



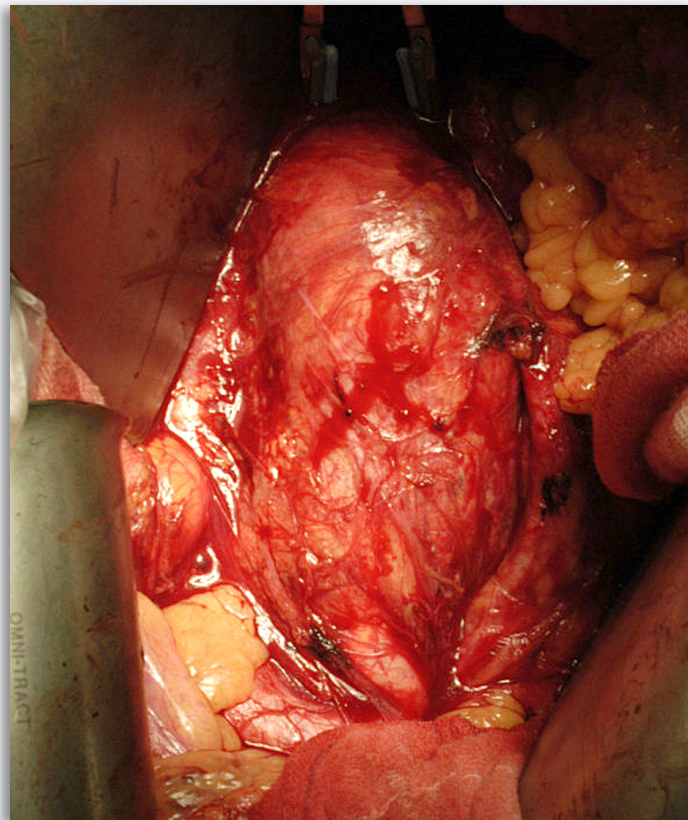
Otago Spotlight Series  
Cardiovascular Disease

# Aortic Aneurysm

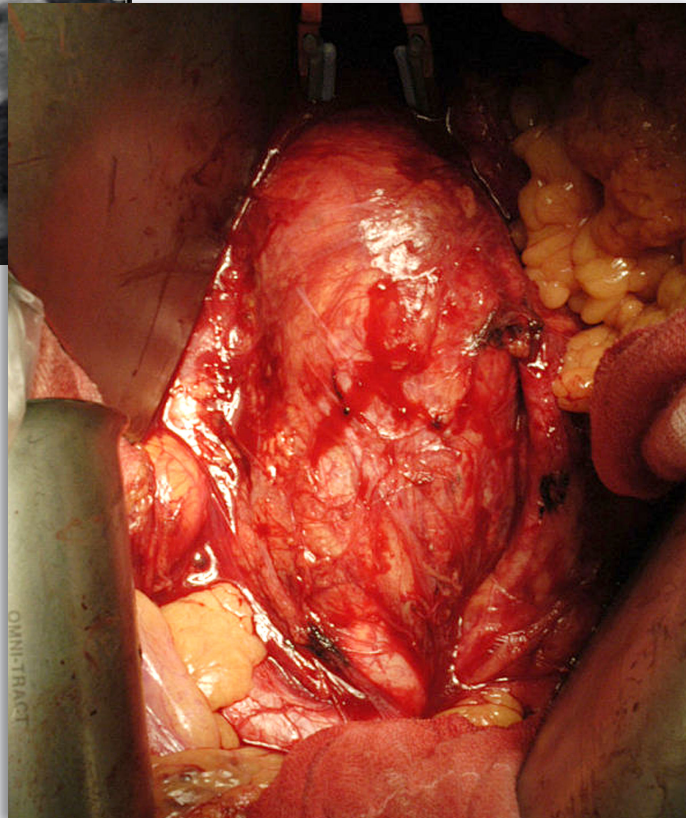
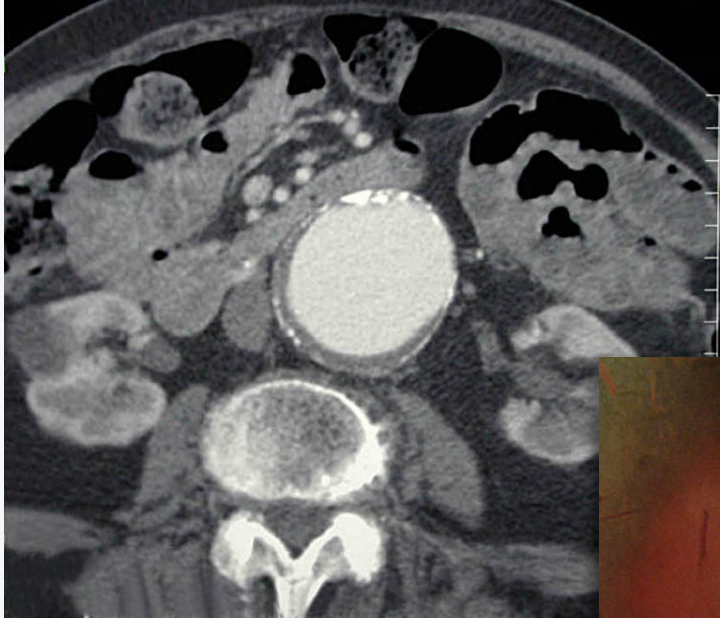
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Prof. Andre van Rij  
Vascular Research Group  
Department Surgical Sciences  
Dunedin School of Medicine

# AAA a silent killer

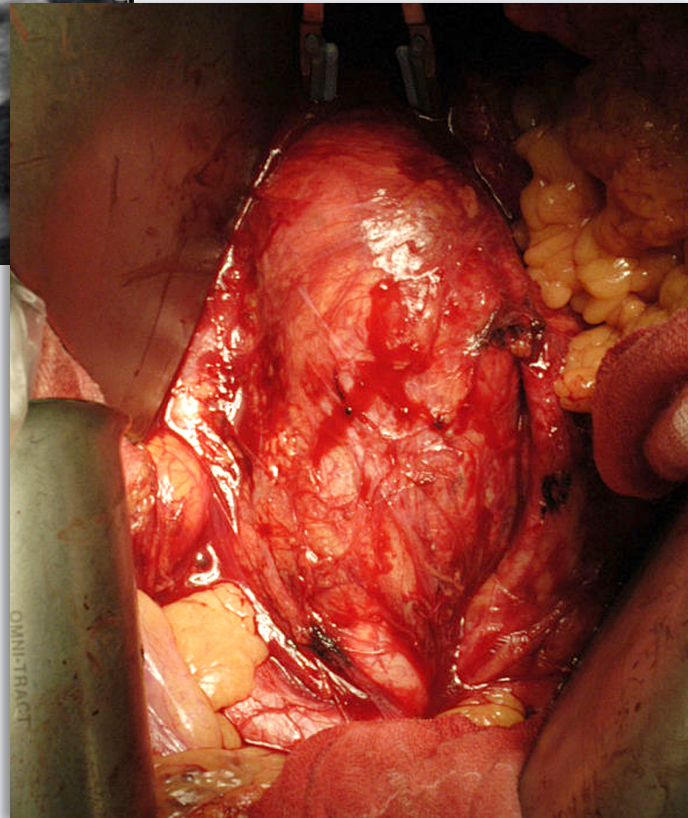
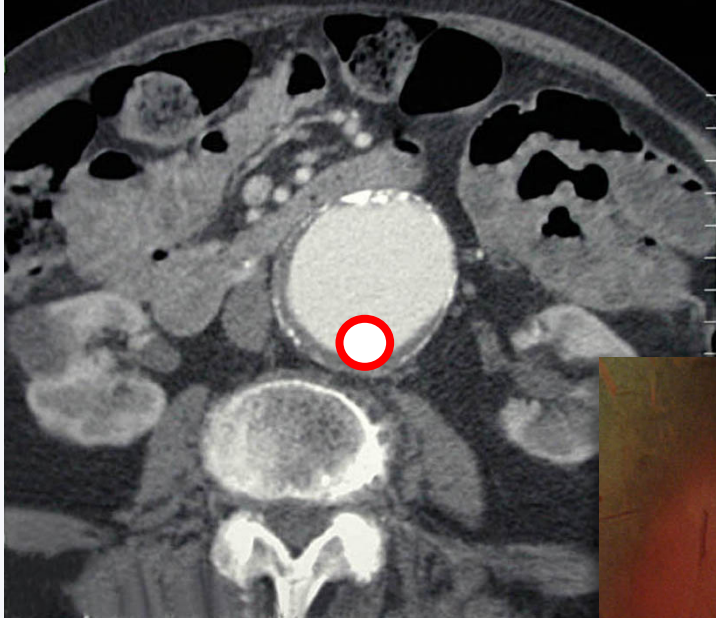


