



Poll 1

Have you ever used (or developed) an open source model?

Multiple choice

- Yes (in precision medicine)
- Yes (not in precision medicine)
- No



Improving healthcare decisions

Open source in precision medicine: the perfect fit?

Chris Sampson, Office of Health Economics On behalf of the Open Source Models Special Interest Group #ISPORAnnual #OSMSIG @ChrisSampson87



Brought to you by the ISPOR Open Source Models Special Interest Group

- A new SIG, established in 2020
- Current leadership: Chair Me | Past (and founding) Chair Renée Arnold | Chair-Elect Raymond Henderson
- ~150 members across
 - 틀 46% US 🏶 9% UK 💿 7% India
 - 😂 29% academia
- 4 journal clubs, 1 webinar
 - Watch them online!
- 1 publication

ISPOR Report

Opportunities and Barriers to the Development and Use of Open Source Health Economic Models: A Survey

Xavier G.L.V. Pouwels, PhD, Christopher J. Sampson, PhD, Renée J.G. Arnold, PharmD, RPh, On behalf of the Open Source Models Special Interest Group

Join us!

www.ispor.org/member-groups/special-interest-groups/open-source-models



Our objectives

To identify **opportunities and challenges** for open source modelling in precision medicine.

To explore **technical aspects of modelling** in precision medicine and their link to open source practices

To consider **strategic questions** for the development of open source models

To **discuss** your views!

OHE

Open source is source code that is made freely available for possible modification and redistribution (says Wikipedia)

- ✓ Transparent reporting
- ✓ Sharing underlying code
- ✓ Removing restrictions on use

- ! Inclusive approach
 - ! 'Free' as in freedom *or* 'free' as in free beer
- ! As much about intention as realisation
 - ! 100% open source is often impossible

Why open source?

Good science

Efficiency savings

Improved methods

Better decisions

Learning















Why precision medicine?

Improve cost-effectiveness

Recognise patient trajectories

Therapeutic adjacency

Decision complexity

Software flexibility







Improving healthcare decisions

Today's speakers

Susan Snyder

Co-Chair, Precision Medicine and Advanced Therapies SIG Georgia State University

Deborah Marshall University of Calgary

Koen Degeling

Lumen Value & Access

Generic Modeling for Precision Medicine:

A Pharmacogenomic Decisionmaking Tool

Presented at ISPOR 2022 in Washington, DC



Susan R. Snyder, PhD, MBA Associate Professor School of Public Health | Georgia State University Co-Chair ISPOR Precision Medicine and Advanced Therapies SIG, Next Generation Testing Project

Case Example: Pharmacogenomic Open-Source Model and Decision Tool

Research Article

Public Health Genomics

Public Health Genomics DOI: 10.1159/000500725 Received: January 22, 2019 Accepted: April 16, 2019 Published online: June 12, 2019

Generic Cost-Effectiveness Models: A Proof of Concept of a Tool for Informed Decision-Making for Public Health Precision Medicine

Susan R. Snyder^a Jing Hao^a Larisa H. Cavallari^b Zhi Geng^a Amanda Elsey^b Julie A. Johnson^b Zahurin Mohamed^c Nathorn Chaiyakunapruk^{d-g, n} Huey Yi Chong^d Maznah Dahlui^h Fatiha H. Shabaruddinⁱ George P. Patrinos^{j, k} Christina Mitropoulou¹ Marc S. Williams^m

Study funded by the US National Human Genome Research Institute (research grant number U01 HG007269).



Why Open-Source Generic Model?

- Value-based decisionmaking
- Emerging evidence base
- Disparate modeling approaches
- Transparency
- Efficiency

Challenges?

- Generalizability
- Validity
- Usability
- Relevance







Generic Pharmacogenomic Screening Economic Model: Adult-Onset Epilepsy



Economic evaluation of HLA-B*I5:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand



Generic Economic Evaluation Decision Analysis Model and Tool Development Process

1. Team Create a generic model development team with relevant stakeholders and expertise represented (e.g., clinical, economic, pharmacogenomics, policy) to employ a consensus-based review process. 2. Original model(s) Modify at least one existing peer-reviewed model to make it generalizable by completing a detailed review of the model structure, variables and assumptions. 3. Evidence Complete evidence reviews and obtain expert opinion as needed to provide supporting documentation for the new generalizable assumptions and parameter values. 4. Generic model Identify which model variables and assumptions will be default values only, input values only or offer default and input options.

