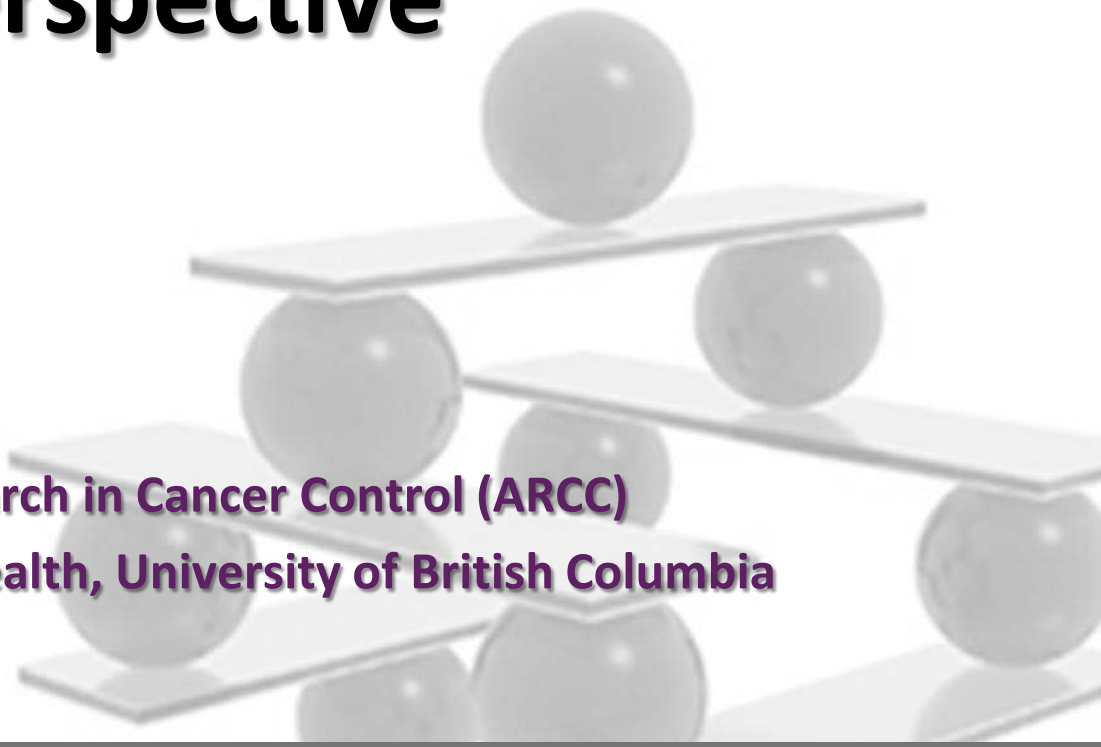
ARCC

Canadian Centre for Applied Research in Cancer Control

Personalized health care: an economic perspective



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Overview

- Background – emerging trends in cancer drugs
- The burgeoning role of health economics in drug reimbursement decisions
- Personalized medicine – a cancer case study
- Some challenges ahead – reconciling individual and population ‘paradigms’

Mirror.co.uk
NEWS

Gene drug heralds cancer's end game

By Danny Buckland 16/09/2010

Find 'as big as penicillin'

A crucial breakthrough in the fight against cancer was unveiled yesterday.

Scientists said the "end game" was in sight after the successful trial of a wonder drug able to genetically target tumours.

Mail Online

Is this cancer's 'penicillin moment'? Gene targeting drug could herald 'end game' for disease

By FIONA MACRAE
Last updated at 1:40 AM on 16th September 2010

A pill that rapidly shrinks the most deadly of skin tumours has been hailed as the dawn of a new era in cancer treatment.