# AAA a silent killer



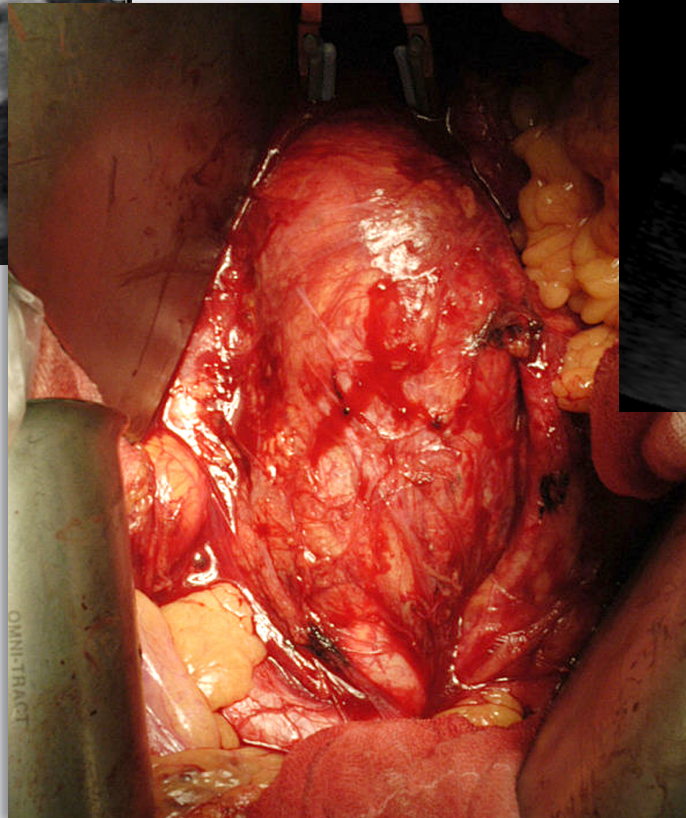
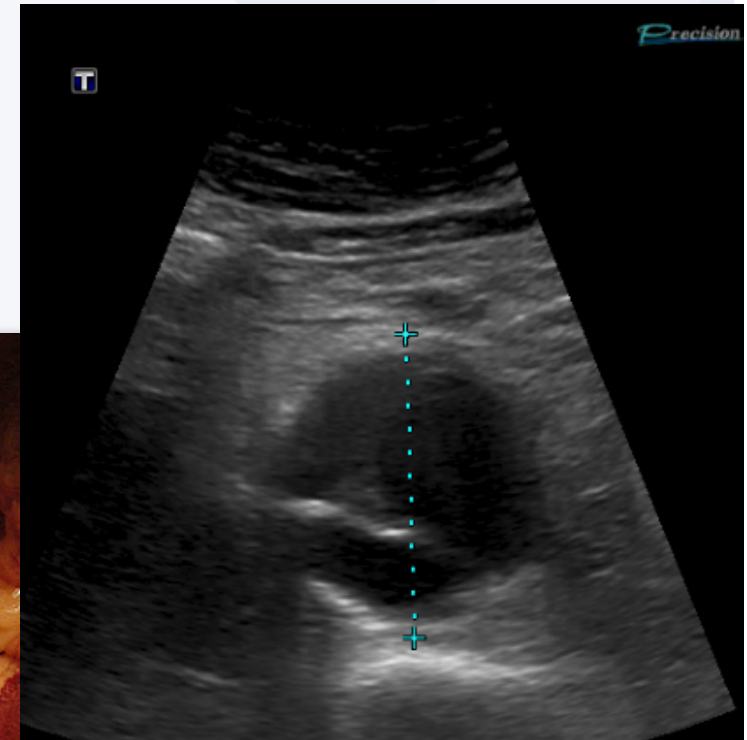
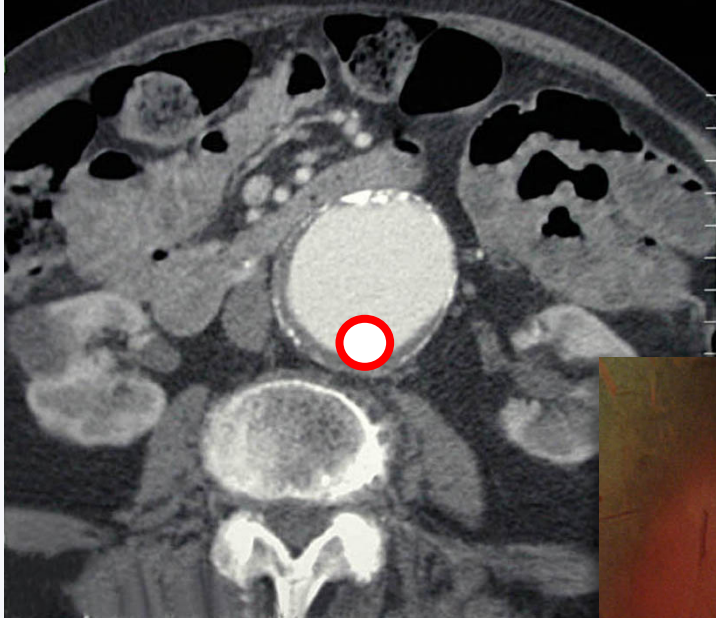


