Precision medicine and MSAC - the way forward

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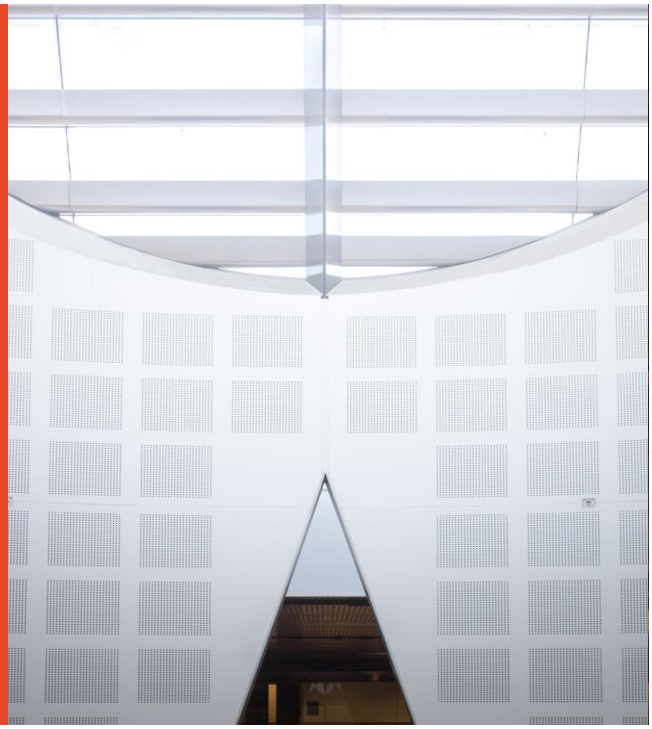
Plenary 3:
Role of clinical trials in health service decisions and policy

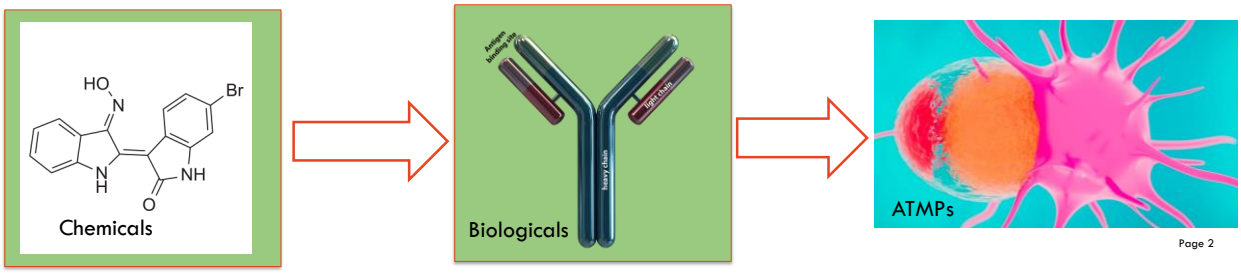
THE UNIVERSITY OF SYDNEY



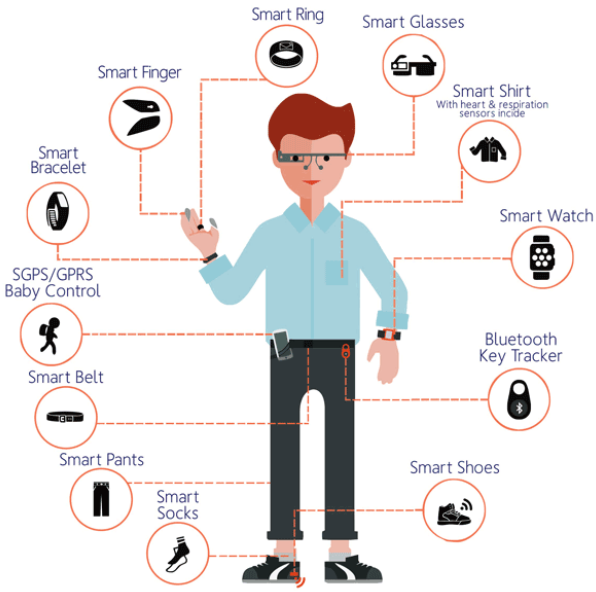
Disruptive technologies – omics, wearables, digital everything "drugs" are changing

