Considering Non-Health Benefits and Preferences in Personalised Medicine (PM)

Session: Health Economic Benefits: Beyond Cost Effectiveness

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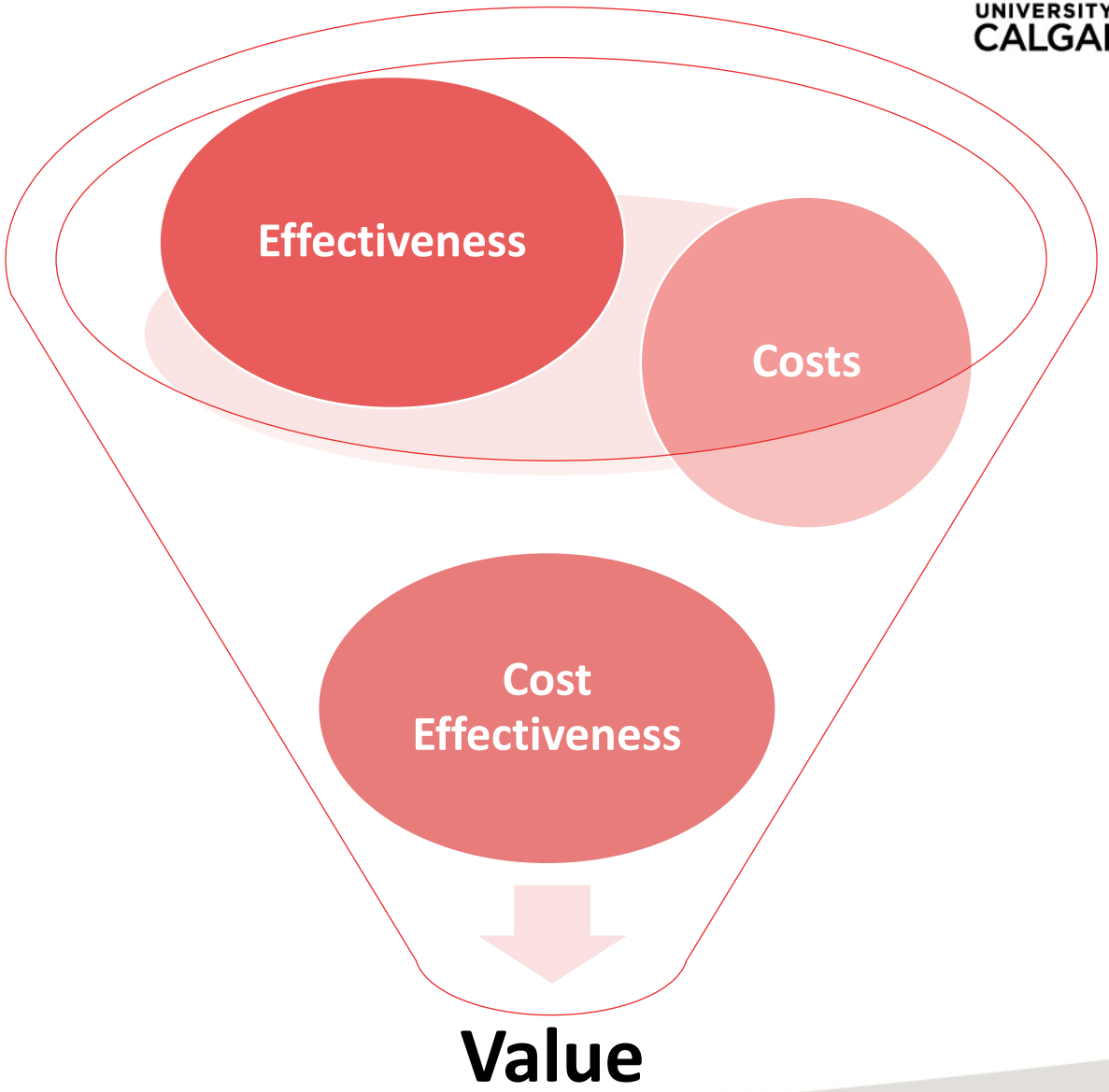
Overview

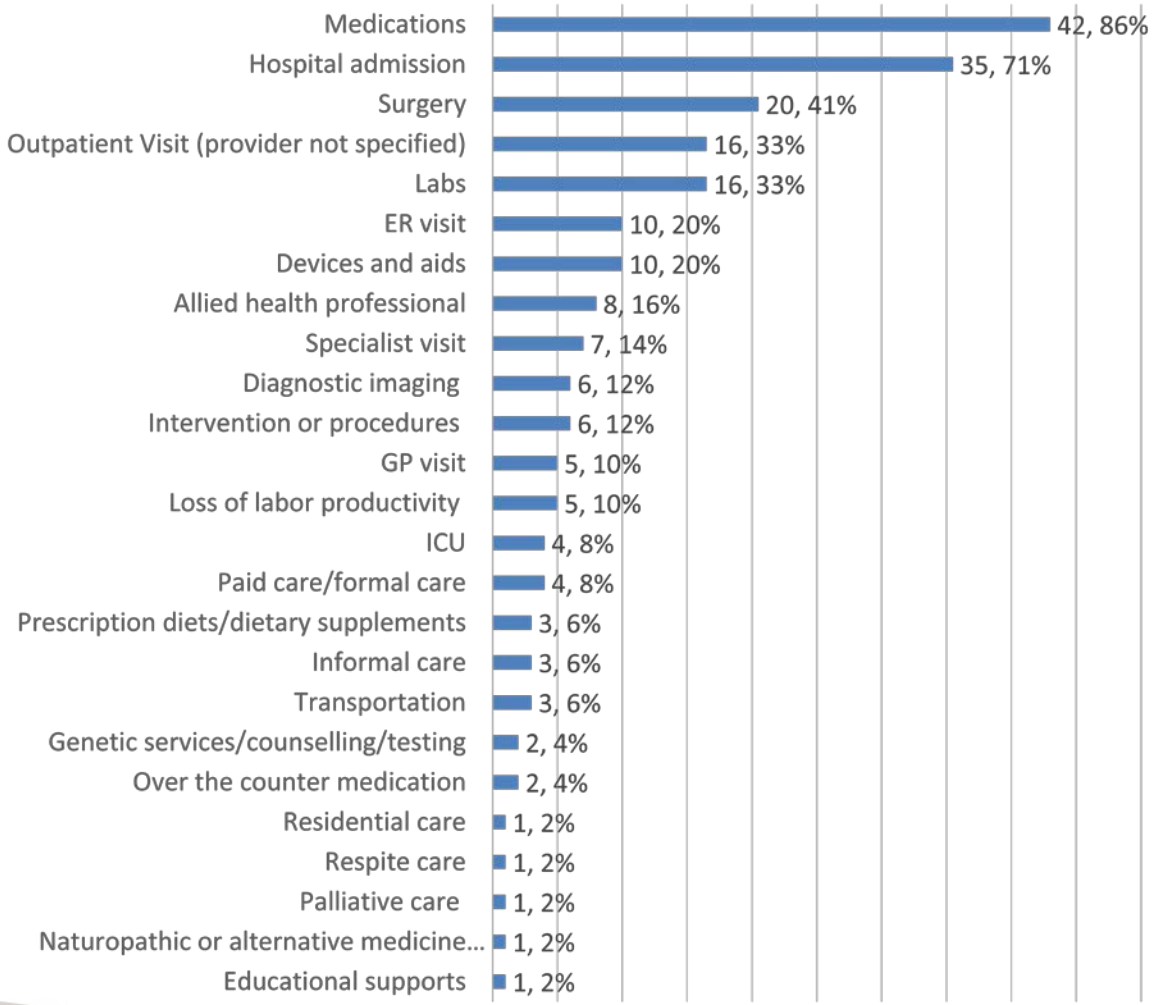
- Measuring Value in PM: What Matters to Patients
  - Productivity Costs/Losses
  - Spillover Effects
  - Non-Health Outcomes: Patient and family preferences
- Methods to Measure Value in PM
  - Patient preferences for personal utility, willingness-to-pay, uptake, and benefit-risk trade-offs
  - Simulation modeling and downstream consequences