# AAA a silent killer

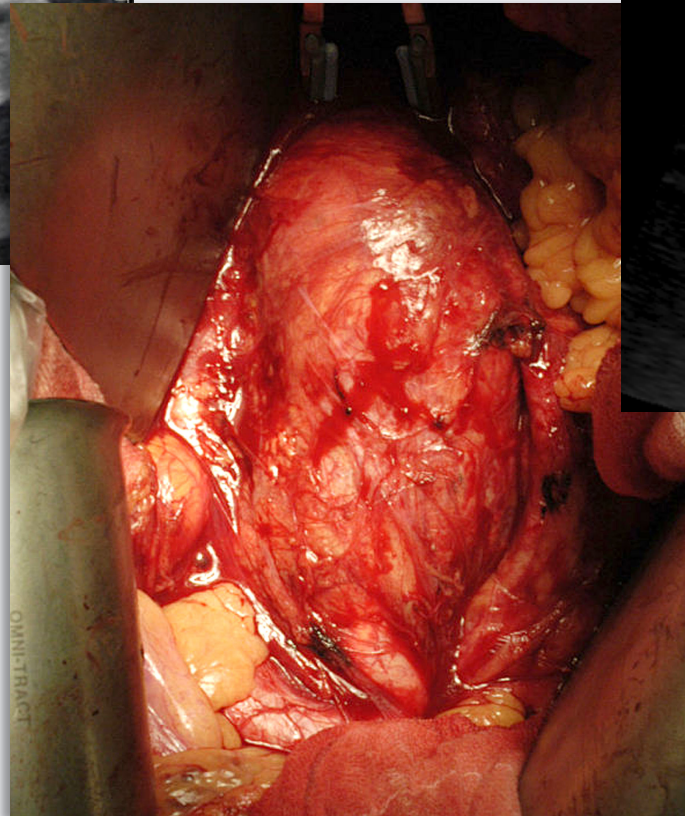
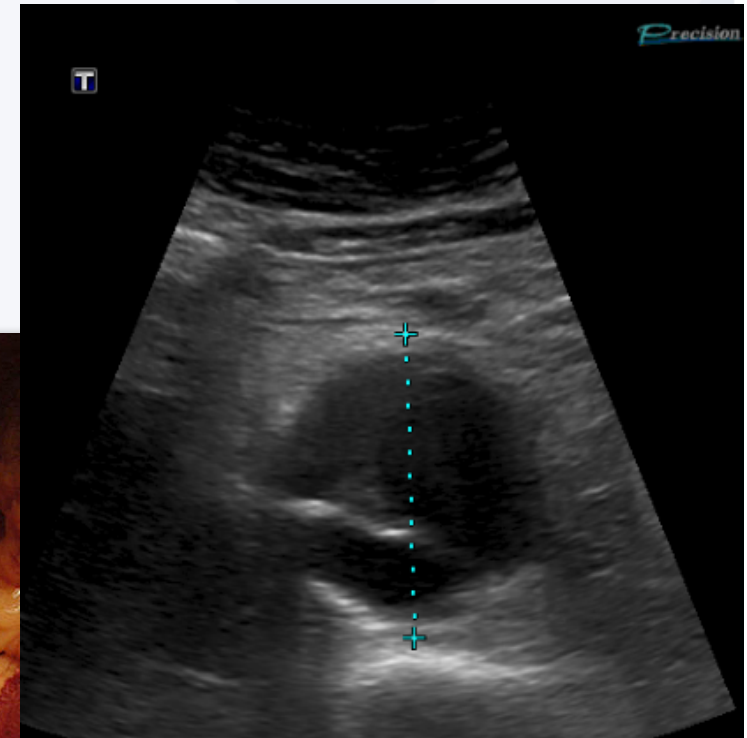
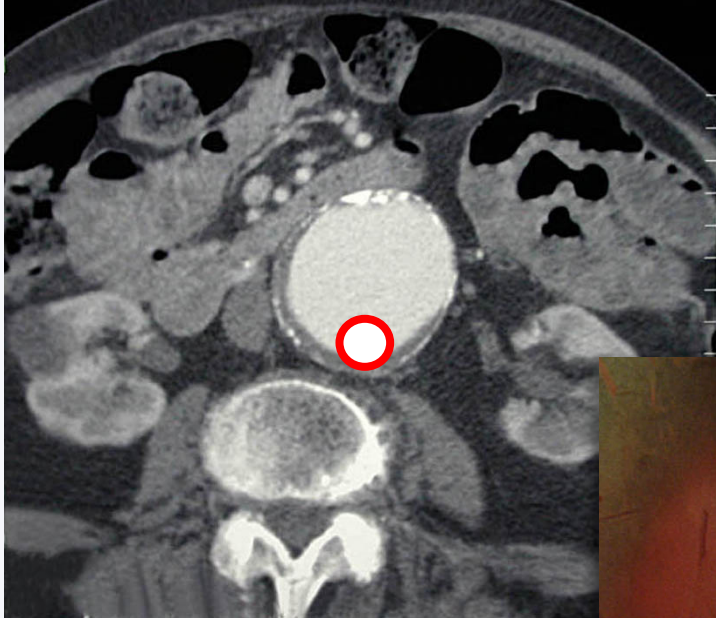




# AAA a silent killer



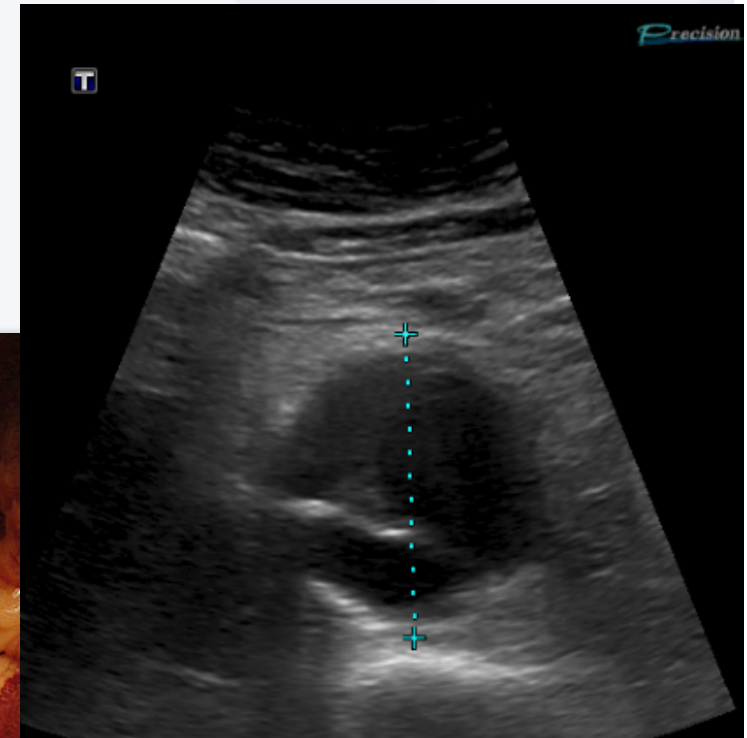
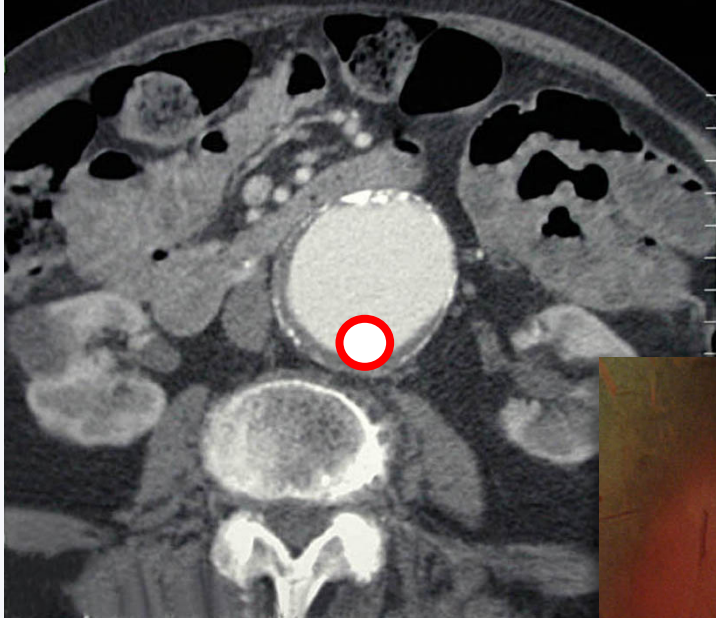
# AAA a silent killer