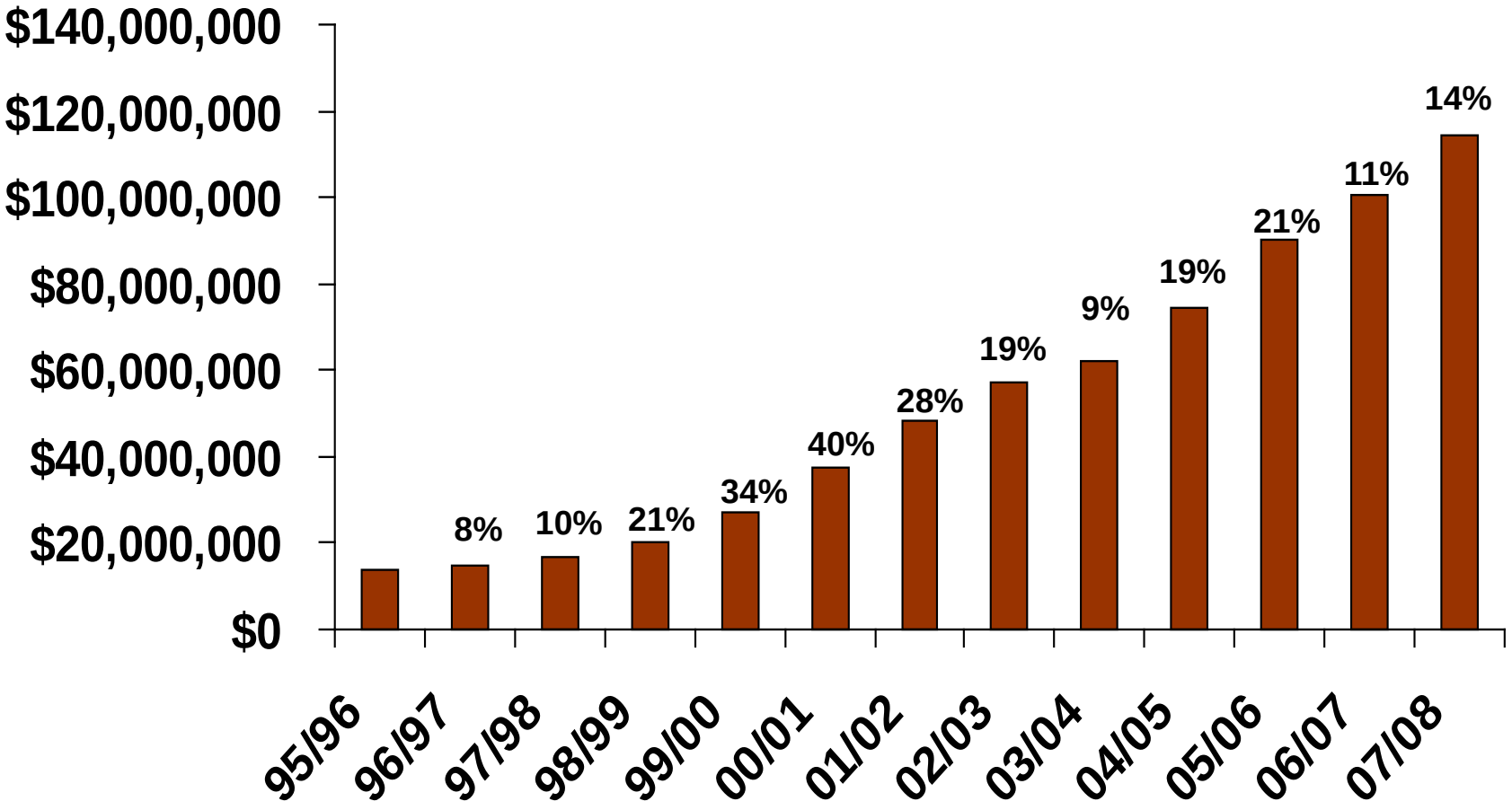
The finding has been likened to the discovery of penicillin.

Known as PLX4032, it is the first cancer drug to harness knowledge from the full decoding of human DNA, and has produced 'spectacular' trial results.

"Today's remarkable medical technologies and therapies are the direct result of an innovation process that takes place not so much in quantum leaps but more in steady, iterative steps. This continually improving, evolutionary cycle is neither linear nor predictable."