Perspective on Value: Typically Cost-Effectiveness from the Payer Perspective

- Effectiveness: Outcomes associated with the intervention (e.g. life years, quality-adjusted life years)
- Costs: Monetary expenditures associated with direct costs of health services
- Cost-effectiveness: Incremental cost-effectiveness ratio (ICER) measures efficiency as marginal cost per unit of effectiveness (PM vs standard of care)



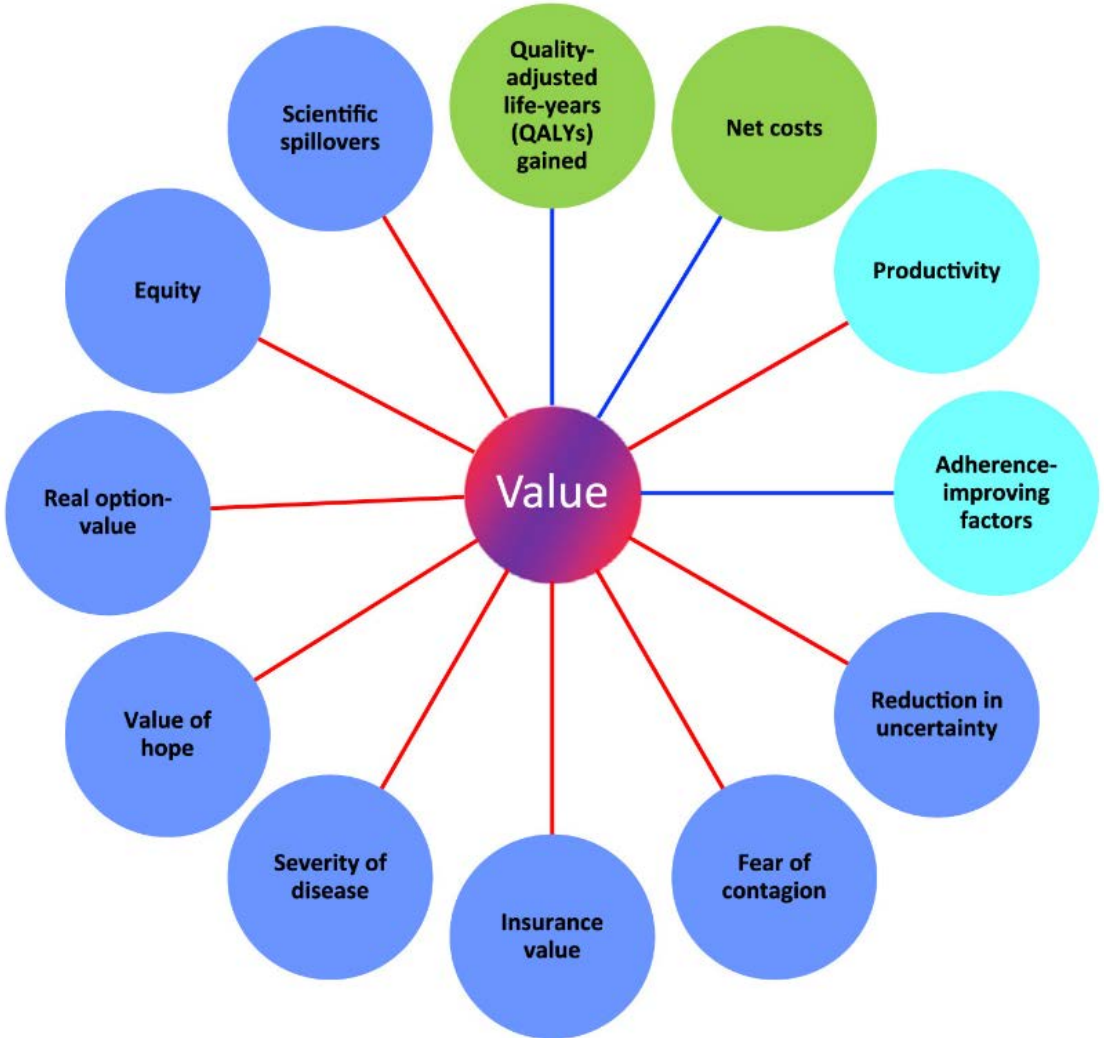
Systematic Review: Costs Reported in Economic Evaluations for Rare Diseases



- Only 7/49 studies used a societal perspective; others used healthcare system and payer perspectives
- Medical costs (e.g., medications, hospitalizations, outpatient visits, laboratory tests and surgery) were the most commonly reported costs.
- Few studies reported costs to patients and families such as productivity, transportation, informal care, over the counter medication or educational supports
- **Unique aspects to PM: advanced genetic testing, use of private labs or out of country travel for testing, participation in research, physician advocacy time**

- Currie GR et al. Developing a Framework of Cost Elements of Socioeconomic Burden of Rare Disease: a Scoping Review. CIHR Knowledge Synthesis, Under Review

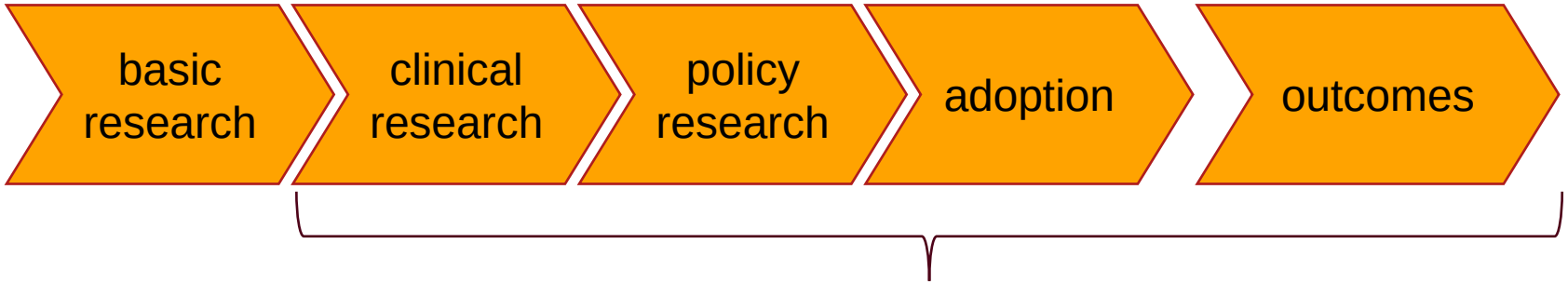
Broadening our View of Value: Extended Cost-Effectiveness



