Pharmacometric-based cost-effectiveness analyses

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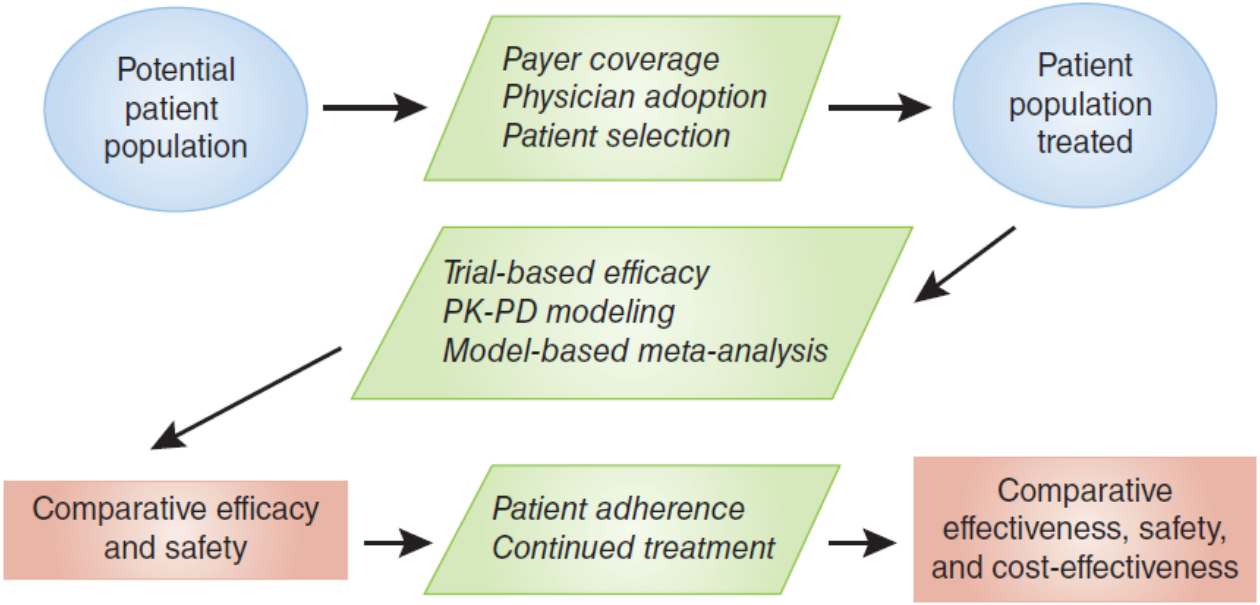
“Marriage of pharmacometrics and pharmacoeconomic modeling”



Lalonde et al, Clin Pharmacol Ther 2011; 10(6): 761-3

LEADING ARTICLE

Pharmacoeconomics 2001; 19 (11): 1069-1077
1170-7690/01/0011-1069/$22.00/0

Economic Evaluations During Early (Phase II) Drug Development

A Role for Clinical Trial Simulations?

Dyfrig A. Hughes and *Tom Walley*

Prescribing Research Group, Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool, UK

- First proposition of the methods

Hughes, Walley. Pharmacoeconomics. 2001;19(11):1069-77

Pharmacoeconomic modelling

Conventional modelling

- Data driven
- Empirical
- Extrapolations based on heroic assumptions
- Unreliable outside of defined parameters
- Limited capacity for early estimation of cost-effectiveness

Pharmacometric-based modelling

- Exploits knowledge of the relationship between dose and response, and co-variate effects
- Compatible with model-based drug development
- Useful to inform clinical trial design, pricing

Applications

1. Providing early indications of cost-effectiveness before large-scale trial data become available;
2. Estimating the cost-effectiveness of complex pharmaceutical interventions (e.g. pharmacogenetic testing);
3. Assessing subgroups, dosing schedules, non-adherence and protocol deviations;
4. Directing future research based on the cost of reducing uncertainty;
5. Informing strategic research & development and pricing decisions

Swift, Hughes et al. Clin Transl Sci. 2018. doi: 10.1111/cts.12559

APPLICATION 1

Early indications of cost-effectiveness

ORIGINAL RESEARCH ARTICLE

Pharmacoeconomics 2012; 30 (5): 413-429
1170-7690/12/0005-0413/$49.95/0

Mechanism-Based Approach to the Economic Evaluation of Pharmaceuticals

Pharmacokinetic/Pharmacodynamic/Pharmacoeconomic Analysis of Rituximab for Follicular Lymphoma

Joshua Pink,[1] *Steven Lane*[2] and *Dyfrig A. Hughes*[1]

1 Centre for Health Economics and Medicines Evaluation, Institute of Medical and Social Care Research, Bangor University, Bangor, Wales
2 Department of Biostatistics, University of Liverpool, Liverpool, England

Lewis Sheiner Prize, PAGE 2011, Athens

Pink et al, Pharmacoeconomics. 2012;30(5):413-29.

