Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

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Horizon Scanning Technology Prioritising Summary

Targeted screening for abdominal aortic aneurysm

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PRIORITISING SUMMARY

REGISTER ID: **000377**

NAME OF TECHNOLOGY: **SCREENING FOR ABDOMINAL AORTIC ANEURYSM**

PURPOSE AND TARGET GROUP: **TO IDENTIFY MEN AT RISK OF ABDOMINAL AORTIC ANEURYSM**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐   Yet to emerge   ☐   Established

☐   Experimental   ☐   Established *but* changed indication or modification of technique

☒   Investigational   ☐   Should be taken out of use

☐   Nearly established

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐   Yes   ARTG number

☐   No

☒   Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia	✓		
United States	✓		
Canada	✓		
Denmark	✓		
Ireland	✓		
United Kingdom		✓	

IMPACT SUMMARY:

This prioritising summary examines current issues in screening for abdominal aortic aneurysm (AAA) in Australia.

BACKGROUND

Aneurysms are usually defined by a 50 per cent increase in vessel diameter. Even in the absence of overt coronary disease, aortic diameter will increase with age. The abdominal aorta, between the renal arteries and the iliac bifurcation, is a common site of aneurysm formation and is referred to as an abdominal aortic aneurysm (AAA). An AAA may occur when this vessel expands to a diameter of 3.0 cm or greater. Elective surgical repair of an AAA is usually only undertaken when the size of the aneurysm is

≥ 5.5 cm in diameter. Although AAA may remain asymptomatic for many years, it has been estimated that if left untreated, one in three will rupture. The majority of patients (50-80%) with a ruptured AAA will die out of hospital or pre-surgery. For those patients who do survive until surgery, mortality is high with only 10-25 per cent of patients with a ruptured AAA surviving until hospital discharge (Baxter et al 2008; Fleming et al 2005).

Ultrasound of the abdomen is an accurate and reliable method of identifying the presence of an AAA, and has been suggested as a means of screening and identifying asymptomatic individuals deemed to be at risk of rupture. Currently the identification of individuals at risk is serendipitous, with patients being identified after undergoing ad hoc imaging for conditions other than suspected AAA. Screening may reduce mortality in these at risk patients as mortality is lower in patients undergoing elective AAA surgery than in those who experience a rupture (Cosford & Leng 2007; Norman et al 2004).

The detection of individuals at risk of AAA therefore fulfils the criteria of the UK National Screening Committee in that the condition is an important health problem, it can be easily detected and can be treated more effectively during the asymptomatic stage rather than when rupture has occurred (Brearley 2008).

However, critics of AAA screening programmes point out that not all patients with an aneurysm will die from it; awareness of a small, non-life threatening aneurysm may be a source of intense anxiety for some patients and elective surgical repair of an AAA is associated with significant mortality (Cosford & Leng 2007).

CLINICAL NEED AND BURDEN OF DISEASE

The number of public hospital separations for AAA with rupture (ICD-10 code I71.3) has been steadily decreasing over time in Australia. In 1998-99 there were 902 separations, with 825 separations reported in 2004-05. The majority of these cases were male patients (73%) aged > 60 years (95.9%). The average length of stay for these separations was 9.2 days in 1998-99, down to 8.5 days in 2004-05. However, the number of separations for AAA without rupture (ICD-10 code I71.4) has increased slightly from 3,730 in 1998-99 to 4,077 in 2004-05. Similarly the majority of these patients were male (80.8%) aged >60 years (95.4%). The average length of stay for these patients in 2004-05 was 6.9 days (AIHW 2008b). No data were available on mortality. However, diseases of the arteries, which includes AAA, was the 12th leading cause of death in Australia during 2005 for both men (n=1,090, 2.2%) and women (n=1,110, 2.1%) aged 65 years and over (AIHW 2008a).

Similar trends were observed in New Zealand. The number of public hospital separations for AAA with rupture (ICD-10 code I71.3) decreased only slightly from 236 in 1999-2000, to 198 in 2003-04. In 2003-04, the majority of patients were male (76.8%) aged over 60 years (96%) and the average length of stay was 12.1 days. For

AAA without rupture (ICD-10 code I71.4) there were 530 separations in 2003-04. No New Zealand mortality data were available (data supplied by the NZ Health Information Service).

It has been estimated that 5-10 per cent of men aged 65-79 years have an AAA. The likelihood of rupture is approximately two per cent for aneurysms <4 cm, and 25 per cent in aneurysms >5 cm. As previously stated, mortality after rupture is high. Death occurs in approximately 80 per cent of patients who reach hospital and in 50 per cent who undergo emergency surgery. Elective surgical repair of AAA and the 30-day operative mortality is approximately 5-6 per cent (Cosford & Leng 2007).