- Going beyond the impact on the individual, and looking at the broader effects on the families and caregivers
- Work productivity and employment effects of caregiving
- Spillover effects
  - Caregiver and family member quality of life
  - Time spent on caregiving

- Lakdawalla D, Doshi J, Garrison L et al. Defining elements of value in healthcare-a health economics approach: an ISPOR Special Task Force Report [3]. Value Health. 2018;21(2):131-13

Challenges to Assessing Value in PM



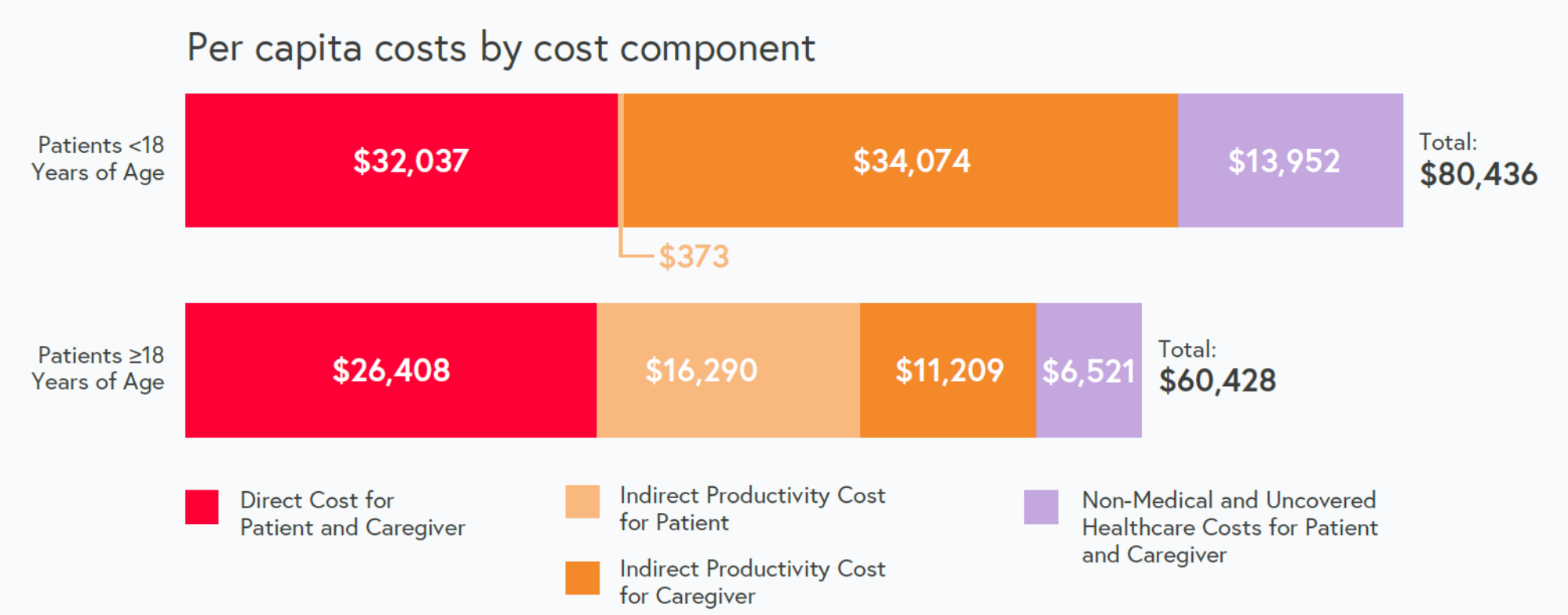
1) PM testing results in multiple actionable and non-actionable results with potential downstream implications for both the patient and their families
2) PM associated with health, non-health and process outcomes

- *Phillips KA, Deverka PA, Marshall DA et al. Methodological challenges and solutions for assessing economic value of next generation sequencing tests. Value in Health 2018; 21(9): 1033-1042*

Hidden Consequences PM Testing and Treatment

- Testing Consequences - False positives and false negatives
- Productivity loss for patients, families and communities
- Lost educational and employment opportunities
- Non-Health Benefits
- Costs to Other Government Sectors
- Patient and Family Costs (e.g., out of pocket expenses) and disability related costs
- Personal Utility/Disutility

Productivity Costs > Direct Medical Costs in Rare Diseases



- Total economic burden on 379 rare diseases in one year
- Derived from analysis of claims data and survey of ~1400 families (USA)

The National Economic Burden of Rare Disease Study Infographic, February2021

Productivity Loss Among Parents of Children with Arthritis: Work Productivity and Activity Impairment Questionnaire (WPAI)

- 12% of parents had made changes in their work commitment due to their child's JIA

73% reduced working hours

13% stopped working altogether

Absenteeism

- Parents missed an average 3.2 hours of work

Presenteeism

- Mean Impairment to productivity: 20%

- For those working, overall work impairment = 26%
- Mean impairment to usual activities: 20%

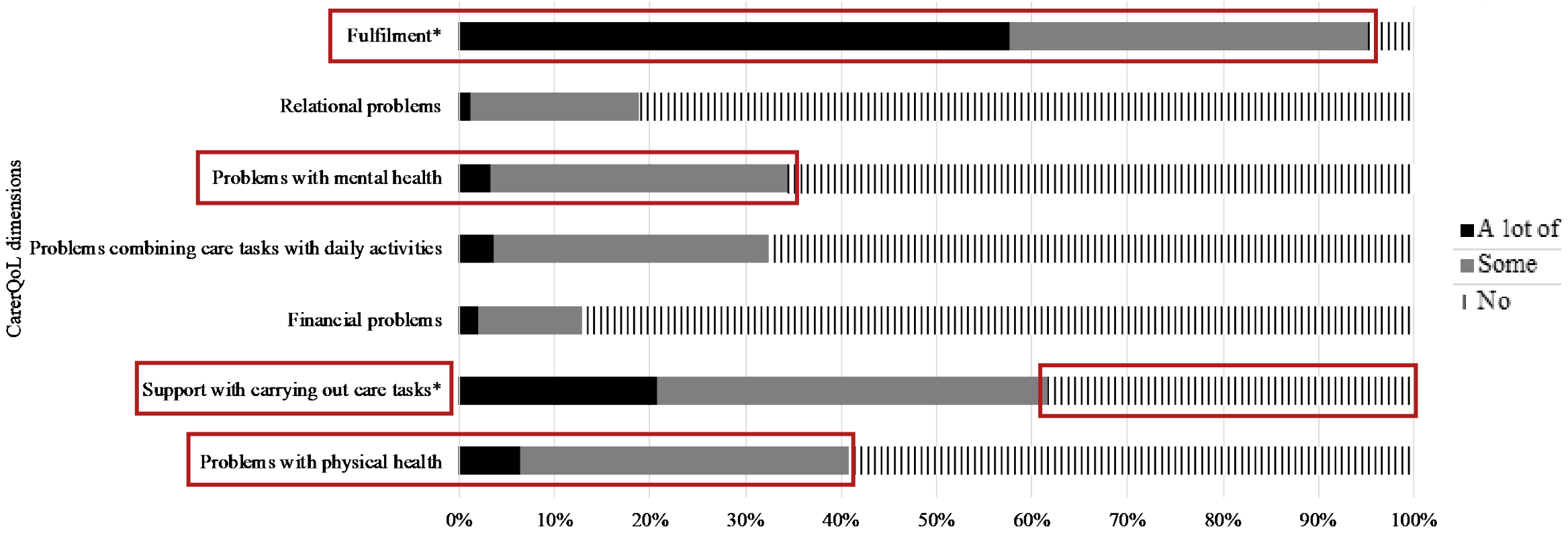
- Grazziotin et al. What is the impact on workplace productivity and usual activities for caregivers of children with juvenile idiopathic arthritis (JIA)? Under review