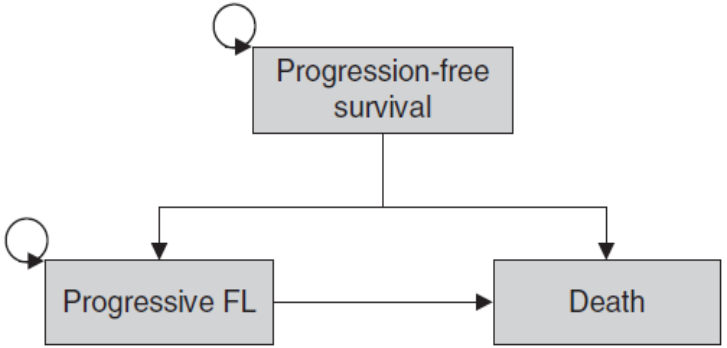
PK-PD and economic models

$$Cl = CL \times \left(\frac{BSA}{1.79}\right)^{\theta BSA\_CL} \times (1 + \theta_{SEX\_CL})$$

$$Vc = VC \times \left(\frac{BSA}{1.79}\right)^{\theta BSA\_VC} \times (1 + \theta_{SEX\_VC})$$

$$Cm(t) = \frac{\int_{t_n}^{t} C(\varphi)d\varphi}{t - \tau_v}$$

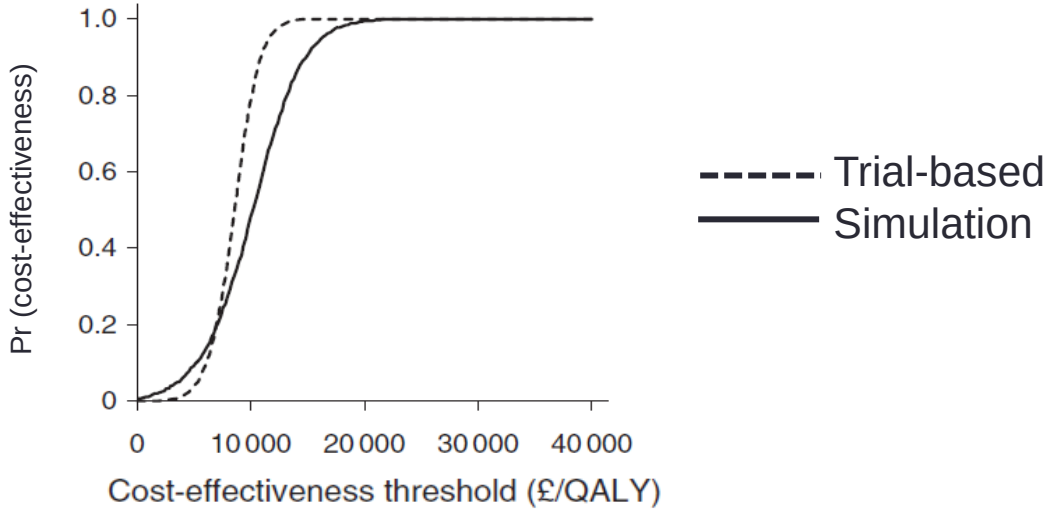
$$PFS(t) = e^{-\lambda_{max}\left(1 - \frac{Cm^{\gamma}}{Cm_{50}^{\gamma} + C_m^{\gamma}}\right)t}$$



Ternant et al. Br J Clin Pharmacol 2009; 68: 561-73

Results – simulation vs trial

	Rituximab maintenance therapy	
	Simulation	Trial-based
Mean time in PFS (years)	3.507	3.417
QALYs	3.696	3.333
ICER (£/QALY)	£9,076	£7,721