Mortality 35-70%



# AAA a silent killer

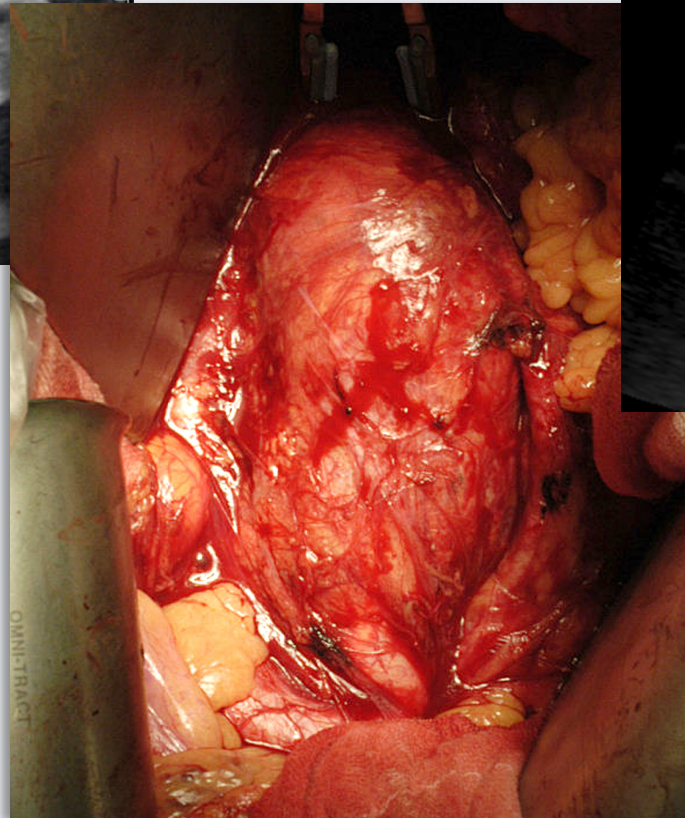
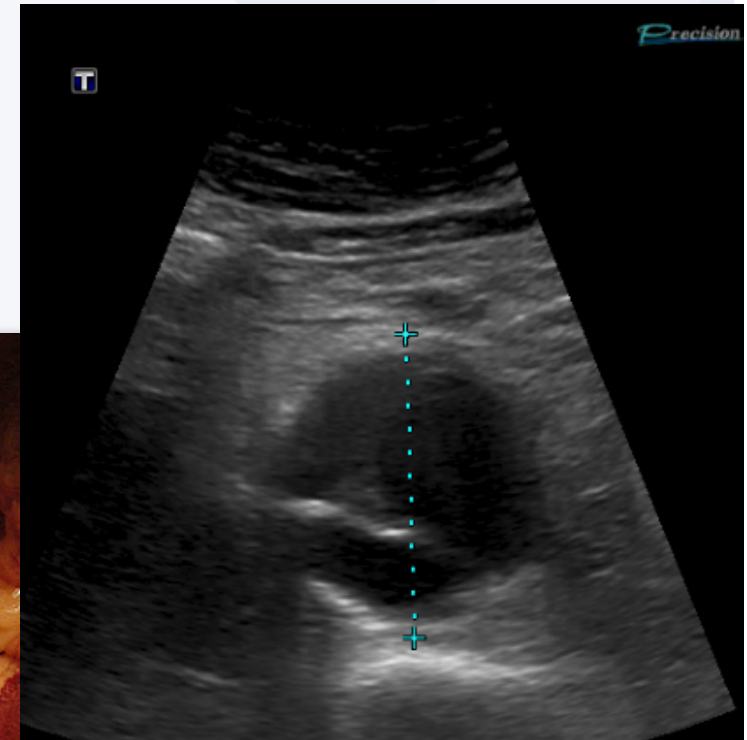
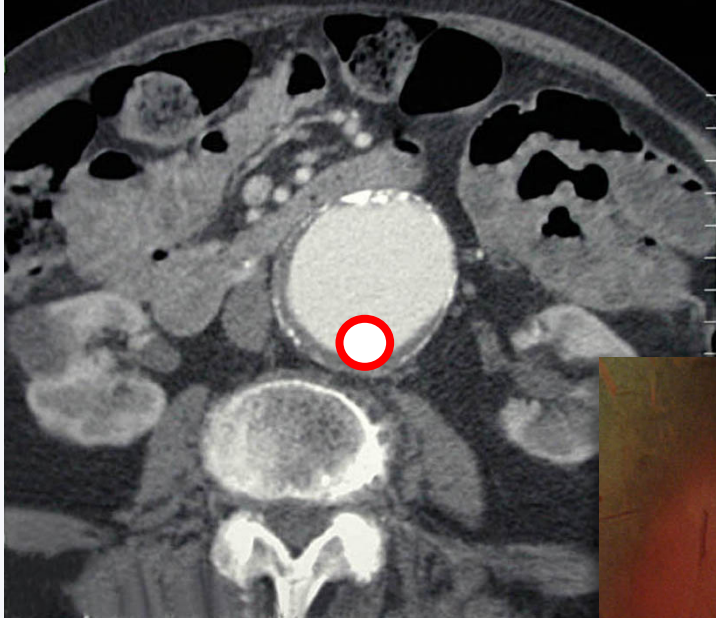