Spillover Effects on Caregivers and Family Members

- Spillover effects – HRQoL effects for caregivers and family members – are rarely considered in cost-effectiveness analysis.
- Systematic review (n=80 studies); only 10 (8%) reported spillovers
- Most studies did not include a comparator, limiting ability to infer spillover effects
- Some national guidance bodies are now recommending inclusion of spillover effects
  - Research gaps remain to be addressed in estimation and incorporation methods to increase the adoption of inclusion of these measures

- Wittenberg E, James LP and Prosser LA. Spillover Effects on Caregivers' and Family Members' Utility: A Systematic Review of the Literature. PharmacoEconomics 2019; 37:475–499.

Caregiving Quality of Life in Parents (n=250)

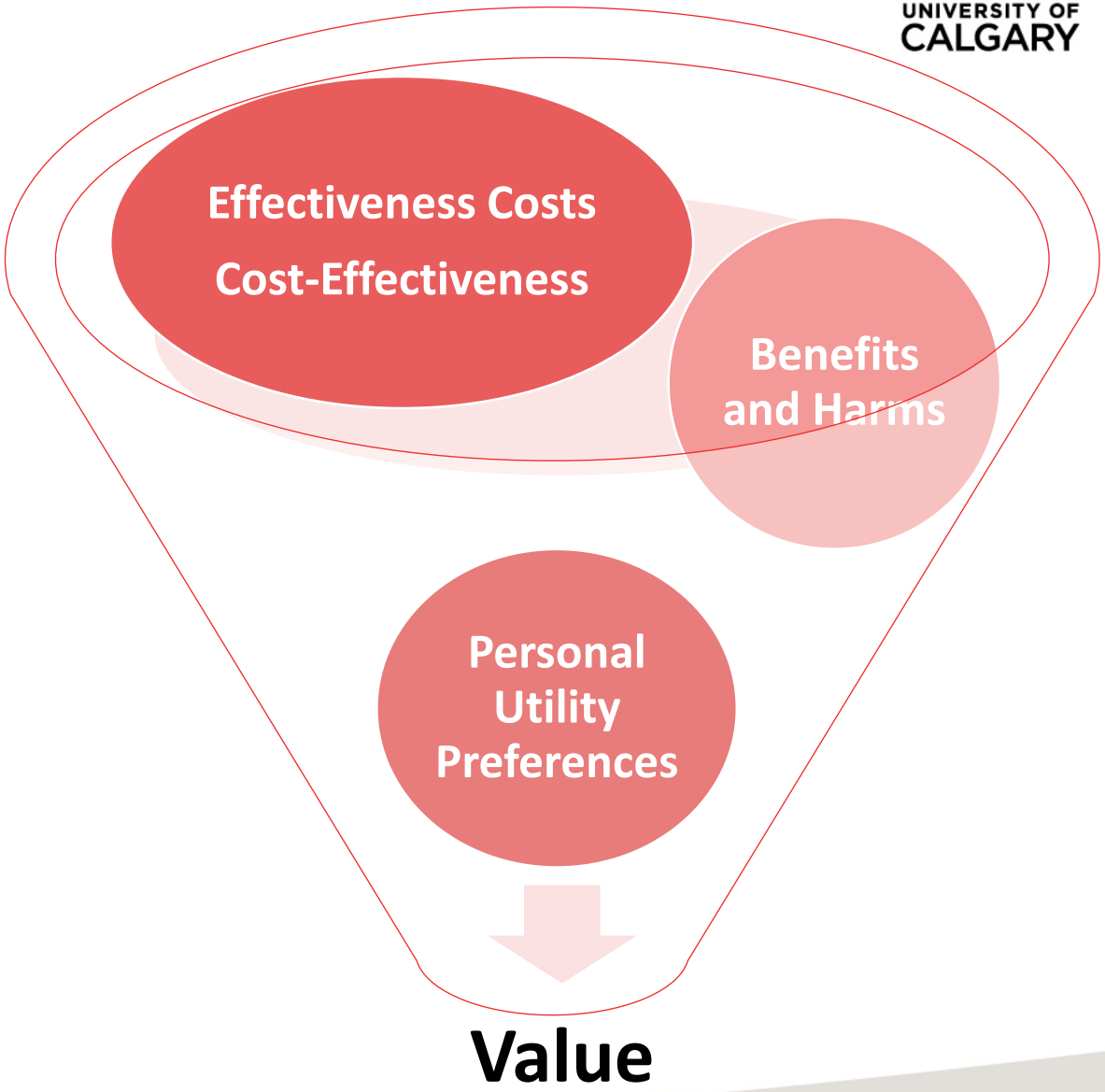


- 95% report some or a lot of fulfilment from carrying out care tasks
- 38% report having no support for carrying out care tasks
- 39% and 34% report some or a lot of problems with physical health and mental health respectively

- Grazziotin et al. Factors Associated with Care- and Health-Related Quality of Life of Caregivers of Children with Juvenile Idiopathic Arthritis. Pediatric Rheumatology 2022;20:51

