriate first-line treatment.[14]

Calcium channel blockers minimise symptoms of angina by dilating coronary and other arteries and increasing coronary blood flow. Non-dihydropyridine calcium channel blockers (verapamil and diltiazem) also reduce myocardial contractility and heart rate and decrease myocardial oxygen demand.[12]

All calcium channel blockers are effective in the treatment of stable angina. Long-acting calcium channel blockers, e.g. amlodipine, or sustained released formulations of short-acting calcium channel blockers, e.g. felodipine, nifedipine, verapamil and diltiazem, are preferred.[12] Short-acting calcium channel blockers, particularly nifedipine, are not recommended because they cause reflex tachycardia which may exacerbate ischaemia and have been associated with an increased risk of cardiovascular events.[15]

A rate limiting calcium channel blocker such as verapamil or diltiazem is a suitable alternative for patients who have had a previous MI who do not tolerate beta-blockers or have a contraindication to their use.[12] However, verapamil is not suitable in patients with heart failure.

If combining beta-blockers and calcium channel blockers, it is appropriate to use a non-rate limiting (dihydropyridine) calcium channel blocker such as felodipine or amlodipine. Diltiazem may be cautiously used in combination with a beta-blocker when heart rate remains above 60 beats per minute despite maximum tolerated doses of beta-blocker. Verapamil is not suitable in combination with beta-blockers because severe bradycardia and heart failure can occur.[1]

A long-acting nitrate can be used if a beta-blocker or calcium channel blocker are not tolerated or contraindicated

Long acting nitrates, e.g. isosorbide mononitrate, are a suitable choice as monotherapy for people who are intolerant of beta-blockers or calcium channel blockers or if those medicines are contraindicated. They may also be used in combination with a beta-blocker or calcium channel blocker. Nitrates produce venous and arterial dilatation, reducing ventricular pre-load and after-load which lowers myocardial oxygen demand and improves subendocardial blood flow.[8]

Nitrate tolerance is a major problem with long-term use, and needs to be avoided because it diminishes the response to short acting nitrates.[16] A "nitrate-free" interval of 12–14 hours each day is required to avoid nitrate tolerance. This is achieved with once daily dosing of modified release tablets, e.g. Corangin, Duride.

Other medicines used to treat angina

Nicorandil is an option if other treatments have failed, are not tolerated or are contraindicated, however, it is not funded in New Zealand. Nicorandil is a potassium channel activator with nitrate like effects. Tolerance to its effects may occur with chronic dosing, however, cross tolerance with nitrates does not appear to be a problem.[12] Nicorandil can be used as monotherapy or in combination with a beta-blocker or calcium channel blocker if symptoms are not controlled.[14]

Perhexiline may be used when angina is unable to be managed with pharmacological treatment or surgery, but it can cause serious adverse effects such as peripheral neuropathy.[20] It is only available in New Zealand under Special Authority.

Revascularisation to treat symptoms of angina

Revascularisation involves either percutaneous coronary intervention (PCI) or coronary-artery bypass surgery (CABG). Revascularisation is most frequently performed for symptom relief but a small percentage of patients also have a prognostic benefit (usually those who are at high risk). Stress testing or similar further risk stratification is required in all patients with stable angina unless co-morbidities would prohibit revascularisation.

Patients who may benefit from revascularisation include:

- Those at high-risk, e.g. patients with symptomatic multi-vessel disease, proximal left anterior descending or left main artery disease, left ventricular systolic dysfunction, diabetes or a large ischaemic burden (referring to all angina episodes, including silent angina).[2]
- Those who have failed to respond to pharmacological treatment, i.e. patient is still experiencing symptoms while on two anti-anginal drugs.

Secondary prevention measures are still important because PCI does not change the natural history of coronary artery disease where non-obstructive plaques may suddenly progress to high grade stenosis or even total vessel occlusion.[21] Repeat revascularisation may be necessary after PCI or CABG, but is more common after PCI.[21]

Optimal medical treatment or revascularisation?

Clinical trial evidence suggests that revascularisation initially provides better symptom control than pharmacological treatment,[21] but in the long-term, it appears that there is little difference between the two approaches to angina symptom control.

