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Health economics – How did it start and where are we heading?

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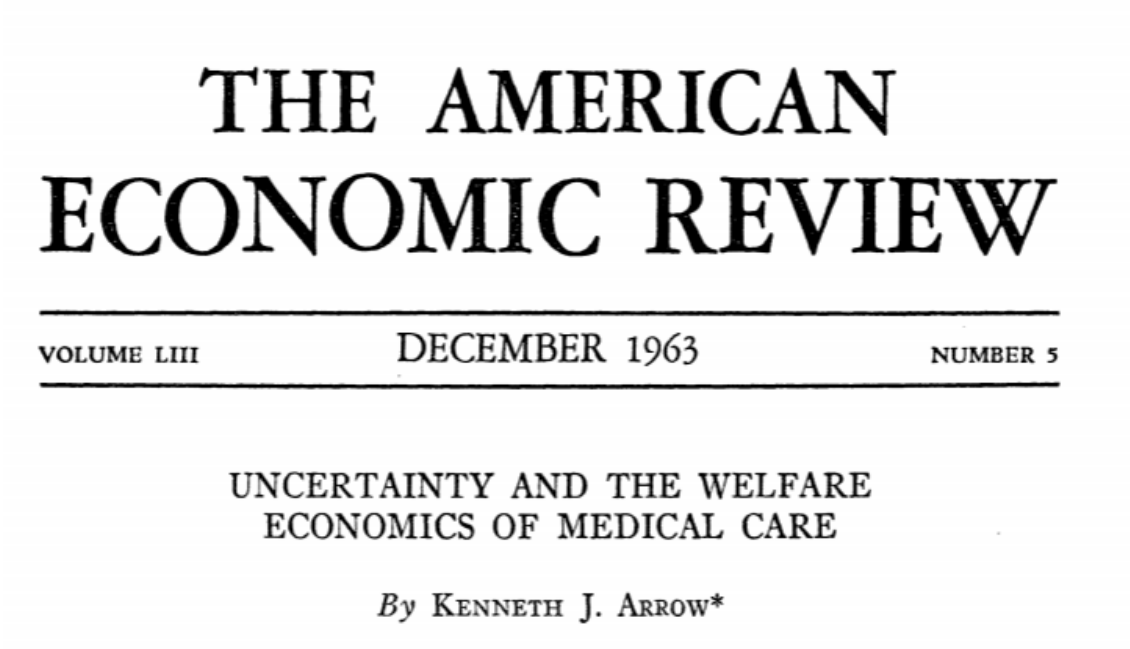
IHE 40TH ANNIVERSARY CELEBRATION
6 SEPTEMBER 2019

My agenda

1. Health economics by the decade – one theme per decade
2. The R&D “machine” of the industry. Is it broken?
3. The WHO Fair Pricing Challenge
4. Where are we heading – issues for the future

The 1960s : Health Economics Emerges

1. OHE started in 1962
2. Speek (1966) first major health economics paper in the Nordic countries
3. 1963 Arrow article – uncertainty around medical care – potential for market failure, and the role for insurance
   - Arrow said insurers should provide procedures where benefits exceeded costs.
   - How do we measure health benefits?
4. Marty Feldstein got his Oxford Ph.D. in 1967 with “a doctoral thesis trying to show how economic analysis and econometric methods could be used to reduce hospital costs”



THE AMERICAN ECONOMIC REVIEW

VOLUME LIII DECEMBER 1963 NUMBER 5

UNCERTAINTY AND THE WELFARE ECONOMICS OF MEDICAL CARE

By KENNETH J. ARROW*

The 1970s : the QALY emerges

- Origins of the QALY are not in a straight line.
- Seems to be US with Weinstein, M.C., Stason, W.B., (1977). But earlier mentions were in Zeckhauser, R., Shephard, D., (1976).. and Bush, J.W., Fanshel, S., Chen, M., (1972)..
- There were parallel strands of activity taking place in Canada with George Torrance and in the UK with Rachel Rosser and Alan Williams.
- Bengt Jonnson's 1976 PhD on Cost-benefit analysis in public health and medical care" cites both Bush et al. (1973) "estimated value of improved health in function years" and Culyer et al. (1971) "The York health index"
- IHE established