Perspective on Value: Moving Beyond CEA and QALYs

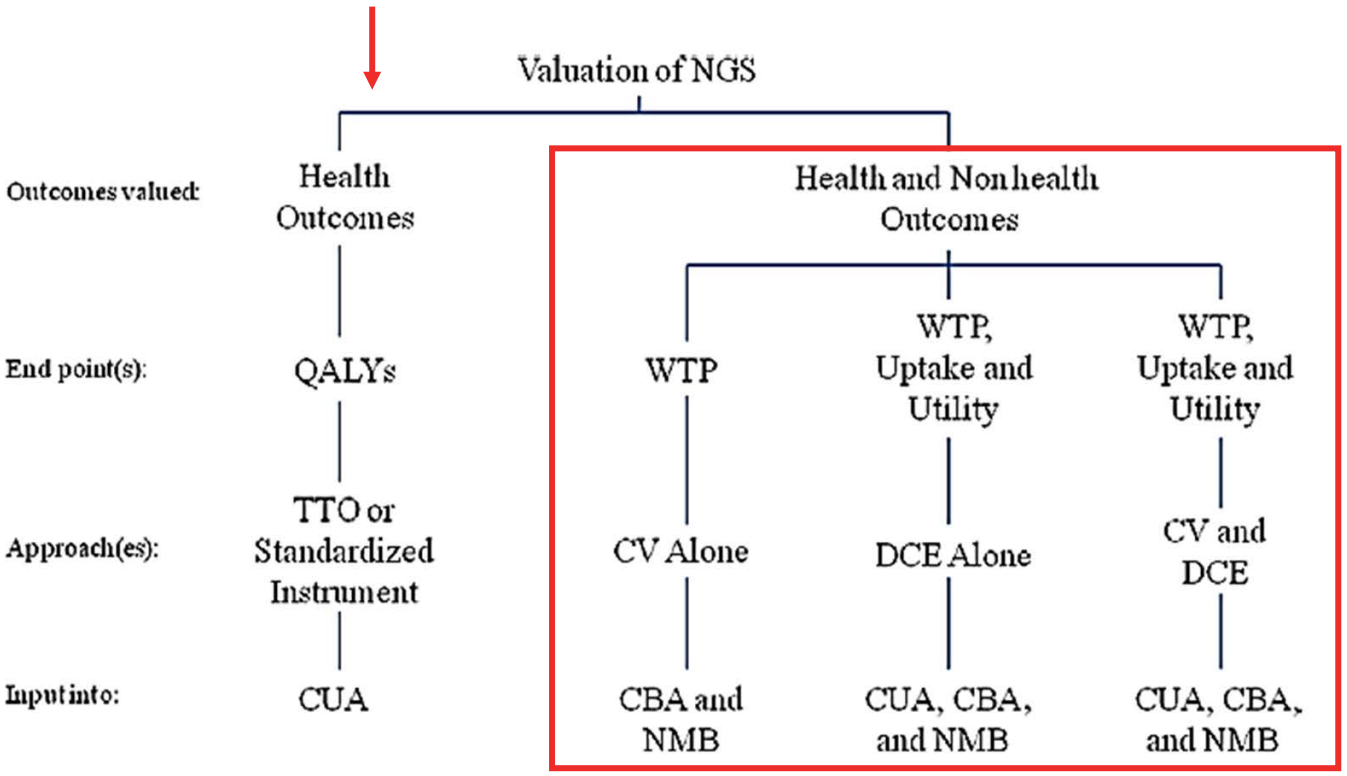
- PM highlights the need for analyses beyond traditional economic evaluation to support decision making
- Personal Utility and Preferences: Non-health value associated with the process, outcomes and features
  - *Desirability: preferences for positive aspects (benefits)*
  - *Acceptability: aversion to negative aspects (harms or risks)*



- *Husereau D, Marshall DA, Levy AR et al. Health technology assessment and personalized medicine: are economic evaluation guidelines sufficient to support decision making? IJTAHC 2014 30(2): 179-187.*

Moving Beyond QALYs…Preference-based Approaches to Valuation of Next Generation Sequencing (NGS)

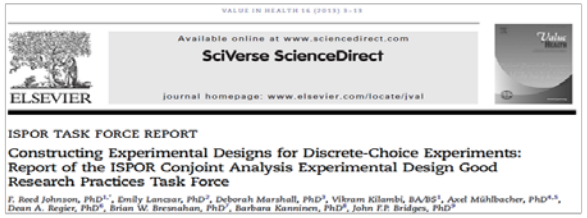
Typical Approach

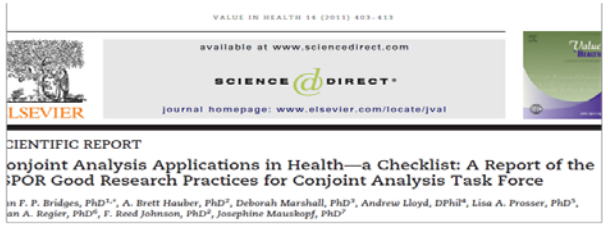


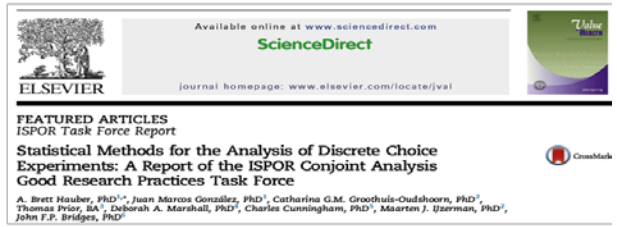
- Preference-based approaches thinking about value beyond QALY (willingness to pay, uptake, utility)
- We have well defined, theory based methods to measure value

- Regier DA, Weymann D, Buchanan J, Marshall DA, Wordsworth S. Valuation of Health and Nonhealth Outcomes from Next-Generation Sequencing: Approaches, Challenges, and Solutions. Value Health. 2018 Sep;21(9):1043-1047

Measuring What Matters to Patients: Preferences in Health







https://www.ispor.org/workpaper/ConjointAnalysisGRP.asp

In Progress Preferences Task Force #4: A Framework for Measuring Patient Preferences to Inform Decision Making in Health Good Practices Task Force Proposal Co-Chairs: John Bridges, Deborah Marshall, Esther de Bekker-Grob

ISPOR Task Forces on Good Research Practices

Why Patient Preferences?

"Aligning health care policy with patient preferences could improve the effectiveness of health care interventions by *improving adoption of, satisfaction with, and adherence* to clinical treatments."

Example: Value of Information for PM Testing Results
Method: Contingent Valuation

- *Marshall DA, Gonzalez JM, MacDonald KV, Johnson FR. Estimating Preferences in the Context of Complex Health Technologies: Lessons Learned and Implications for Personalized Medicine. Value in Health, 2017; 20(1): 32-39.*

- *Marshall DA, Gonzalez JM, Johnson FR, MacDonald KV, Pugh A, Douglas MP, Phillips KA. Who decides and what are people willing-to-pay for whole genome sequencing information? Genetics in Medicine. 2016; 18(12): 1295-1302. doi:10.1038/gim.2016.61.*

Preferences to Value PM Test Information: Whole Genome Sequencing (WGS)