Nelson, Health Affairs 1994

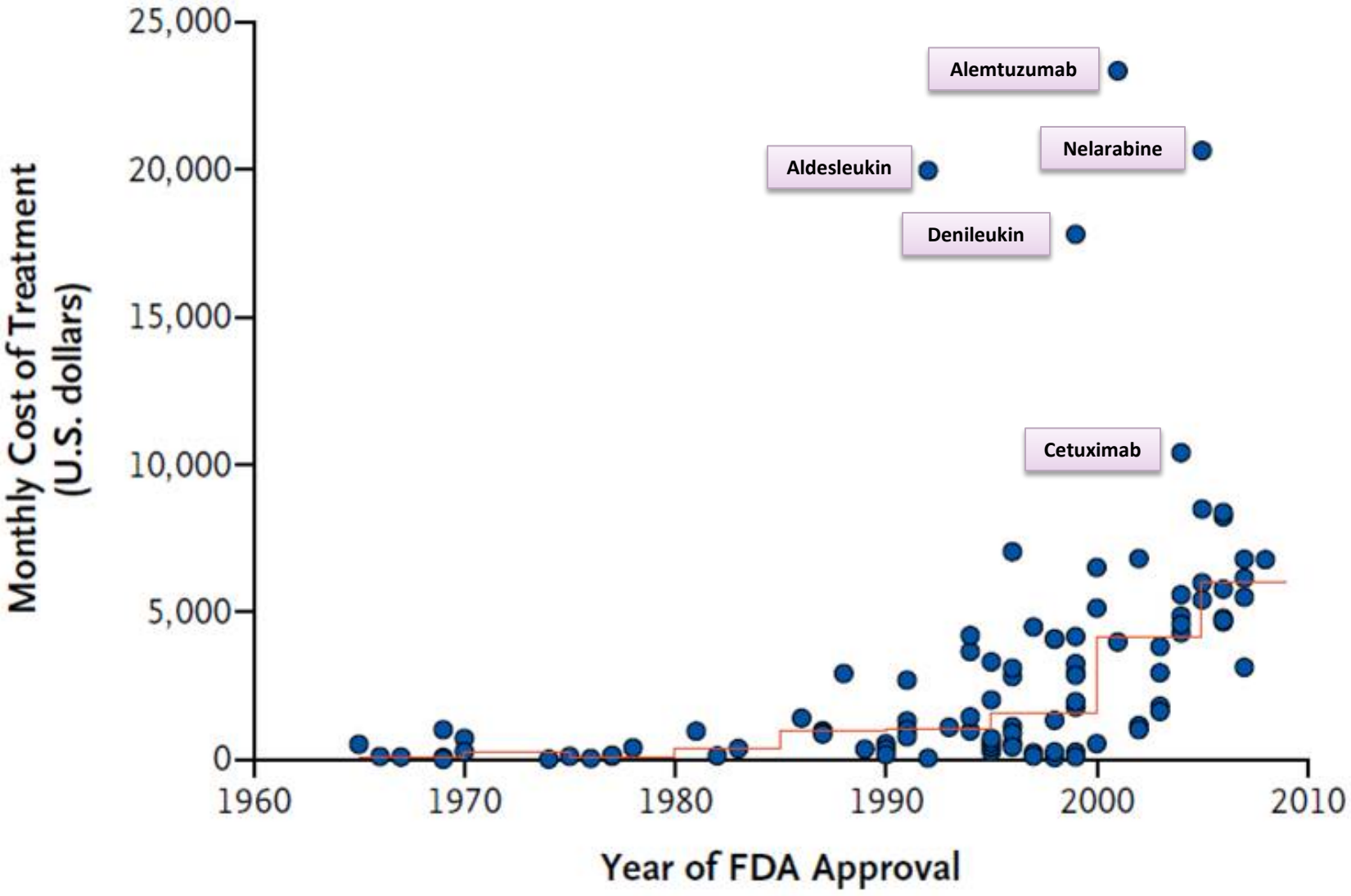
Oncology drugs in BC



Top ten drugs in BC 2007/08

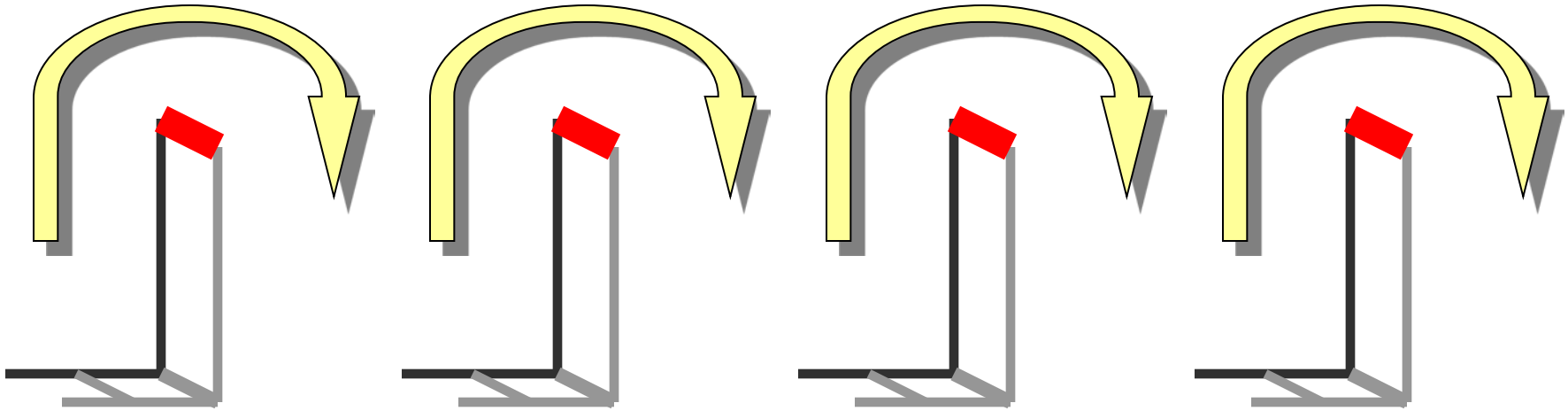
TUMOUR SITE	TYPE	DRUG	COST
Lymphoma	Curative & Chronic	Rituximab	$ 16,787,572
Breast	Curative & Chronic	Trastuzumab	$ 15,621,847
Prostate	Curative & Chronic	LHRH	$ 14,449,370
Leukemia & Sarcoma	Curative & Chronic	Imatinib	$ 10,991,744
Breast	Curative & Chronic	Aromitase Inhibitors	$ 8,026,114
Breast, Lung, Prostate	Curative & Chronic	Docetaxel	$ 5,543,786
Colon	Curative & Chronic	Oxaliplatin	$ 5,320,446
Pituitary & Carcinoid	Long-term Symptom Control	Octreotide	$ 3,905,787
Colon	Chronic	Bevacizumab	$ 3,847,817
Lung, Pancreas, Ovarian & Breast	Chronic	Gemcitabine	$ 2,920,565