Two large, recent clinical trials have compared the effectiveness of pharmacological treatment to revascularisation in the management of chronic stable angina. Earlier trials may no longer be relevant to modern clinical practice due to advances in PCI techniques (e.g. the use of stents) and improvements in the optimal use of medicines for both symptom control and risk factor reduction.

The Clinical Outcomes Utilising Revascularisation and Aggressive Drug Evaluation (COURAGE) trial was a randomised controlled trial (RCT) which randomly assigned 2287 patients with angina and significant coronary artery disease to either optimal medical treatment alone or PCI and optimal medical treatment.[22] High-risk patients who were likely to have a survival benefit from revascularisation (usually CABG) were excluded from the trial. Optimal medical treatment included medicines to prevent angina; beta blockers, calcium channel blockers, nitrates individually or in combination and an ACE inhibitor or angiotensin receptor blocker (ARB), as well as an antiplatelet medicine and a statin. The results showed no significant difference in the risk of death, myocardial infarction, or rates of hospitalisation between the two groups. Significantly more patients in the PCI group were free of angina at one and three year follow-up, however, by five years there was no significant difference between the groups.[22]

A follow-up study using an angina specific health questionnaire compared the quality of life for patients in each group and found marked improvement in the health status of patients in both groups.[23] Although patients in the PCI group initially reported greater benefit, by three years there was no significant difference in health status between the two groups. The most benefit with PCI, as indicated by quality of life measures, was in a subgroup of patients who, at baseline, had the most severe angina.[23]

The Bypass Angioplasty Revascularisation Investigation 2 Diabetes (BARI) trial, also a RCT involving 2368 patients randomised to PCI and intensive medical treatment or intensive medical treatment alone, reported similar results to those reported for the COURAGE trial, with no significant difference in the primary outcome of death from any cause or in the rate of major cardiovascular events.[24]

ACKNOWLEDGEMENT Thank you to **Dr Gerry Devlin**, Cardiologist and Clinical Unit Leader Cardiology, Cardiac Surgery and Thoracovascular Surgery, Waikato DHB for expert guidance in developing this article.

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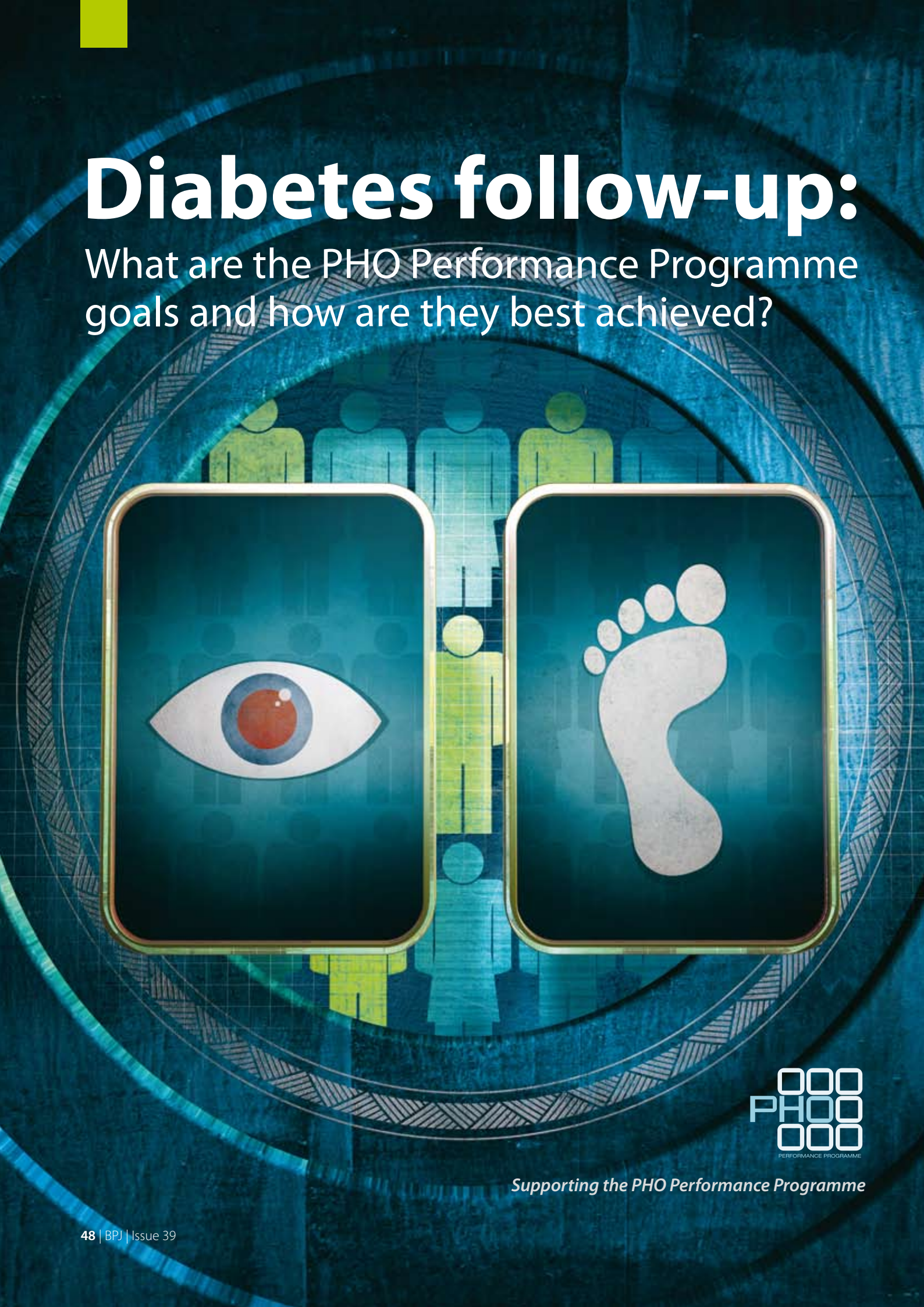
Diabetes follow-up:

What are the PHO Performance Programme goals and how are they best achieved?



PHO PERFORMANCE PROGRAMME

Supporting the PHO Performance Programme

What are the goals?

The PHO Performance Programme was launched in January 2006 in order to:

- Encourage and reward improved performance by PHOs in line with evidence based guidelines
- Measure and reward progress in reducing health inequalities amongst high need populations

Performance based payments are made to PHOs to improve key indicators which are reviewed annually. Individual PHO indicators are adjusted to take into account factors such as age and ethnicity which may vary from region to region. Those indicators which are currently funded are shown in Table 1.[1]

See "BPJ 36 (Jun, 2011), BPJ 37 (Aug, 2011) and BPJ 38 (Sep, 2011) for previous articles in this series.

Diabetes follow-up

The purpose of the diabetes follow-up indicator is to determine what proportion of the population estimated to have diabetes has had an annual diabetes review.[1]

Annual diabetes review

An annual review for people with diabetes includes assessment of:[2]

- HbA_{1c}
- Blood pressure
- Fasting lipids
- Microalbuminuria
- Feet
- Retinal health
- Follow-up care plan

An annual review can be scheduled for a specific consultation, or data can be collected over a series of visits.

N.B. It was recently announced that the Ministry of Health's "Get Checked" programme, which encouraged free annual diabetes reviews, is due to cease. The Ministry of Health is expected to release further details shortly, including possible replacement services.

Table 1: Funded PHO Performance Indicators for the period commencing 1 January, 2011

Chronic conditions	Cervical cancer screening Breast cancer screening Ischaemic cardiovascular disease detection Cardiovascular disease risk assessment Diabetes detection **Diabetes follow-up after detection** Smoking status
Infectious disease	Influenza vaccine in people aged over 65 years Age appropriate vaccinations for children aged two years
Financial	GP referred laboratory expenditure GP referred pharmaceutical expenditure

Targets and funding

The PHO performance indicator and target for diabetes follow-up is: For 80% of enrolled patients aged between 15 and 79 years expected to have diabetes, to have had an annual diabetes review.*[1]

Diabetes follow-up accounts for 9% of a PHO's performance payment, with 6% allocated for achieving the target in the total population and 3% for achieving the target in the high needs population (Māori and Pacific peoples and people living in New Zealand Deprivation Decile 9 or 10 socioeconomic areas).[1]

How is the indicator calculated?