Mortality 35-70%

Males 3 : 1



# AAA a silent killer



Mortality 35-70%

Males 3 : 1

Maori and Women  
- worse outcomes

# AAA a silent killer

## Our Research

- The Biology
- Biomarker
- Genetics

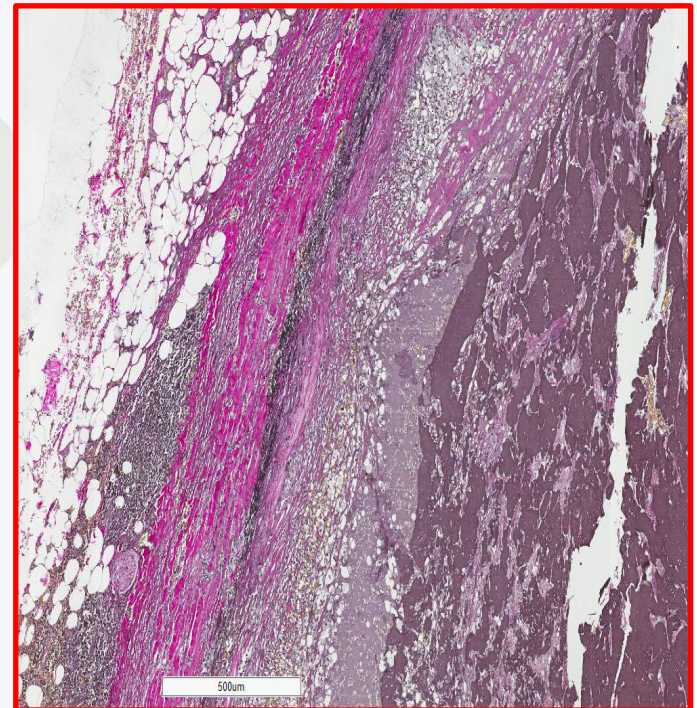
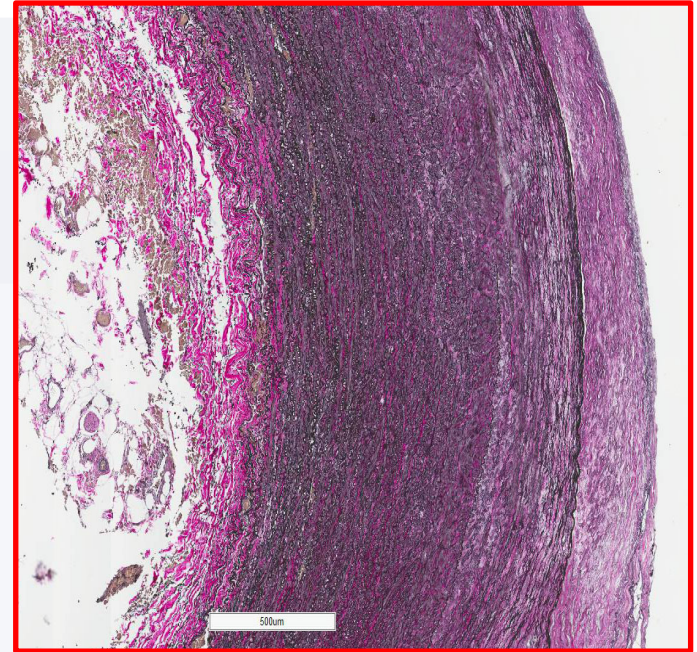
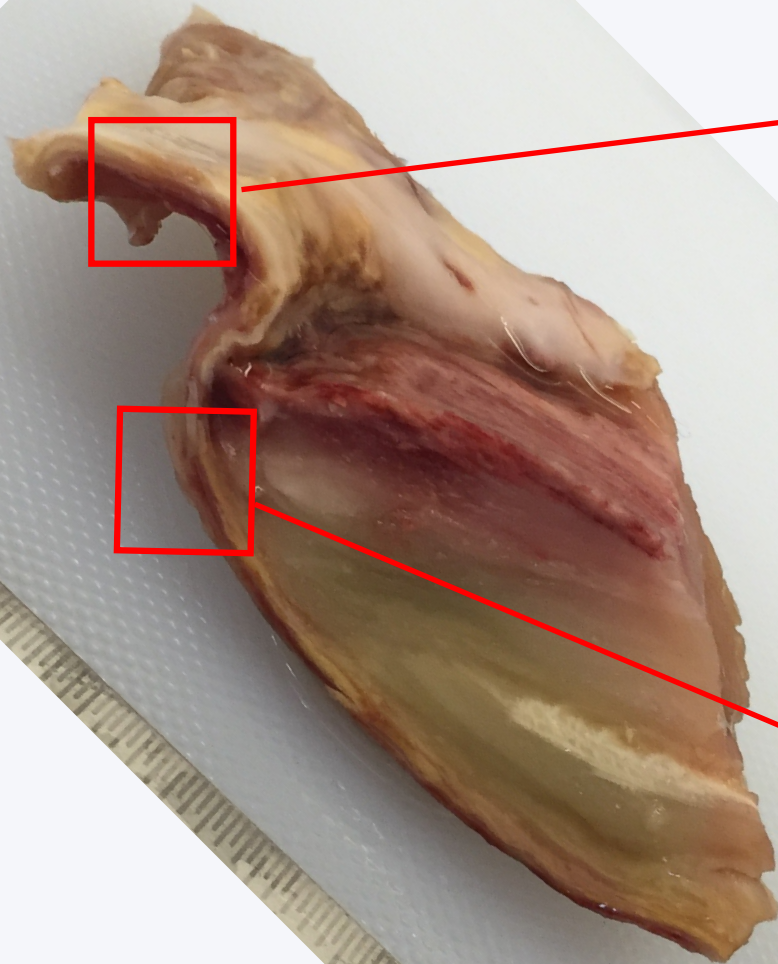
Translation

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- Prevention
- Non surgical treatment
- Early detection



# Biology

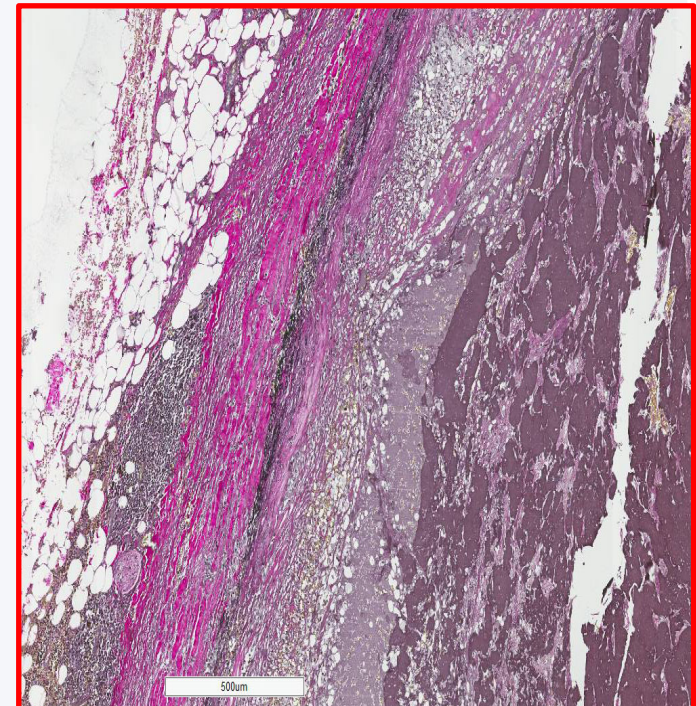
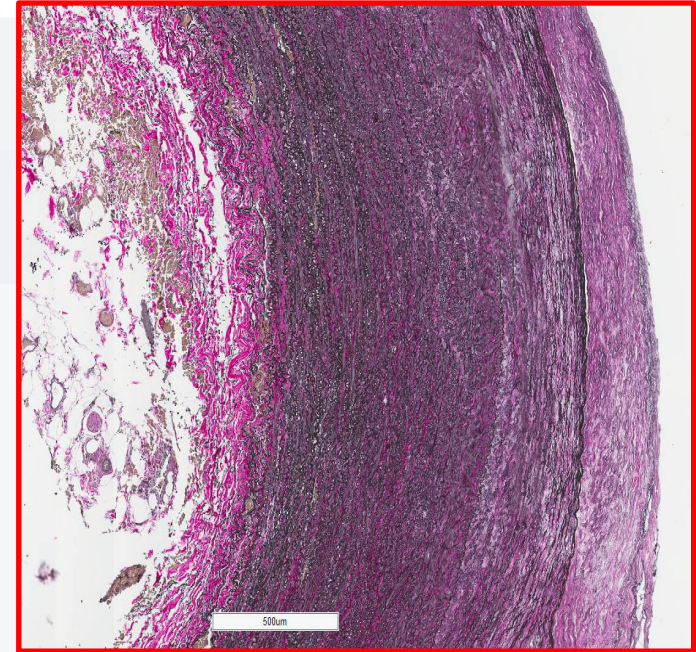