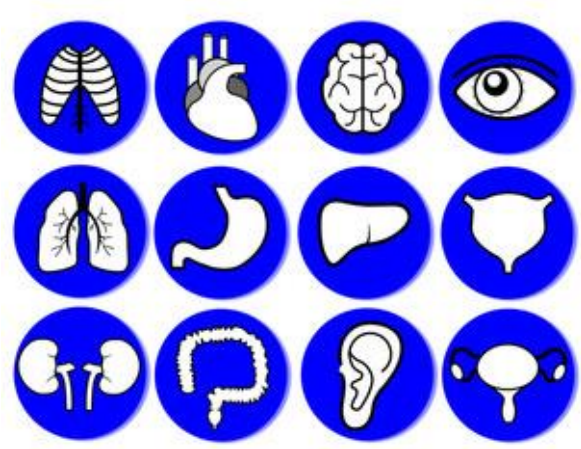
Advanced therapy medicinal product (ATMPs) means any of the following:

- Gene therapy medicinal products
- Somatic cell therapy medicinal product
- A tissue engineered produce – ie engineered [substantial manipulation] cells or tissues administered to human for regenerating, repairing or replacing human tissue



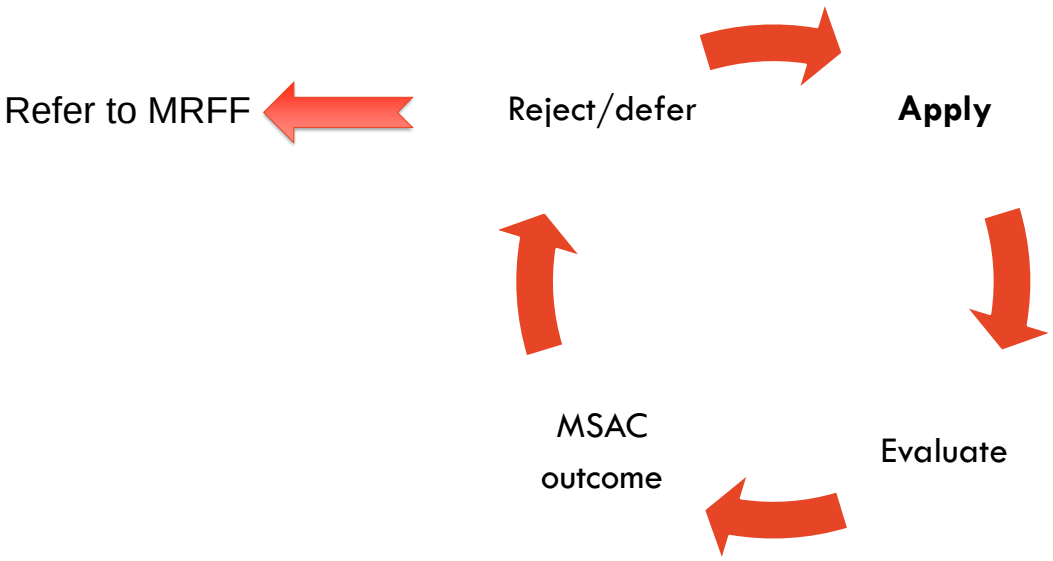
Health policy or health politics





Types of applications to MSAC

- Medical services funded via the MBS
  - therapeutic services
  - investigative services
  - consultative services
- Codependent submissions
  - with PBAC
  - with PLAC
- Nationally funded centres
- Screening - e.g. renewal of cervical cancer screening
- Blood products via the National Blood Authority
- Pharmacy services via the Community Pharmacy Agreement
- Cellular therapy – e.g. CART



Targeted health system and community organisation research

- $39.8 million to support research that addresses specific health system questions which compare the effectiveness of health services and practice

Desired outcomes:

- improve health outcomes for patients
- improve and promote the use of evidence-based treatments
- support evidence-based research to inform healthcare policy decisions
- address areas of healthcare practice with low or insubstantial evidence
- support consumer-driven research that improves clinical practice and health outcomes important to the public.