The number of enrolled people in the PHO with a record of a diabetes review during the reporting period (numerator), is divided by the number of enrolled people in the PHO who would be expected to have been diagnosed with diabetes (denominator). The estimated prevalence of diabetes within a PHO is taken from a national calculation of diabetes prevalence, which is then adjusted to take into account individual PHO differences in age, gender and ethnicity. The national diabetes prevalence data estimate is calculated from the number of people in New Zealand who have had diabetes related health service contact and the number of people in New Zealand either enrolled with a PHO, or who have had contact with the New Zealand health service from the 1st July 2009 to 30th June 2010.[1]

Conditions defined as diabetes

For the purposes of the indicator, diabetes is defined as:[1]

- Type 1 diabetes
- Type 2 diabetes
- Diabetes that may be either type 1 or 2, but is clinically indeterminate

N.B. Gestational diabetes is excluded

*Orinially printed as 'diabetes detection' in error.

How to achieve the target

Diabetes detection

Effective diabetes follow-up relies on sound diabetes detection programmes. Practice wide awareness of the risk factors, symptoms and different diabetes detection methods all assist in maximising diabetes detection.

For further information see: "Diabetes Detection", BPJ 37 (Aug, 2011).

Increasing uptake of the annual diabetes review

Strategies to increase the number of people with diabetes who receive annual follow-ups include:

Send out follow-up letters: An invitation letter including a laboratory form for $HBA_{1c,}$ fasting lipids and microalbuminuria tests is a good way to motivate patients and has the advantage of allowing patients to choose a time that suits them.

Create a PMS alert: Recall alerts can be created for patients overdue for an annual assessment.

For further information see: "Detecting diabetes", Best Tests (Sept, 2008).

Create a diabetes register: An electronic diabetes register allows analysis of a practice's population, which can highlight patients overdue for review and those not achieving treatment targets.

Elect a chronic conditions "champion": Allocate specific roles for members of the primary care team to oversee aspects of the diabetes programme and patient recall.

Promote patient awareness: High visibility posters, leaflets and advertising in the practice may encourage patients to attend annual assessments.

Text alert reminders: Text alerts are a simple, cheap and non-intrusive way to remind patients when their annual assessments are due.

Take any opportunity that arises: Discuss testing during any consultation, when time permits.

The benefits of follow-up

Regular diabetes follow-up allows for assessment of glycaemic control and earlier detection of, and intervention for, diabetes related complications. It also creates an opportunity to regularly review and assess individual treatment plans and enable specialist support if required. Additionally, the information gained from diabetes follow-up provides up to date data for diabetes registers, which in turn drives improvements in diabetes service delivery.

A focus on follow-up

The diabetic foot

Foot ulceration is a common complication of diabetes, which, if not detected early, can ultimately result in amputation. The peripheral neuropathy and peripheral arterial disease which cause this complication can be delayed through strategies targeting; glycaemic control, reduction of hypertension and blood lipid levels, smoking cessation and weight management. Other factors which increase the risk of a person with diabetes developing foot complications include:[3]

- Previous foot ulceration
- Co-existing abnormalities of the foot
- Plantar callus
- Smoking
- Age over 70 years
- Pacific or Māori ethnicity
- Long duration, or poor control of diabetes
- Retinopathy or other diabetic complications
- Renal impairment
- Wearing inappropriate footwear
- Inability to maintain foot hygiene and prevent trauma
- Living in a lower socioeconomic area

People with diabetes should have their feet checked at least once every year, or more regularly (every three to six months) if there is an increased risk of complications developing. Patients should also be encouraged to check their own feet, or to enlist the help of a family member. Treatments which reduce foot pressure, including callus debridement, shoe inserts and specialised footwear all reduce the risk of ulceration.[2]

There are two broad types of "diabetic foot":[4]

- **Neuropathic feet** which are generally warm, dry and numb with a detectable pulse. The most common complications are neuropathic joints and neuropathic ulcers which occur mainly on the soles. Minor lesions, such as blisters, can develop into chronic ulcers which progress due to a lack of sensitivity in the foot.
- **Neuro-ischaemic feet** are frequently cold with no detectable pulse. Complications may include those described above and intermittent limping, pain at rest and gangrene. Ulcers from pressure damage are generally found on the edges of the feet.

