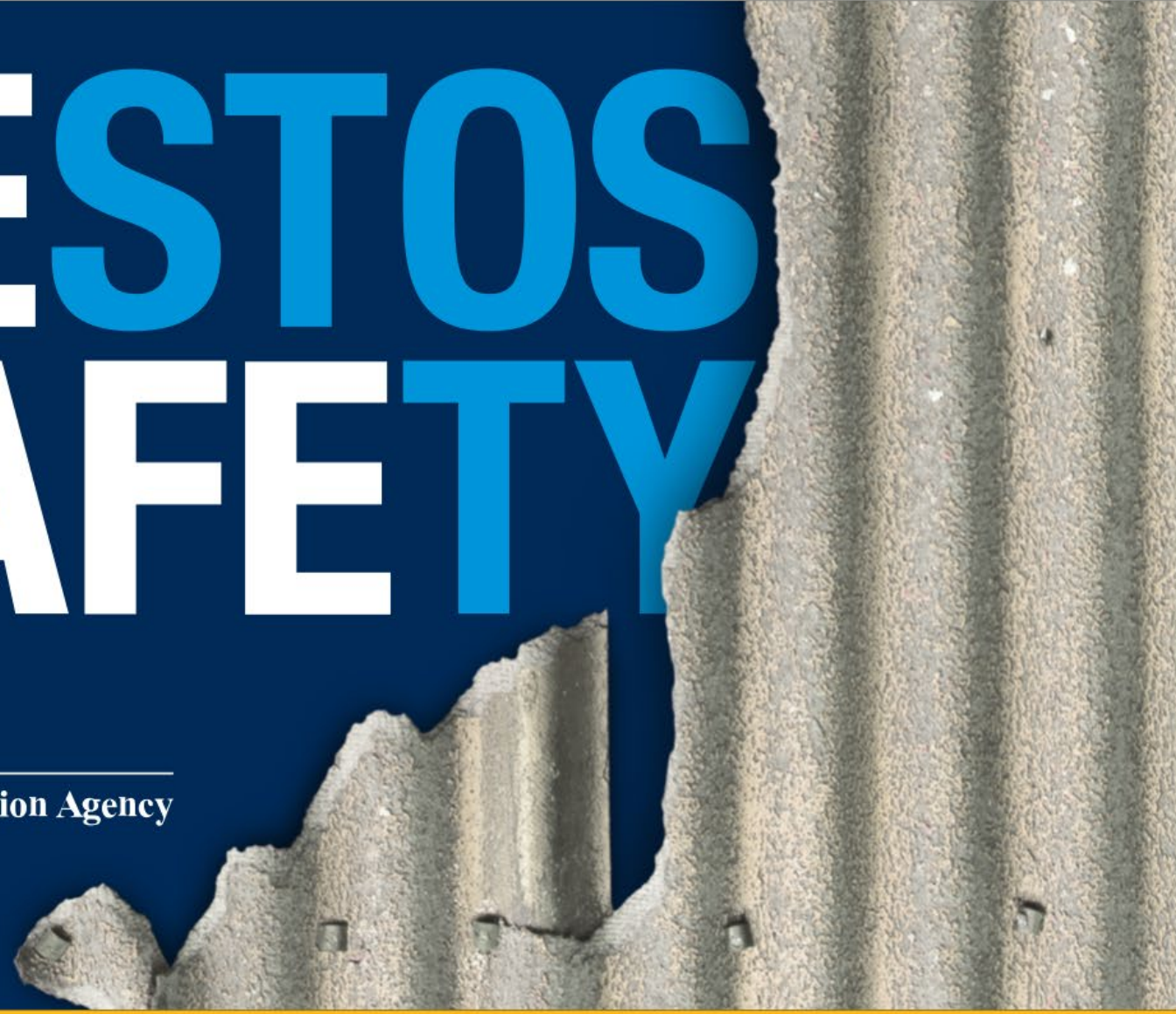
ASBESTOS SAFETY 2019 CONFERENCE



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Asbestos Safety and Eradication Agency

11-13 NOV PERTH, WA

Australian Government
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Welcome to Country

Mr Samuel Pilot-Kickett

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Australian Government
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Facilitator Welcome

Ms Karen Tighe

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Commemoration of Lives Lost

Robert Vojakovic & Melita Markey

Asbestos Diseases Society of Australia

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Conference Welcome

Diane Smith-Gander AO

Chair – Asbestos Safety & Eradication Council

Justine Ross

CEO – Asbestos Safety & Eradication Agency

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Plenary Panel: Breakthroughs in Medical Research

QUESTIONS: www.slido.com #ASEACONF2019

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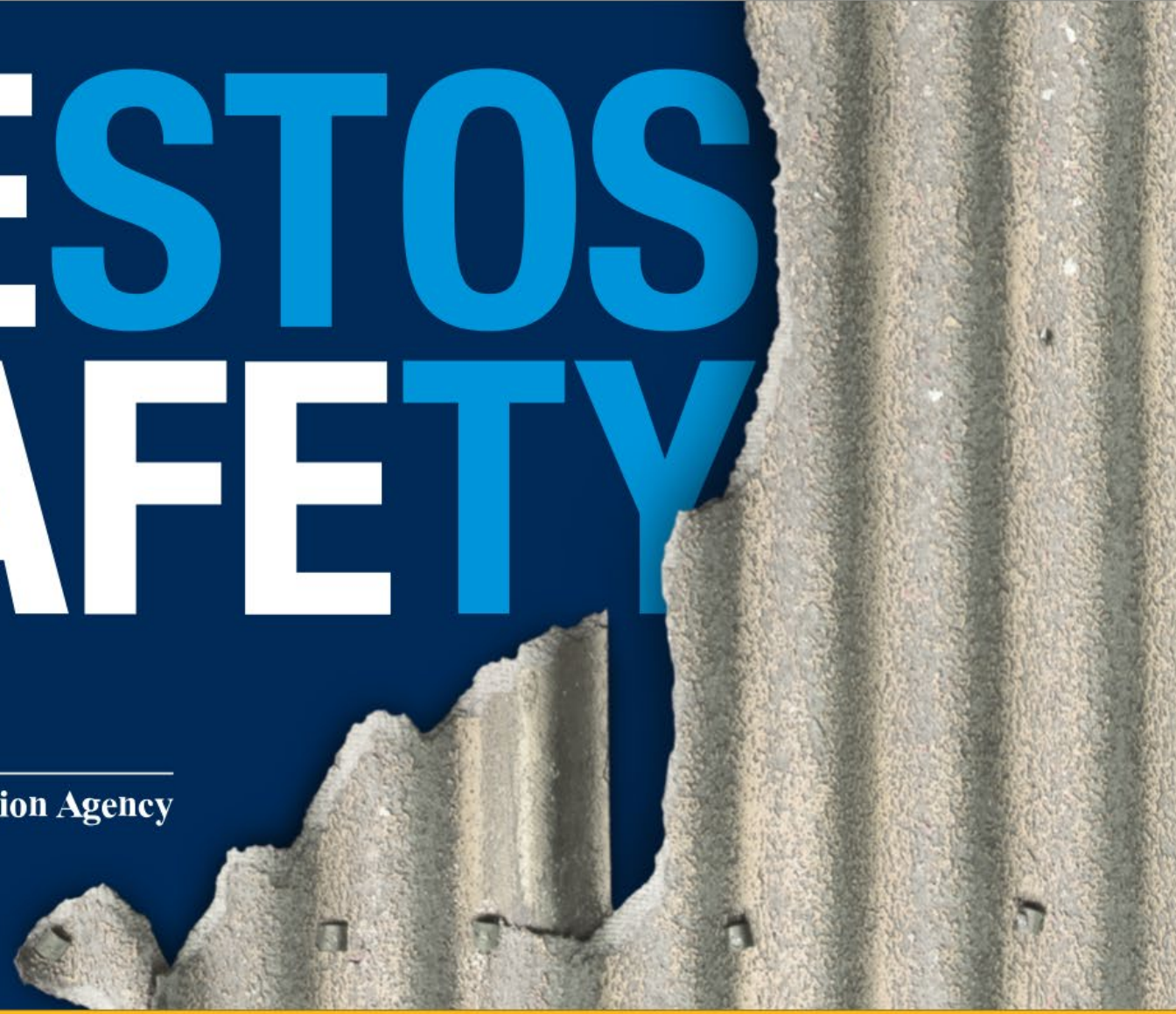

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National Centre for Asbestos Related Diseases
an Australian Research Cooperative

The MexTAg Collaborative Cross

Understanding how host genetics impacts asbestos related disease

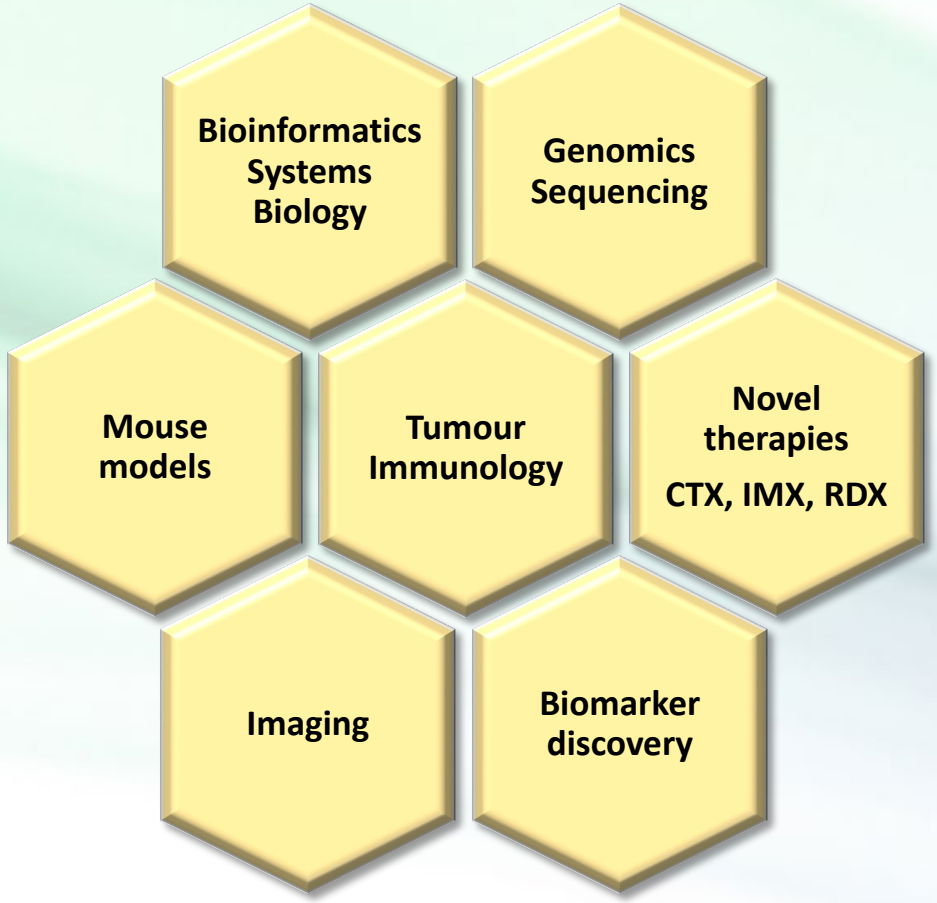
Scott Fisher PhD

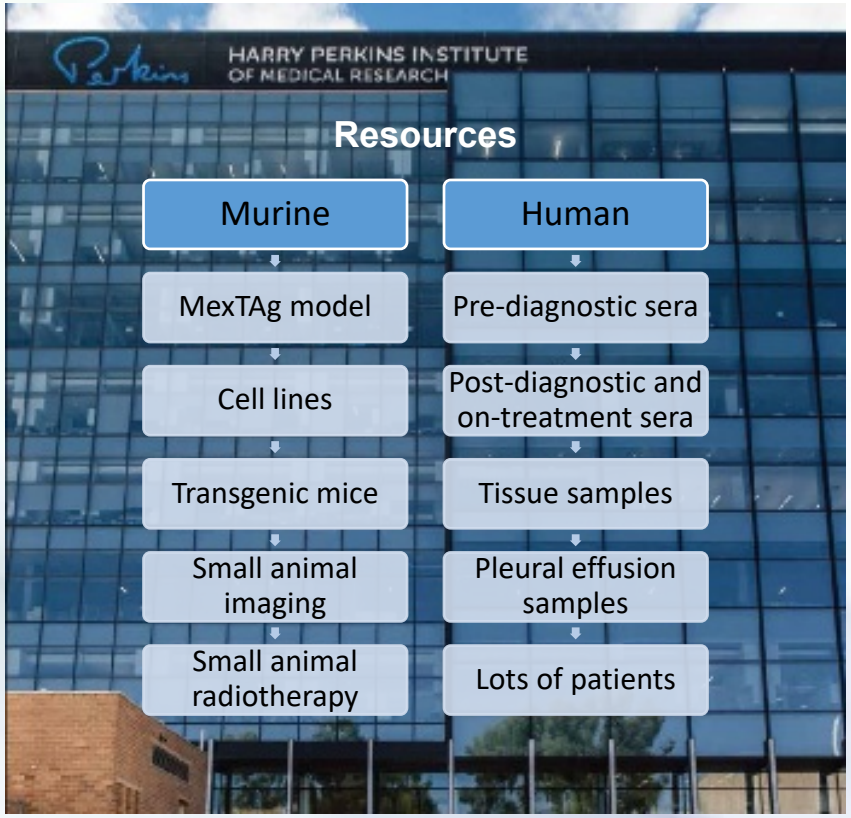
National Centre for Asbestos Related Diseases

an Australian Research Cooperative

30+

Clinicians
Scientists
Students

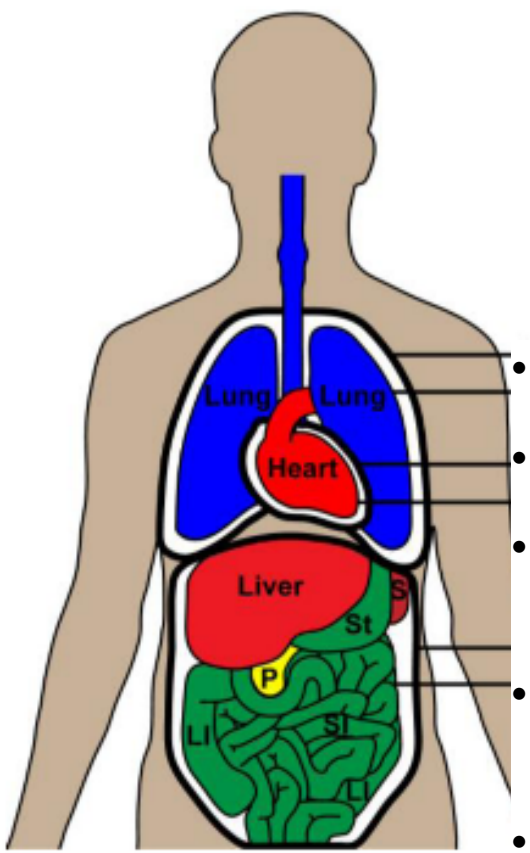




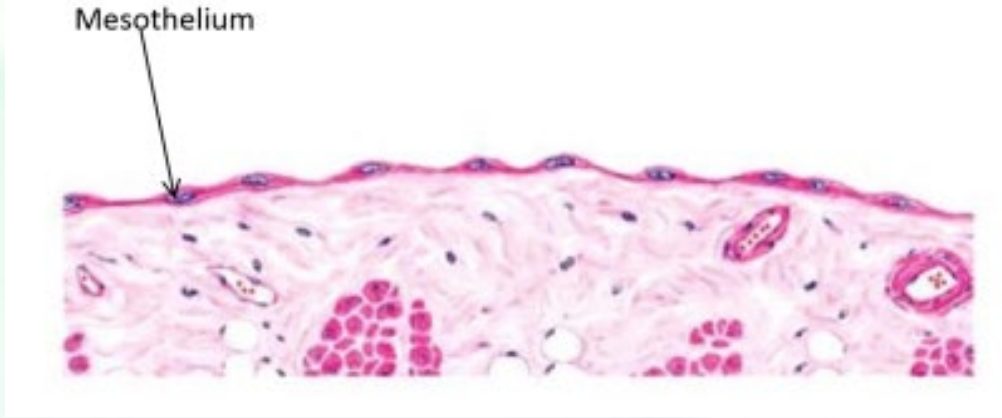
Leading innovation and discovery to improve the lives of people affected by asbestos related disease