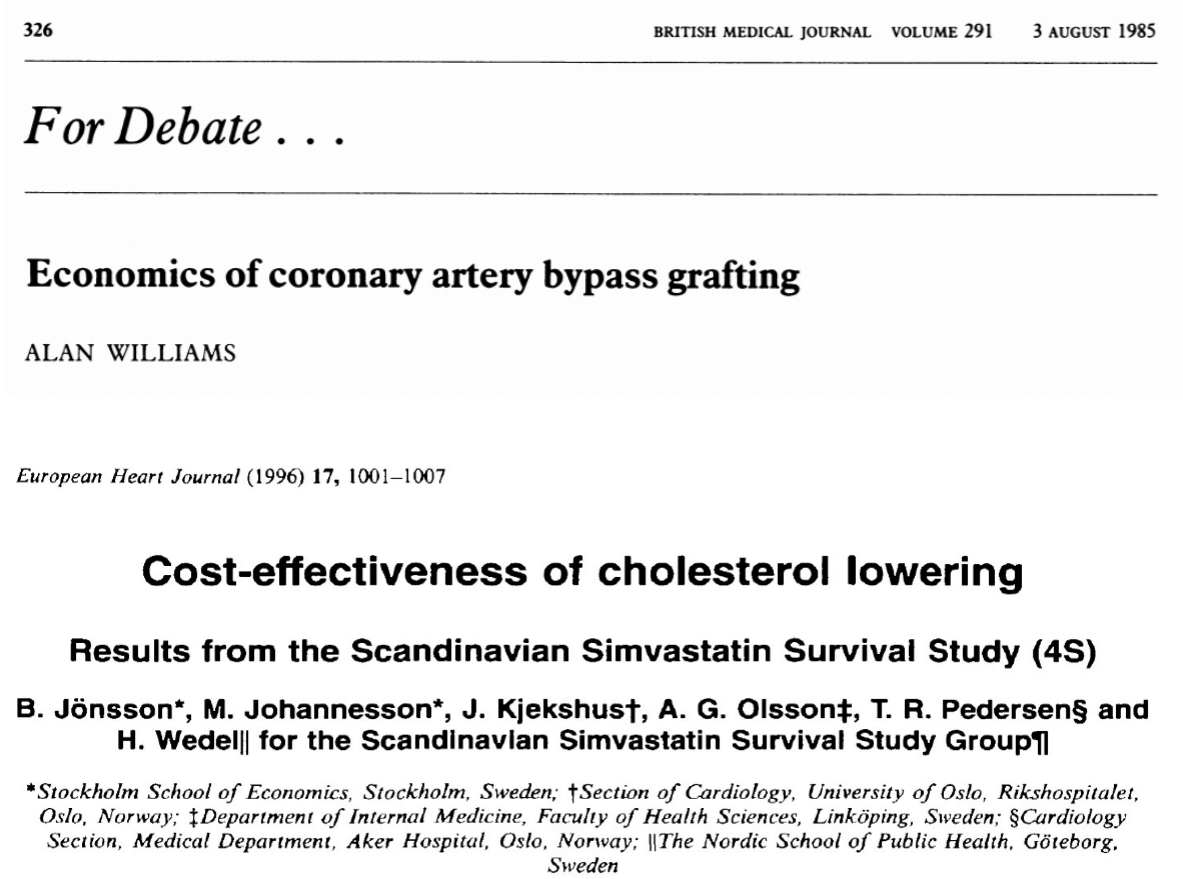
We had a lucky escape ….

"Our term QALY is a variant of Robert Inman's suggestion to us of quality-adjusted citizen year (pronounced quacky). which we felt to be fowl usage."

Zeckhauser, R., Shephard, D., (1976)

The 1980s: the case for cost-per-QALY rationing emerges

1. Moving from QALYs to cost-per-QALY takes us into the 1980s with a seminal paper by Alan Williams on CABG in the BMJ (1985)
2. It was another decade before we had health economics evidence being collected in, and alongside clinical trials with modelling, of which the 4S study was the text book classic
3. We also had
   - SBU established in 1987.
   - The RAND Health Insurance Experiment reported (an experimental study from 1974 to 1982 of health care costs, utilization and outcomes in the United States)



326 BRITISH MEDICAL JOURNAL VOLUME 291 3 AUGUST 1985

For Debate . . .