Risk factors for AAA of >4 cm include smoking (3-5 times elevated risk compared to never smokers), a family history (OR=1.94), coronary artery disease (OR= 1.52), hypercholesterolemia (OR= 1.44) and cerebrovascular disease (OR= 1.28) (Fleming et al 2005).

DIFFUSION

General population screening for AAA is not currently conducted in Australia or New Zealand. The United Kingdom has recently established a pilot screening programme to screen all men over the age of 65 years (National Library for Health 2007). In addition, a recent United States task force recommended the screening of men aged 65 to 74 years of age (Fleming et al 2005).

COMPARATORS

Currently the identification of asymptomatic AAA patients is conducted in an ad hoc manner. The number of patients identified may be increasing with the increased availability and use of ultrasound by general practitioners (Norman et al 2004).

SAFETY AND EFFECTIVENESS ISSUES

The UK National Screening Committee cited three main papers as the source of evidence leading to a change in the policy of screening for AAA: the systematic Cohrane review by Cosford and Leng (2007), the systematic review by Fleming et al (2005) and the randomised controlled trial by Ashton et al (2002) (National Library for Health 2007).

Although both systematic reviews included the Western Australian randomised controlled trial (RCT) by Norman et al (2004) (level II screening evidence), it has been assessed in more detail in this summary as it may give an Australian context. The RCT intended to target only men aged 65-79 years, however due to poorly recorded data on the electoral roll and time delays in screening (completed over a 32 month period) the age range increased to include men aged 65-83 years. This population screening study randomised 41,000 men, identified from the Western Australian electoral roll, to an intervention group (screening with ultrasound) or control group (usual care). Initially 19,352 men were assigned to each group, however

only 12,203 completed a valid ultrasound scan (63%). Follow-up consisted of electronic data linkage to hospital databases for all men admitted to hospital for AAA surgery and death registration with AAA as a cause of death (median follow-up of 43 months).

The numbers of procedures and deaths following randomisation are summarised in Table 1. There were 875 cases of aortic aneurysm (aorta ≥ 30mm) detected, a crude prevalence of 7.2 per cent. This rate was markedly reduced when only men aged 65-69 years were considered (4.8%). Of the 875 cases, 699 (79.9%) had an aorta 30-44 mm in diameter, 115 (13.1%) were 45-54 mm and 61 (7%) were ≥55 mm in diameter. Twice as many men in the intervention group elected to have surgery compared to the control group (107 vs 54, p=0.002). Total post-operative 30-day death following elective surgery was 7/161 (4.3%) and there was no difference between the control and intervention groups (5.6% vs 3.7%, p=0.59). There were 33 ruptures in the intervention group, 13 of whom died before surgery. Nine individuals underwent emergency surgery, with one post-operative death. In the control group, there were 38 ruptures, 19 of whom died before surgery. Eight of these individuals underwent emergency surgery and three of these patients died post-operatively. The age standardised mortality per 100,000 at the end of follow-up (median 43 months) was 60 per cent lower in men who actually attended screening compared to the control group (7.48 vs 18.91). Results were stratified for age, comparing mortality for men aged 65-74 years and >75 years. In the younger age group, there were no deaths in men who underwent scanning and two deaths in the intervention group who did not undergo scanning, compared to 10 deaths in the control group (data not shown), translating to an odds ratio of 0.19 (95% CI [0.04, 0.89], p=0.01). However this benefit in the younger age group was not detected when all deaths were included from time of randomisation (OR= 0.82 [0.37, 1.84], p=0.06). The authors concluded that although there was benefit for men who attended screening, this benefit was reduced by deaths that occurred in the men who did not attend screening and that subgroup analysis indicates that screening should target men aged 65-74 years. In addition, although there was a large reduction in the relative risk of death between those individuals screened and those in the control group, the absolute risk reduction would be small due to the rarity of the condition (Norman et al 2004).