Mesothelioma

Derived from normal mesothelium

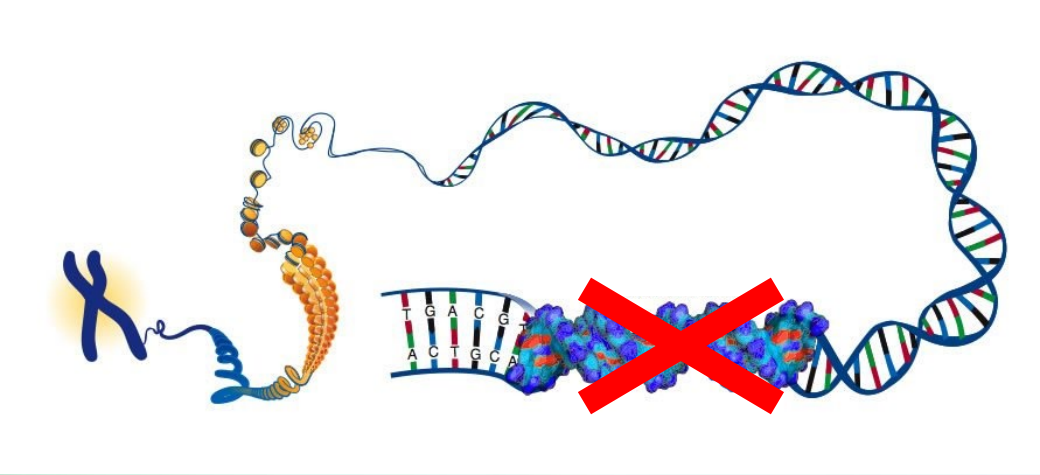


- Around the lungs
- Around the heart
- Around abdominal organs
- Facilitates movement of organs
- Barrier function



Mesothelioma is a genetic disease

- Mesothelioma is a disease of genetic loss

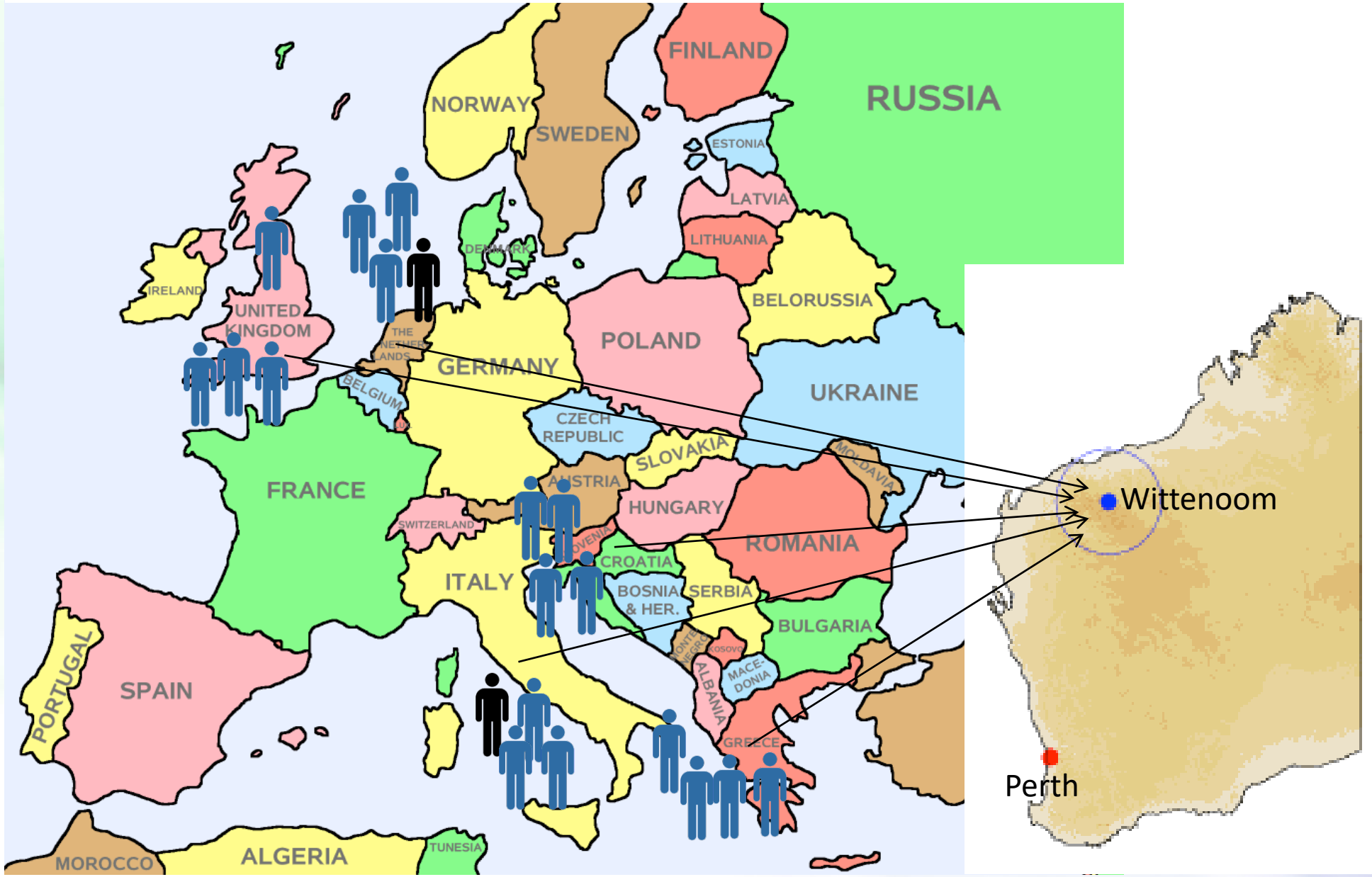


- Mesothelioma develops in a minority of asbestos exposed individuals

Why do some people develop mesothelioma while others don't?

Does your genetic makeup influence mesothelioma development?

How to link genes to mesothelioma risk?



Genetic factors associated with mesothelioma risk

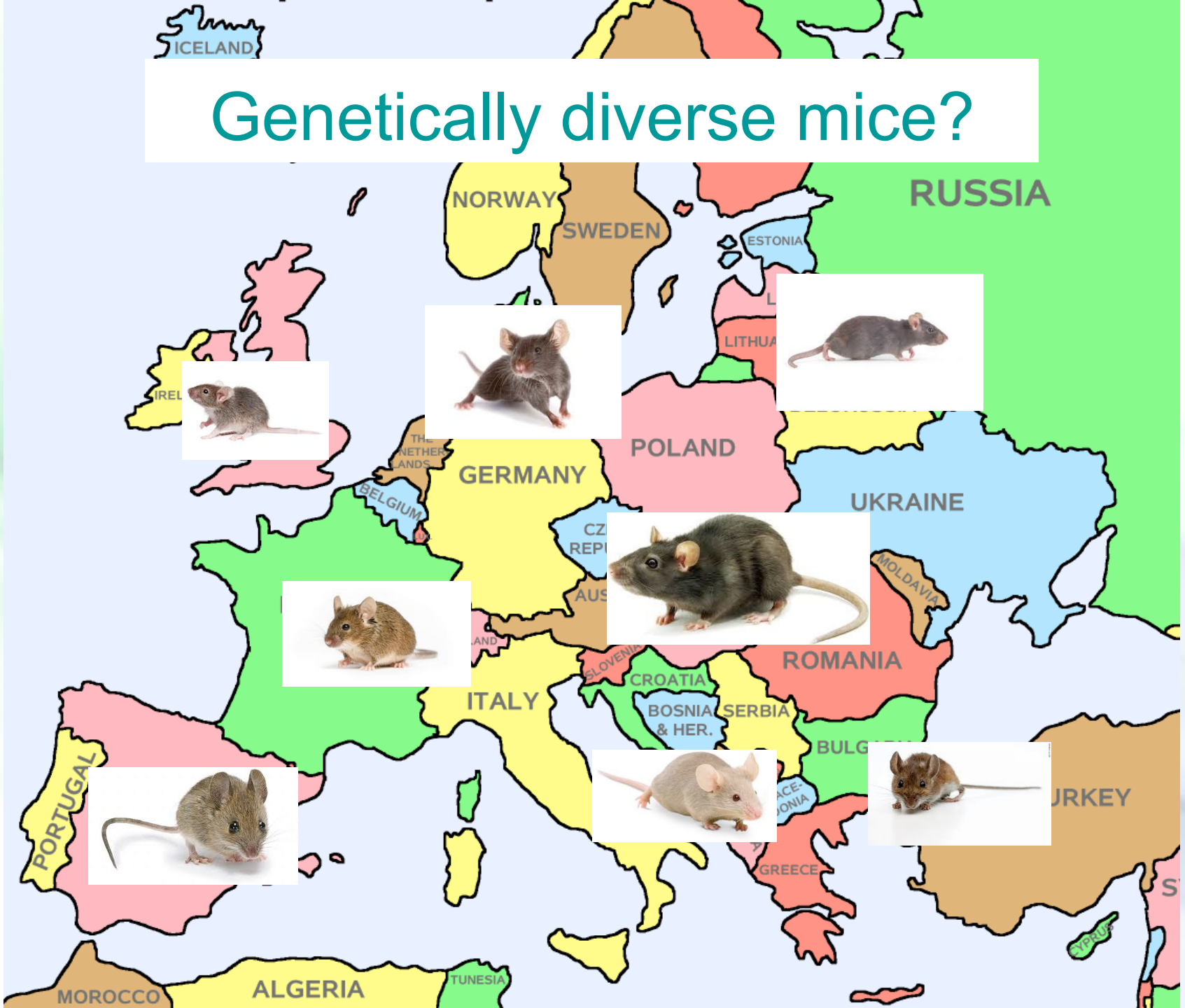
- Mesothelioma GWAS studies not consistent
  - Cadby *et al., Lung Cancer 82 (2013) 1–8:*
  - Betti *et al., Mutation Research 708 (2011) 11–20:*
  - Dianzani *et al., Mutation Research 599 (2006)*
  - Ugolini *et al.,* Mutation Research 658 (2008) 162–171*:*

- Confounding factors:
  - sequencing platforms, modest sample size
  - likely modest effects of these genes on mesothelioma risk

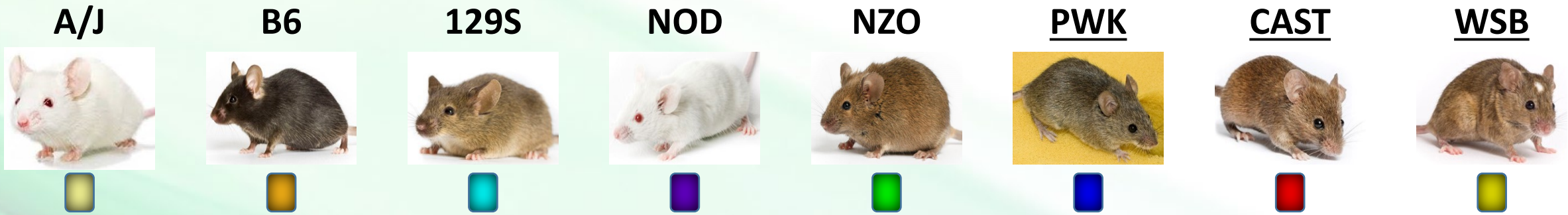
- modifier genes / biological pathways remain unknown

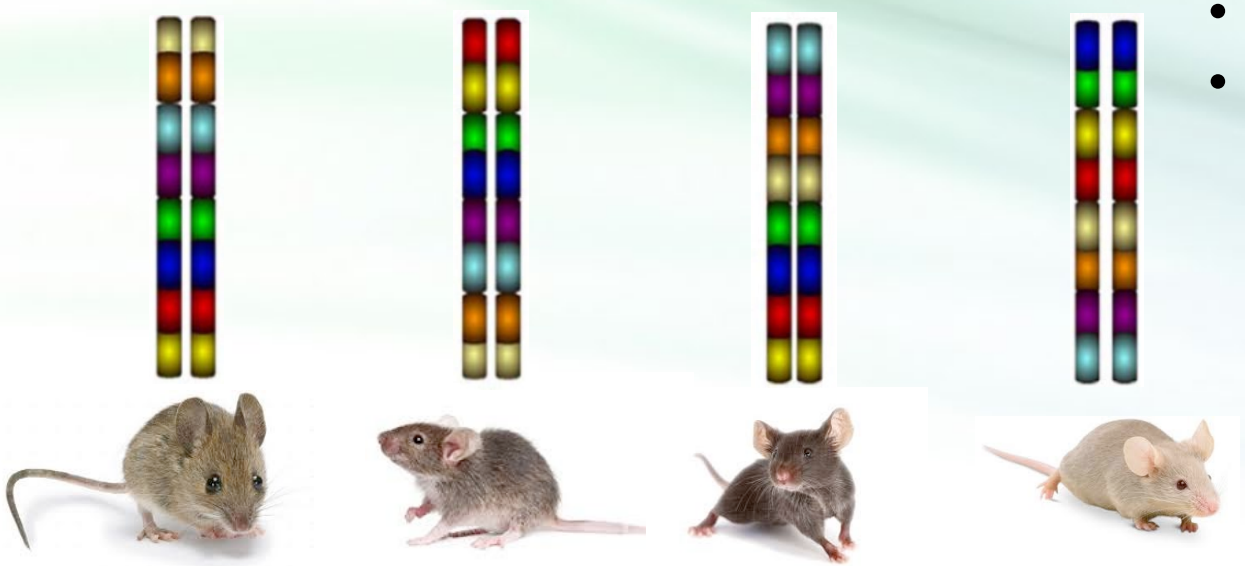
How do we get around this problem?

Genetically diverse mice?



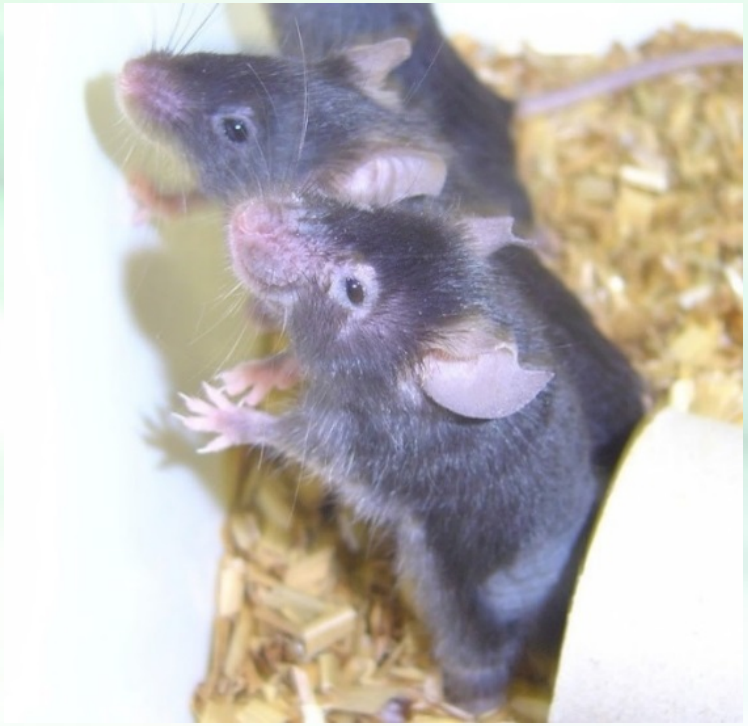
The Collaborative Cross (Gene Mine)

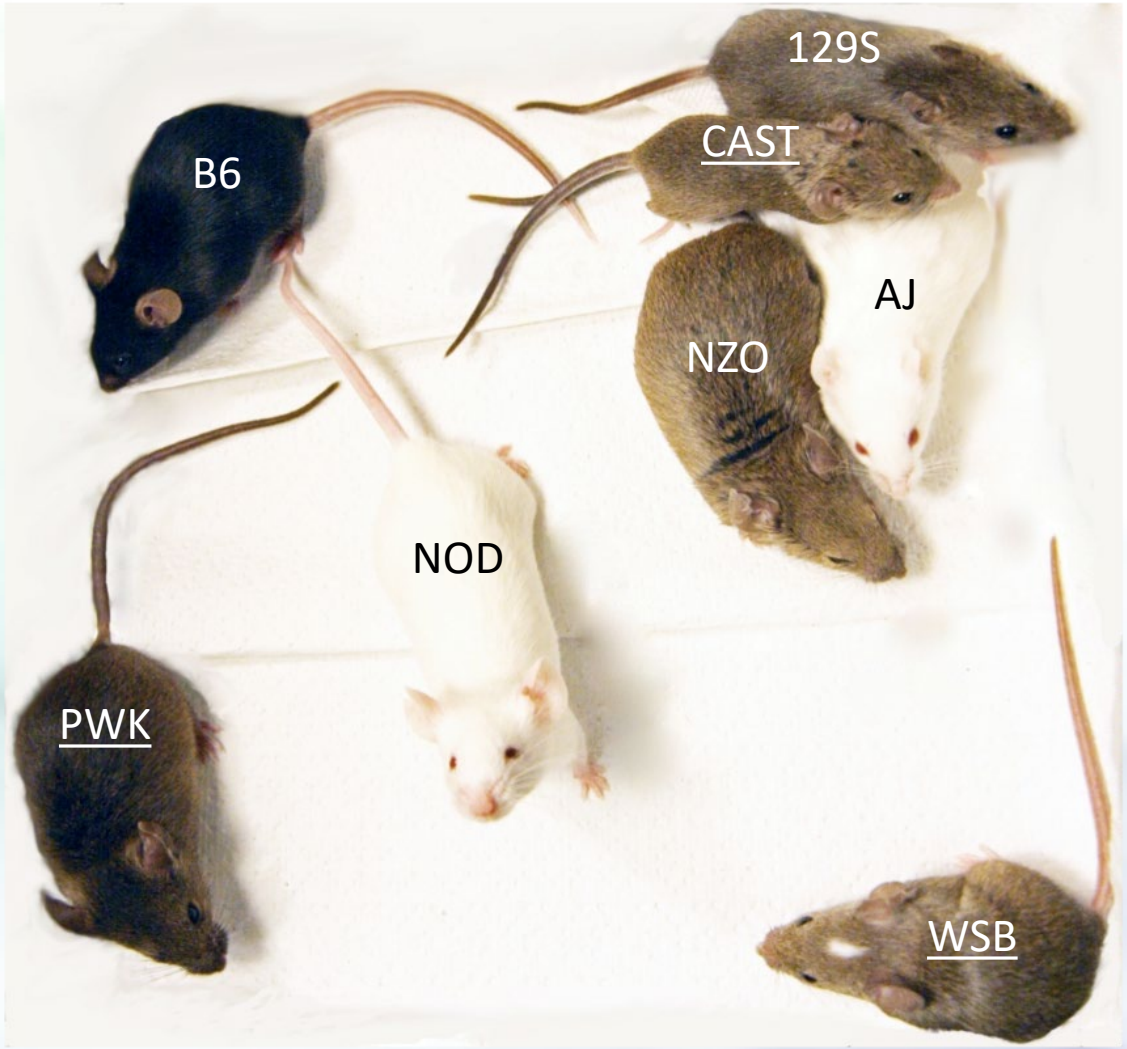




- 100 x CC distinct strains >90% allelic diversity
- Genetically stable, controlled reference population
- Founder and CC strains fully sequenced
- Imputation of allele sequences
- Unprecedented mapping resolution (~40kbp)