Economics of coronary artery bypass grafting

ALAN WILLIAMS

European Heart Journal (1996) **17**, 1001–1007

Cost-effectiveness of cholesterol lowering

Results from the Scandinavian Simvastatin Survival Study (4S)

B. Jönsson*, M. Johannesson*, J. Kjekshus†, A. G. Olsson‡, T. R. Pedersen§ and H. Wedel‖ for the Scandinavian Simvastatin Survival Study Group¶

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The 1990s : HTA and cost-effectiveness hits the mainstream

1. Guidelines for economic evaluation were introduced into Australian decision making (PBAC) in 1990 with mandatory submissions of health economic evidence from 1993.
2. CCOHTA/ CADTH first guidelines issued in 1994, NICE established in 1999
3. LFN / TLV established 2002 /2008
4. Significant intellectual developments in decision analytical modelling, in particular the presentation of uncertainty to decision makers (e.g. CEAC, CEAF, VoI) by Briggs, Claxton and others
   - Tension between frequentist and Bayesian approaches to evidence assessment
5. Other:
   - Rikard Althin's PhD on Measurement of Producer Performance with use of both parametric and non-parametric (including Malmquist) approaches

The 2000s : Falling drug productivity and regulatory fast track proposals

1. Concern that the numbers of new drugs being launched was falling and too many of them were “me too” drugs. The R&D machine of the industry not delivering
2. The FDA's Critical Path Initiative effort was launched in March 2004; FDA Fast Track (1997), Breakthrough Therapy (2012), Accelerated Approval (1992), Priority Review (2007)
3. EMA had a budget deficit due to low throughput. EMA Conditional Marketing Authorisation (2006), PRIME (2016)
4. Pammolli, F., Magazzini, L. and Riccaboni, M. (2011) The productivity crisis in pharmaceutical R&D. *Nature Reviews Drug Discovery*. 10, 428-438:
   - shift of effort to more difficult therapy areas
5. Other: BMGF founded (2000), Sachs WHO Report MacroEconomics and Health (2001), PEPFAR (2003)

The current decade : rising drug productivity but can we afford it?

1. Rising output of cancer drugs and of orphan drugs
2. Immunotherapy - multiple indications
3. Hep C treatments – “cost-effective but not affordable”
4. AMTPs including CAR-T and gene therapy
5. Evidence of recent upsurge of R&D productivity within the industry
6. Is it all too much? Can health systems pay for these drugs?
7. Calls for “de-linkage” and for “transparency”

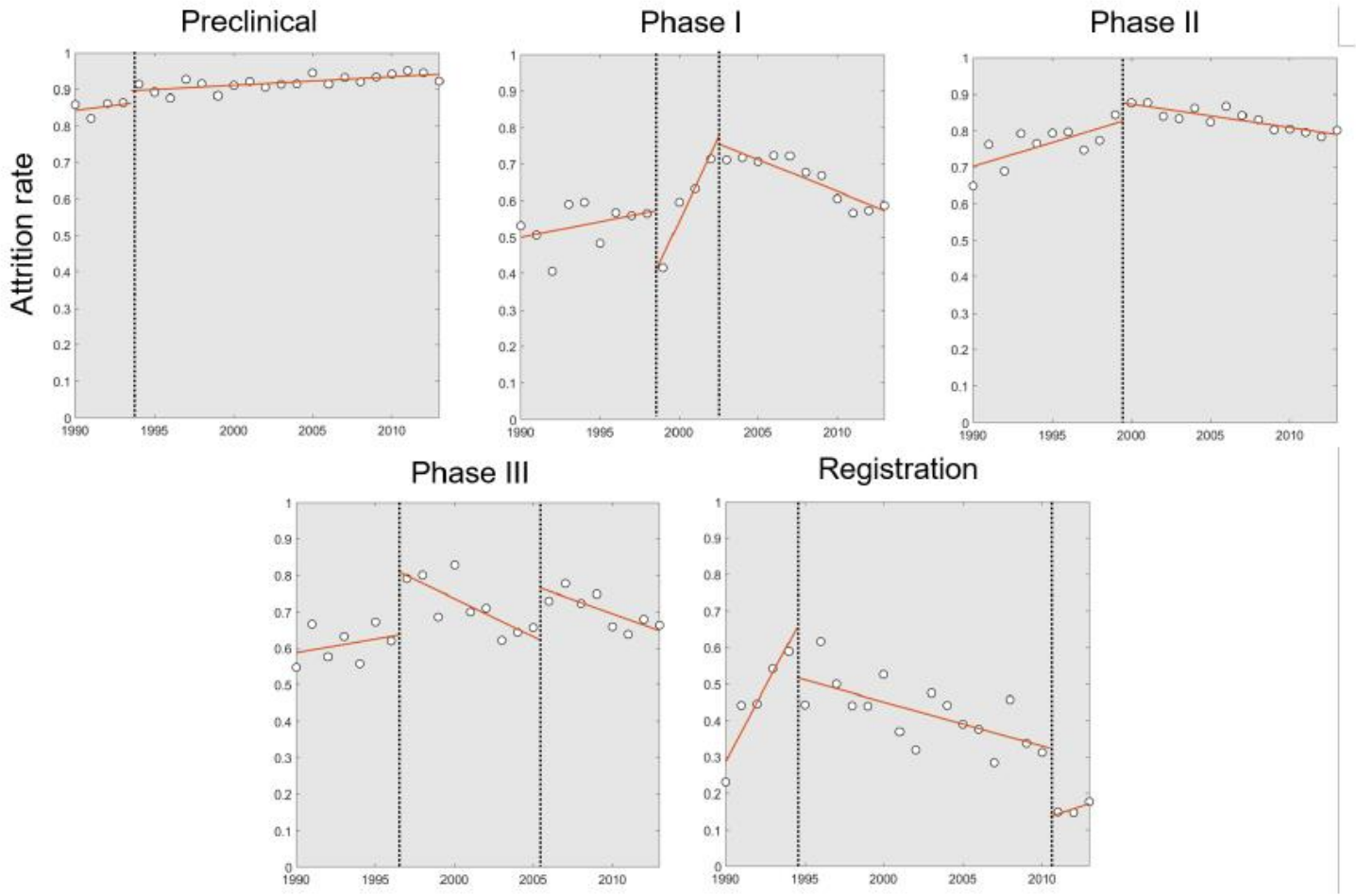
The Endless Frontier? The Recent Upsurge of R&D Productivity in Pharmaceuticals