Georgia<u>State</u> University.

Generic Model Inputs



Variables and assumptions retained requiring an input value assigned to three categories

1) Input value only

User-specified value (e.g., all medical cost variables, population allele prevalence for pharmacogenomics test) (Table1)

2) **Default value only**

- Supported by very strong evidence (e.g., test sensitivity and specificity)
- Likely unavailable due to very limited evidence (e.g., health state utility of a very rare disease), or otherwise required by the model to meet certain logic requirements (e.g., health state utility value is constrained by its relationship to other state values).

3) **Default value with an input option**

Allowed user to select either approach to address the need for information for an input value which is not readily available by providing a default based on available evidence

Generic Economic Evaluation Decision Analysis Model and Tool Development Process





Generic Model Cross-Validation: Country-Specific Input Values & Models

Thailand Model



	Baseline	Option 1	Option 2	Baseline	Option	1	Optio	n 2			0.5	
Result (THB)	Current practice	HLA- B*1502 screening	No HLA- B*1502 screening	Current practice	HLA-B*1 screeni	502 ng	No HI B*15 screer	_A- 02 ning				
Cost	17,915	26,006	61,104	16425	24,	752	61	1,212				
QALYs	25.18	25.21	25.22	13.81	13	3.83	-	13.83				
ncremental cost	-	8,091	43,190	-	8,	327	44	1,787				
ncremental QALYs	-	0.032	0.038	-	0.	017	(0.017				
CER	-	250,896	1,140,944	-	493,	483	2,651	1,431				
Threshold CFR	160, 000					Base	Sir eline	ngapore M Option 1	lodel Option 2	Generic Moo Baseline	lel with Singa Option 1	Option 2
	Res (US		Resu (US D	ult Dollars) pr		rent ctice	HLA- B*1502 screening	No HLA- B*1502 screening	Current practice	HLA-B*1502 screening	No HLA- B*1502 screening	
				Cost	Cost		4,110	4,680	6,780	1,203	1,668	3,016
				QALY	′s	18	8.846	18.865	18.865	17.88	17.92	17.92
				Incre cost	mental		-	570	2,100	-	465	1,813
				Incre QALY	mental ′s		-	0.019) –	-	0.048	0.048
				ICER			-	29,750	-	-	9,717	37,834
				Three	shold	50	0,000					

Generic Model with Thailand Inputs

Generic Model & Decision Tool: Input Table

		<u>Required Input Variables</u>		<u>Input Value</u>		Georgi	aState
		Prevalence				Univ	versity.
Overvie	W	Prevalence of HLA-B*1502 allele (carrier status) in study	Mean	0.1487			
		population, please note that this is not allele frequency, it	Min	0.11			
		is twice the allele frequency	Max	0.1874			
Model Diagrams	rams	Cost			Ontional Input Variables		Innut value
		Selected Currency		US dollars	<u>Probabilities</u>		
		Base year		2010	Probability of CBZ-induced SJS/TEN in HLA	A-	0.0506
Input Tab		Cost of HLA-B*1502 screening test (includes all costs		270	B*1502 +ve patient		0.0390
input fables	les	related to screening test)		270	<u>Utility</u>		
		Cost of SJS/TEN treatment (1 year): Annual direct		10.250		Mode	0.907
		medical cost of CBZ-induced SJS/TEN		10,230	Utility score of patient with epilepsy	Min	0.7
Results		Cost of follow up with SJS/TEN sequelae: Annual direct	Min	42.5		Max	0.999
		medical cost of sequelae (base-case value assume \sim dry		170	170		0.68
		eye syndrome)	Iviax	170	Utility score of patient with SJS/TEN sequela	ae <u>Min</u>	0.57
		Cost of disease treatment				Max	0.79
ICER		Annual direct medical cost of epilepsy treatment with		170	<u>Treatment Duration</u>		
		CBZ			Treatment duration of epilepsy		7
		Annual direct medical cost of epilepsy treatment with			<u>Discount rate</u>		0.00
CE Plane		VPA		470	Discount rate for costs		0.03
		Ceiling ratio and threshold value			Discount rate for outcomes		0.03
CEAC		Maximum acceptable ceiling value for use in the maximum acceptable ceiling ratio (in selected currency/QALY gained)		200,000			
		Cost-effectiveness threshold value (in selected currency/QALY gained)		50,000			