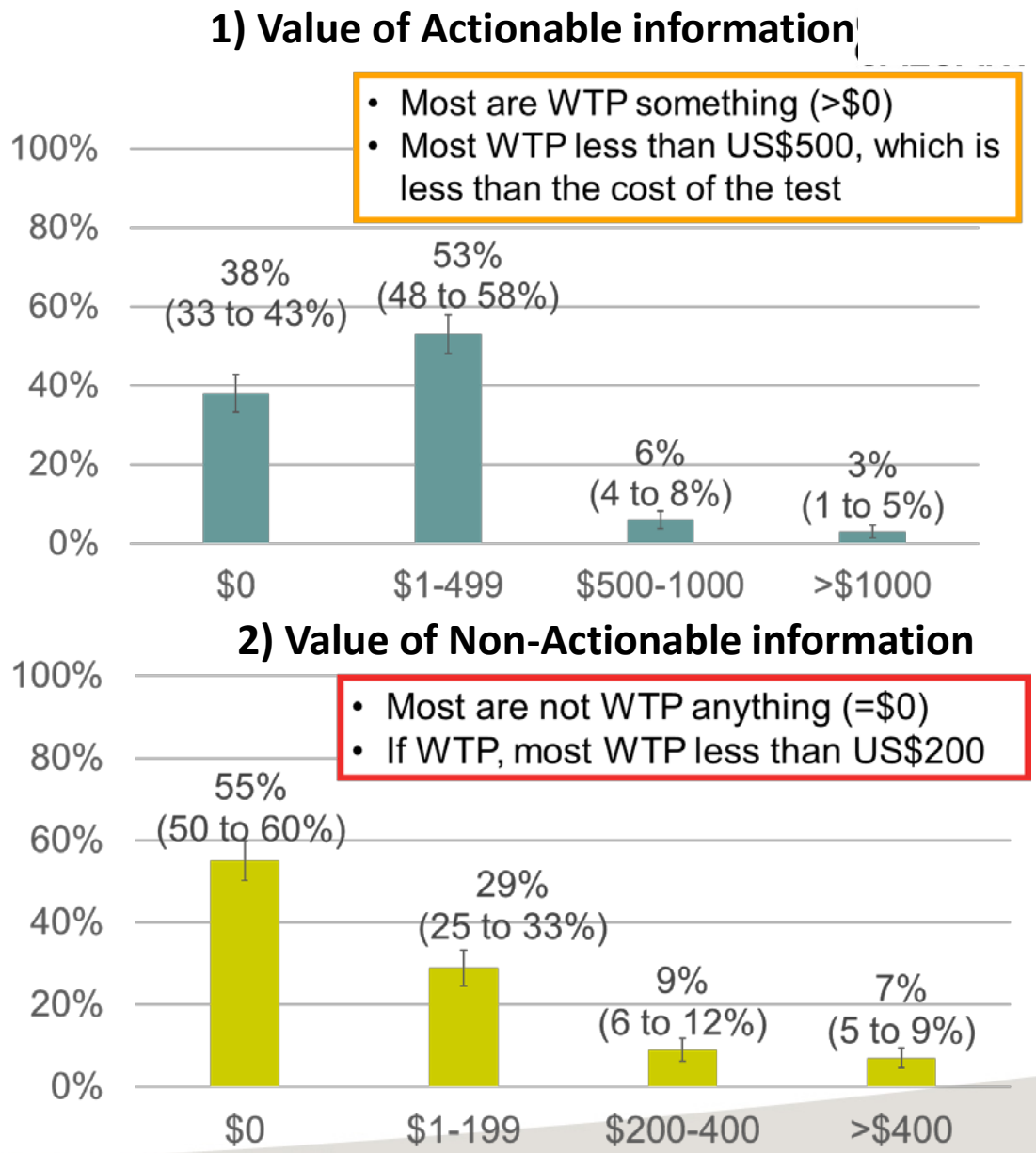
- WGS Testing is now being offered in clinical care and is expected to become more widely used in the near future
- What about the down stream consequences of testing
- What about the potential effect on others – e.g. family members

Value and Preferences for WGS?

- Joint production problem - WGS testing reports produce both beneficial and undesirable information
- Incidental information can have negative utility – more information is not always better

What are people willing-to-pay for PM? Value of Testing Information

- Despite valuing actionable information more, some respondents perceive genetic information could negatively impact them.
- Heterogeneity in preferences should be considered in the development of WGS policies, particularly in integrating patient preferences with PM and shared decision making.



Example: Personal Utility
Method: Discrete Choice Experiment

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Estimating the Value of Whole Exome Sequencing (WES) for Parents of Children with Rare Genetic Diseases

(GELS Activity Lead: Deborah Marshall)

CARE forRARE

UNIVERSITY OF CALGARY

CHEO Research Institute Institut de recherche

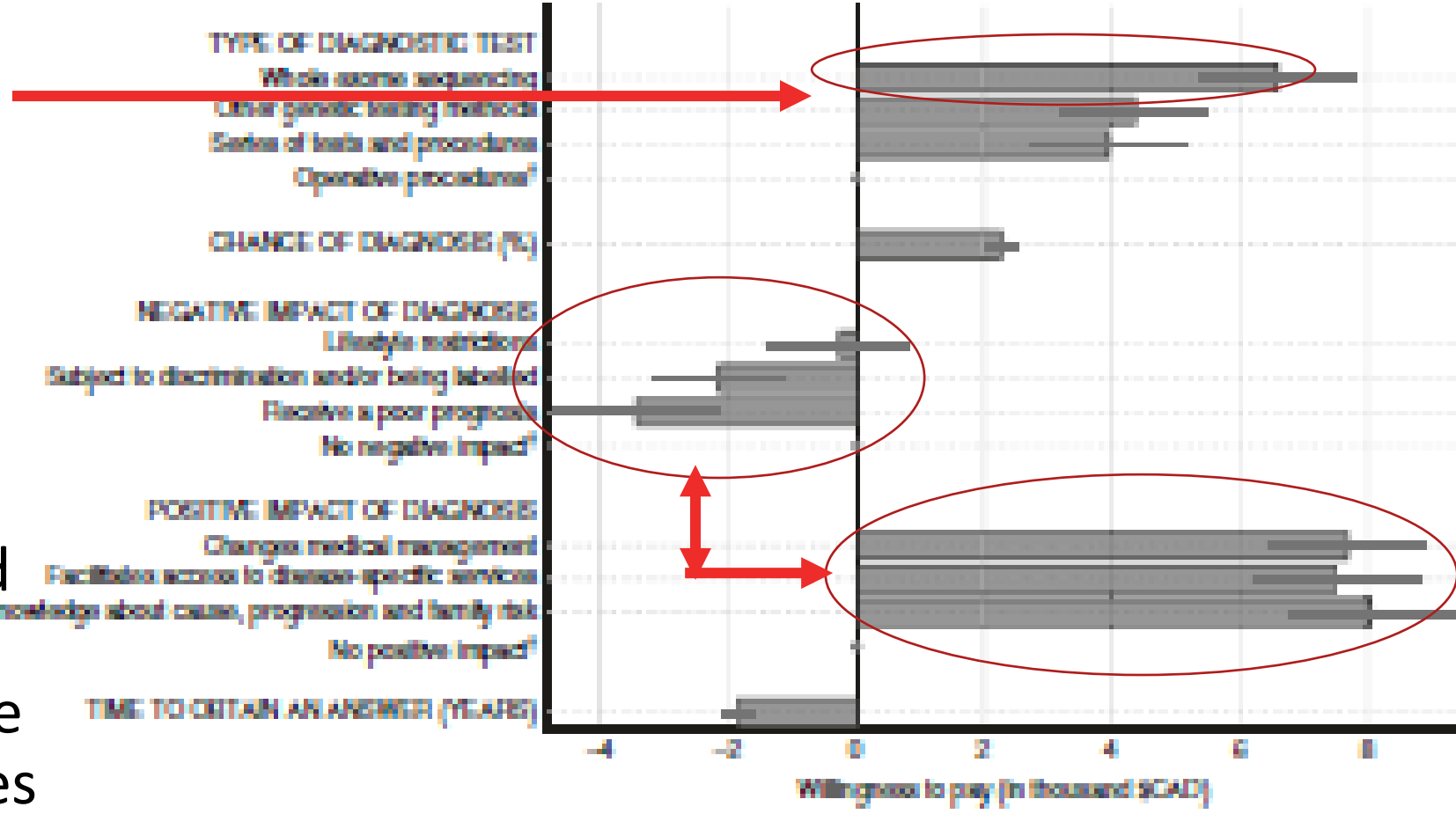
GenomeCanada

CIHR IRSC Canadian Institutes of Health Research Instituts de recherche en santé du Canada