Monthly and median costs of FDA approved cancer drugs (2007 US$)



Source: Bach, NEJM 2009

Why is economic evaluation important?

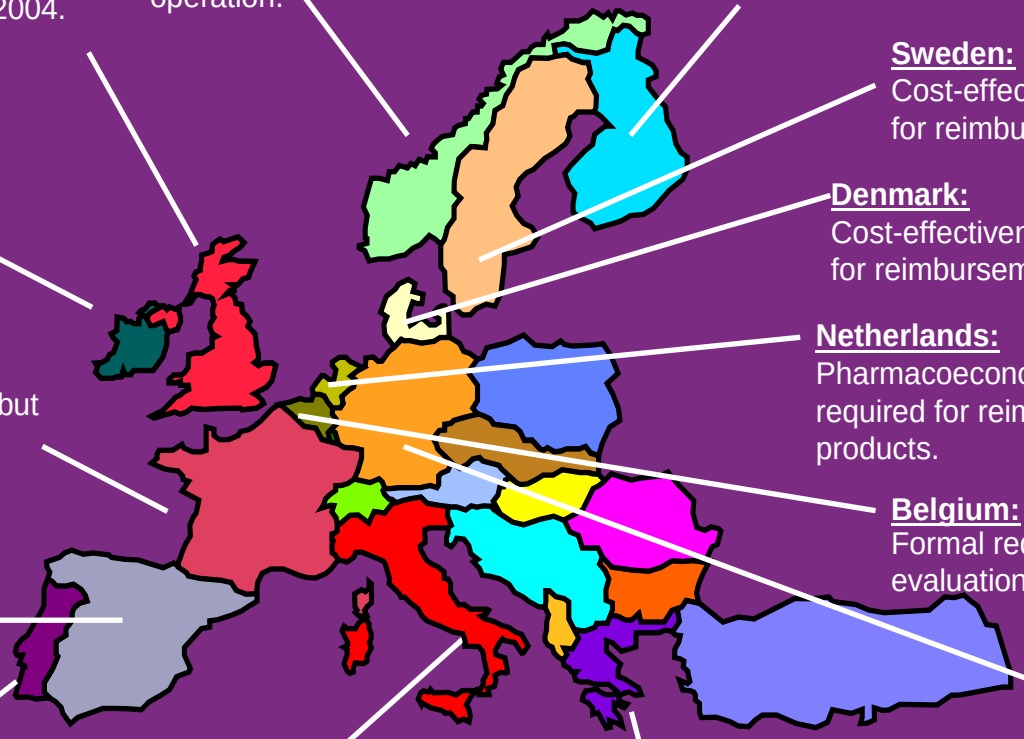


The Fourth Hurdle

Economic evaluation for reimbursement decisions

- Many jurisdictions now require economic evaluation for reimbursement decisions (primarily for drugs)
  - Accompanied by guidelines for pharmaceutical companies
  - Pricing decisions maybe linked with reimbursement decisions
- Australia: Pharmaceutical Benefits Advisory Committee (PBAC)
- England and Wales: National Institute for Health and Clinical Excellence (NICE)
- Based on 'Acceptable' Incremental Cost-Effectiveness Ratios (ICERs)

Economic Evaluation in Europe



Britain:
NICE evaluates the cost effectiveness of medicines. Guidelines updated April 2004.

Norway:
Pharmacoeconomic data required for reimbursement; official guidelines in operation.

Finland:
Pharmacoeconomic evidence mandatory for evaluating new therapies for reimbursement and may also be requested for existing therapies.

Sweden:
Cost-effectiveness data required for reimbursement.

Ireland: Guidelines for pharmacoeconomic studies prepared; cost-effectiveness data may be requested.

Denmark:
Cost-effectiveness data may be requested for reimbursement decisions.

France:
Not a formal requirement but increasingly used in reimbursement decisions. Guidelines prepared.

Netherlands:
Pharmacoeconomic evidence explicitly required for reimbursement of new products.

Belgium:
Formal requirement for economic evaluation.

Spain:
Health technology assessment at a regional level.

Germany:
Guidelines prepared. Institute for Quality and Efficiency in the Health Service established in 2004.