The MexTAg Collaborative Cross

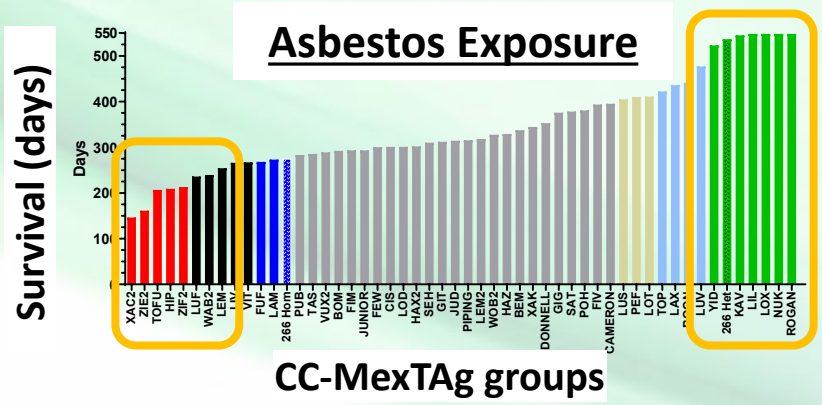




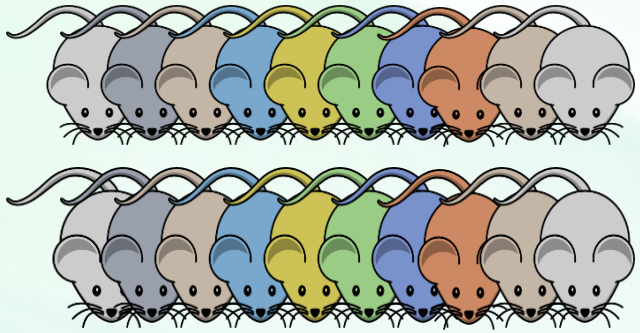
Identifying modifier genes associated with mesothelioma

CC-MexTAg study design

Study 1
Genomic analyses



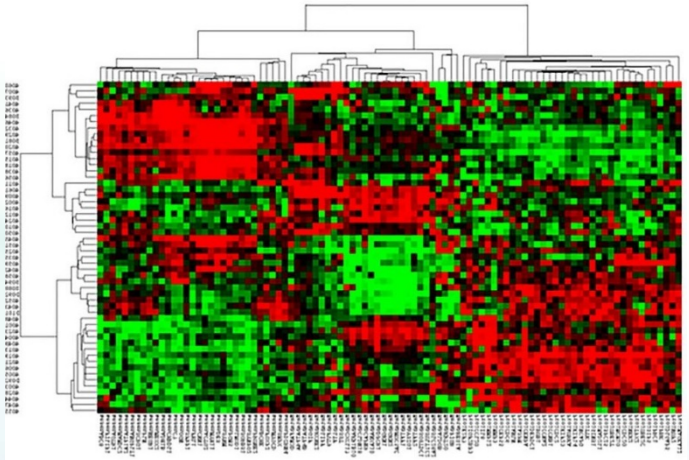
CC-MexTAg model



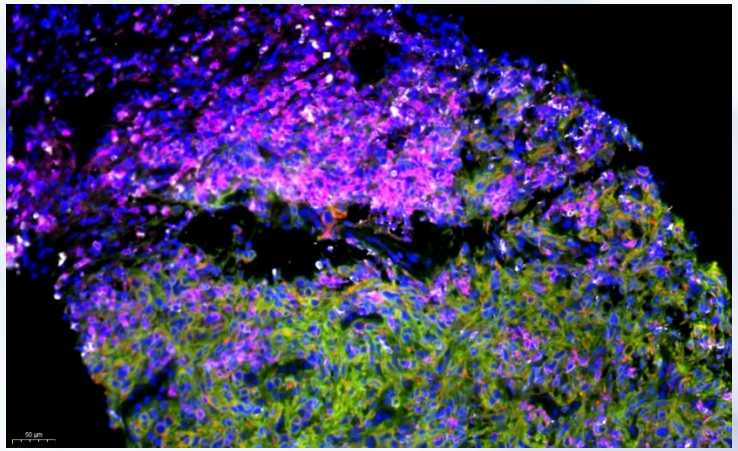
CC-MexTAg strains (n=74)

Study 2
Transcriptomic analyses

Tumour gene expression profiling



TME Immunofluorescence



Analysis

CC Genotype-mesothelioma phenotype correlation

↓

Genes identified

↓

Interrogate human datasets

Biological samples

tumour samples
ascites cell lines
tumour cell lines
histology samples

CC-MexTAg study stats

58/75
(77%)

50/58
Complete data

7
On study
(18 months/group)

125 Tumours

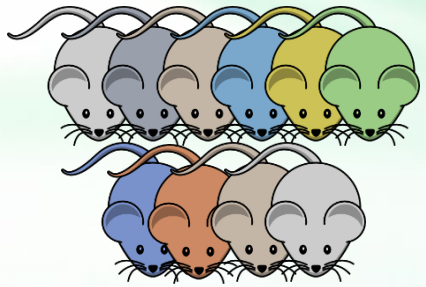
65 Tum cell lines

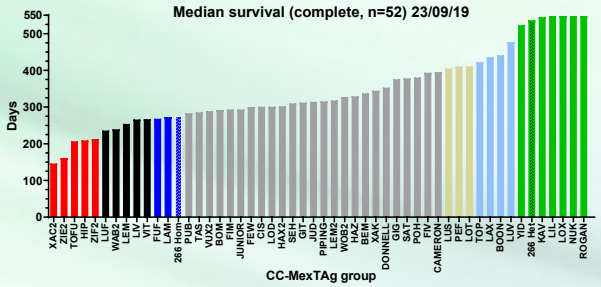
17
Breeding
(2-3 months)

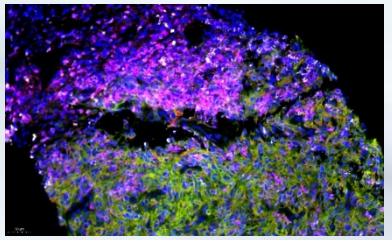
645 ascites cell lines

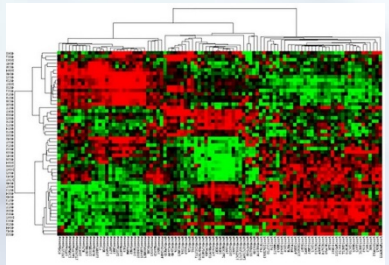
1898 histology

Asbestos exposed
CC-MexTAg groups



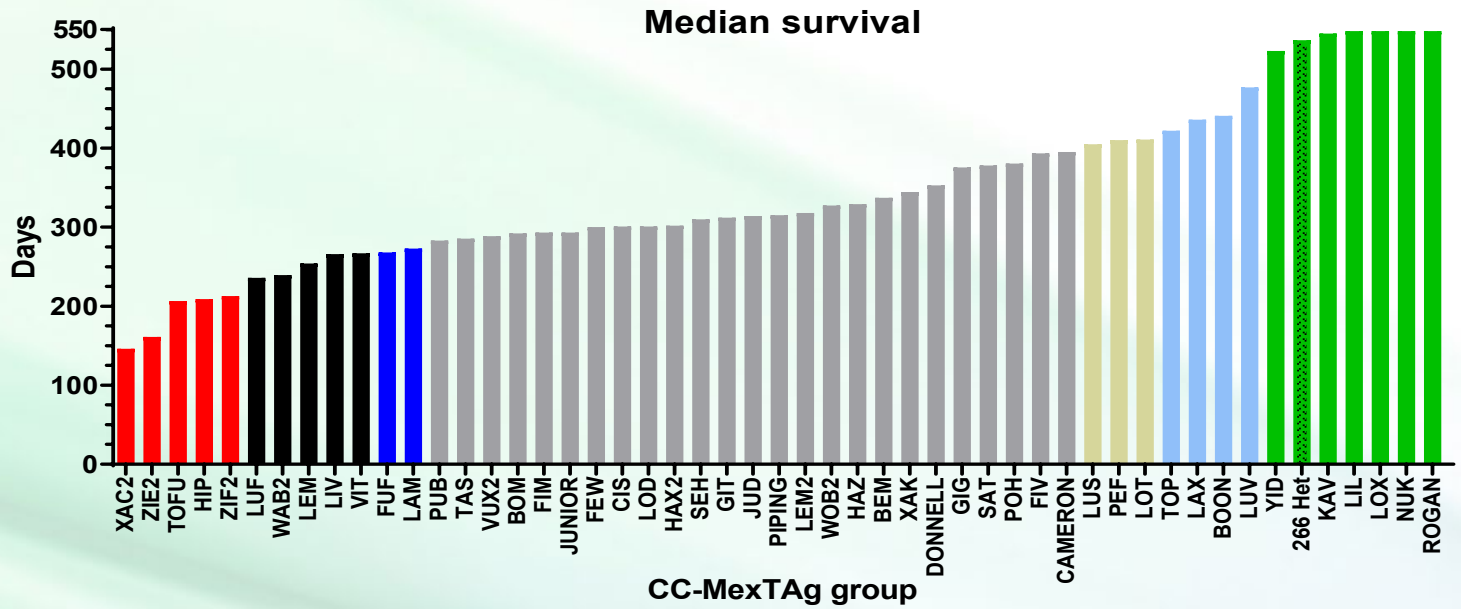


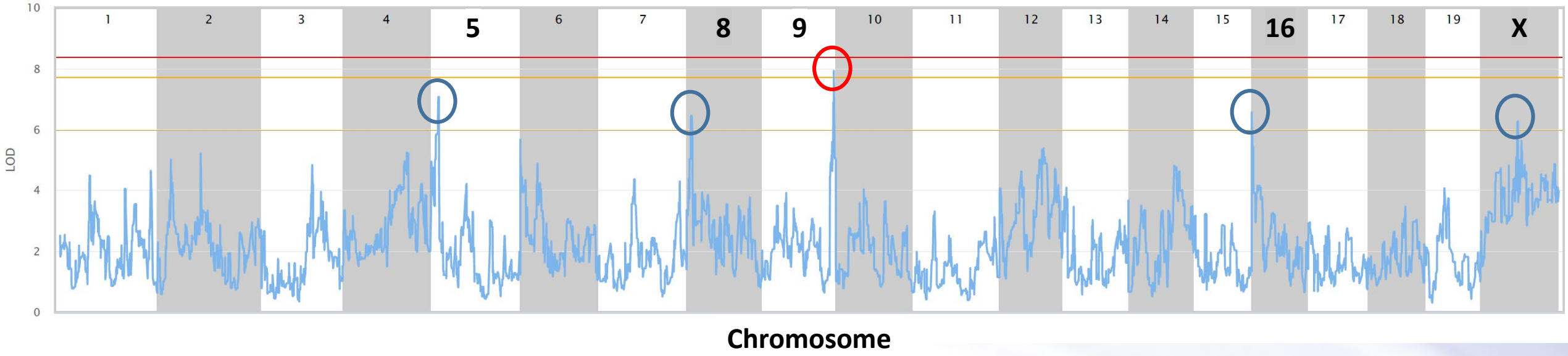




Program started 20/01/16 (~3.8 yrs)

Proof of concept: Host genetics affects ARD in CCMT





CC-MexTAg Program: Overall Summary

- Systems genetics approach to identify modifier genes and their biological pathways associated with asbestos related disease
  - Part I: 75% complete
  - Part II: just beginning …
- Comprehensive genetic and phenotypic analysis of CCMT samples correlated with disease outcome
- Understand how host genetics affects asbestos related disease

Acknowledgements

icare dust diseases care

Congressionally Directed Medical Research Programs
CDMRP
Department of Defense

Australian Government
National Health and Medical Research Council
NHMRC

National Centre for Asbestos Related Diseases
an Australian Research Cooperative

CC-MexTAg Team

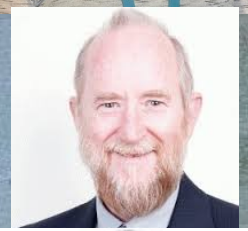
Richard Lake **Kimberley Burton**
Grant Morahan Raphael Bueno
Sylvia Young Joost Lesterhuis
Anna Nowak Kiarash Behrouzfar

NCARD Team

Bruce Robinson
Jenette Creaney

Special help

Tracy Seymour
Emma Port
Nathan Eckhardt



Thank You

Early registration closes 18th December 2019

iMig2020
MARCH 25 - 28, 2020
BRISBANE, AUSTRALIA
www.iMig2020.org

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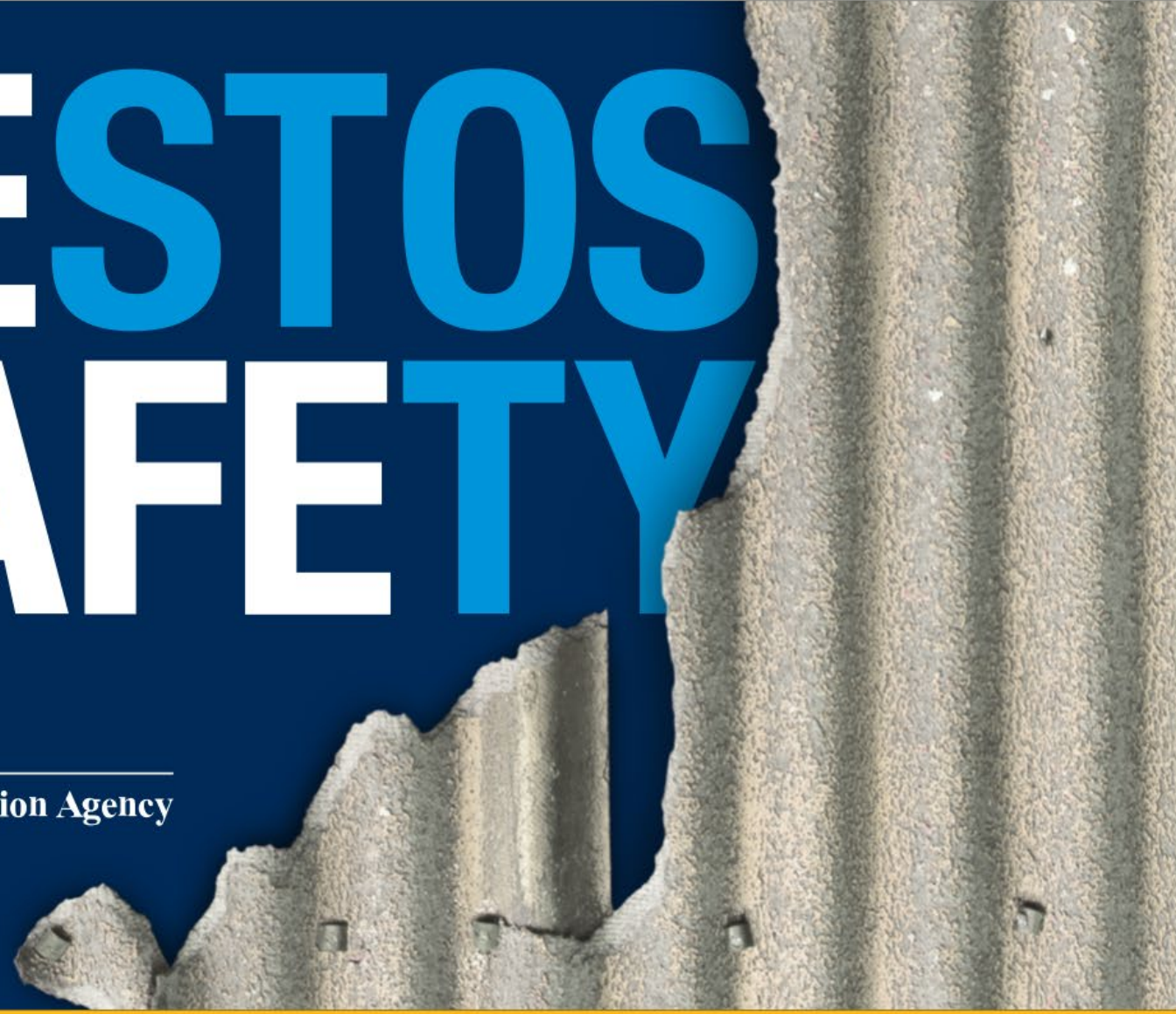

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Role of immunotherapy in treatment of malignant mesothelioma

Melvin Chin

Medical Oncologist - Sir Charles Gairdner Hospital
PhD candidate - National Centre for Asbestos Related Diseases

QUESTIONS: www.slido.com #ASEACONF2019

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Background

- Immunotherapy treatment is an additional line of treatment in multiple cancers such as melanoma and lung cancer
- Immunotherapy works in a different way to chemotherapy, by stimulating the immune system to attack cancer cells
- Immunotherapy is an active area of medical research in mesothelioma because it potentially affords more treatment options to patients

Topics to discuss

- Two recent clinical trials in mesothelioma

- Will discuss three aspects of each study:
  1. the study design,
  2. the results, and
  3. the interpretation

- Future directions and unanswered questions

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DREAM: Phase II Trial of First-line Combination Durvalumab Plus Chemotherapy in Advanced Mesothelioma

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DREAM: study design

- Phase II trial – 52 patients
- First-line treatment for patients with malignant pleural mesothelioma
- All patients received initial chemotherapy with immunotherapy, followed by maintenance immunotherapy for up to a year
- Question: Is combination treatment with chemo-immunotherapy superior to chemotherapy alone?