HC1341, M, 69 years



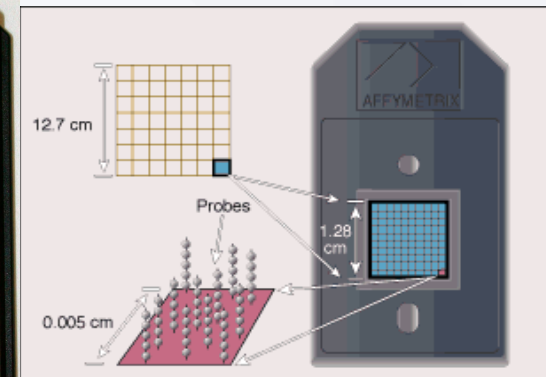
# Biology

- Angiogenesis
- Inflammation
- Gender
- Smoking
- Atherosclerosis
- Diabetes (-)
- Familial



# Genetics – GWAS for AAA

## Building the Resource



# Genetics – GWAS for AAA

## Building the Resource

- Local
- National
- International

Summer students programme

Long term recruitment Strategy



# Genetics – GWAS for AAA

## Building the Resource

- Local
- National
- International



# Genetics – GWAS for AAA

## Building the Resource

- Local
- National
- International



# Genetics – GWAS for AAA

Building the numbers

**AAA subjects**

**vs**

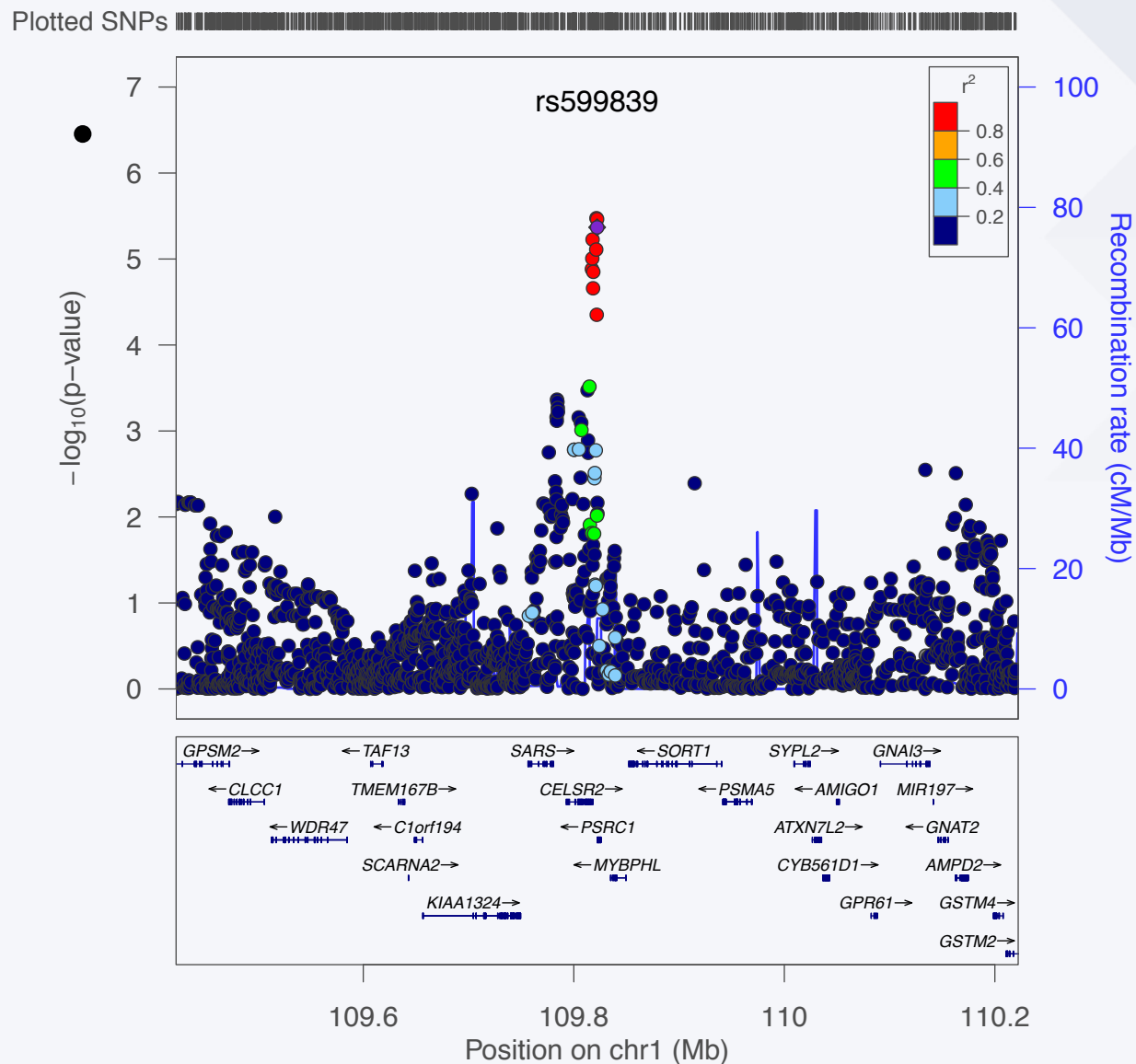
**Non AAA subjects**

5 million SNP differences

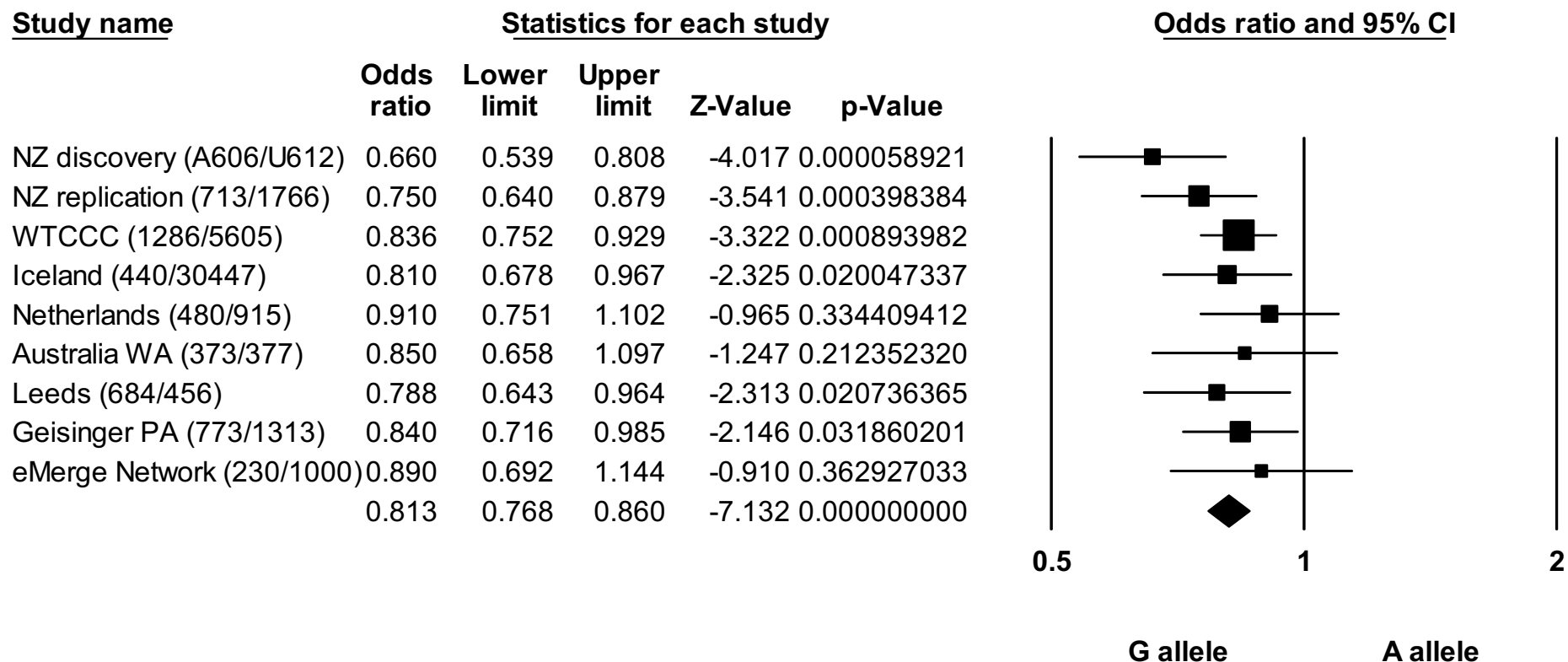




# GWAS for AAA



# AAA Associated 1p13 locus, rs599839



**7048 AAA cases compared with >40,000 controls**

**G allele carrier OR 0.81,  $p=7.2 \times 10^{-14}$**

## LETTERS

nature  
genetics

---

Genome-wide association study identifies a sequence variant within the *DAB2IP* gene conferring susceptibility to abdominal aortic aneurysm



JONES\_CIRCRES/2016/308765\_R1

## **Meta-Analysis of Genome-Wide Association Studies for Abdominal Aortic Aneurysm Identifies Four New Disease-Specific Risk Loci**

## **Meta-Analysis of Genome-Wide Association Studies for Abdominal Aortic Aneurysm Identifies Four New Disease-Specific Risk Loci**

### **meta-analysis of 6 GWAS**

10,204 cases and 107,766 controls

Confirmed 5 AAA associated SNPs

4 new SNPs specific for AAA





# Spin Offs

nature

Vol 452|3 April 2008|doi:10.1038/nature06846

## LETTERS

### **A variant associated with nicotine dependence, lung cancer and peripheral arterial disease**

**Cardiometabolic effects of genetic upregulation of the interleukin 1 receptor antagonist: a Mendelian randomisation analysis**

*Lancet Diabetes Endocrinol 2015*

*The Interleukin 1 Genetics Consortium\**

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

Variant *ASGR1* Associated with a Reduced Risk of Coronary Artery Disease



# Translational Spin Off



# Translational Spin Off

## Predicting AAA Risk

Possible maximum score 54



# Translational Spin Off

## Predicting AAA Risk

<b>Male gender</b>	5 points	<b>Diabetes</b>	-1 point
<b>Age:</b> 60-64yrs	3	Hx <b>Heart disease</b>	3
65-69yrs	6	Hx <b>Hypertension</b>	4
70-74yrs	12	<b>AIP +</b>	4
75+	24	<b>CRP &gt;4.5mg/L</b>	6
<b>Smoking pack years:</b>			
1-10yrs	3		
11-25	6		
25+yrs	8		

Possible maximum score 54

**Demographic Score >28: AAA odds ratio 7.3 (95% CI 5.9-8.9,  $p < 10^{-30}$ )**





# Early Detection Screening

- Limitations of the Abdominal Ultrasound one shot 65 yr male model
  - Inequities: gender
  - Maori
  - Changing prevalence
  - Aging
  - Expensive