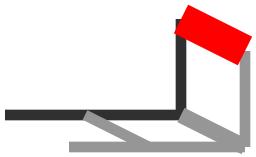
Portugal:
Cost-effectiveness data incorporated into reimbursement decisions.

Italy:
Cost-effectiveness considered in pricing and reimbursement decisions.

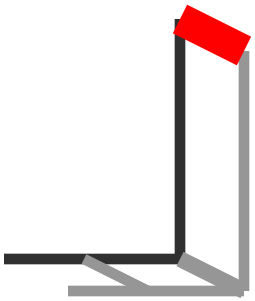
Greece: Guidelines for pharmacoeconomic studies prepared; cost-effectiveness data may be requested.

Source: National Centre for Pharmacoeconomics, Ireland

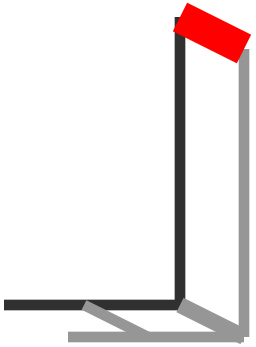
How big is the hurdle?



$100,000/ QALY



$60,000/ QALY



$50,000/ QALY

ICER thresholds in Australia

Number	Incremental cost per additional life-year gained at 1998/1999 prices ($AU)	PBAC decision
1	5517	Recommend at price
2	8374	Recommend at price
3	8740	Recommend at price
4	17387	Recommend at price
5	18762	Recommend at price
6	18983	Recommend at price
7	19807	Recommend at lower price
8	22255	Recommend at price
9	26800	Recommend at price
10	38237	Recommend at price
11	39821	Recommend at price
12	42697	Reject
13	43550	Reject
14	43550	Recommend at price
15	56175	Reject
16	57901	Recommend at price
17	63703	Reject
18	71582	Recommend at price
19	75286	Recommend at price
22	85385	Recommend at lower price
21	88865	Reject
22	98323	Reject
23	229064	Recommend at lower price
24	231650	Reject
25	256950	Reject