Foot checks should begin as soon as a person has a confirmed diagnosis of diabetes and should include a visual inspection for: redness, swelling, ulceration, deformity, tinea pedis, vulnerable pressure sites, poor self-care (lack of cleanliness and untrimmed nails) and skin abrasions. The foot should be checked to see if joint movement is fixed or flexible. Ask the patient if they have trouble walking or experience pain (burning or tingling) and what the normal temperature of the foot is. Peripheral neuropathy can be assessed with a monofilament (touch pressure-testing) and by testing vibration sensation with a biothesiometer or tuning fork. Peripheral circulation can be checked through palpation of pedal pulses. Evidence of neuropathy and an absence of pedal pulse elevate the risk of ulceration, while additional skin changes and deformity place a person at

high risk of ulceration. It is important to remind people with diabetes of the importance of appropriate footwear and foot hygiene at every oppurtunity.[4,5]

Diabetic foot ulcers should be cleaned, debrided (if appropriate) and covered with a dressing able to absorb any exudate without plugging the lesion. Pain management should be given where appropriate. The foot should be rested and therapeutic footwear worn while the lesion is healing. Regular assessments should be made until the ulcer heals, followed by checks every one to three months. Urgent referral (within 24 hours) should occur if:

- An ulcer shows no sign of healing or becomes necrotic
- Significant swelling or discolouration of any part of the foot is present
- There is suspicion of bone or joint complications

If the wound appears infected, oral antibiotics can be prescribed initially. Infected foot ulcers are often colonised by a variety of organisms, therefore a broad spectrum antibiotic such as amoxicillin clavulanate is appropriate.[6] Refer to a podiatrist or vascular specialist if complications develop, or if there are any concerns. Patients with extensive infection, or who are systemically unwell should be referred to hospital for IV antibiotic treatment. It is important to refer the patient for radiological assessment if osteomyelitis is suspected.

For further information see: "Screening and management of the 'diabetic foot'", BPJ 31 (Oct, 2010)

Diabetic retinopathy

Loss of vision due to diabetic retinopathy is a preventable complication that affects many adults with diabetes in New Zealand. Primary care plays an important role in ensuring that people with diabetes receive regular retinal screening and prompt treatment before visual deterioration begins. Estimates suggest that 30% of people with diabetes have some degree of retinopathy, with 10% having sight-threatening retinopathy.[7] The longer a person has diabetes, the greater the chance they will develop retinopathy.

Diabetic retinopathy is generally asymptomatic, until it reaches an advanced stage which is often beyond treatment. Early detection and prevention are the key responsibilities of primary care and are best achieved through:

- Ensuring retinal screening occurs at least every two years
- Improving glycaemic control and reducing high blood pressure and lipids

A referral for retinal screening should be made at the time a diagnosis of diabetes is confirmed. Screening should occur more frequently for people showing early signs of retinopathy. As diabetic retinopathy can progress rapidly during pregnancy, women with diabetes who are pregnant should be screened in the first trimester of their pregnancy. The goals of screening are to identify people with early microvascular disease to allow optimal management of risk factors, and to refer those with significant retinopathy to specialist care.

DHBs have individual arrangements with local retinal screening providers – contact your local DHB for details.

Managing the risk of retinopathy in people with diabetes can be achieved by:

- Maintaining good glycaemic control with an individualised HbA_{1c} target
- Reducing blood pressure to ≤ 130/80 mm Hg[3]
- Reducing blood lipid levels towards a total cholesterol target of < 4.0 mmol/L[8]
- Smoking cessation, exercise and a healthy diet

For further information see: "Screening for diabetic retinopathy in primary care", BPJ 30 Aug, 2010).

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Dual reporting of HbA_{1c} laboratory results has ended

As of 1 October 2011, laboratories are reporting HbA_{1c} results in millimoles per mole (mmol/mol) only. For the preceding two years, results have been reported in both percentages (%) and mmol/mol to allow time for both practitioners and patients to become familiar with the mmol/mol system.