DREAM: results

- Positive trial – patients treated with combination **had a slower time to disease progression than those with chemotherapy alone**
- **More shrinkage of tumour with combination treatment as compared to chemotherapy alone**

DREAM: interpretation

- Opens the possibility for a Phase III study in a larger patient population

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Promise-MESO: Pembrolizumab immunotherapy versus standard chemotherapy for advanced pre-treated malignant pleural mesothelioma

Promise-MESO: study design

- Phase III trial – 73 patients
- Pre-treated malignant pleural mesothelioma
- Randomised to either to immunotherapy or chemotherapy
- Question: Is immunotherapy superior to second-line chemotherapy in patients who have received prior treatment for their mesothelioma?

Promise-MESO: results

- Negative trial
- Did not show that immunotherapy was superior to chemotherapy in the second-line setting

Promise-MESO: interpretation

- Both immunotherapy and chemotherapy are reasonable options in second line treatment
- Choice of treatment can be tailored to the patient – cost, physical fitness and patient preference come into consideration

Future directions and unanswered questions – two important research issues

- The effectiveness of first-line chemo-immunotherapy needs to be tested in a larger number of patients
- If combination chemo-immunotherapy is effective, what is the optimal sequence of treatments for patients in the second or third line setting?

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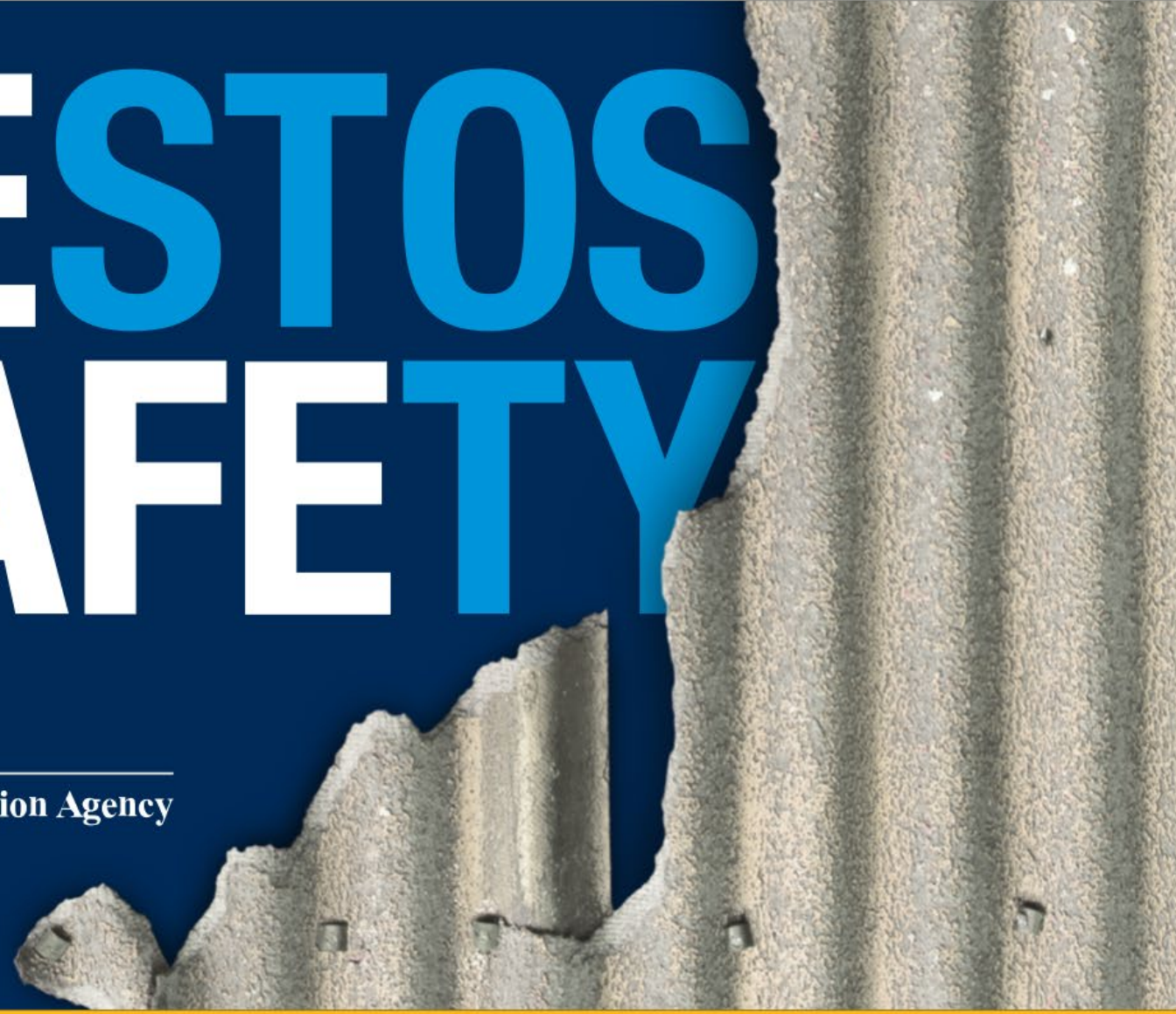

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Clinical Trials in Mesothelioma and Malignant Pleural Disease

Deirdre B Fitzgerald
Clinical Research Fellow
Pleural Medicine Unit, SCGH

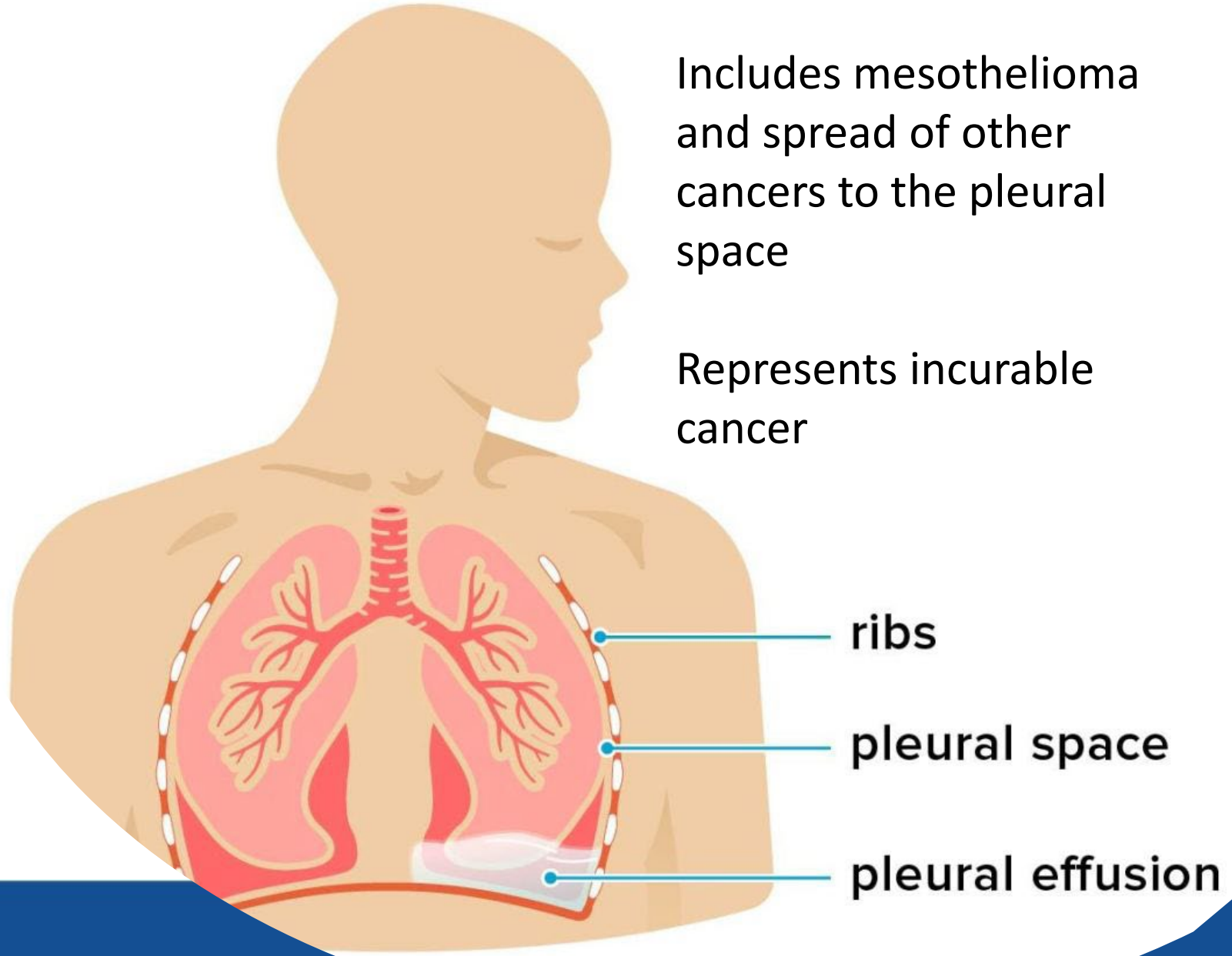
QUESTIONS: www.slido.com #ASEACONF2019

Overview

- Mesothelioma and Malignant Pleural Disease
  - How they affect patients
- Clinical Trials in Malignant Pleural Effusion Management
- Clinical Trials in extra-Effusion Management

Includes mesothelioma and spread of other cancers to the pleural space

Represents incurable cancer



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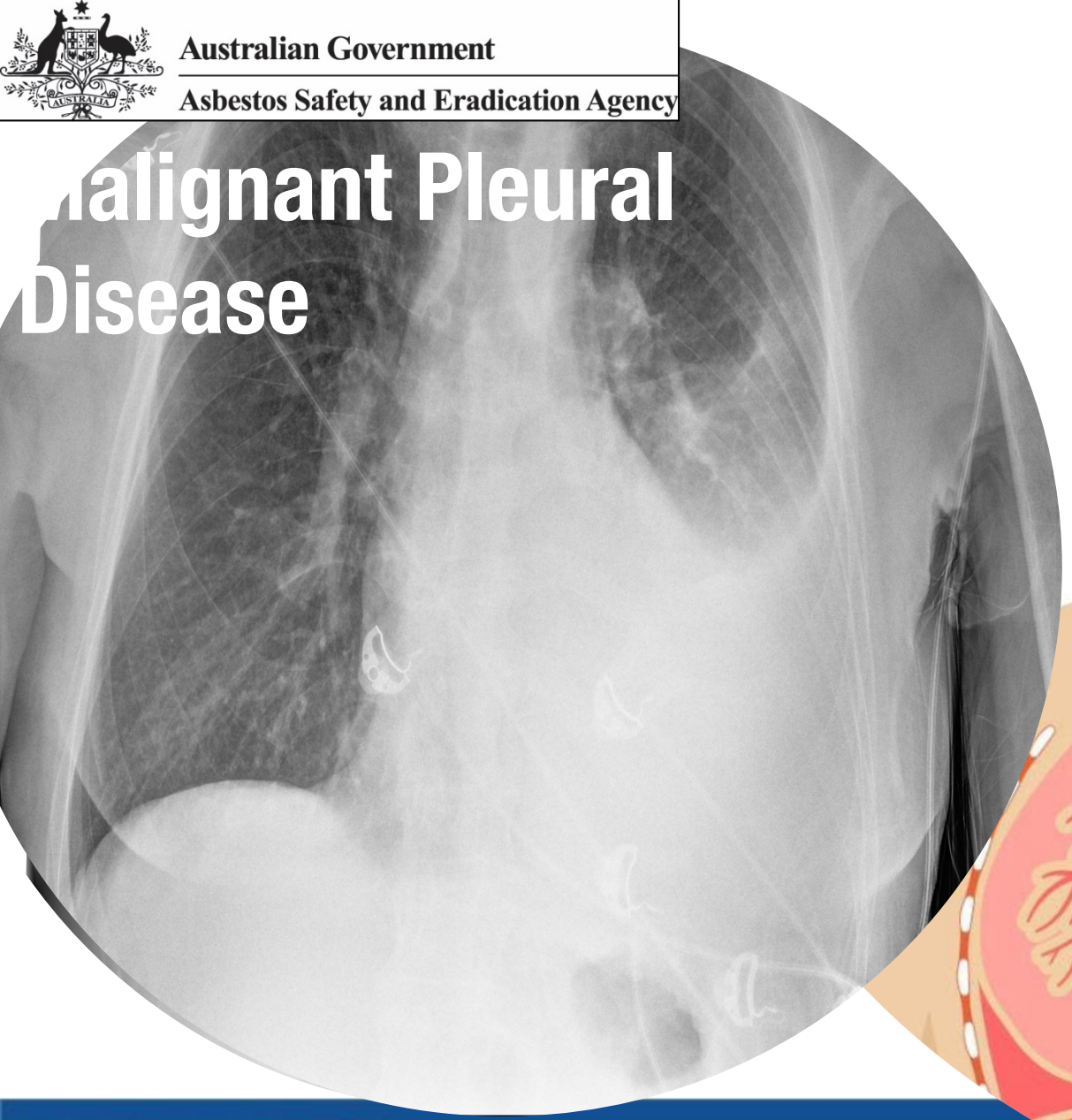
Malignant Pleural Disease



Includes mesothelioma and spread of other cancers to the pleural space

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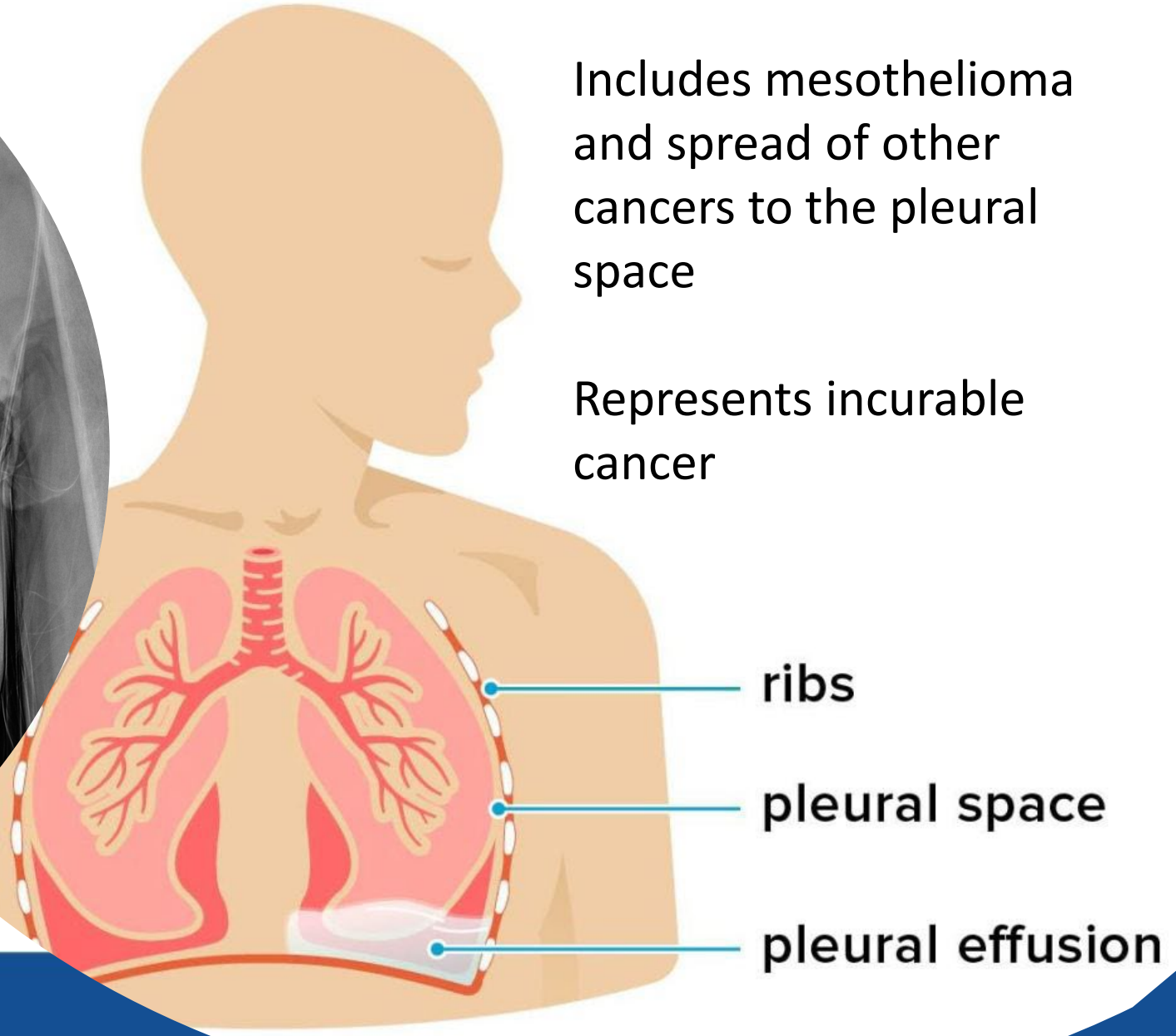