Fabio Pammolli*† Lorenzo Righetto‡ Sergio Abrignani§¶ Luca Pani‖**
Pier Giuseppe Pelicci†† Emanuele Rabosio‡‡

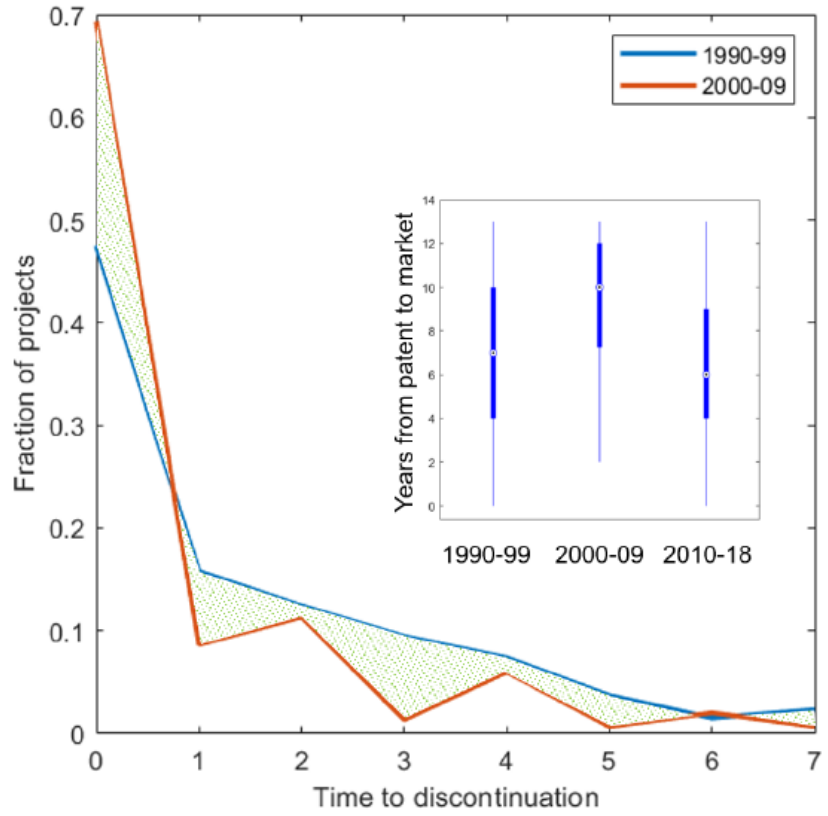
May 2019

- Polarization towards high-risk/high-reward indications, with a strong focus on oncology.
- Attrition rates decreasing at all clinical stages
- Increase of early failures in preclinical research
- Significant reduction of time required to discontinue.
- Projects increasingly based on novel mechanisms of action and indications with small patient populations.

Pammolli et al. 2019



Attrition rates in time for different stages of drug development



Fraction of projects that are discontinued after x years from the start of preclinical research

The R&D “machine” of the industry. Is it broken? (1)

1. Doesn’t mean the science is broken “love the science” – but rather the cost of delivering it to health systems
2. Estimates of $2.6bn - $3bn for the cost of an NCE / NBE / NME (DiMasi et al. 2016) . Much disputed (e.g. Prasad and Mailankody, 2017) but …
3. Will fast-track access reduce R&D cost? Or shift to the post launch setting?
4. Earlier access means higher expenditure as far as payers are concerned.
5. And payers are asking for more evidence not less.