Source: George et al. Pharmacoeconomics 2001

Cancer ICER thresholds in England and Wales

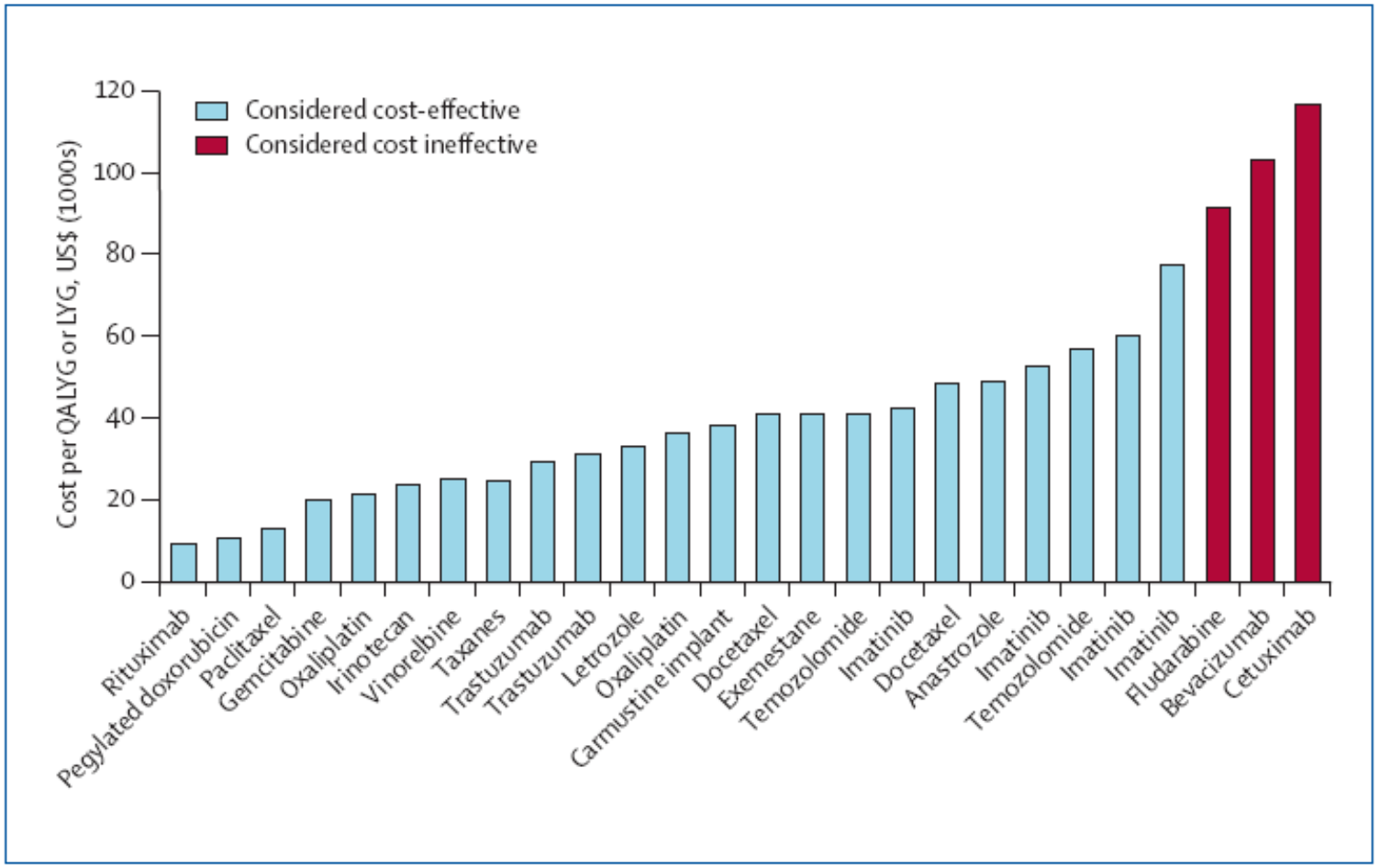


Figure 1: ICERs expressed as US$ (at purchasing power parity) per QALYG or LYG for condition–treatment pairs appraised by NICE