The reason for the change in units is due to a decision made by the International Federation of Clinical Chemistry (IFCC), which will make it easier to compare HbA_{1c} results from different laboratories and trials throughout the world.[1]

New Zealand guidelines recommend that people with diabetes should aim for a target HbA_{1c} range of 50–55 mmol/mol – or as individually agreed.[2]

There may be concern that glycaemic control will deteriorate in some cases if patients or carers become confused due to the new reporting method. General practitioners are advised to explain to their patients that this is not a new method of testing, but an alternative way of reporting the same test results.

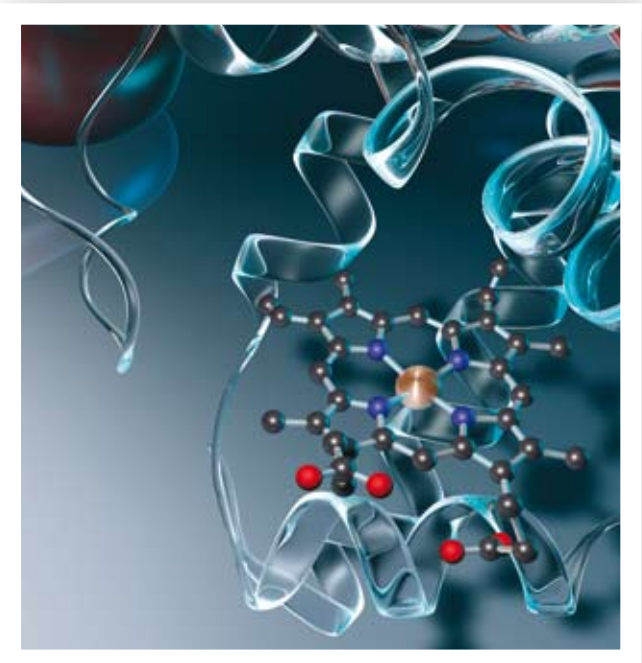

Table 1 shows the equivalency of HbA_{1c} mmol/mol and HbA_{1c} %.

Table 1: Equivalence of HbA_{1c} units[2]

HbA_{1c} mmol/mol (new units)	HbA_{1c} % (old units)
42	6.0
48	6.5
53	7.0
59	7.5
64	8.0
75	9.0
86	10.0
108	12.0

If an exact conversion from HbA_{1c} mmol/mol to % is required, the following formula can be used:[3]

$$HbA_{1c}\ (mmol/mol) = (HbA_{1c}\ (\%) - 2.15) \times 10.929$$

An electronic version of this tool is available on the bpac^{nz} website: **www.bpac.org.nz**

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New diabetes resources for primary care

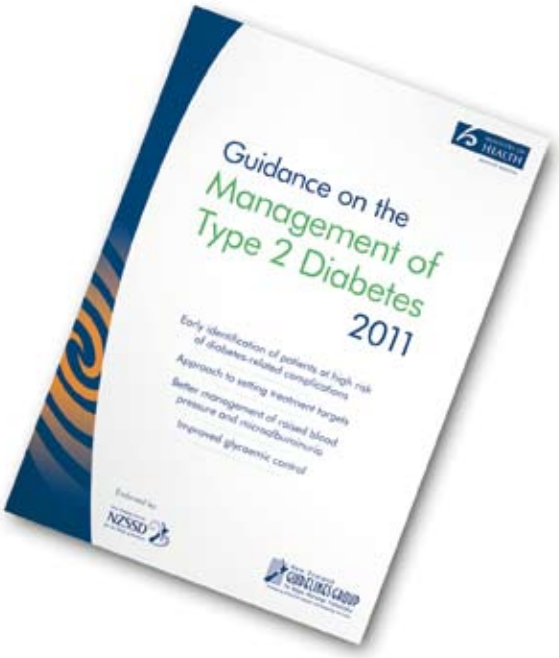
New resources for primary care on the management of type 2 diabetes have been recently released by the New Zealand Guidelines Group (NZGG).