Generic Model Decisionmaking Tool: Cost-Effectiveness Results

Deterministic/Race Case	Baseline	Option 1	Option 2		
(US Dollar)	Current practice	HLA-B*1502	No HLA-B*1502		
	ourient practice	screening	screening		
Cost	1,203	1,668	3,016		
QALYs gained	17.88	17.92	17.92		
Incremental cost		465	1,813		
Incremental QALYs		0.048	0.048		
ICER		9,717	37,834		
Threshold ICER	50,000				
	Number Needed	to Screen and Ca	ses Prevented		
Cases prevented by screening 1 epilepsy patient	0.0089				
Number needed to screen to prevent 1 SJS/TEN		113			





Generic Model Applications

> Pharmacogenomics J. 2021 Aug;21(4):476-483. doi: 10.1038/s41397-021-00225-9. Epub 2021 Apr 6.

Cost-effectiveness analysis of genotyping for HLA-B*15:02 in Indonesian patients with epilepsy using a generic model

Rika Yuliwulandari ¹², Jae Gook Shin ³⁴, Erna Kristin ⁵, Fransiscus D Suyatna ⁶, Iwan Dwi Prahasto ⁵, Kinasih Prayuni ⁷, Surakameth Mahasirimongkol ⁸, Larisa H Cavallari ⁹, Christina Mitropoulou ¹⁰, George P Patrinos ¹¹¹², Jing Hao ¹³, Marc S Williams ¹⁴, Susan R Snyder ¹⁵

GENERAL DERMATOLOGY

BJD British Journal of Dermatology

Is universal *HLA-B*15:02* screening a cost-effective option in an ethnically diverse population? A case study of Malaysia

H.Y. Chong,¹ Z. Mohamed,² L.L. Tan,³ D.B.C. Wu,¹ F.H. Shabaruddin,⁴ M. Dahlui,⁵ Y.D. Apalasamy,² S.R. Snyder,⁶ M.S. Williams,⁷ J. Hao,⁶ L.H. Cavallari⁸ and N. Chaiyakunapruk^{1,9,10,11}







Thank you Susan R. Snyder

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Case Example UCAN CAN-DU: Precision Health in Childhood Arthritis

Presented by: Deborah A Marshall, PhD

Professor and Arthur J.E. Child Chair Rheumatology Outcomes Research Cumming School of Medicine, University of Calgary

ISPOR Conference, Washington, May 2022









Recommendation

Total of 21 recommendations:

- general principles (1–3)
- ethics (4–7)
- paediatric principles (8-9)
- consent to paediatric research (10–14)
- paediatric databank and biobank (15-16)
- sharing of data and samples (17–19)
- commercialisation and third parties (20-21)

Kuemmerle-Deschner JB, Hansmann S, Wulffraat NM, Vastert SJ, Hens K, Anton J, Avcin T, Martini A, Kone-Paut I, Uziel Y, Ravelli A, Wouters C, Shaw D, Ozen S, Eikelberg A, Prakken BJ, Ruperto N, Horneff G, Constantin T, Beresford MW, Sikken M, Foster HE, Haug I, Schuller S, Jagle C, Benseler SM. Recommendations for collaborative paediatric research including biobanking in Europe: a Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) initiative. Ann Rheum Dis. 2018;77(3):319-27

Recommendations for collaborative paediatric research including biobanking in Europe: a Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) initiative

WEF White paper



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COMMITTED TO IMPROVING THE STATE OF THE WORLD

White Paper

Global Data Access for Solving Rare Disease A Health Economics Value Framework

• Highlights that access to global data critical

Framework identifying the **benefits of data sharing** in federated data system, potential for return on investment across four major areas:

- **Diagnostic benefit**: The identification of pathogenic or likely pathogenic variants in known disease genes
- Clinical benefit: Changes in the medical or surgical management of patients as a result of the diagnosis being made
- Clinical trial benefit: Changes related to the improvement of clinical trial operations
- **Personal benefit**: The presence of non-clinical outcomes that are important from a personal point of view to patients.