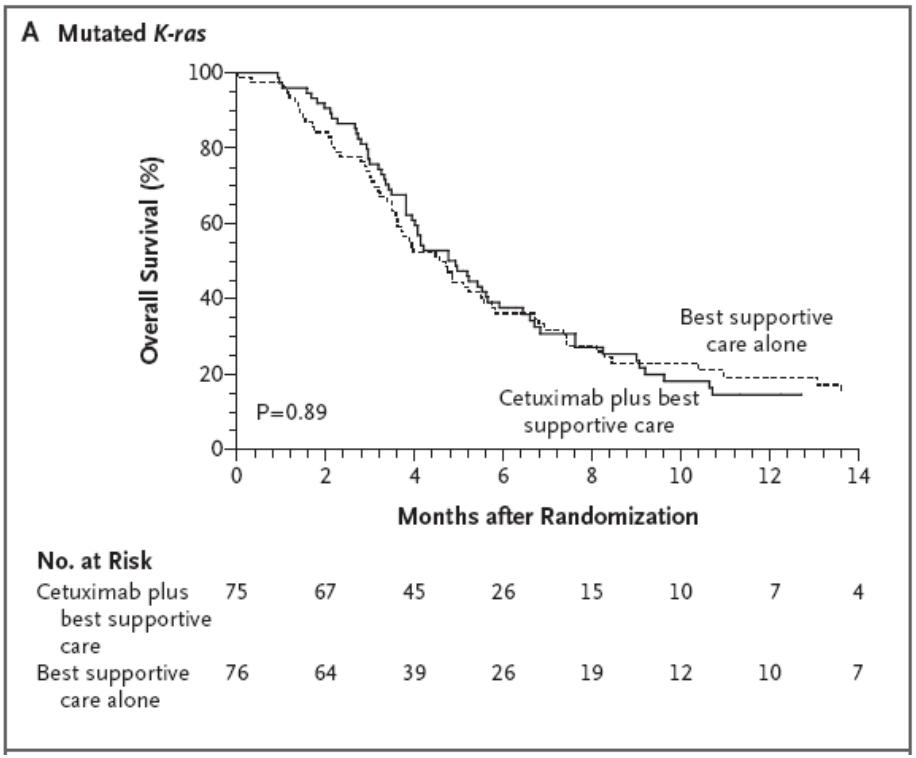
Source: Rawlings. Lancet Oncology 2007

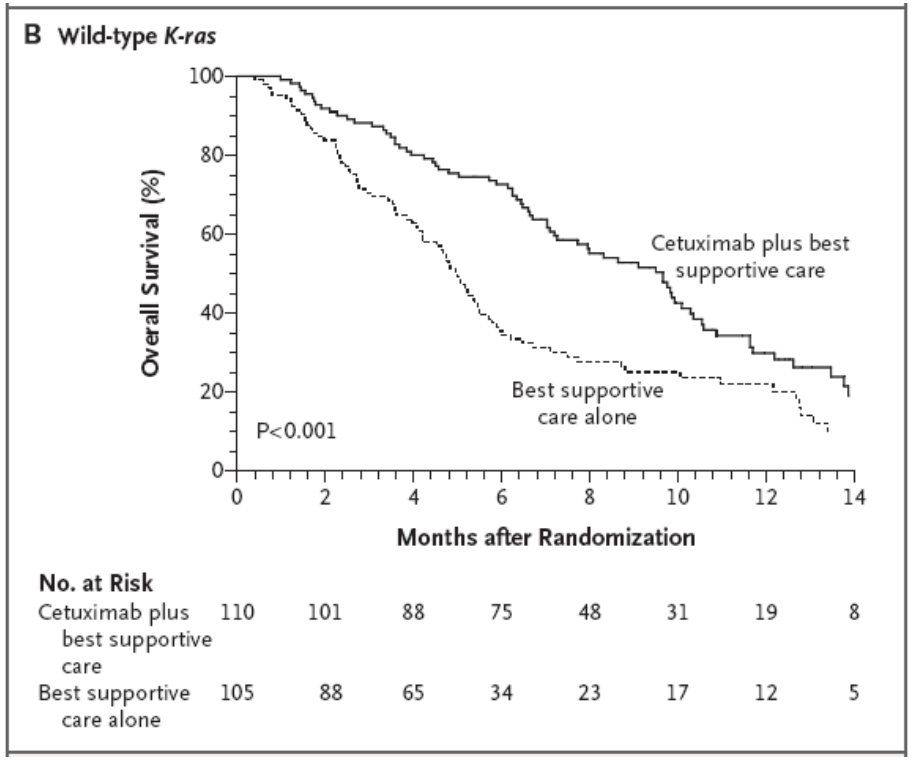
A personalized medicine case study: Cetuximab (Erbitux) in advanced colorectal cancer (CRC)

Cetuximab in Advanced Colorectal Cancer

- Treatment for advanced colorectal cancer (CRC) – improves overall and progression-free survival compared to best supportive care[1]
- Mechanism of action - monoclonal antibody that targets epidermal growth factor receptor (EGFR), modulating tumor cell growth[2]
- Resistance to cetuximab is common (>50% after one treatment) - Caused by mutations in component of EGFR: *K-ras* protein, which occur in ~40% of patients[3]

Cetuximab in Advanced Colorectal Cancer





Effectiveness of cetuximab (overall and progression-free survival) is significantly associated with *k-ras* mutation status (p>0.001)

- **Patients with wild-type *k-ras* tumors did benefit (overall survival 9.5 months)**
- **Patients with mutated *k-ras* tumors did not benefit (overall survival 4.8 months)[3]**

Source: Karapetis et al, NEJM, 2009

Cetuximab in Advanced Colorectal Cancer

Cost-effectiveness

- Cetuximab may increase the already significant cost of managing advanced CRC, especially when provided to all patients
- Drug and administration cost of cetuximab $71,000/patient[4]
- K-ras testing $450/patient[4]

Cetuximab in Advanced Colorectal Cancer

Cost-effectiveness cont…

- Providing drug to all patients is not cost effective
- Incremental cost effectiveness ratio (ICER) ~$300,000 per QALY gained[5]
- Targeting the therapy to patients with wild-type *k-ras* improves cost-effectiveness
- ICER ~$180,000/QALY[5]
- Theoretical cost-savings associated with treating only wild-type *k-ras,* $740 million (US), accounting for cost of *k-ras* testing

Some challenges ahead

Identifying the costs of testing strategies

- Current reimbursement systems for diagnostic tests are cost based rather than value based
- Tests for multiple markers cost thousands of dollars
- Technology is changing – cost per single-nucleotide polymorphism (SNP) analyzed is falling rapidly
- True opportunity cost is often unknown – testing may result in changes to medical utilization
- Difficult to estimate a true economic value at any given time

Complexity, complexity, complexity

- Genetic tests share the same concerns about sensitivity and specificity as older diagnostics
- Patient outcomes are likely to be influenced by multiple genes, and each gene can influence multiple outcomes
- Each outcome is modified by interactions with other genes and environmental exposures – including diets, drugs and disease states

Lack of effectiveness data

- Lack of data on patient and clinician behaviour following the results of diagnostic tests, and associated patient outcomes
- Issue gets more complicated if the test indicates a patient should not get a drug
- Are there alternatives?
- If so, how does the analysis factor in the timing and sequencing of alternatives?

Lack of effectiveness data cont …

- Inconclusive or contradictory results from small (n < 200) RCTs may be insufficient for robust estimates of effectiveness
- More decision analytic modelling required, with careful consideration of parameter and decision uncertainty
- Use of surrogate end-points, e.g. progression free survival, is likely to increase
- Cumulative synthesis of RCTs needed

Coverage with evidence development (CED)

- Uncertainty with the clinical value of new technologies will likely mean that the value of additional research and policy options, such as CED, should be considered
- CED = provisional approval for coverage by payers on condition that additional data on effectiveness are collected through RCTs or patient registries
- Registries and linkable administrative data sets will only become more important

Some concluding thoughts

Individual vs. population 'paradigms'