The resources focus on three priority areas:

1. Early identification of patients at high risk of diabetes-related complications
2. Management of blood pressure and microalbuminuria
3. Management of glycaemic control, including initiation of insulin treatment

In addition to the guidance document, the suite of resources produced by NZGG includes a primary care practitioner quick reference card, a presenter slide set to support CME and CNE, and a RNZCGP-accredited online CME unit. The content of these resources was developed by an Advisory Group, drawing on evidence from the Scottish Intercollegiate Guidelines Network (SIGN) Guideline 116: Management of Diabetes (2010).

The guidance document and all resources are now available to download at: **www.nzgg.org.nz**



Warfarin or dabigatran for atrial fibrillation?

Dear Editor,

I have a patient currently taking warfarin for atrial fibrillation (AF) and aspirin for embolic stroke prevention (secondary to AF). She was discharged from hospital on both medications a few years ago. She has a normal heart and is keen to go onto dabigatran to avoid the hassle of getting regular INR tests done, because she is elderly, lives rurally and prefers to avoid driving where possible.

I have searched for information on what to do in this situation and have been unable to find specific recommendations. I know the aspirin raises the risk of a major bleed with both medications. Could the aspirin be stopped?

General Practitioner, Hawke's Bay

This question raises several issues and is likely to be a common scenario in managing patients in primary care who require antithrombotic treatment.

Firstly, it is unclear why the patient is taking both aspirin and warfarin as it appears that they are both being given for the same indication. It is also unclear if the patient has had a previous cardiovascular event, but we can presume that the medicines are being given for primary stroke prevention. We also presume that the AF is non-valvular and permanent.

- Anticoagulation with warfarin or dabigatran is indicated for the primary prevention of stroke in people with AF, who have a moderate to high risk of stroke
- Aspirin may be considered for people with AF who have a low risk of stroke or those who are unsuitable for anticoagulation, e.g. patients with severe liver disease, recent history of gastrointestinal bleeding
- Aspirin and warfarin or dabigatran in combination for the primary prevention of stroke is not recommended

The risk of stroke in people with AF can be calculated using assessment tools such as $CHADS_2$, CHA_2DS_2-VASc and HAS-BLED (see Page 14 for these tools). If the $CHADS_2$ score is ≥ 2, the patient should be anticoagulated. If the $CHADS_2$ score is less than 2, CHA_2DS_2-VASc can be used to further evaluate risk. Anticoagulation is recommended for people with a CHA_2DS_2-VASc score ≥ 1.

HAS-BLED can be used to calculate the risk of bleeding when considering anticoagulant use. A score of ≥ 3 indicates a patient who may be at high risk of bleeding complications. This is of particular significance in the present scenario as the patient lives in a rural area, therefore access to medical services is likely to be delayed if a bleeding event did occur.

Therefore the choices needed to be made for this patient are:

- What is her stroke risk?
- Should she be on aspirin or an anticoagulant? (or possibly even no treatment?)
- If an anticoagulant is the appropriate choice, should this be warfarin or dabigatran?