Topics to date

Round 1: opened December 2018/closed Feb 2019
Melanoma Surveillance Photography and Breast MRI

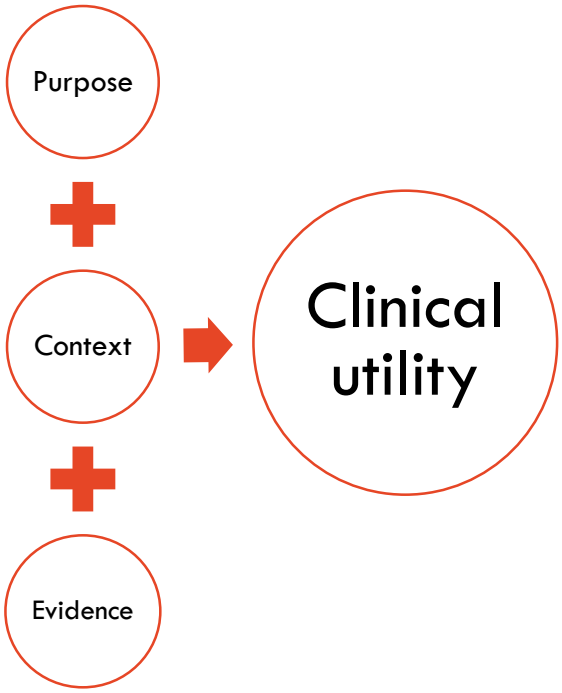
Round 2: closed April 2019
Mobile X-rays in Residential Aged Care Facilities
Economic impacts and costs associated with Chronic Fatigue Syndrome

Purpose of "omic" tests

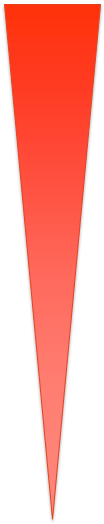
- Diagnostic
- Prognostic
- Predictive
- Treatment outcome assessment
- Monitoring
- Heritable risk assessment
- Population screening

Does policy for health technology assessment apply to "omics"

Clinical effectiveness	Cost effectiveness	Budgetary impact	Other factors
• Clinical utility	• Inputs	• Who pays	• Roll-out
• Evidence base	• Modelling	• How we pay	• Access



Clinical utility preference scale



1. Improve health outcomes – live longer, live better
2. Change clinical practice – improved health outcomes likely
3. Change family planning options
4. Diminish diagnostic odyssey
5. Value in naming – to support classification of disease, prognosis or disease risk
6. Value in knowing - provide confirmation of diagnosis and or management plan

Clinical effectiveness:

Is everything "omic" good for our health?

Clinical effectiveness – the Mammaprint™ example

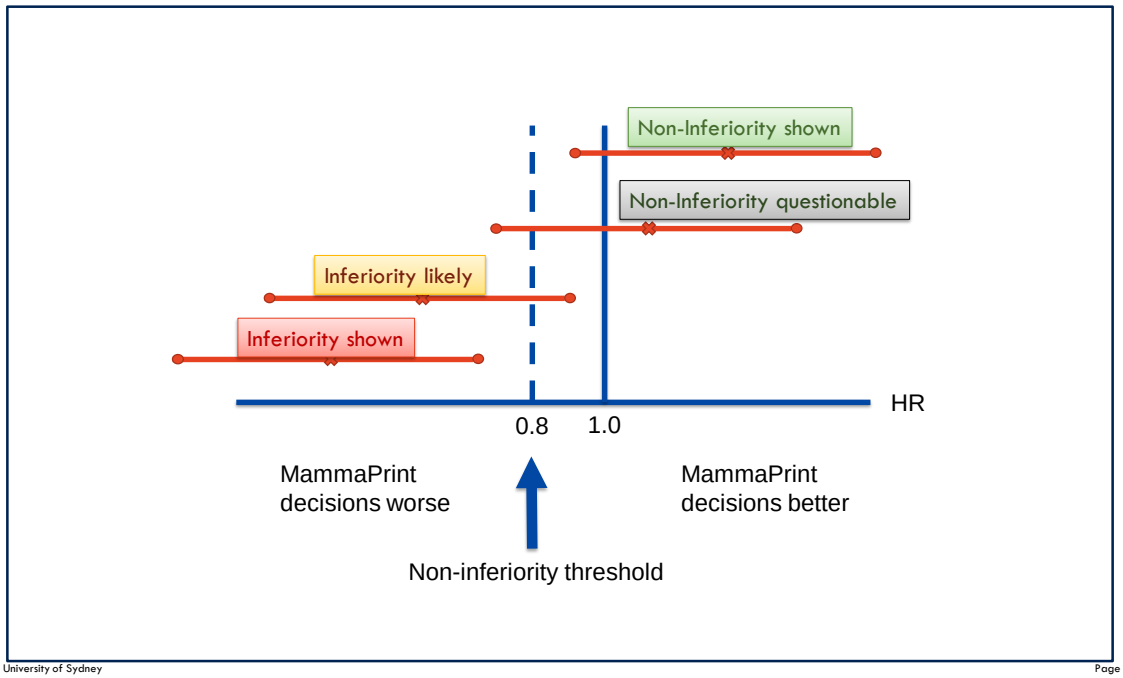
- MammaPrint™ - a 70 gene signature test for breast cancer
- Proposed as a way of identifying high risk patients who dont need adjuvant chemotherapy