The R&D “machine” of the industry. Is it broken? (2)

1. Industry argues that higher R&D cost means higher prices
2. But if payers pay for value, then costs are irrelevant
3. Let’s dissect this a little:

- Yes, costs are irrelevant in the static sense, but not dynamically
- Competition should drive down prices, but willingness to invest in R&D depends on costs as well as revenues.
- So R&D costs provide a floor to prices. Lower R&D costs mean more competition and lower prices in the long run
- But there is an endogeneity here as well. High returns stimulates higher cost (risk) R&D, so the signals from payers need to be right as well.

The R&D “machine” of the industry. Is it broken? (3)

1. We have the US market, where it is much less clear that payers are necessarily paying for value - particularly in the area of oncology
2. One could argue that the US oncology market is distorting the global market for innovation. It is so profitable. High prices, low R&D costs.
3. Although we have to note, a forthcoming paper by DiMasi and Grabowski on R&D cost arguing that oncology R&D costs are high, because of (i) low success rates and (ii) the number of indications – lots of trials, and, cumulatively, lots of patients

The R&D “machine” of the industry. Is it broken? (4)

1. Can we revolutionise R&D costs? I think the only way is through IT. If we are able to track patients through EHRs and these capture health status and interactions with the health system, then we can change the costs of both RCTs and of RWE collection.

- What about patent pools, open innovation, and open source innovation?

2. An obvious counterfactual for us to think about is what happens if prices in the US do come down (or stop rising). What will happen to industry R&D? Two scenarios perhaps:

- “soft landing” and a “hard landing”

Questions

1. Can we reduce confirmatory trial and post launch development costs?

   • Why are health systems so useless at implementing IT and collecting meaningful and consistent / readable data in EHRs? (Or is it just the UK NHS?)

2. RCTs v. observational studies – will the divide narrow? (methodologically and/or politically?)

   Oncology - so many combinations – how do we collect evidence?

3. Can we do anything at an earlier R&D stage:

   Patent pools, open innovation, and open source innovation

4. If industry R&D fell by 50% what impact would that have?

Incentivising R&D in global health and antibiotics when the market is not delivering? The WHO “Fair Pricing” saga (1)

1. Transparency of costs and prices are key activist demands. Recently both Donald Trump and the Italian health minister have argued for transparency.
2. Two potential motivations. One is a mistaken belief that price transparency will reduce prices. The other is to move towards cost-plus pricing.
3. Activists seem to want an environment in which pharmaceutical companies become regulated utilities rewarded for investment on a cost-plus basis.
4. The underlying preference of many is to “nationalise” the R&D process and have it push funded, with successful products being supplied at generic prices. No need for IP protection. R&D is delinked from prices.

Incentivising R&D in global health and antibiotics when the market is not delivering? The WHO “Fair Pricing” saga (2)

1. Do we really want the government and health systems to pay for effort and not for outcomes? Do we think the profit motive increases or reduces R&D efficiency?
2. The industry also has to make a choice which it seems to reluctant to do. If it doesn’t want to be rewarded on a “cost-plus” basis then it has to embrace getting rewarded in relation to value.
3. In a world of 3rd party payers, this means a proxy assessment of value using a form of HTA – whether cost-effectiveness analysis or therapeutic value added. And willingness to pay depends on ability to pay (budgets) and on what else the money can be spent on (opportunity cost).
4. Scope to argue about elements of value, decision making criteria and processes, budgets devoted to health, and estimates of opportunity cost, but industry should accept, and indeed ask, governments and health systems to embrace HTA.

Where are we heading? Issues for health economists for the future

1. Making the case for value-based pricing. Addressing pricing models and contracting issues ranging from performance-based risk sharing, differential pricing, indication-based pricing, division of value as between tests and drugs (combination therapy), availability (Netflix) type contracts
2. Measuring the efficiency of health systems, and advising on policy around the organisation of health systems. This has to include a great understanding of opportunity cost – what is happening at the margin in health systems, and understanding the gap between c-e thresholds and citizen WTP for health gain.
3. Promoting the routine collection of better health outcomes data.
4. Use of real world evidence – analytical and methodological issues – not least transferability of evidence
5. Exploring the efficiency and practicality of open innovation and open source innovation
6. Elements of value beyond QALY health gain and savings to the health system – revisiting the societal perspective
7. Supporting decision-making (MCDA v. deliberation v. algorithms)
8. The global health challenges of (i) neglected diseases (including AMR) and (ii) UHC for MLICs

To enquire about additional information and analyses, please contact:

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