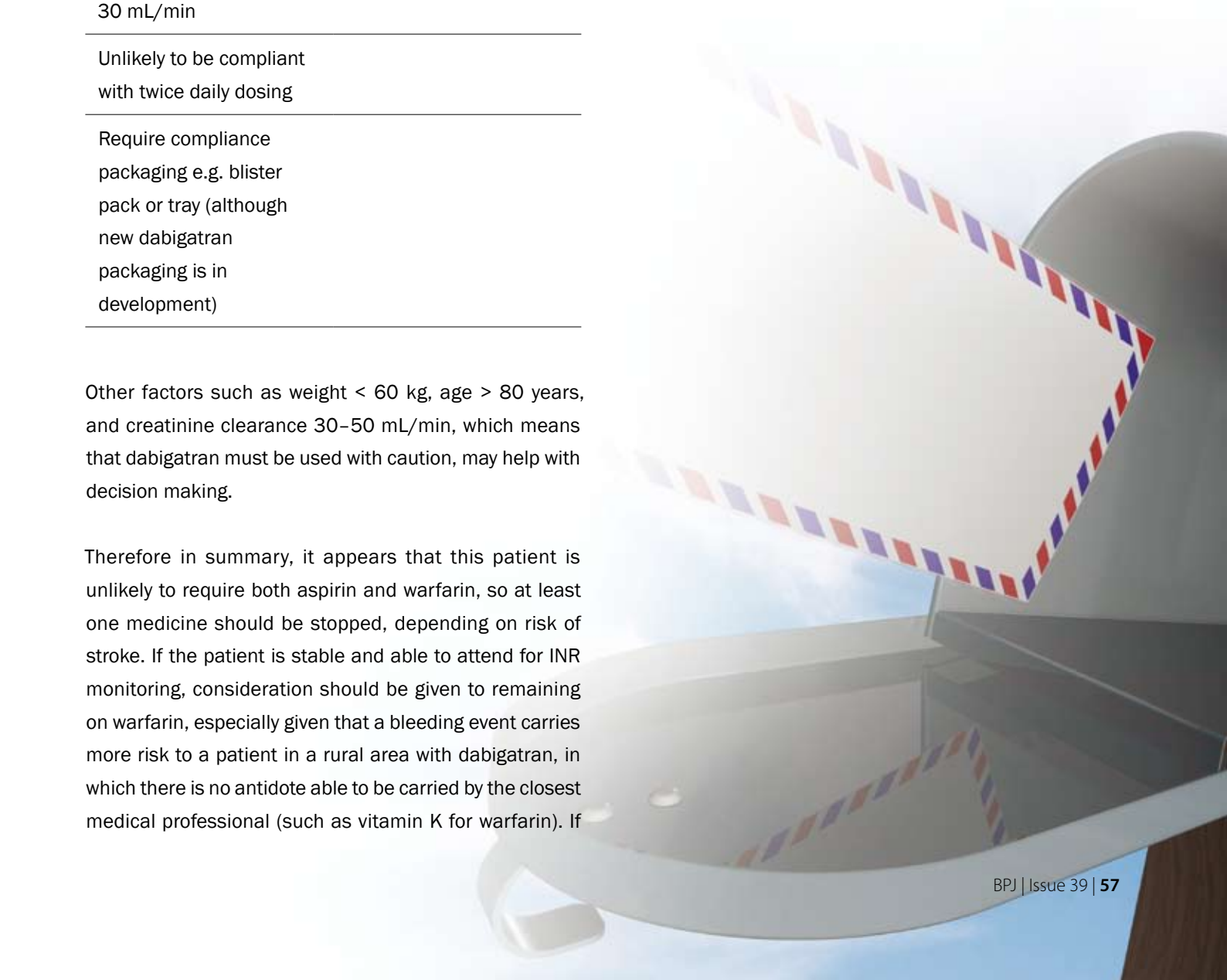
Factors to consider when choosing between warfarin and dabigatran for this patient (with non-valvular AF and already on warfarin) include:

Stay on warfarin	Change to dabigatran
Stable INR	Difficult to control INR
Comfortable with the need for monitoring	Monitoring poses difficulties
Taking medicines that may interact with dabigatran, e.g. verapamil or amiodarone for AF	Taking medicines which interact with warfarin
Creatinine clearance < 30 mL/min	
Unlikely to be compliant with twice daily dosing	
Require compliance packaging e.g. blister pack or tray (although new dabigatran packaging is in development)	

Other factors such as weight < 60 kg, age > 80 years, and creatinine clearance 30–50 mL/min, which means that dabigatran must be used with caution, may help with decision making.

Therefore in summary, it appears that this patient is unlikely to require both aspirin and warfarin, so at least one medicine should be stopped, depending on risk of stroke. If the patient is stable and able to attend for INR monitoring, consideration should be given to remaining on warfarin, especially given that a bleeding event carries more risk to a patient in a rural area with dabigatran, in which there is no antidote able to be carried by the closest medical professional (such as vitamin K for warfarin). If the decision is made to swap to dabigatran, ensure that INR is less than 2, check creatinine clearance and ensure that the correct dose is given for the patients age (i.e. < 80 years: 150 mg, twice daily, ≥ 80 years: 110 mg, twice daily).

We value your feedback. Write to us at: Correspondence, PO Box 6032, Dunedin or email: editor@bpac.org.nz



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