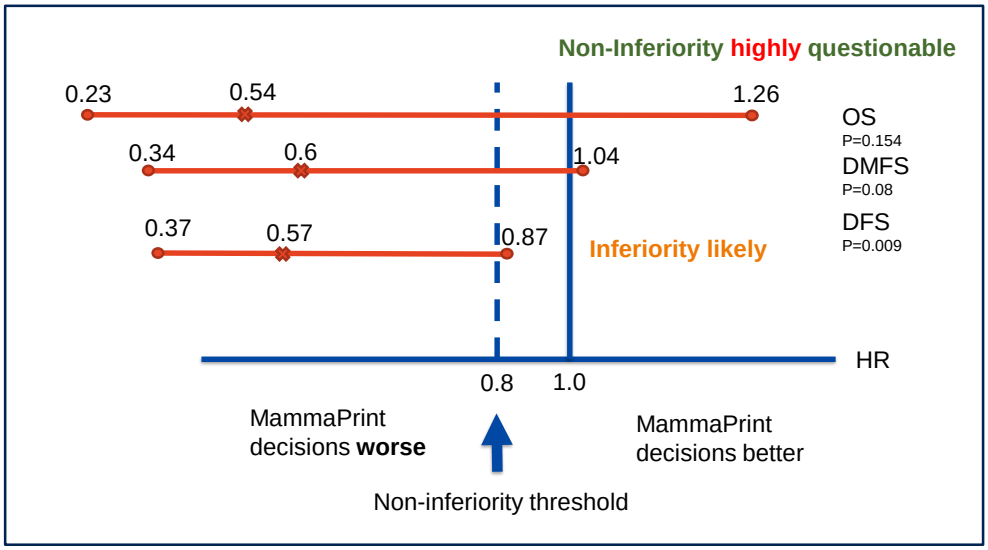
Does adding Mammaprint to clinical review reduce the need for adjuvant chemotherapy **WITHOUT** impacting negatively on survival? (i.e a non-inferiority claim)

MINDACT study; NEJM 2016; 6693 person RCT

Management changes using Mammaprint™

Risk at clinical review	High	Low	Low	High
Risk at genomic review	High	Low	High	Low
Management change	No Continue chemoRx	No Continue without chemoRx	No Continue without chemoRx	Yes Do not give chemoRx





Per protocol sensitivity analysis – ie PP but with patients enrolled between 24th May, 2009 – 30th Jan 2010 excluded