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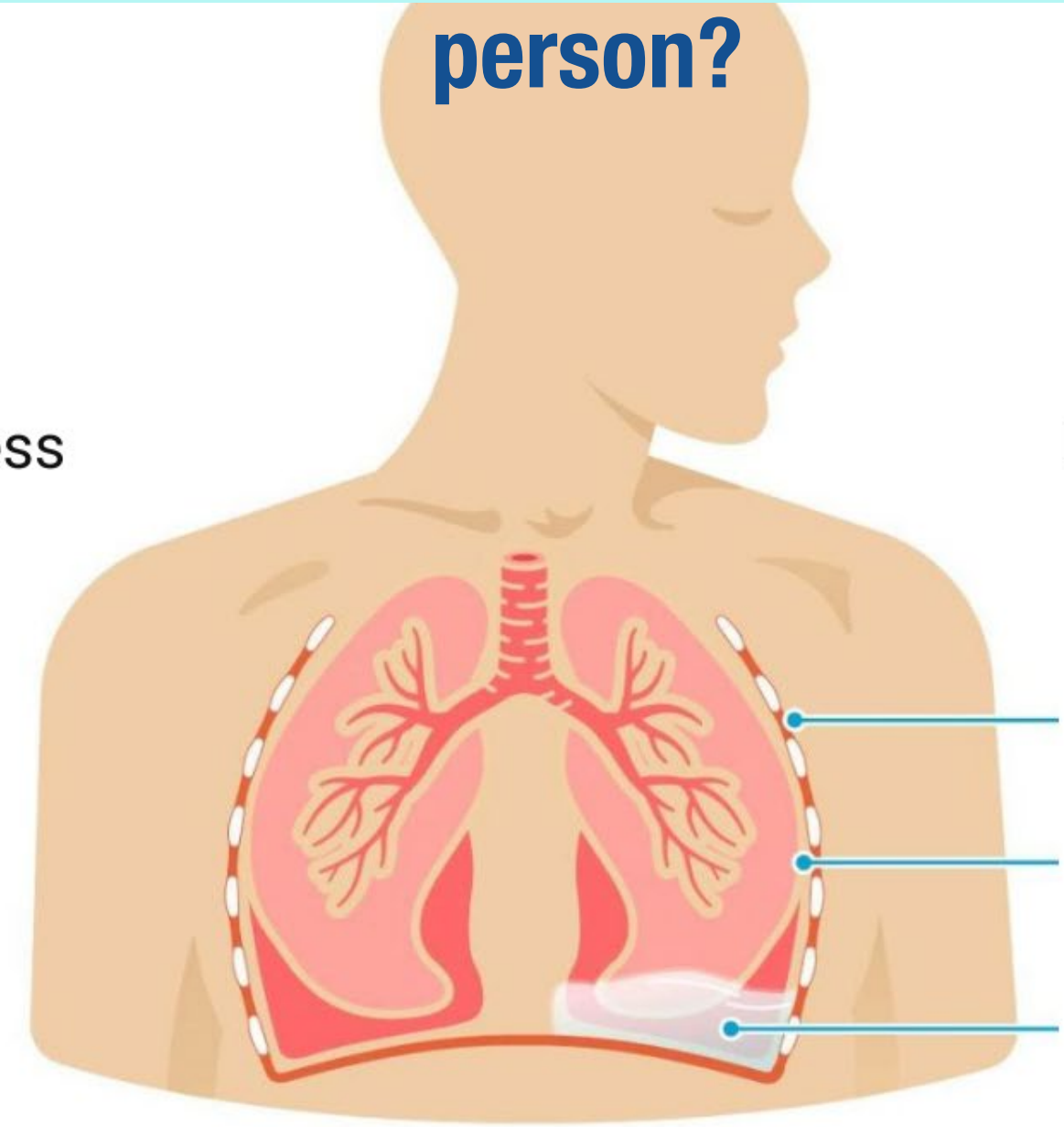
How does malignant pleural disease/effusion affect a person?

Anxiety/Stress

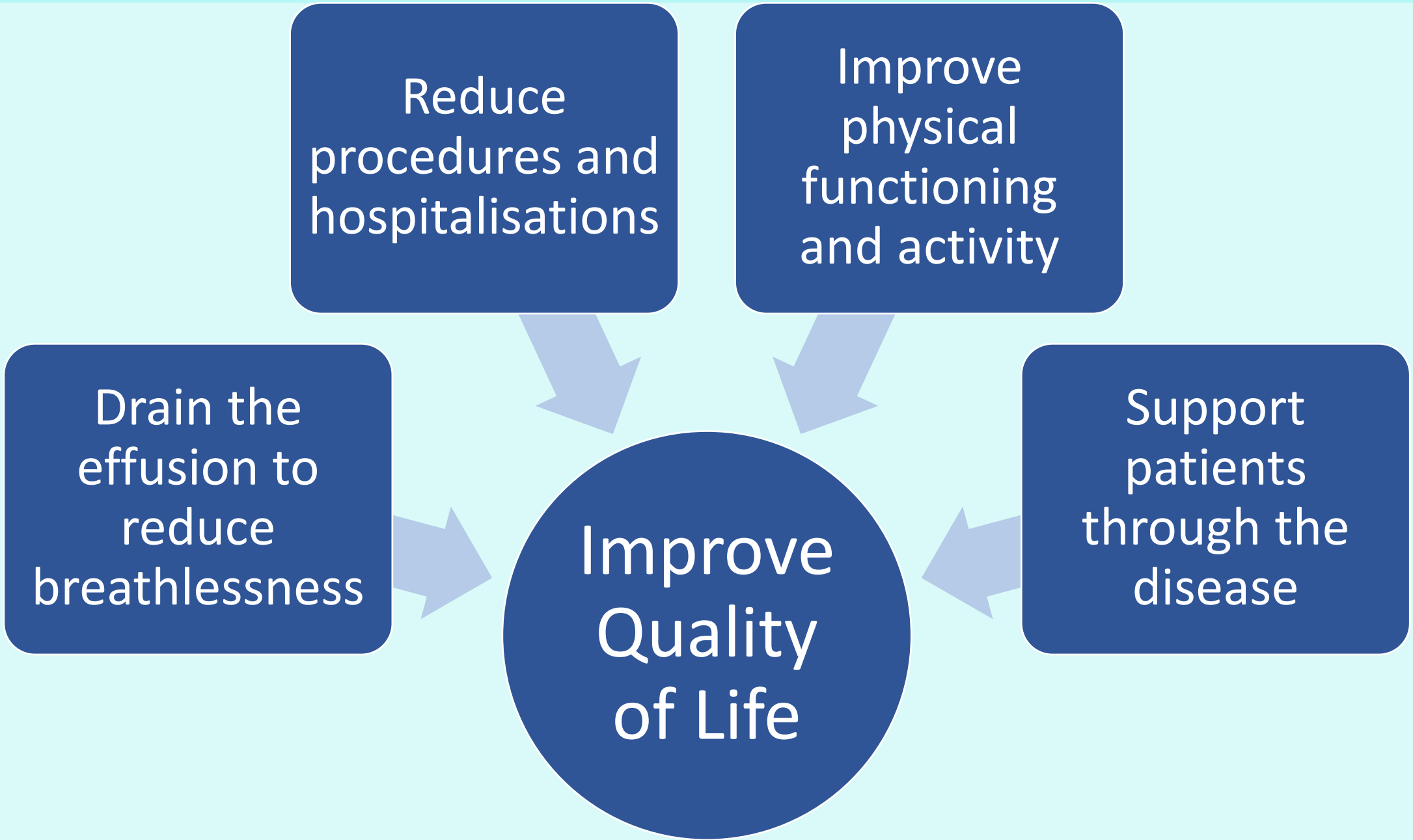
Breathlessness

Procedures

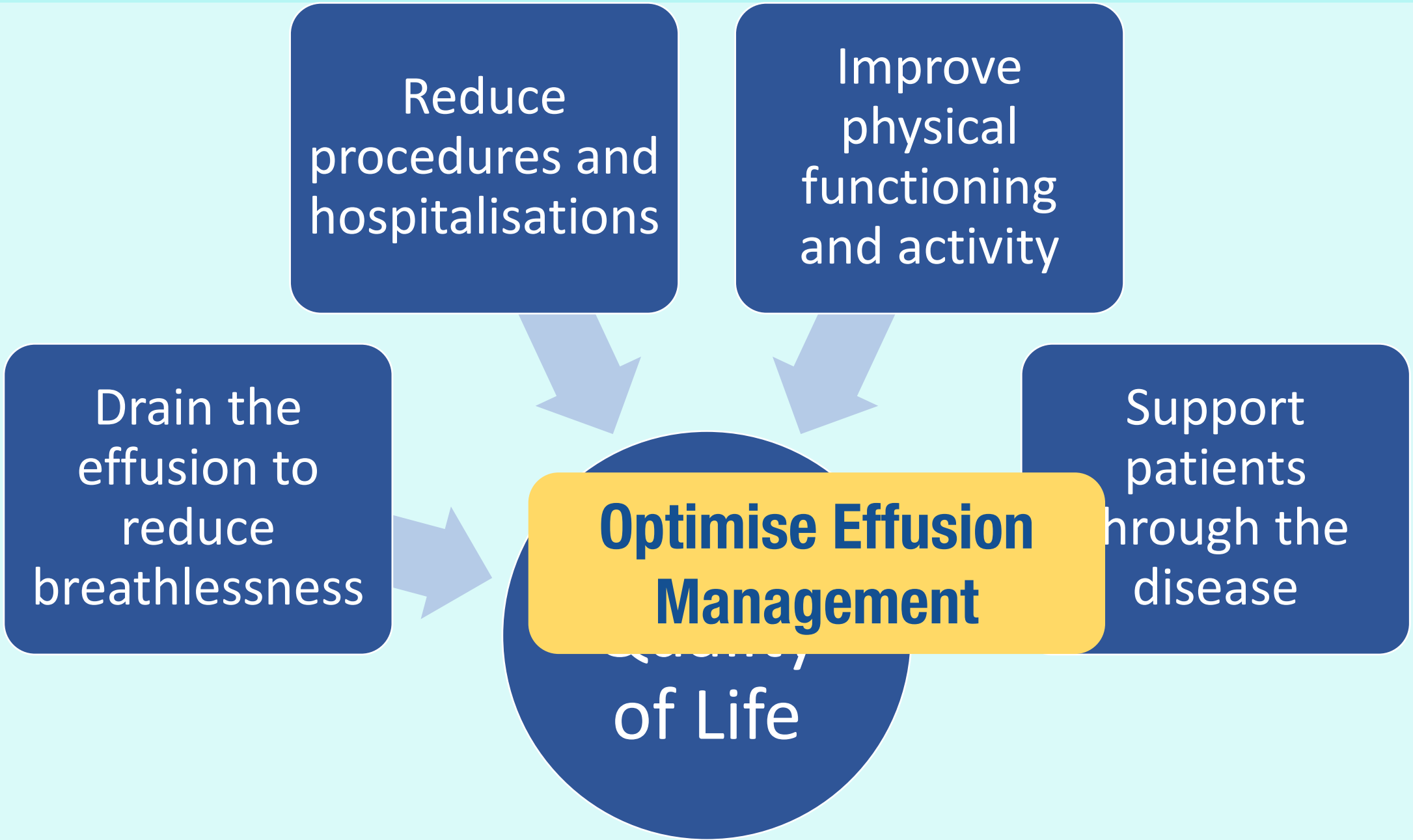
Hospitalisation



Our Goals


Reduce procedures and hospitalisations
Improve physical functioning and activity
Drain the effusion to reduce breathlessness
Support patients through the disease
Improve Quality of Life

Our Goals


Reduce procedures and hospitalisations
Improve physical functioning and activity
Drain the effusion to reduce breathlessness
Support patients hrough the disease
Optimise Effusion Management
of Life

Australasian Malignant PLeural Effusion (AMPLE) Clinical Trial Network

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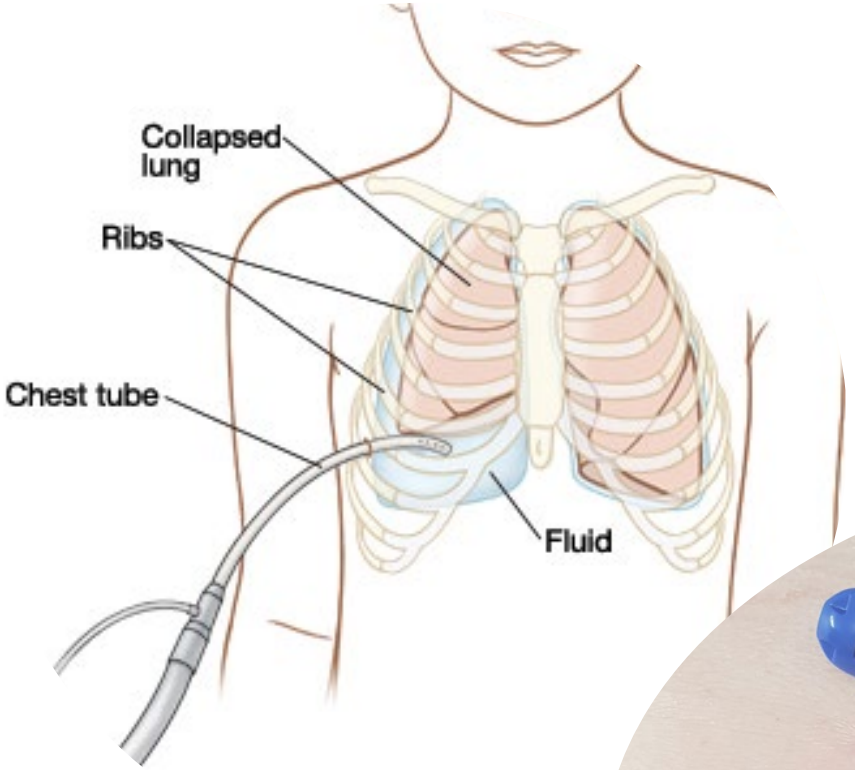
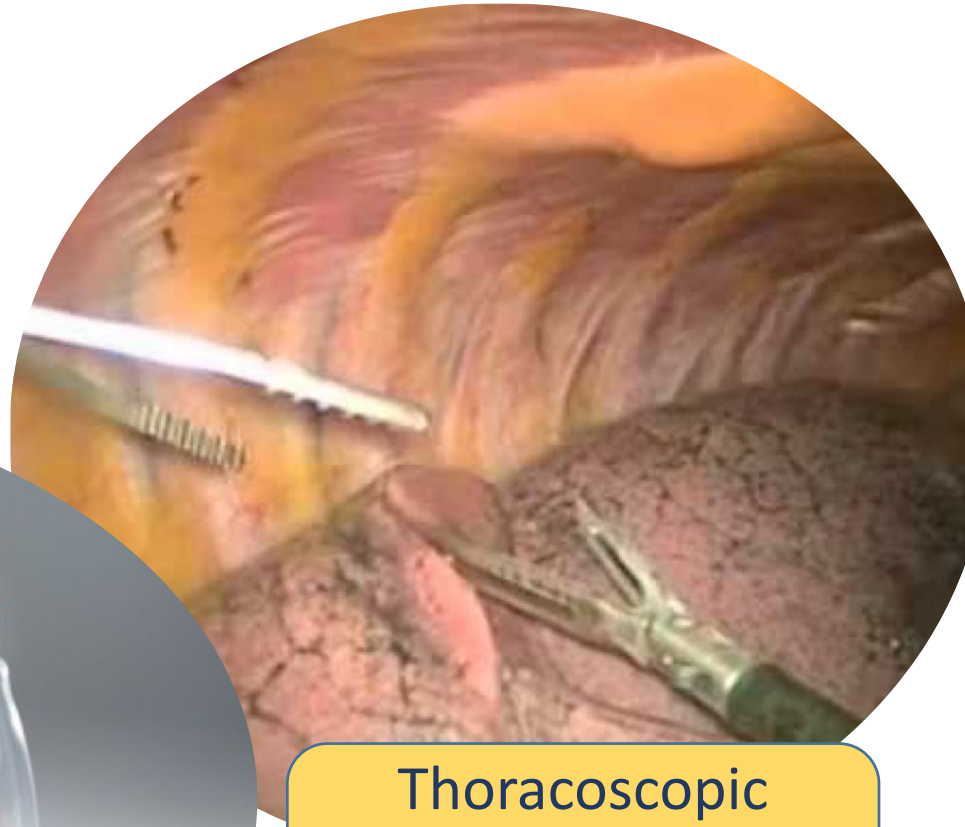