- Marshall DA, MacDonald KV, Heidenreich S, Hartley T, Bernier FP, Gillespie MK, McInnes B, Innes AM, Armour CM, Boycott KM. The value of diagnostic testing for parents of children with rare genetic diseases. Gen Med 2019 21(11):2662.

Preferences for Whole Exome Sequencing (WES)

- Preference for WES over alternatives
- Positive impacts affected choices more than negative impacts
- Increased knowledge and changes in management or access to services were the most valued attributes

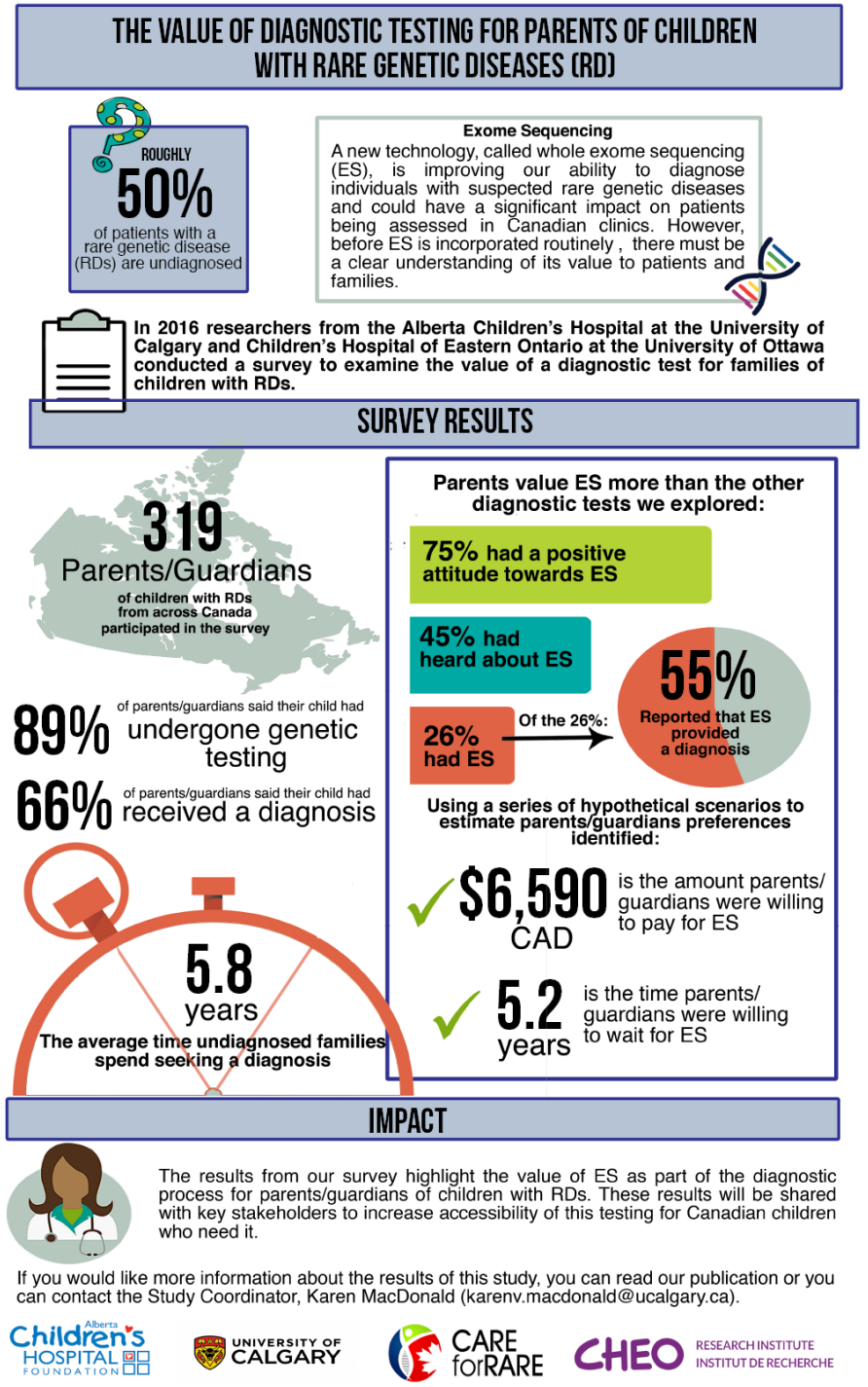


Value of WES Diagnostic Testing for Rare Diseases (n=319)

Preference for ES and other genetic tests

- Parents were willing to pay ~CAD$6,500
- Willing to wait 5.2 years to obtain diagnostic test results from ES