First do no harm: concern about worse cancer outcomes

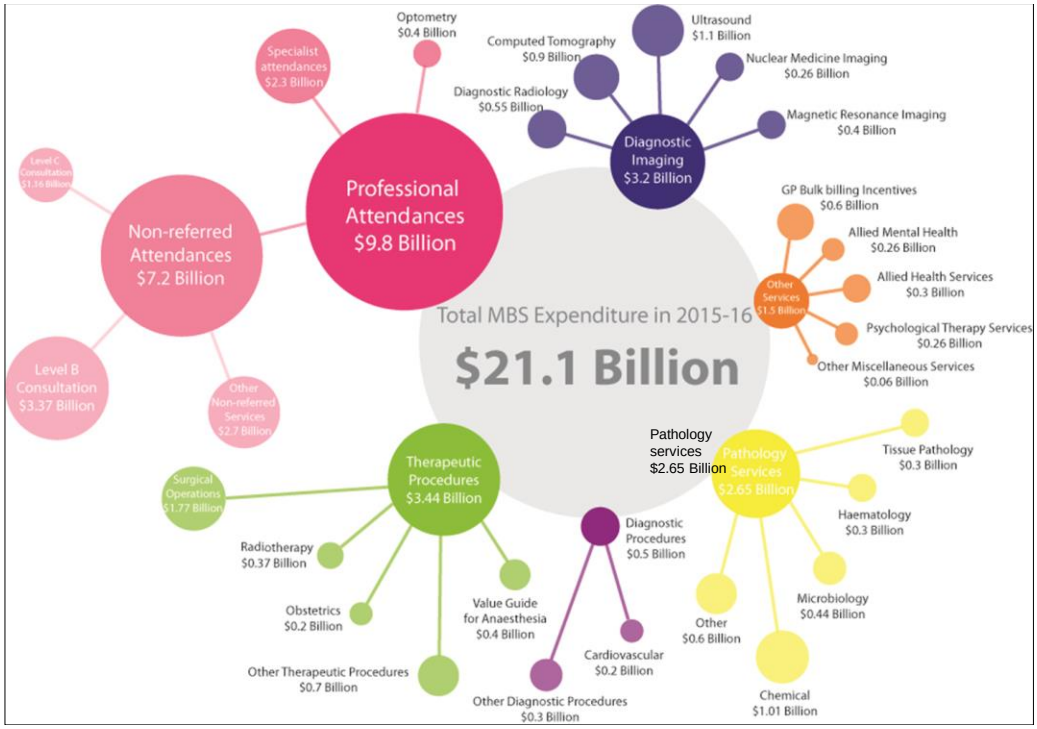
Assume 1000 patients tested per year (optimistic two-thirds of 1,500 patients eligible per year) with public funding. Of these, over five years*:

- 770 would have no change in clinical management
- 223 more would no longer receive chemotherapy
- 2 more would live with a local recurrence of their cancer
- 1 more would live with a metastatic recurrence of their cancer
- 4 more would die

* Based on MINDACT proportions with high clinical risk/low genomic risk, per protocol analysis of the randomised comparison of this group with and without adding chemotherapy, and assuming 100% compliance with MammaPrint genomic risk recommendation

MSAC's concluded disease free survival was poorer in patients who didn't receive chemotherapy compared with those who did:

– five year DFS in the PP population was 93.3% in the chemotherapy group and 90.3% in the non-chemotherapy group — an absolute **risk decrement** of 3.0%



Cost-Effectiveness and Targeting

Ramsay SD et al. JCO
Doi:110.150.005.080

TABLE 1. Clinical and Economic Outcomes in Practice Settings for a Test With 99% Sensitivity and 95% Specificity for a Tumor Mutation at Varying Levels of Mutation Prevalence Across Tumor Types

Clinical and Economic End Points	Cancer Type		
	Non–Small-Cell Lung Cancer	Prostate Cancer	Thyroid Cancer
Clinical end points			
Prevalence of mutation, %	1	10	20
Population, No.	1,000	1,000	1,000
Mutation, No.	10	100	200
No mutation, No.	990	900	800
TP, No.	10	99	198
FP, No.	50	45	40
TP plus FP, No.	60	144	238
F1 score	0.29	0.81	0.90
PPV, %	17	69	83
Economic end points*			
Total cost, targeted therapy strategy, $	26,660,000	32,384,000	28,768,000
Total cost, standard therapy strategy, $	24,000,000	24,000,000	24,000,000
Survival with targeted therapy strategy, life-years gained	1,005	1,094.5	1,194
Survival with standard therapy strategy, life-years gained	1,000	1,000	1,000
Incremental cost effectiveness (cost per life-year gained), $	532,000	88,720	76,124

Abbreviations: FP, false positive; PPV, positive predictive value; TP, true positive.
*Model assumptions: targeted therapy screening test cost, $500; drug cost, targeted, $15,000/month, standard, $4,000/month; treatment duration, responders (targeted and standard), 6 months; treatment duration, nonresponders, 2 months; survival, targeted treatment, 2 years, standard treatment, 1 year; survival decrement, false-positive targeted test, 0.1 years. No difference in lifetime costs of care beyond drug costs.