Table 1   Elective and emergency procedures from AAA

Elective and emergency procedures from AAA *between scheduled screening* and the end of follow-up (median 43 months)								
	Elective procedures		Emergency procedures					
	Operation	Post-operative death (%)	All ruptures	Operation	Post-operative death	Fatal rupture without surgery	Total deaths (%)	Age standardised mortality per 100,000* [95% CI]
Intervention group								
Scanned (n=12,203)	86	4 (4.7)	3	0	0	3	7 (0.6)	7.48 [1.91, 13.05]
Not scanned (n=7,149)	21	0	30	9	1	10	11 (0.15)	18.27 [7.08, 29.46]
Total invited (n=19,352)	107	4 (3.7)	33	9	1	13	18 (0.09)	11.51 [6.16, 16.86]
Control group								
Total (n=19,352)	54	3 (5.6)	38	8	3	19	25 (0.13)	18.91 [10.97, 26.85]
Elective and emergency procedures from AAA *between randomisation* and the end of follow-up								
Intervention group								
Scanned (n=12,203)	86	4 (4.7)	3	0	0	3	7 (0.06)	7.48 [1.91, 13.05]
Not scanned (n=7,149)	26	1 (3.9)	35	11	2	21	24 (0.29)	46.56 [24.7, 68.4]
Total invited (n=19,352)	112	5 (4.5)	38	11	2	24	31 (0.15)	23.55 [13.79, 33.31]
Control group								
Total (n=19,352)	60	4 (6.7)	41	10	5	28	37 (0.18)	27.83 [16.89, 38.77]

* At the end of follow-up (median 43 months)

The Cochrane systematic review included four RCTs which compared screening vs no screening (level I screening evidence). The Chichester (UK) RCT enrolled 15,775 *men and women* aged 65-80 years who were randomised to screening (n=7,887) or control groups (7,888). Overall acceptance of screening was 68.4 per cent with a mean follow-up of 30.5 months. The UK Multi-centre Aneurysm Screening Study (MASS) enrolled 67,800 men aged 65-74 years, with a screening uptake of 80.2 per cent and mean follow-up of 4.1 years. The Viborg RCT conducted in Denmark enrolled 12,658 men aged 65-73 years, with a screening acceptance rate of 76 per cent and a mean follow-up of 5.1 years. The RCT by Norman et al (2004) was also included. Results for men and women were analysed separately.

Overall there was a significant decrease in mortality from AAA favouring screening (from rupture and emergency or elective surgery) with an odds ratio of 0.60, 95% CI [0.47, 0.78] in men (*p*=0.0001) but not for women (OR=1.99, *p*=0.4). There was no significant difference (*p*=0.4) between the intervention screening group compared to controls for *all-cause* mortality in men or women (OR = 0.95 and 1.06, respectively), which again is expected due to the rarity of mortality with AAA as a cause. In the screened group there was a significant decreased incidence of rupture in men (OR= 0.45, 95% CI [0.21, 0.99], *p*=0.05) but not in women (OR = 1.49, *p*=0.7). There was a significant increase in the rate of surgery as a result of screening with an odds ratio of 2.03 (95% CI [1.59, 2.59], *p*<0.00001). The systematic review concludes that there is evidence of a significant reduction in mortality with ultrasound screening for AAA in men, but not women, aged 65-79 years (Cosford & Leng 2007).

The same four RCTs were identified in the systematic review for the US Preventative Services Task Force (Fleming et al 2005) (level I screening evidence) with the same results being reported. In addition, Fleming et al reported on the results of repeated screening for AAA in patients who negative on their first screen. The Chichester RCT prospectively followed a cohort of 1,011 men for 10-years who had a negative initial screen with an aorta <3.0 cm at age 65 years. The incident rate for new AAAs was four per cent and none of these were greater than 4.0 cm in diameter. It was postulated that it would be unlikely that these aneurysms would become clinically relevant as the men in this cohort were in their mid to late seventies. The authors therefore concluded that repeated screening of negative individuals would not be warranted. Several other cohort studies reported similar findings.

Ashton et al have recently (2007) published a15-year follow-up of an original randomised controlled trial published in 2002, the findings of which formed the basis of the MASS study which was included in both systematic reviews summarised above. A total of 6,040 men aged 65-80 years were randomised into the ultrasound screening group (n=2,995) and control group (n=3,045). Uptake of screening was 74 per cent. The relative risk reduction in AAA-related mortality in those invited for screening, reported in previous publications, was 42 and 21 per cent at five and 10 years, respectively. In the control group, 19 and 21 men underwent elective and

emergency AAA surgery, respectively. In the intervention group 41 and 16 men underwent elective and emergency AAA surgery. There were no post-operative deaths in either group for elective surgery, compared to the high mortality rate of 20/37 (54%) in patients undergoing emergency surgery. At 15-year follow-up, there were 54 AAA-related deaths in the control group (1.8%) and 47 in the intervention group (1.6), 20 of whom had refused screening. Although in real terms this represents an 11 per cent decrease in the AAA mortality rate with screening, the difference between the two groups was not significant. In the men who did receive a scan, AAA-related death occurred in 10/2046 who were diagnosed as normal. The mean time between the normal scan and death was 10.8 years (range 3.8-15 years). At initial scan, AAA was detected in 170 men, 17 of whom died from an AAA-related cause. Seven of these deaths were deemed preventable (patients declined elective surgery, did not attend follow-up or undergoing surgery for other causes). The authors concluded that although small, the benefit of a one off ultrasound screen was evident 15-years after the initial scan.