⁻ Belsey J, Chaihorsky L, Chediak L, Currie GR, Goranitis I, Marshall DA. Global Data Access for Solving Rare Disease: A Health Economics Value Framework. World Economic Forum, February, 2020. (http://www3.weforum.org/docs/WEF Global Data Access for Solving Rare Disease Report 2020.pdf)



Expanding Use of Clinical Genome Sequencing and the Need for More Data on Implementation

Kathryn A. Phillips, PhD

Center for Translational and Policy Research Personalized Medicine (TRANSPERS), Department of Clinical Pharmacy, University of California, San Francisco, and Philip R. Lee Institute for Health Policy Studies, University of California, San Francisco.

Michael P. Douglas,

MS Center for Translational and Policy Research on Personalized Medicine (TRANSPERS), Department of Clinical Pharmacy, University of California, San Francisco.

Deborah A. Marshall, PhD

Cumming School of Medicine, Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; and O'Brien Institute for Public Health, University of Calgary, Calgary, Alberta, Canada.

Author Audio

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Supplemental content

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Center for Translational and Policy Research on Personalized Medicine (TRANSPERS), Department of Clinical Pharmacy, University of California, San Francisco, 490 Illinois St, Third Floor, PO Box 0613, San Francisco, CA 94143-2510 (kathryn, phillips@ucsf.edu). (NGS) has transitioned from research to clinical use.¹ At least 14 countries have created initiatives to sequence large populations (eg, All of Us, Genomics England), and it is projected that more than 60 million people worldwide will have their genome sequenced by 2025.¹ However, there has not been an assessment of global NGS implementation (defined here as the use of testing in routine clinical care as measured by clinical applications, utilization, and coverage/funding/ reimbursement). Implementation is a key pillar in the translational continuum of discovery, utility, implementation, and population health impact.² Understanding how NGS is being used and paid for is critical

standing how NGS is being used and paid for is critical for determining its clinical and economic benefits and addressing current and future challenges to appropriate implementation.

What Is NGS and How Is It Used in Clinical Care?

NGS is a broad term that encompasses several modern sequencing technologies that measure variations in genes that are present at birth or emerge later in life (eg, cancers or viruses). Many NGS tests are available for clinical care and are being used for clinical applications, including risk assessment, diagnosis, prognosis, and therapy selection. The eTable in the Supplement provides examples of tests currently in use in countries that have widespread NGS implementation, as well as several emerging and future tests. Emerging tests (eg, liquid biopsy tests for cancer screening) could influence clinical outcomes and health care budgets. Thus, the identification of emerging and future tests can guide the collection of data needed by clinicians and policy makers to inform

appropriate implementation. This Viewpoint examines use, payment/coverage, and gaps in data availability on implementation of NGS worldwide using 3 common tests³ as examples of NGS: (1) noninvasive prenatal testing (NIPT), (2) whole-exome sequencing (WES)/whole-genome sequencing (WGS) for suspected genetic disorders.

Use of NGS Around the World

and (3) tumor sequencing (TS)

NIPT is widely used and is currently available in at least 90 countries. In the commercially insured population in the US, almost a half-million NIPT tests were reimbursed in 2019, along with 5600 WES tests and 70 300 TS tests.⁴ There is increasing, but variable, use of NIPT, WES/WGS, and TS in Canada, Europe, the Middle East, and Asia, and to a more limited extent in Central/South America and Africa. Even some middle-income countries are implementing NGS in clinical care.

During the past 5 years, next-generation sequencing Payment and Coverage

Whether tests are covered or funded varies by the type of health care system (private or public). The UK is recognized as a leader in nationally funded coverage for NGS testing, although several other European and Asian countries also have national coverage for some NGS tests.

The US provides an example of how coverage varies depending on the clinical scenario and payer type.⁵ Almost all (97%) insured individuals have NIPT coverage, although about half (48%) of this coverage is for women in high-risk categories (eg, advanced maternal age, family history of abnormal pregnancy) only. Most Medicaid enrollees (90%) also have NIPT coverage, but a greater percentage (62%) of this coverage is for women in high-risk categories only. More than half of insured individuals (63%) have WES and/or WGS coverage, although the percentage of Medicaid enrollees with coverage is lower (39%). Most insured individuals (80%) have coverage for TS, although this declines

als (80%) have coverage for TS, although this declines to 56% of Medicaid enrollees having coverage. In contrast, all Medicare enrollees have select TS coverage based on a 2018 National Coverage Determination.