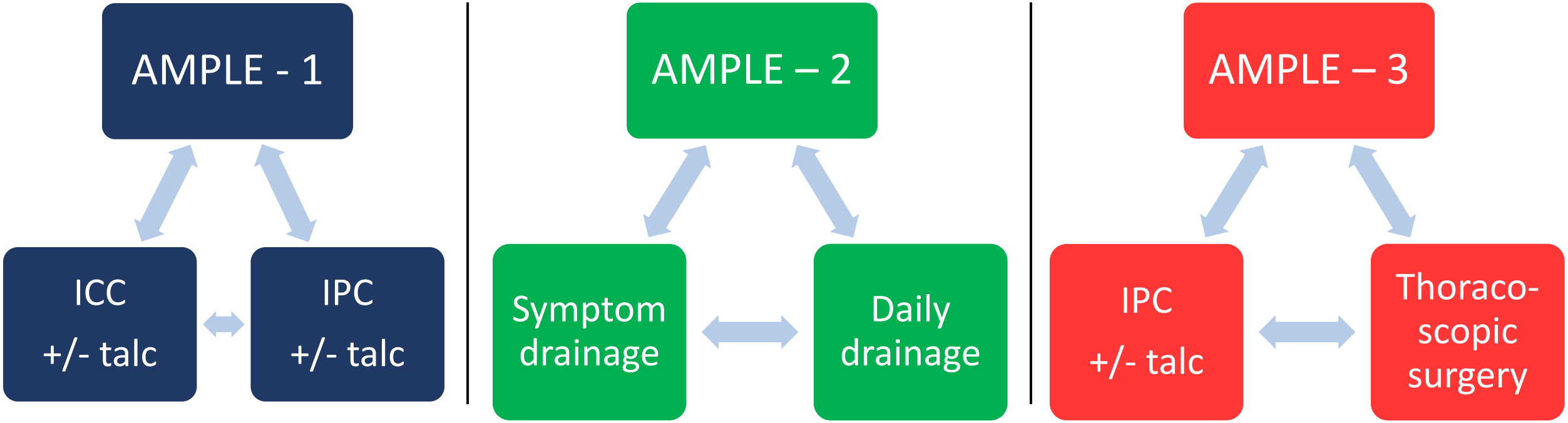
Intercostal catheter
(Chest tube)
+/- talc

Indwelling pleural
catheter (IPC)
+/- talc



Thoracoscopic
surgery
+/- talc

AMPLE Trials

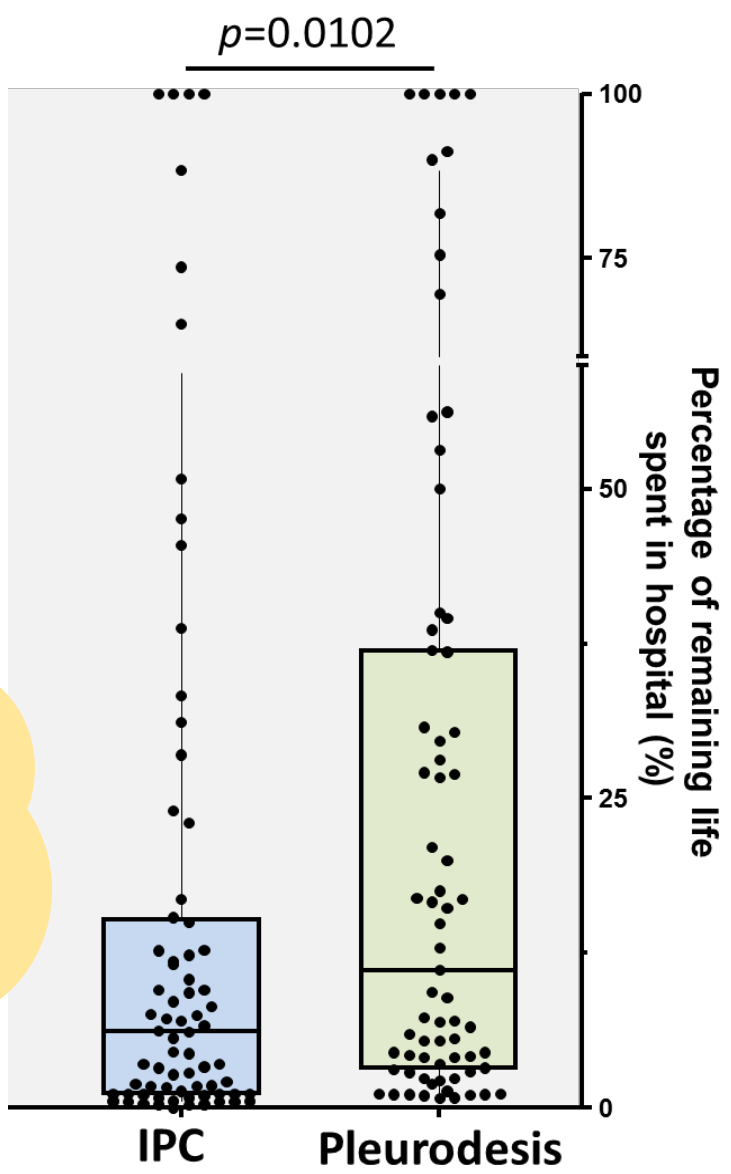


AMPLE - 1

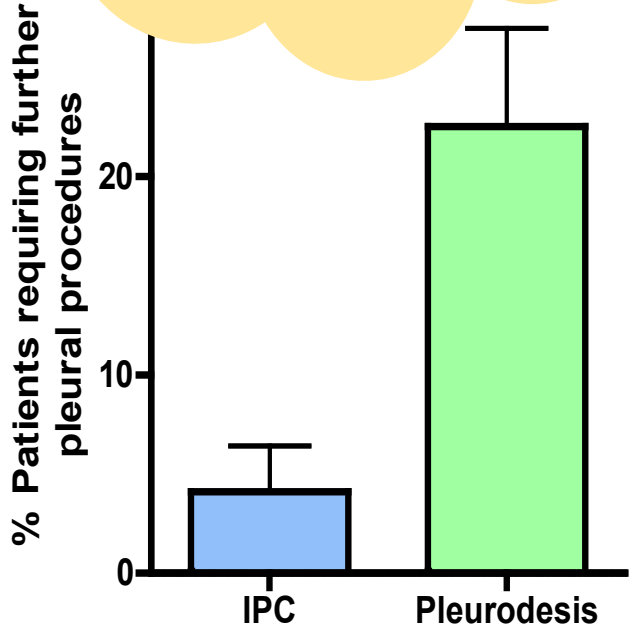
ICC

+/-

IPC reduces the percentage of the patient's remaining life spent in hospital



IPC reduces the number of repeat drainage procedures required

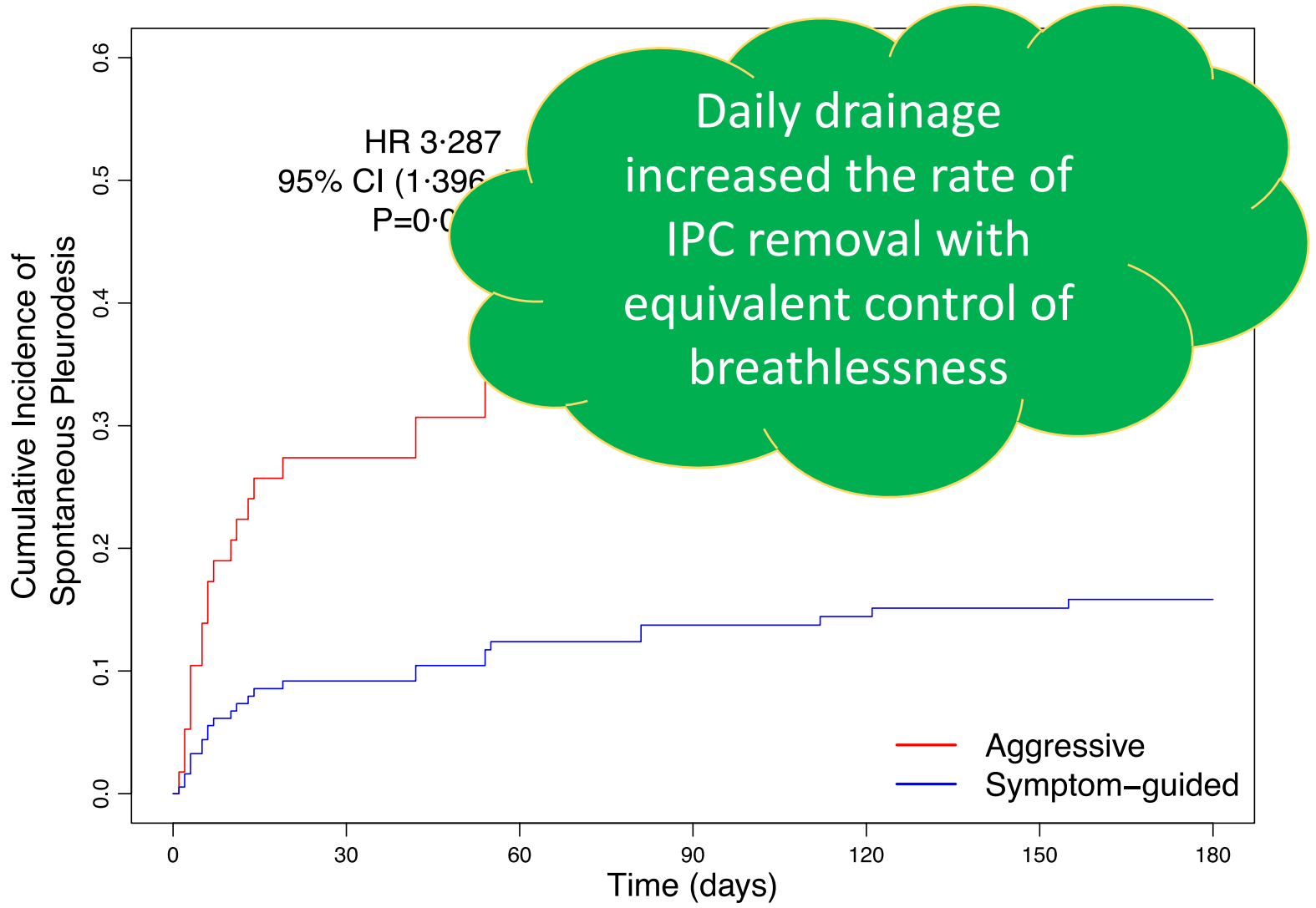


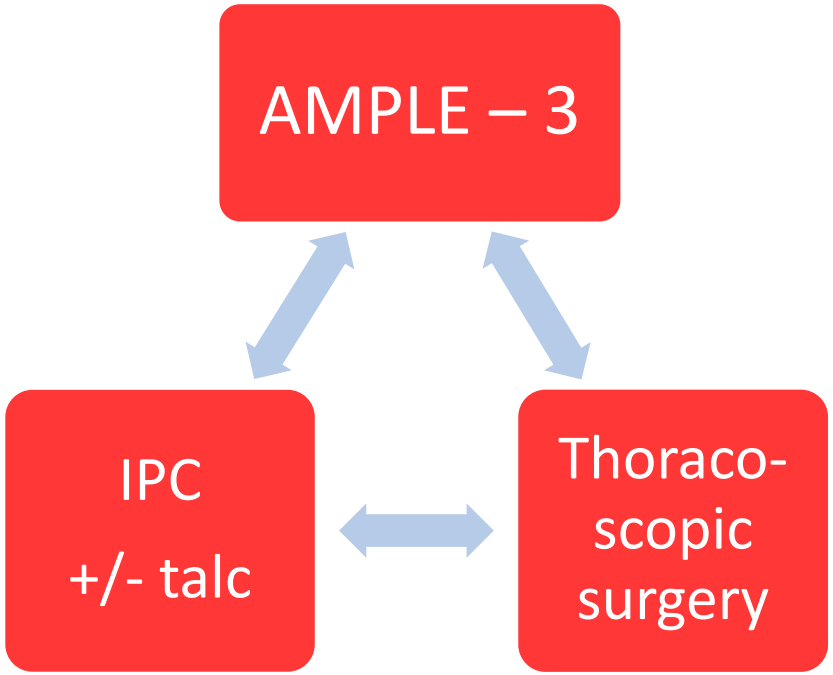
Research
JAMA | Original Investigation

AMPLE – 2

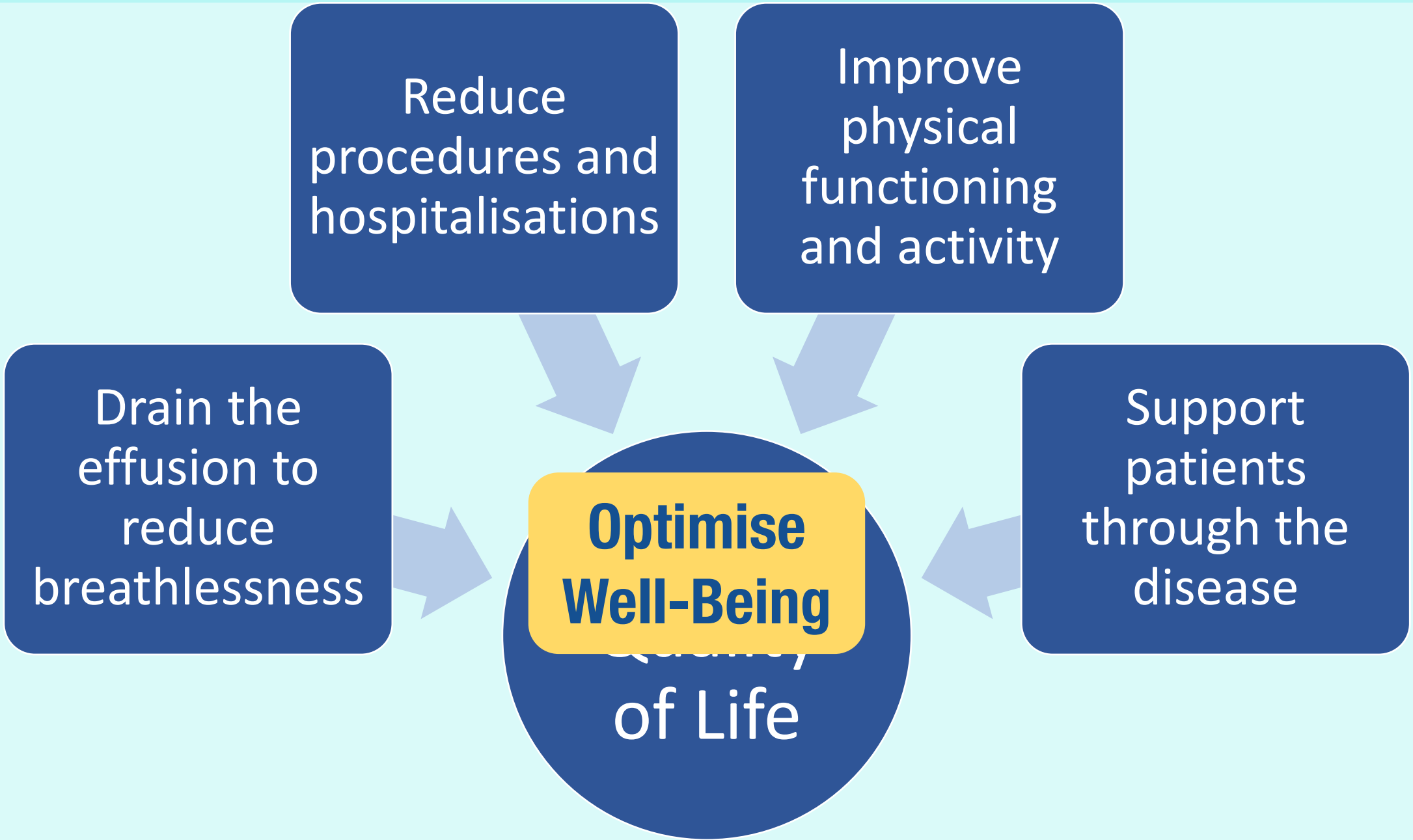
Symptom drainage

Daily drainage




AMPLE – 3
IPC
+/- talc
Thoraco-
scopic
surgery

Our Goals


Reduce procedures and hospitalisations
Improve physical functioning and activity
Drain the effusion to reduce breathlessness
Support patients through the disease
Optimise Well-Being
of Life