APPLICATION 2

Cost-effectiveness of complex pharmaceutical interventions

Warfarin pharmacogenetics

- Variability in response to warfarin can be partly explained by genetic polymorphisms in
  - *CYP2C9 , VKORC1*
- People with variant alleles are at an increased risk of over-anticoagulation and bleeding
- Dosing algorithms based on pharmacogenetics may result in better INR control, and hence better clinical outcomes

BMJ

BMJ 2011;343:d6333 doi: 10.1136/bmj.d6333 Page 1 of 14

RESEARCH

Dabigatran etexilate versus warfarin in management of non-valvular atrial fibrillation in UK context: quantitative benefit-har

OPEN ACCESS

Joshua Pink *PhD student*[1], Steven Lane *le*
of clinical pharmacology[3], Dyfrig A Hughes

nature publication group ARTICLES

Comparative Effectiveness of Dabigatran, Rivaroxaban, Apixaban, and Warfarin in the Management of Patients With Nonvalvular Atrial Fibrillation

J Pink[1], M Pirmohamed[2] and D

Received 21 September 2012; accepted 1 A

CLINICAL PHARMACOLOGY & THERAPEUT

nature publication group ARTICLES

Cost-Effectiveness of Pharmacogenetics-Guided Warfarin Therapy vs. Alternative Anticoagulation in Atrial Fibrillation

J Pink[1], M Pirmohamed[2], S Lane[3] and DA Hughes[1]

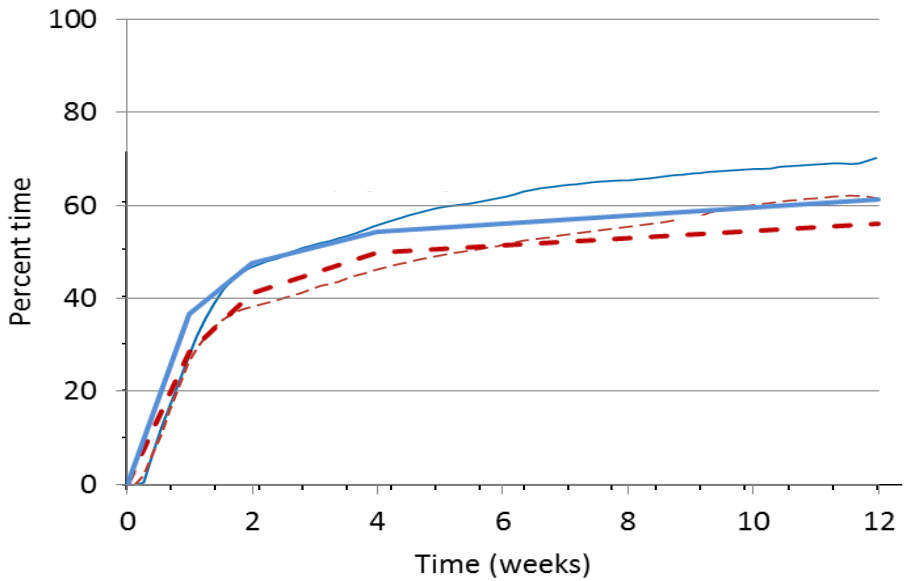
Received 25 April 2013; accepted 7 September 2013; advance online publication 6 November 2013. doi:10.1038/clpt.2013.190

CLINICAL PHARMACOLOGY & THERAPEUTICS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Genotype-Guided Dosing of Warfarin



Genotype-guided group

Clinical algorithm

Pirmohamed et al. N Engl J Med. 2013;369(24):2294-303

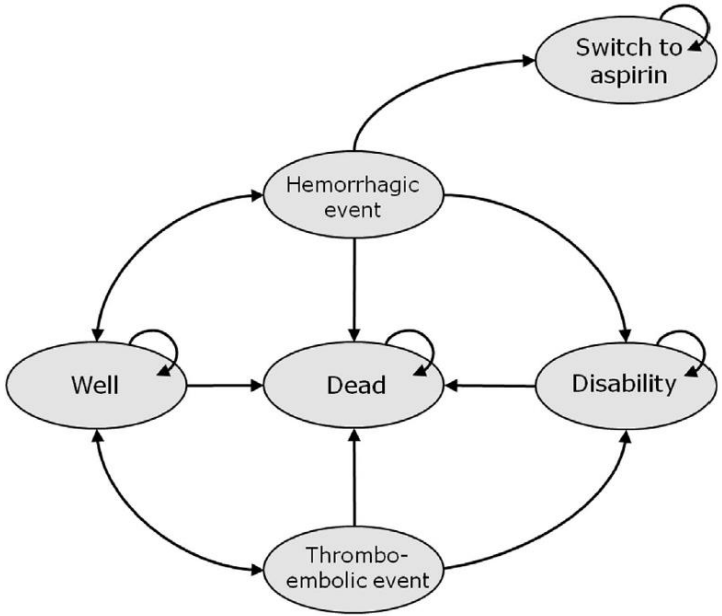
The Pharmacogenomics Journal (2016), 1–7