NIPT and small TS panels (<50 genes) have the lowest reimbursement rates (up to approximately \$1000), whereas WES/WGS and comprehensive TS have the highest (up to approximately \$5000). Patients in the US who self-pay can obtain NIPT for \$99 and exome sequencing (trio) for \$2500.⁵ Despite the high costs of some NGS tests, expenditures for NGS in the US represent a small percentage of health care expenditures (approximately 0.13% of Medicare expenditures).⁶

Gaps in Data Availability on Implementation

There is no central source of information on implementation across countries and clinical applications. Much of the available data are from the US only; in many other countries, little or no data are publicly available. A consistent gap is data on usage, with sparse data available on how many tests are performed even in countries with high implementation, such as the US. Peer-reviewed publications only provide data on select tests and specific health care systems and are based on historical vs current data. As a result of these gaps, data on implementation must be compiled across diverse sources. For example, some data can be found in the gray literature (eg, white papers, health system reports, market analyses, regulatory filings, company websites, news reports, national/international consortia websites) and some data can be obtained from administrative/clinical resources (eg, electronic health records, claims data, fee schedules, industry databases. registries). Much of the needed data are proprietary, costly to obtain, or both, such as lab data and market

Need for Open Source Health Economics Modeling in Precision Medicine

....key next step is to integrate information on both clinical utility and implementation to assess the overall impact...

Global Economics and Evaluation of Clinical Genomics Sequencing Working Group (GEECS) health economists and policy researchers on genomics into clinical care

https://pharm.ucsf.edu/transpers/grants-programs/pghe-working-group

- Phillips KA, Douglas MP, Marshall DA. Expanding Use of Clinical Genome Sequencing and the Need for More Data on Implementation. JAMA 2020;324(20):2029-2030. doi:10.1001/jama.2020.19933

UCAN CAN-DU and beyond: Towards a global genomics partnership for childhood arthritis (JIA)



Overall Aim: To create a transformative roadmap for global, secure sharing of genomic, phenotypic and health economic data across borders that considers genomic, clinical and economic data mandates and is guided by diverse legal, ethical and regulatory requirements across borders.

Aim 1. To develop a deep understanding of the current provincial, national and international childhood arthritis datasets, related data sources such as administrative datasets and their specific ethical, legal and technical frameworks.

Aim 2. To establish a UCAN stakeholder team enriched by ethics and legal experts to define the organizational principles of a federated, transparently interconnected database system.

Aim 3. To take steps towards transforming the Dutch-Canadian UCAN data framework into aglobal federated database systems that integrate the Global Alliance for Genomics in Health data access and sharing standards and FAIR principles.



Project Overview – Integrated Thematic Activities







Integrated Health Economics



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(GE³LS) Genomics Ethical, Environmental, Economic Legal and Social Aspects



Complexity of Treatment Patterns in Childhood Arthritis

- Assessment of treatment sequences for different drug classes in current routine practice
- 112 unique treatment sequences in cohort of 325 patients over 5 years



- Grazziotin, L.R., Currie, G., Twilt, M. et al. Real-world data reveals the complexity of disease modifying anti-rheumatic drug treatment patterns in juvenile idiopathic arthritis: an observational study. Pediatr Rheumatol 2022; 20, 25.

Modeling Care Pathways for Individual Patients



* Only events until the age of 18 years are captured in the model

High Performance Computing for Health

- Compute cloud framework as node in the Compute Canada supercomputing infrastructure
- Capable of processing large genomics or other types of data sets ("Big Data")
- Enterprise level governance, management and technical support
- Best practices to maintain patient data confidentiality
- Houses all UCAN CANDU research participant data, eHealth application webservers and webapps for demographic, clinical, patient reported outcomes measures, bioassay data and genomic data











- UCAN data management compliant with GDPR effected by Data and Material Transfer Agreements and a Data Processing
- Data is harmonized and stored using codified standardized vocabularies and allows integration with various third-party systems
- Data protection officer (DPO) ensures adherence to FAIR principles.
- FAIR: Findable, Accessible, Interoperable, Reusable (syntaxes, codes, protocols made available to researchers)

Data management following GDRP and FAIR principles enables sharing of data in real-time and integration of real-time data in analytic models throughout the study course.