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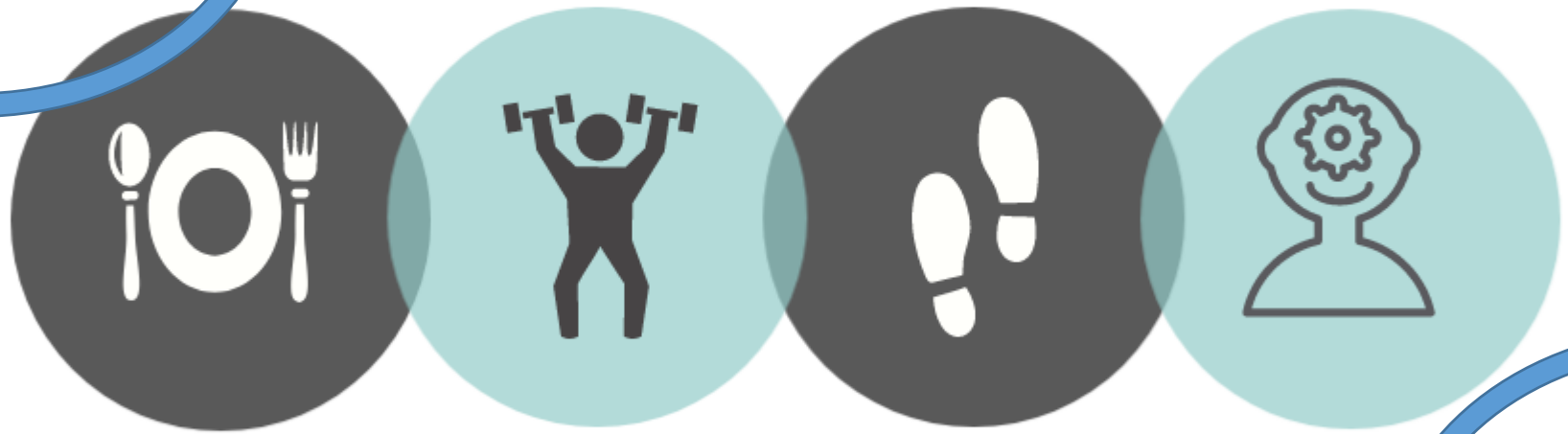
Allied Health Research
Pleural Medicine Unit

Exercise

Improving patient outcomes through exercise medicine

Measuring Phyiscal Activity

Objective measures of activity as clinical trials outcome



Nutrition

Nutritional status composition research

Psychology

psychosocial experiences and needs of people living with mesothelioma

Multidisciplinary Research

Single group pilot study to examine the feasibility and effects of resistance exercise training in patients with malignant pleural disease

Week 0

Baseline Assessment

Exercise intervention

Resistance exercise training

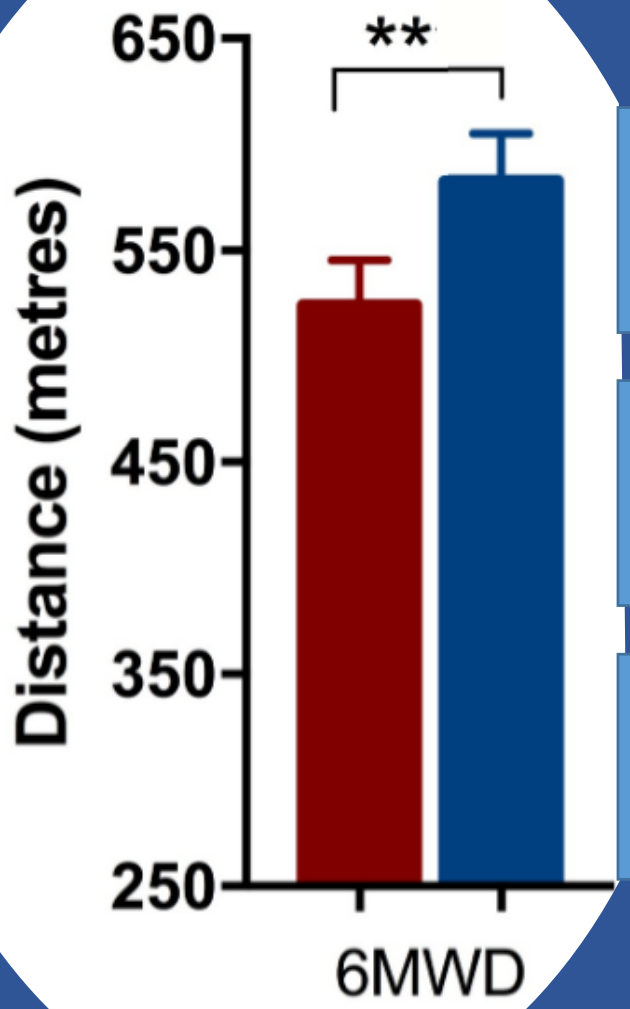
Three times a week for 6 weeks

Week 7

Post Intervention Assessment

Changes in functional capacity

Distance walked in six minutes



- ✓ Significantly increased walk distance
- ✓ Increased by 59m, 11% (p=0.002)
- ✓ Clinically meaningful change >42m

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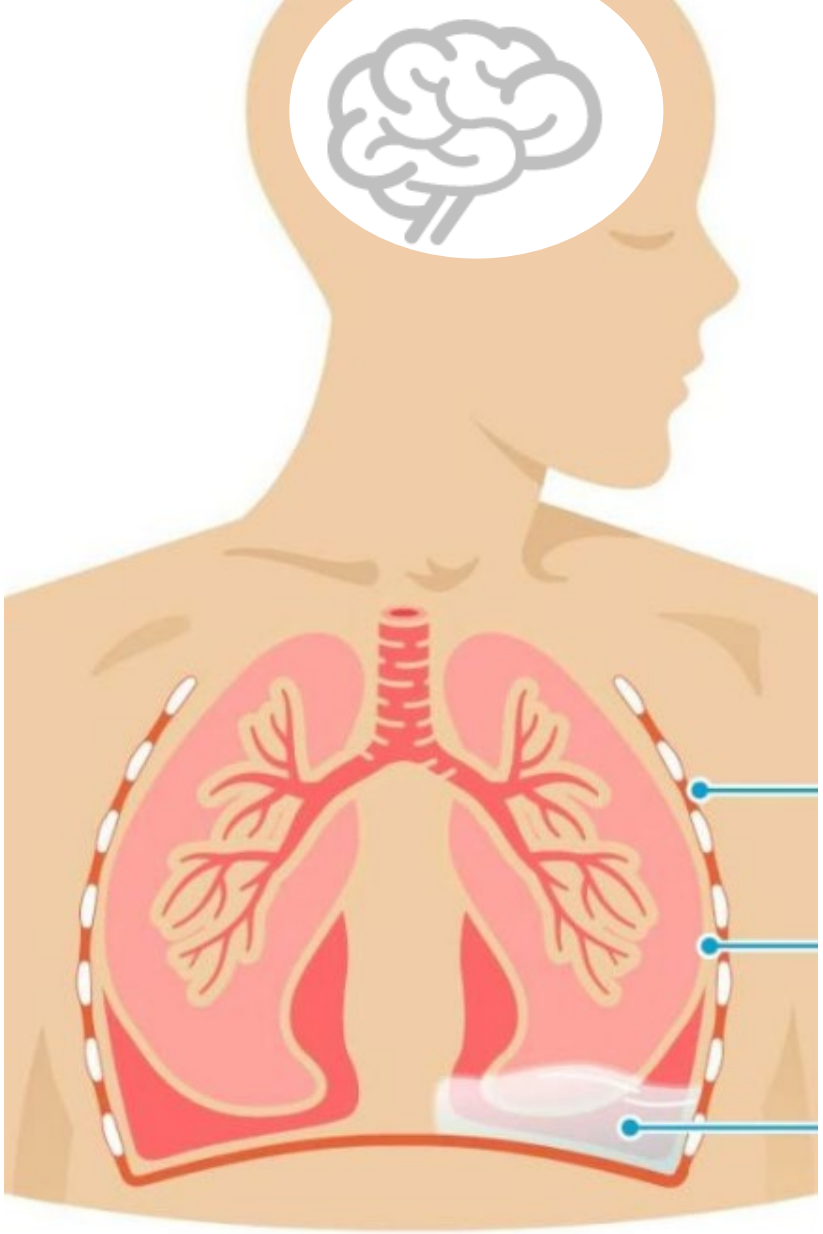
EXPAND
The Psychosocial Experience, Needs and Priorities of Care for People Living with Mesothelioma and their Family Members/Carers

Exploratory cross-sectional study, interviewing patients and carers regarding their experiences



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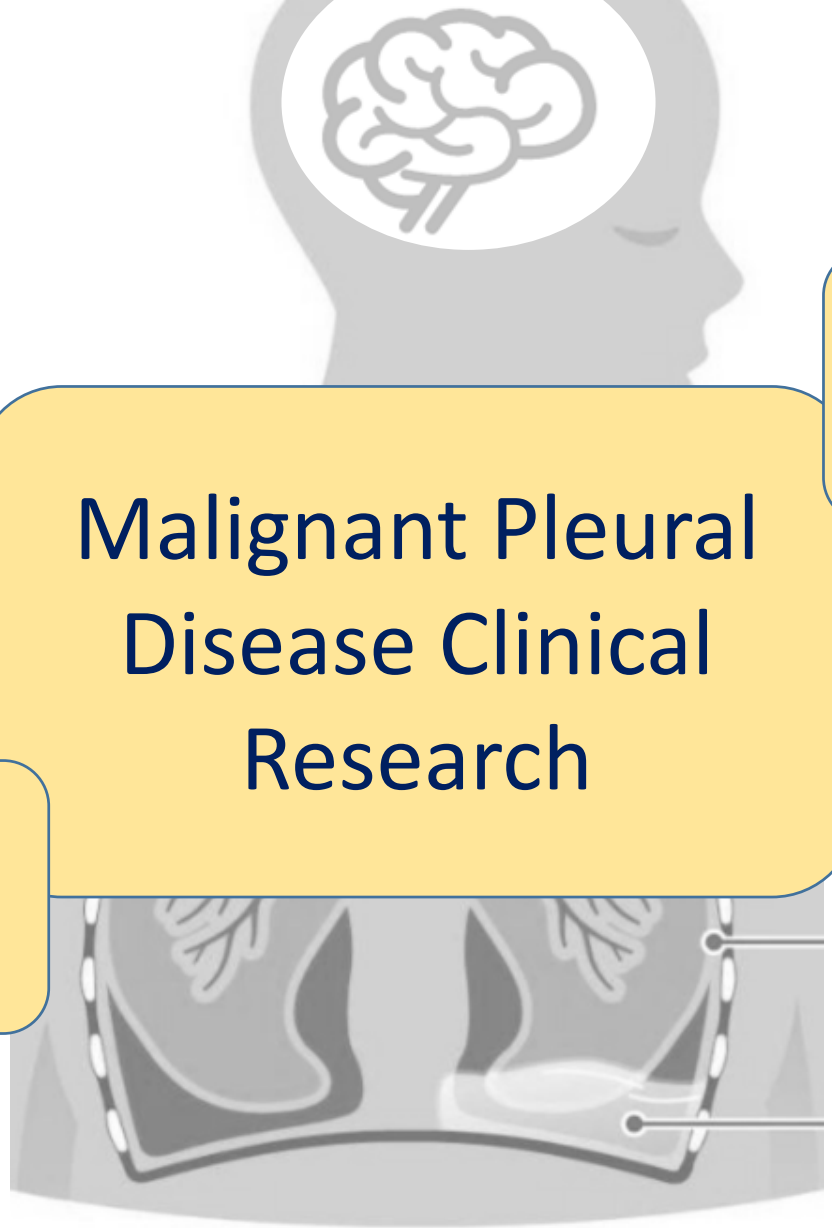

Psychosocial

Malignant Pleural Disease Clinical Research

Physcial

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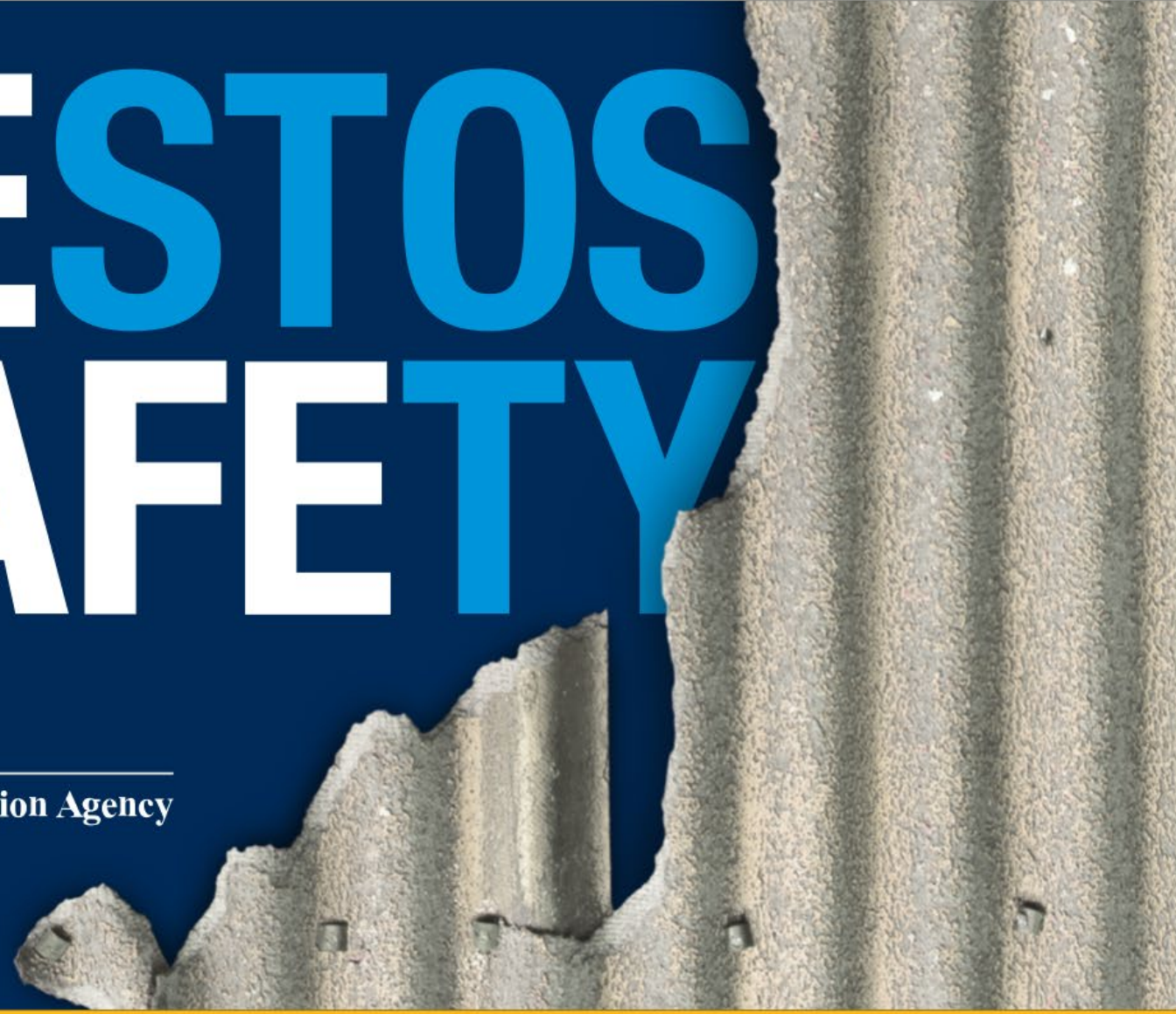

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Australia's response to HIV/AIDS 1982-2019

Bill Bowtell AO

Kirby Institute, UNSW Sydney

Pacific Friends of the Global Fund to Fight AIDS, Tuberculosis, and Malaria

Perth, November 2019

QUESTIONS: www.slido.com #ASEACONF2019

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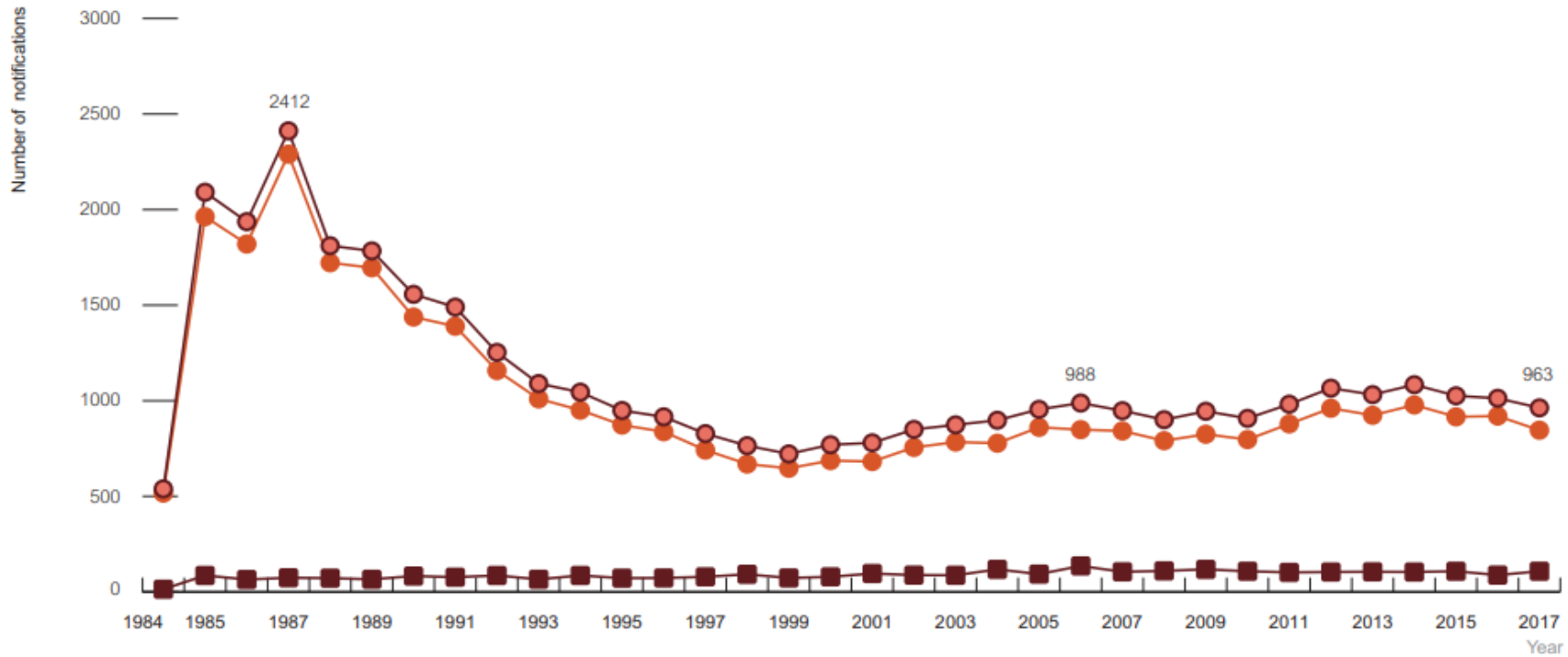
Australian HIV caseload as at end 2017, new HIV diagnoses in 2017, and deaths from AIDS