www.nature.com/tpj

ORIGINAL ARTICLE

Cost-effectiveness of pharmacogenetic-guided dosing of warfarin in the United Kingdom and Sweden

TI Verhoef[1,2], WK Redekop[3], S Langenskiold[4,5], F Kamali[6], M Wadelius[7], G Burnside[8], A-H Maitland-van der Zee[2], DA Hughes[9] and M Pirmohamed[8]



	ΔCosts	ΔQALYs	ICER
Simulation	£41	0.0031	£13,226
Evaluation	£26	0.0039	£6,702

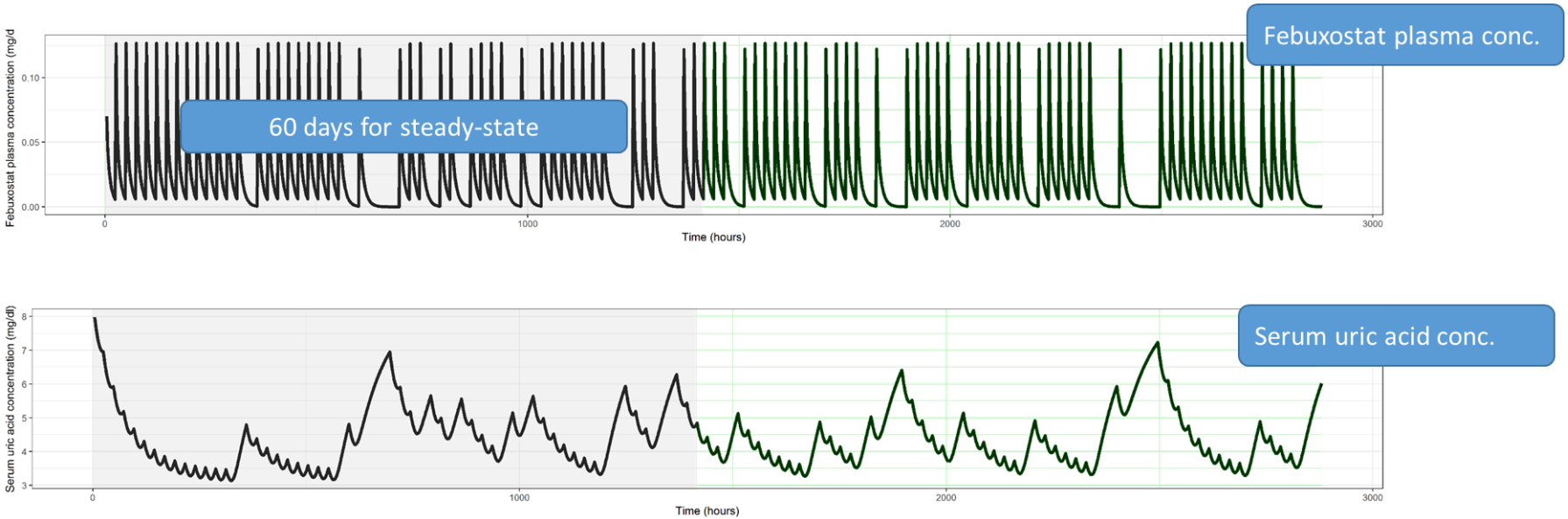
APPLICATION 3

Impact of non-adherence on cost-effectiveness

Urate lowering therapies

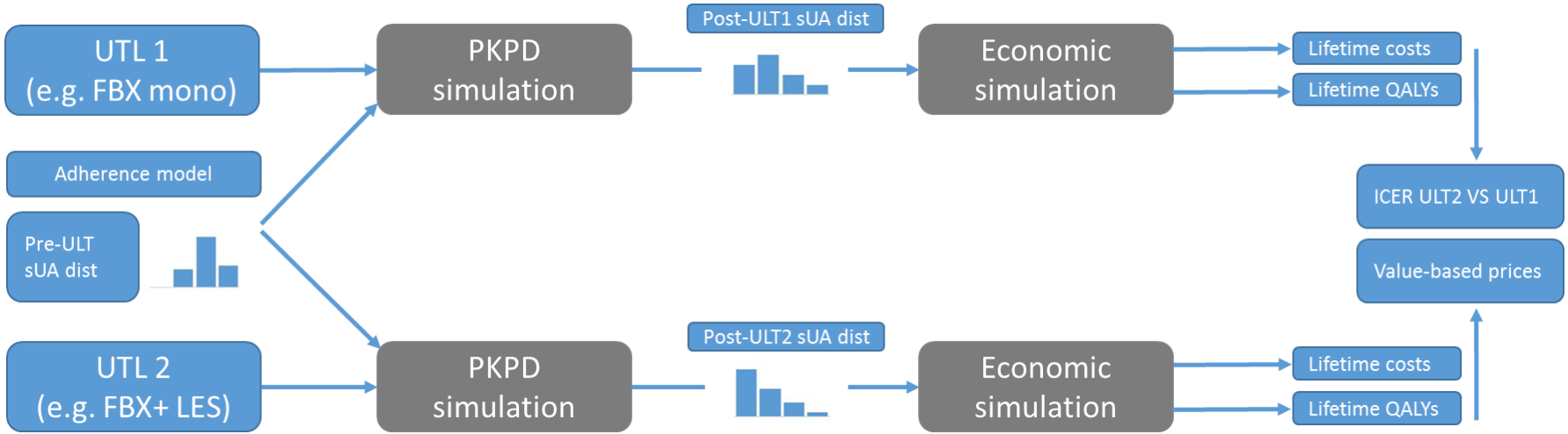
- Adherence to ULTs in gout is notoriously low
- Conventional economic evaluations unable to consider the relationship between missed doses, changes in serum uric acid, and cost-effectiveness

PK-PD simulation



Hill-McManus et al. Br J Clin Pharmacol. 2018;84(1):142-152

Modelling framework



OTHER EXAMPLES

Citation: CPT Pharmacometrics Syst. Pharmacol. (2015) 4, 374–385; doi:10.1002/psp4.48

ORIGINAL ARTICLE

Integrated Simulation Framework for Toxicity, Dose Intensity, Disease Progression, and Cost Effectiveness for Castration-Resistant Prostate Cancer Treatment With Eribulin

JGC van Hasselt[1,2,3*], A Gupta[4], Z Hussein[4], JH Beijnen[1,5], JHM Schellens[2,5] and ADR Huitema[1,2]

Incorporating harm

VALUE IN HEALTH 19 (2016) 1026–1032

Translating Pharmacometrics to a Pharmacoeconomic Model of COPD