[otago.ac.nz/cvd](http://otago.ac.nz/cvd)

Leading article

British Journal of Surgery

## Aortic aneurysm screening

A. M. van Rij and G. T. Jones

Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand  
(e-mail: [andre.vanrij@otago.ac.nz](mailto:andre.vanrij@otago.ac.nz))



PODCAST  
AVAILABLE  
ONLINE

Published online in Wiley Online Library ([www.bjs.co.uk](http://www.bjs.co.uk)). DOI: 10.1002/bjs.9830



# Early Detection Screening

- Innovations for a NZ context

Leading article

British Journal of Surgery

## Aortic aneurysm screening

A. M. van Rij and G. T. Jones

Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand  
(e-mail: andre.vanrij@otago.ac.nz)



Published online in Wiley Online Library (www.bjs.co.uk). DOI: 10.1002/bjs.9830



# Early Detection Screening

- Low cost scanning

Nguyen *et al. Cardiovascular Ultrasound* 2013, **11**:42  
<http://www.cardiovascularultrasound.com/content/11/1/42>



CARDIOVASCULAR  
ULTRASOUND

**RESEARCH**

**Open Access**

## Novices may be trained to screen for abdominal aortic aneurysms using ultrasound

Anh TV Nguyen, Geraldine B Hill, Matthew PT Versteeg, Ian A Thomson and Andre M van Rij\*





# Early Detection Screening

- Focused screening  
based on CVD risk

Original article

## Comparison of three targeted approaches to screening for abdominal aortic aneurysm based on cardiovascular risk

G.T. Jones<sup>1</sup>, B. G. Hill<sup>1</sup>, N. Curtis<sup>1</sup>, T. D. Kabir<sup>1</sup>, L. E. Wong<sup>1</sup>, M. W. Tilyard<sup>2</sup>, M. J. A. Williams<sup>3</sup>  
and A. M. van Rij<sup>1</sup>

Departments of <sup>1</sup>Surgical Sciences, <sup>2</sup>General Practice and Rural Health, and <sup>3</sup>Medicine, University of Otago, Dunedin, New Zealand

Correspondence to: Associate Professor G. T. Jones, Vascular Research Group, Department of Surgical Sciences, University of Otago, PO Box 913, Dunedin, New Zealand (e-mail: greg.jones@otago.ac.nz)



# Early Detection Screening

- Alternative biomarkers to US

ORIGINAL RESEARCH



**Two C-C Family Chemokines, Eotaxin and RANTES, Are Novel Independent Plasma Biomarkers for Abdominal Aortic Aneurysm**

Gregory T. Jones, PhD; L. Victoria Phillips; Michael J.A. Williams, MBChB; Andre M. van Rij, MBChB; Tasnuva D. Kabir, MBChB, PhD



# Early Detection Screening

- Screening in Parallel

## CT colonography

Kashram M, Jones G, Roake J. Prevalence of Abdominal Aortic Aneurysm (AAA) in a Population Undergoing Computed Tomography Colongraphy in Canterbury, New Zealand. *Eur J Vasc EndoVasc Surg* 2015;49: 1-7.

## Echocardiography

Majeed K, Hamer AW, White SC, Pegg TJ, Wilkins GT, Williams SM *et al*. Prevalence of abdominal aortic aneurysm in patients referred for transthoracic echocardiography. *Intern Med J* 2015; 45: 32-39.