COST IMPACT

The most recent economic assessment of screening for AAA conducted by Montreuil and Brophy (2008) used Markov modelling to assess the cost-utility of an AAA screening programme in Canada. The model compared invitation to ultrasound screening to current practice of opportunistic detection using a hypothetical cohort of men aged 65 years. The model assumed that absence of AAA at aged 65 inferred a life-time freedom from AAA and re-screening would not be offered. Attendance rates and transition probabilities were obtained from systematic reviews of the literature and outcomes of emergency and elective surgery were derived from Canadian studies. Direct costs included the cost of abdominal ultrasound, pre-hospitalisation workup, inpatient care for surgical treatment of ruptured and non-ruptured AAAs, professional fees and the lifetime costs of complications.

An invitation to attend screening resulted in an undiscounted gain in life expectancy of 0.049 years and a gain in discounted QALY[1] of 0.019 for an estimated incremental lifetime cost of Can $118[2]. Therefore the estimated incremental cost-utility ratio was Can $6,194 per QALY gained (95% CI [1,892, 10,837]). To prevent one AAA death, 187 (95% CI [130, 292]) men needed to be invited to attend screening and 137 (95% CI [85, 213]) needed to be screened. The model appears to support that screening men over the age of 65 years for AAA with a one-off abdominal ultrasound would be cost-effective. The authors suggest that more work should be conducted into the screening of subgroups who may be at greater risk such as smokers.

A similar study conducted in Denmark by Henriksson and Lundgren (2005) reported higher costs. Differences between this study and the one by Montreuil and Brophy

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[1] QALY = quality adjusted life year
[2] 26th June 2008 the Australian dollar was on parity with the Canadian dollar

(2008) included a slightly higher prevalence of AAA (4.9% vs 4.2%), and some higher direct health care costs (elective surgery for AAA €17,769 (~Can $28,126) compared to elective surgery costs in Montreuil & Brophy study of Can $17,991). The cost of the abdominal ultrasound was similar in both studies. The Danish study reported an incremental cost per life-year gained for a screening programme compared to current practice to be €7,760[3] and for a QALY of €9,700. Although these costs are higher than those reported by the Canadian study, the authors concluded that a screening programme for AAA was cost-effective (stating that a QALY below €10,000 is usually considered low), feasible and yielded positive health outcomes for a reasonable cost.

Several earlier studies conducted in the Netherlands (Boll et al 2003), the United States (Lee et al 2002) and Denmark (Lindholt et al 2002) also concluded that a one-off abdominal ultrasound for men aged 65 years was cost effective.
Two Medicare Benefits Schedule item numbers for abdominal ultrasound are listed, 55036 (fee $111.30) and 55037 (fee $37.85).

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

Opponents of screening for AAA have cited the potential psychological harm and anxiety caused by alerting individuals to a condition that may cause sudden death.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

All of the good quality, high level of evidence, studies included for assessment in this summary reported significant decrease in mortality from AAA in men who actually underwent screening. There was no difference in the all-cause mortality, or absolute risk of death between individuals who underwent screening compared to those who relied on standard care and opportunistic detection of AAA, due to the rarity of the condition. More individuals underwent elective AAA surgery as a result of screening which was reflected in a reduced rate of rupture in the screened population. All economic studies reported that a one-off abdominal ultrasound was cost-effective.

HEALTHPACT ACTION:

Based on the high level of evidence available it would appear that a one-off abdominal ultrasound screen for men aged between 65-74 years is effective in terms of reduced mortality. In addition, the cost per QALY makes screening for AAA cost-effective. HealthPACT have therefore recommended that this summary be forwarded to the Clinical, Technical and Ethical Principle Committee (CTEPC) for forwarding to the National Screening Committee for their consideration.

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[3] 26th June 2008: €7,760 = A$12,675and €9,700 = A$15,844

NUMBER OF INCLUDED STUDIES

Total number of studies
Level I screening evidence   2
Level II screening evidence   2

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SEARCH CRITERIA TO BE USED:

Aortic Aneurysm, Abdominal/ mortality
Mass Screening/ methods
Cardiovascular Diseases/ mortality/ultrasonography
Ultrasonography
Aortic Rupture/mortality/ prevention and control