- Personalized medicine produces treatment regimens based on the molecular biology of *individuals* and their diseases
- Economic evaluation (and EBM) produces results based on responses of average patient *populations*, and considers *effectiveness* not just *efficacy*
- RCTs are limited to exceedingly homogeneous populations because of strict inclusion/exclusion criteria and tightly controlled settings

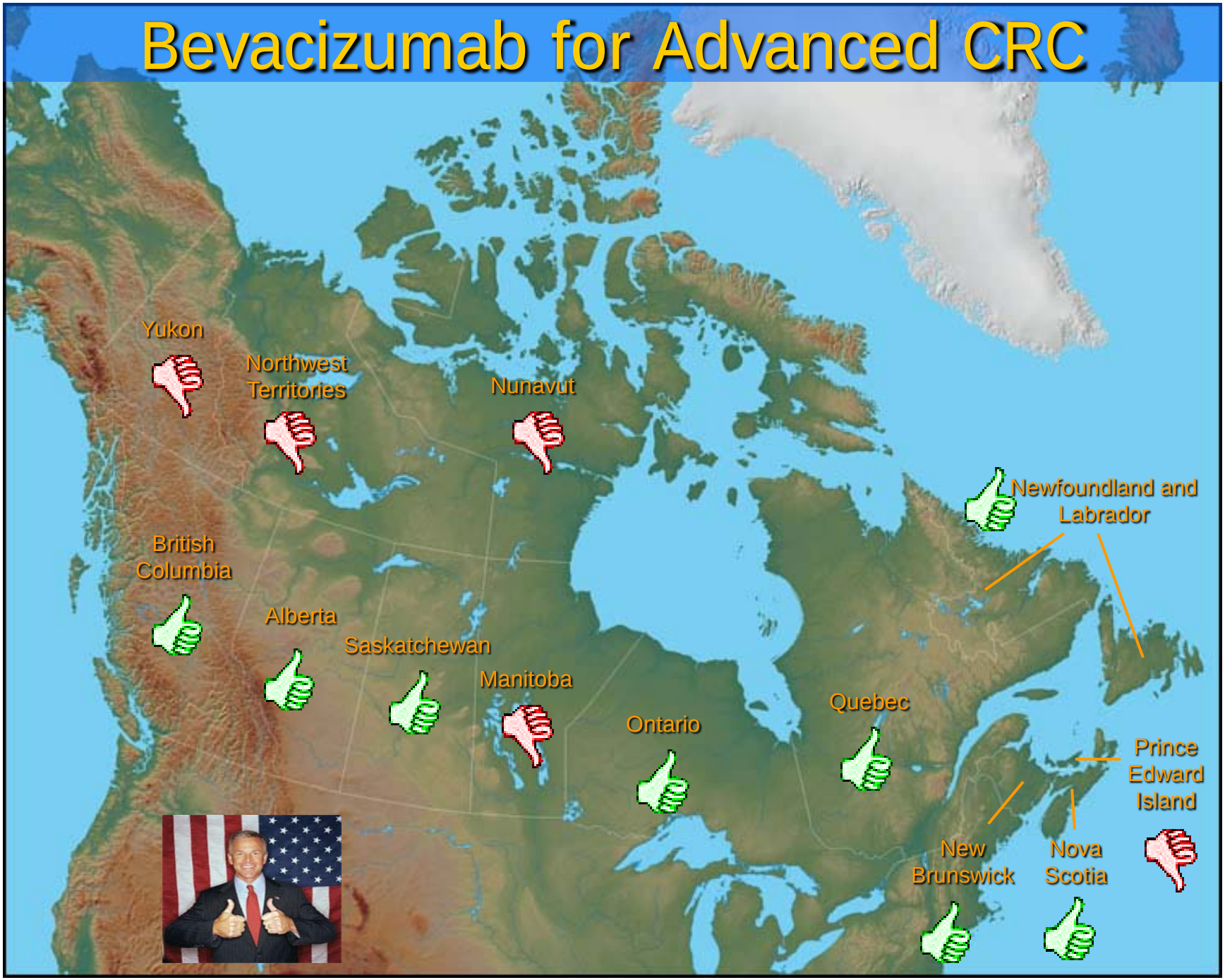
Personalized vs. stratified medicine

- Is personalized medicine more likely to lead to smaller and smaller sub-group analyses rather than 'individualized' care?
- Possibly, because the marginal cost of developing new drugs will outweigh the marginal benefits for pharmaceutical companies
- RCTs and economic evaluation will not become redundant – but they will be more complex and costly
- Linkable administrative data will be very important

Preferences, preferences, preferences

- Personalized medicine promises to provide tailored therapies that take into account individual differences in risk and values
- The balance of risks and benefits for each person will differ because of preference heterogeneity
- Tailoring therapy and determining the optimal strategy will mean listening to patients preferences
- Economic evaluations need to model patient preferences about different treatment options

Bevacizumab for Advanced CRC



Acknowledgements

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