Julia F. Slejko, PhD[1,], Richard J. Willke, PhD[2], Jakob Ribbing, PhD[3], Peter Milligan, PhD[4]*

[1]*Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD, USA;* [2]*International Society for Pharmacoeconomics and Outcomes Research, Lawrenceville, NJ, USA;* [3]*Pharmetheus AB, Uppsala, Sweden;* [4]*Global Clinical Pharmacology, Pfizer, Sandwich, United Kingdom*

Infectious disease

Predicting economic outcomes based on trial design

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2017) **83** 1580–1594 1580

PHARMACOECONOMICS

Interdisciplinary pharmacometrics linking oseltamivir pharmacology, influenza epidemiology and health economics to inform antiviral use in pandemics

Mohamed A. Kamal[1,2], Patrick F. Smith[3], Nathorn Chaiyakunapruk[4], David B. C. Wu[4], Chayanin Pratoomsoot[5], Kenneth K. C. Lee[4], Huey Yi Chong[4], Richard E. Nelson[6], Keith Nieforth[3], Georgina Dall[3], Stephen Toovey[7], David C. M. Kong[4], Aaron Kamauu[8], Carl M. Kirkpatrick[4] and Craig R. Rayner[4,5]

Future directions

- Pharmacometric-based pharmacoeconomic analyses represent an additional step in model-based drug development
- Defining the potential benefit of applying linked pharmacometrics and health economics modelling to inform R&D decisions
- Develop value of information analyses

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