# Early Detection

## pre - Screening

### The Routine Abdominal CT scan

- 3332 scanned
- 187 AAA - Prevalence 5.8%
- 35% unreported
  
- >3000 screening not needed

### Journal of Vascular Surgery

Measuring abdominal aortic diameters in routine abdominal CT scans and implications for AAA screening.

--Manuscript Draft--

Rachel Claridge, Sam Arnold, Neil Morrison and André. M Van Rij

Radiology Department Dunedin Hospital and Surgery Department



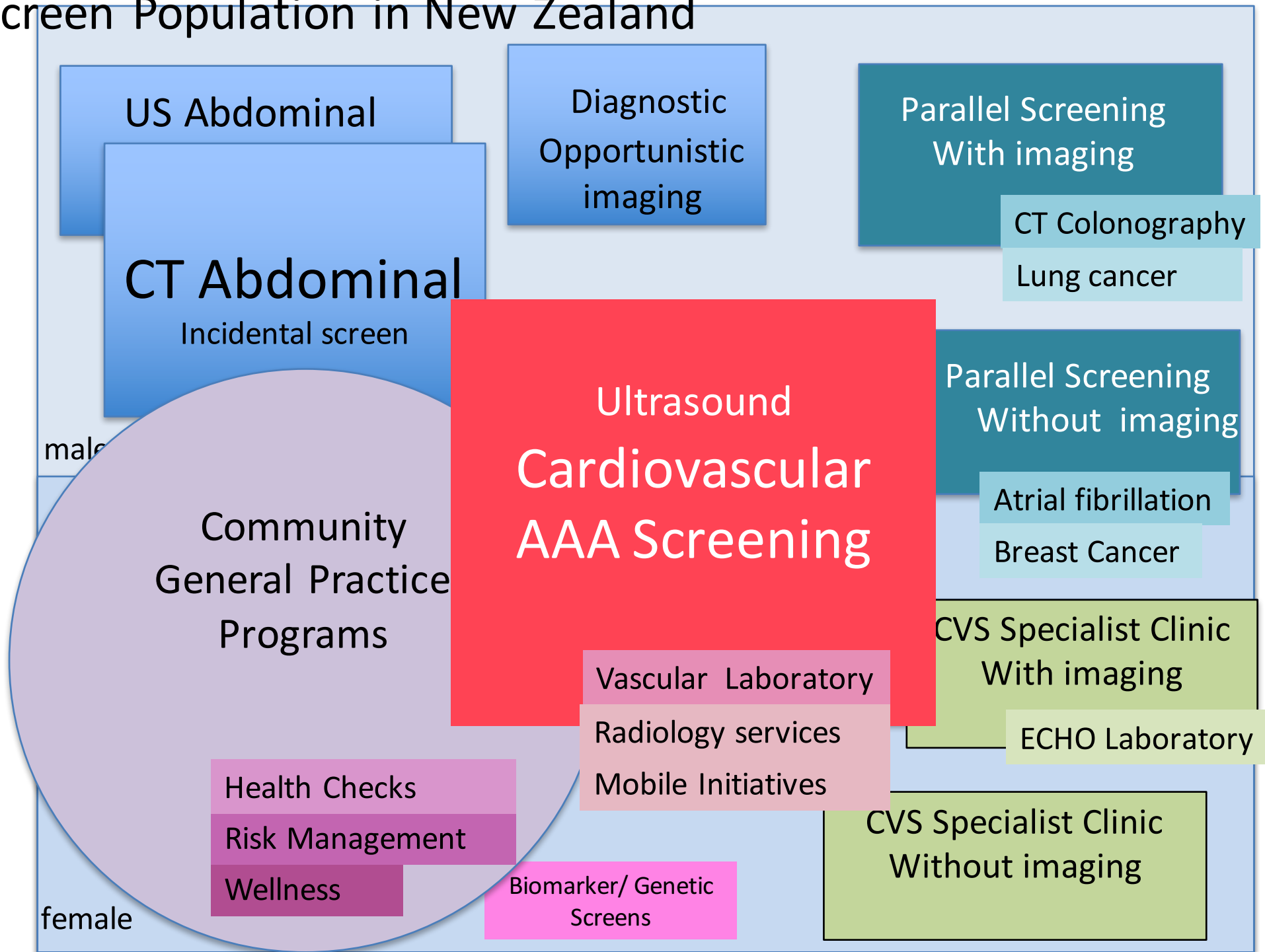
# Early Detection pre - Screening

Personal Genomics

Community

Cardiovascular risk

# Screen Population in New Zealand





# Data Integration and Linkage

All incidental Imagers

All screening  
Initiatives

e-Health record

DATA  
resource

“AAA  
Screen”





## Assoc Prof Greg Jones

### Team

- Vicky Phillips
- Kate Thomas
- Josie Macfarlane
- Matt Versteeg
- Nicole Curtis
- Ian Thomson
- Jo Krysa
- Rachel Claridge
- Anh Nguyen
- Reardon Dickinson
- Gerry Hill
- Greg Tarr
- Tasnuva Kadir
- Jeremy Rosaak
- Lisa Wong
- Jimmy Jin
- Neil Morrison
- Sam Arnold
- Tim

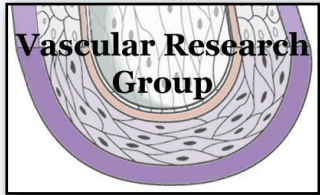
### Collaborators

- Prof Michael Williams
- Prof Sally MacCormack
- Prof Tony Merriman
- Prof Murray Tilyard

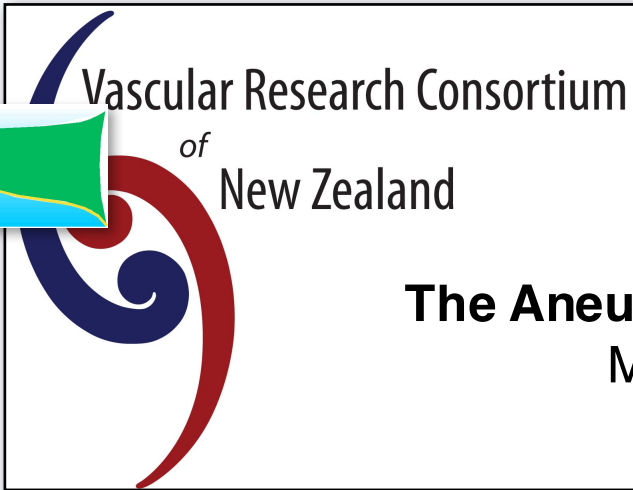
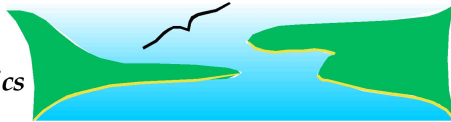


deCODE  genetics

**Thank you**



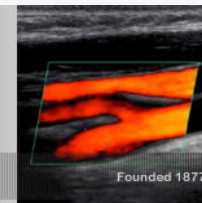
Otago  
Vascular  
Diagnostics



**The Aneurysm Consortium (UK)**  
Matt Bown



**Otago Vascular  
Diagnostics**  
Department of Surgical Sciences  
DUNEDIN SCHOOL OF MEDICINE



[otago.ac.nz/cvd](http://otago.ac.nz/cvd)

# Data Integration and Linkage