…compared with other procedures

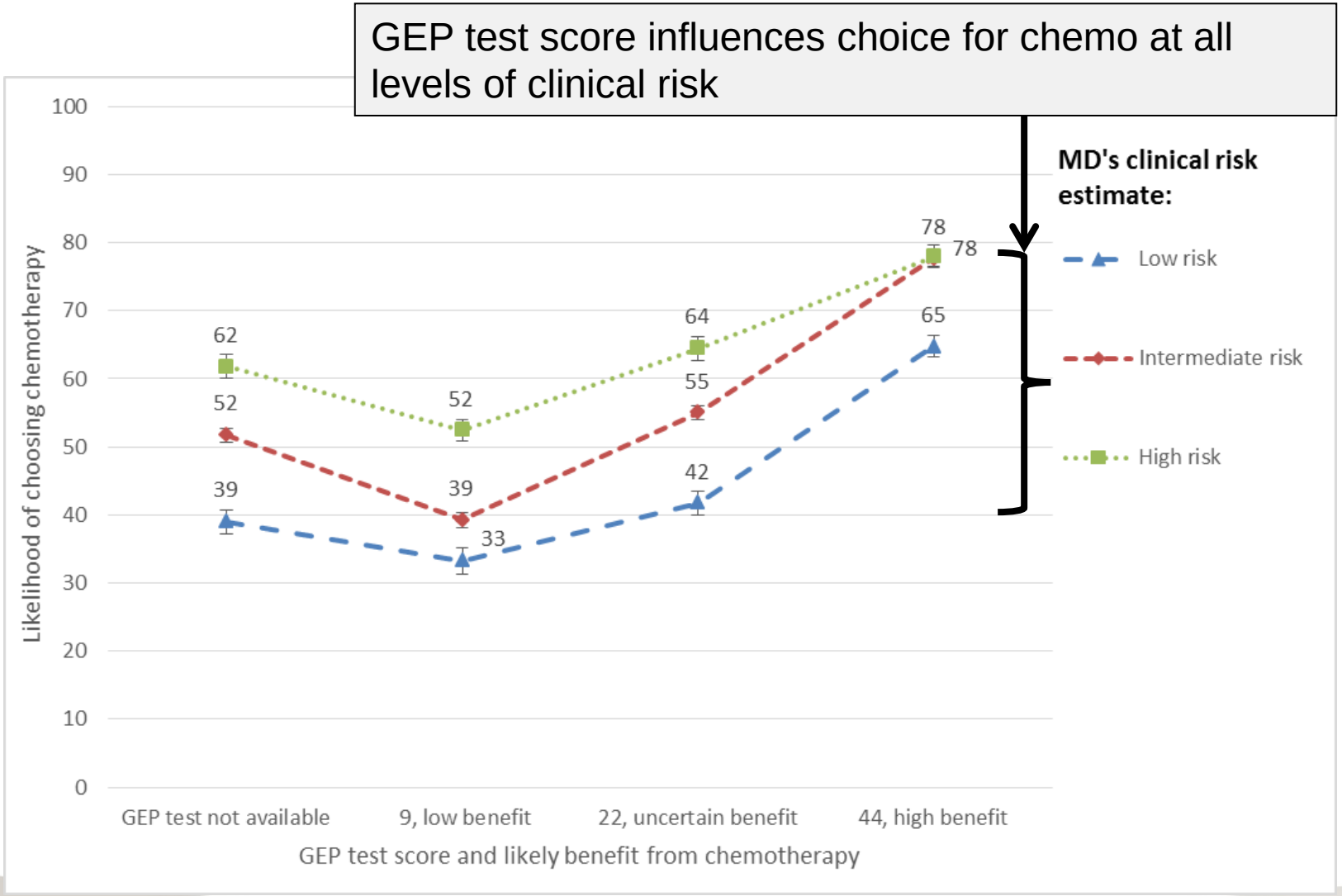


Example:
Understanding Benefit-Risk Trade-offs of Gene Expression Profile (GEP) Testing in Chemotherapy Treatment Decisions for Breast Cancer

- *Marshall DA, Deal K, Bombard Y, Leighl N, MacDonald KV, Trudeau M. How do women trade-off benefits and risks in chemotherapy treatment decisions based on gene expression profiling for early-stage breast cancer? A discrete choice experiment. BMJ Open 2016;6:6 e010981 doi:10.1136/bmjopen-2015-010981*

- *MacDonald KV, Bombard Y, Deal K, Trudeau M, Leighl N, Marshall DA. The influence of gene expression profiling on decisional conflict in decision making for early-stage breast cancer chemotherapy. European Journal of Cancer. 2016;61:85-93.*

GEP Testing Information Influences Stated Uptake of Chemotherapy Treatment



Simulation Modeling to Address Complex Clinical Pathways with PM Testing and Treatment

- *Simulation models (e.g. discrete event simulation) are well suited to PM since PM uses individual patient-specific information to inform selection of therapy tailored to the patient*
- *A systematic review reported increase in patient-level simulation methods in the last decade*

Challenge	Specification of challenge in the checklist	How these challenges are addressed by simulation modeling and limitations compared with traditional health economic modeling
1. Modeling patient-level processes	Is the model defined on a patient level?	Patient-level models reflecting care pathways considering context of delivery
2. Modeling patients' preferences	Are patients' preferences modeled to take their effect on the outcomes into account?	Incorporate at decision nodes the probability of uptake based on patient preferences; issue of availability of the data and the attributes from preferences need to align with variables in the model/ care pathway
3. Modeling physicians' preferences	Are physicians' preferences modeled to take their effect on the outcomes into account?	Incorporate at decision nodes the probability of uptake based on physician preferences; issue of availability of the data and the attributes from preferences need to align with variables in the model/ care pathway
4. Taking into account the diagnostic performance of tests	Is the effect of the sensitivity, specificity, positive predictive value, and/or negative predictive value on the outcomes taken into account?	Include compound probabilities based on patient-specific pathways considering context of care delivery
5. Modeling combinations of tests	Does the modeled process include combinations of tests and/or prediction models?	Include compound probabilities based on patient-specific pathways
6. Modeling companion diagnostics	Does the modeled process include combinations of test(s) and treatment(s)?	Include compound probabilities based on patient-specific pathways
7. Study-specific outcome measures	Does the modeled process include study-specific outcomes, such as disease-specific adverse events?	Patient-level models reflecting care pathways and patient-specific outcomes based on patient characteristics
8. Data gaps	Do the authors mention any evidence gaps? If so, do they mention that these evidence gaps exist because of stratification of patients based on risk models and/or test results?	Simulation models offer greater flexibility to include patient-specific pathways and account for stratification of patients based on risk models and/or test results
9. Greater uncertainty due to more complex analysis	Do the authors mention greater uncertainty with respect to the outcomes, due to more complex analysis, as a result of personalization of the model?	Simulation models offer greater flexibility to include patient-specific pathways and account for uncertainty at a patient level; there remain challenges to aggregate these findings
10. Absence of guidelines	Do the authors mention any difficulties related to the absence of guidelines for health economic modeling in the context of personalized medicine?	There is guidance for simulation modeling from the operations research literature and emerging in health

- *Marshall DA et al. Addressing challenges of economic evaluation in precision medicine using dynamic simulation modelling. Value in Health, May 2020;23(5):566-573*

- *Degeling K et al. A systematic review and checklist presenting the main challenges for health economic modeling in personalized medicine: towards implementing patient-level models. Expert Rev Pharmacoecon Outcomes Res. 2017;17(1):17–25.*

Modeling Care Pathways for Individual Patients

JIA onset

Prescribe NSAIDs / IA injections / DMARDS

Flare (increase medication)

Reduce dose NSAIDs / DMARDs

Stop medication (remission)

Flare (increase medication)

Ineffectiveness

Intolerance

Most relevant predictors?

Targeting interleukin-1 in unique 'window of opportunity ' for JIA

Prescribe biological

Flare (increase medication)

Reduce dose biological

Switch to DMARDs (remission)

Flare (increase medication)

Pause

Vastert S et al. Effectiveness of First-Line Treatment With Recombinant Interleukin-1 Receptor Antagonist in Steroid-Naive Patients With New-Onset Systemic Juvenile Idiopathic Arthritis: Results of a Prospective Cohort Study. Pediatric Rheumatology 2014; 66(4):1034-43

Measuring Value in Personalised Medicine

Measure What Matters to Patients, Families and Their Communities

Evaluate Complex Clinical Pathways Reflecting PM Testing and Treatment Trajectories

Thank you!

Questions and Discussion

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