(Kirby Institute, 2018 and UNAIDS, 2018)

Living with HIV	27,545
New HIV diagnoses in 2017	963
Deaths from AIDS in Australia since 1983	~7,500

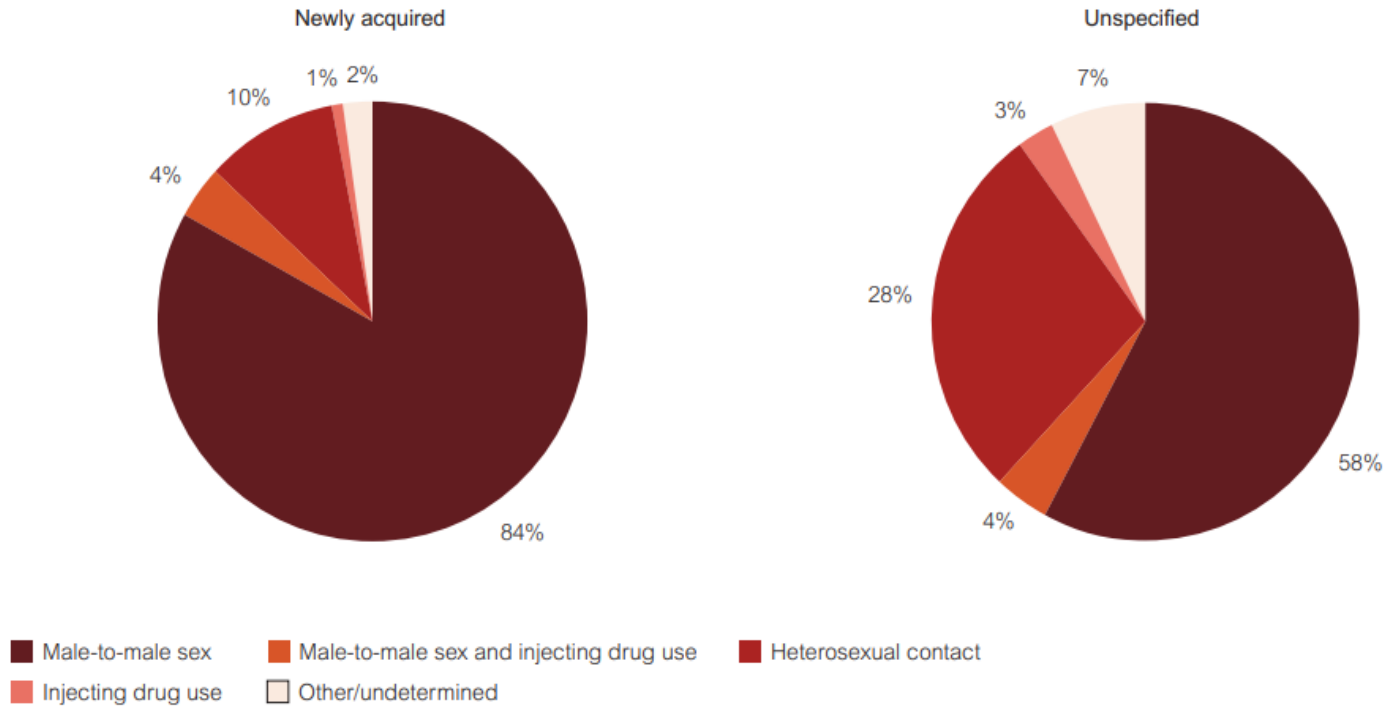
HIV notifications in Australia, 1984-2017, by sex (Kirby Institute, 2018)



	1984	1985	1987	1989	1991	1993	1995	1997	1999	2001	2003	2005	2007	2009	2011	2013	2015	2017
Men	517	1963	2290	1696	1438	1158	951	838	742	647	687	784	861	842	825	879	924	916
Women	14	86	74	66	83	86	86	73	79	73	79	87	93	105	118	102	105	108
Total[a]	539	2091	2412	1784	1557	1253	1045	916	828	722	770	874	955	948	945	982	1032	1026

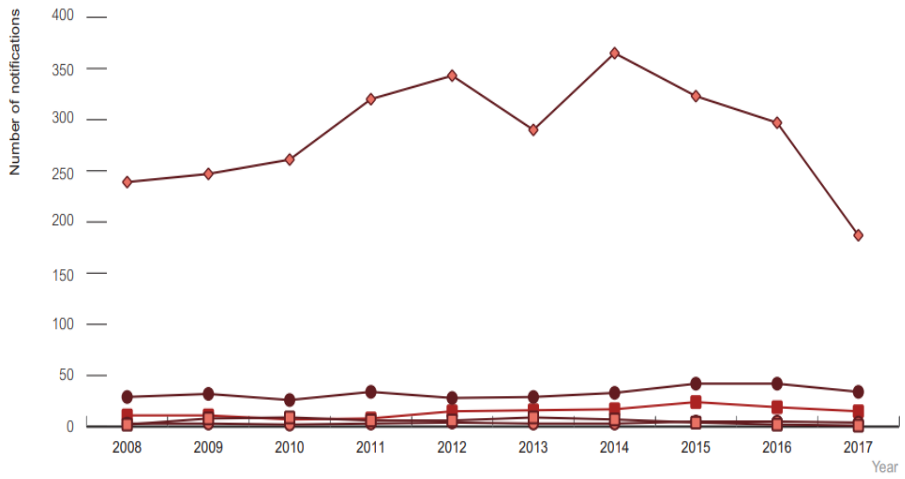
a Total includes transgender people and people for whom data on sex was missing.

HIV notifications classified as newly acquired or unspecified, 2008-2017, by HIV exposure category (Kirby Institute, 2018)



Note: Newly acquired HIV was defined as newly diagnosed infection with a negative or indeterminate HIV antibody test result or a diagnosis of primary HIV within one year before HIV diagnosis. Unspecified notifications are all notifications that do not meet the definition for newly acquired HIV.

Number of HIV infections classified as newly acquired, 2008-2017, by exposure risk category (Kirby Institute, 2018)



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male-to-male sex	239	247	261	320	343	290	365	323	297	187
Male-to-male sex and injecting drug use	11	11	7	8	15	16	17	24	19	15
Injecting drug use	3	3	2	3	4	3	3	5	5	4
Heterosexual sex	29	32	26	34	28	29	33	42	42	34
Other/undetermined	2	8	9	6	6	9	7	4	2	1

Australia's response to HIV/AIDS: Key policies

- Timely, peer-based, explicit education aimed at general public and at-risk groups
- Widespread needle and syringe exchange programs
- Rapid expansion of methadone maintenance programs
- Free- anonymous, universal HIV testing
- Free or subsidised access to antiretroviral therapy
- Safe sex education and access to condoms
- Inclusion of marginal groups in funding, policy-making, and implementations
- Removal of political and legislative barriers to action
- Building of research and reporting capacity

Expenditure ($AUD) and needles distributed by needle and syringe programs in Australia 1999/2000 (Australian Department of Health and Ageing, 2002)

Government Expenditure	Consumer Expenditure	Total Expenditure	Needles distributed
$19,673,000	$3,001,000	$22,674,000	$31,848,000

Australia's response to HIV/AIDS based on key principles

- Beliefs based on evidence as basis for policy-making
- Minimisation of risk for general population
- Promotion of research, especially epidemiological, clinical, and social
- Respect for human rights and legislative change to ensure anti-discrimination against at-risk groups
- Partnership between governments, scientists, and at-risk communities
- Long-term over short-term thinking

Australia's response to HIV/AIDS: Based on TRUST

- Trust in evidence based science as a basis for action
- Trust that HIV/AIDS education could bring about sustained change in at-risk behaviours
- Trust that high-risk groups would educate peers effectively and sustainably
- Trust that government would not resort to punitive measures, sanction, isolation, and quarantine
- Trust that governments would tell the truth about HIV/AIDS

Australia's response to HIV/AIDS required:

- Definition and defence of the public and national interest
- Political leadership and imagination
- Sustained and excellent communities, market research, public relations, and issues management
- Detailed planning but swift implementation
- Working around medical and clinical establishments, practices, and vested interests
- Belief that prevention works
- Action based on reason but informed by emotion

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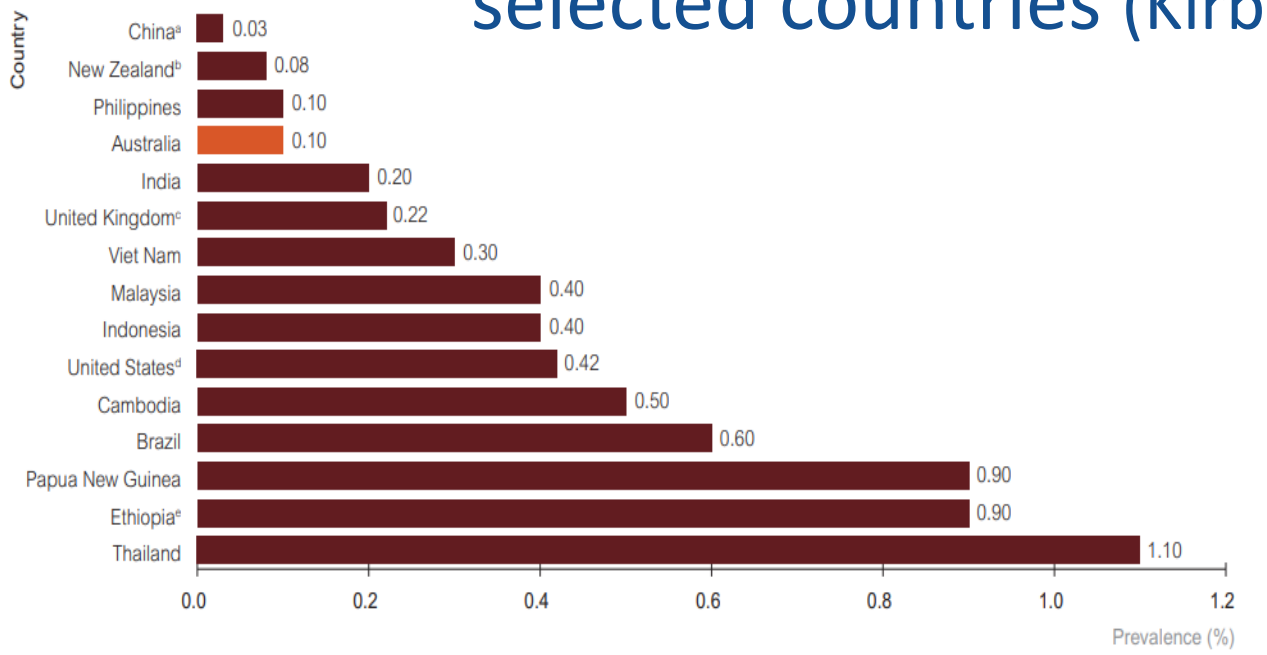
The results of nearly 40 years' application of Australia's HIV/AIDS policies

- Australian HIV/AIDS caseload 10% of US caseload
- Tens of thousands of young Australians NOT infected, dying, or dead from HIV/AIDS
- Resources freed for care and treatment
- Optimal, cost-effective outcome for Australians, economy, and society
- HIV/AIDS under control and management
- HIV/AIDS not an issue of political or social controversy or concern
- Enhanced scientific research base and skills development
- Social cohesion and inclusion

HIV prevalence in persons aged 15-49, in selected countries (Kirby Institute, 2018)



a 2013 prevalence
b 2017 prevalence[11]
c 2016 prevalence[12]
d 2015 prevalence in those aged 13 years and older[13]
e 2015 prevalence

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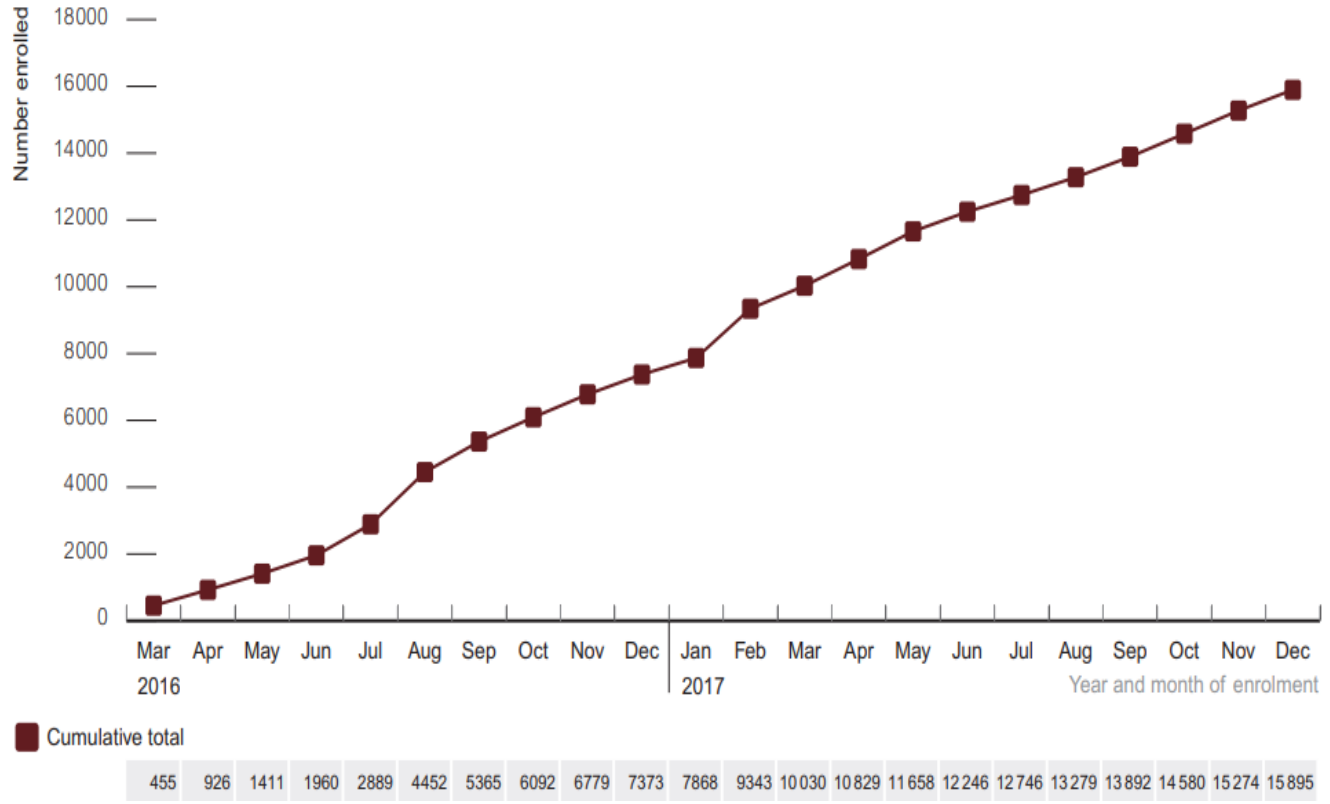
Culminate number of gay men enrolled in PrEP implementation programs, 2016 and 2017, by month (Kirby Institute, 2018)



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Australia's response to HIV/AIDS challenges

- Paradox of prevention – the more successful, the less concern and need for action
- Shaping cultural and political environment – primary of evidence based science as basis for policy over ideology and theology
- Introduction of needle and syringe exchanges in prisons
- Need to re-engage women
- Regional spread of HIV/AIDS
- Engagement with religious leaderships
- Continual education of new cohort of young people using latest and best communications technologies and methods
- Taking HIV/AIDS out of clinical setting through mobilisation of business and economic forces

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Thank you

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