Why Open-Source in Precision Medicine ?



- Efficiency required particularly in rare disease research where sample sizes are small
- In precision health, complexity and heterogeneity of clinical pathways and treatment trajectories with clinical, biologic, genomic, preference, and health care resource use data
- To reap the benefits of considerable infrastructure requirements and data collection efforts to enable open-source modeling !

Thank you! Discussion

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Will the Next Generation of Models Make Open-Source Modeling Take Off?

Koen Degeling, PhD

Research Scientist Health Economic Modeling & Advanced Analytics

Presented at ISPOR 2022 in Washington, DC

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The Next Generation of Models Will Continue to Become Increasingly More "Advanced"

Precision Medicine

Patient-level modeling techniques are required to appropriately represent the complex dynamics of today's and tomorrow's clinical pathways

Changing Evidence

Data analysis and evidence synthesis methods are becoming increasingly sophisticated, and models need to match the evidence

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Life Cycle Approach

Shift from static one-off modeling efforts to dynamic evidence synthesis frameworks that evolve throughout the product life cycle

Next Generation of Modelers

Increased training and comfort with code-based software empower today's graduates to be comfortable applying more advanced methods

The Next Generation of Models Provide Both the Need and the Opportunity for Open-Source Modeling



Putting Words Into Action

PharmacoEconomics https://doi.org/10.1007/s40273-020-00951-1

ORIGINAL RESEARCH ARTICLE



Simulating Progression-Free and Overall Survival for First-Line Doublet Chemotherapy With or Without Bevacizumab in Metastatic **Colorectal Cancer Patients Based on Real-World Registry Data**

Koen Degeling^{1,2} Hui-Li Wong^{3,4} Hendrik Koffijberg¹ Azim Jalali³ Jeremy Shapiro⁵ Suzanne Kosmider⁶ Rachel Wong^{3,7,8} + Belinda Lee^{3,4,9} · Matthew Burge¹⁰ · Jeanne Tie^{3,4,6} · Desmond Yip¹¹ · Louise Nott¹² · Adnan Khattak¹³ · Stephanie Lim¹⁴ · Susan Caird¹⁵ · Peter Gibbs^{3,6} · Maarten IJzerman^{1,2,4}



Collaborators:







Manuscript & **Supplements**



R code & Shiny app

Putting Words Into Action: *Simulating PFS and OS Based on Real-World Data*



Objective

Simulate conditional outcomes for specific patient profiles based on registry data

Challenges

- Missing data on covariates
- Variable selection for parametric survival models
- Missing data <> variable selection
- Validation of multivariable parametric survival models
- Validation of overall (multivariable) simulation model

Solutions

- Discrete event simulation
- Multiple imputation
- Forward and backward selection
- Pooled statistics for variable selection in each step
- Bootstrap approach to correct for optimism in internal validation
- Kaplan-Meier curves and summary statistics for subgroups

Italics indicate codes for which no existing functions/codes were available



Outcomes

- Successful implementation of all steps in R
- Good model performance

- Results suggest treatment targeting could be improved
- Published in PharmacoEconomics

OS = overall survival; PFS = progression-free survival.

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Putting Words Into Action: *Simulating PFS and OS Based on Real-World Data (cont'd)*



Challenges of Going Open-Source

- Complexity of code and analyses: thorough explanation required and discussion of concerns about appropriate use
- Data could not be shared to support transparency



What We Were Able to Do

- Extensive supplementary materials to explain analyses
- Code available in a markdown with explanation *and results*
- Shiny app for exploration of dummy data and model runs



Will the Next Generation of Models Make Open-Source Modeling Take Off?







Will the Next Generation of Models *Will* Make Open-Source Modeling Take Off?!



ISPOR Open-Source Models Journal Club

June 1, 2022 11:00 AM – 12:00 PM ET

> @k_degeling koen.degeling@hcg-int.com







"

Poll 2

Where could open source models be most valuable?

Results will be presented as a word cloud

(single-word answers only)





Poll 3

When will open source become the norm in precision medicine?

Multiple choice

- This year
- Next 5 years
- Next 10 years
- Next 20 years
- Not in my lifetime