Evaluating (& Paying for) Gene Therapies and ATMPs

Andrew Briggs, DPhil

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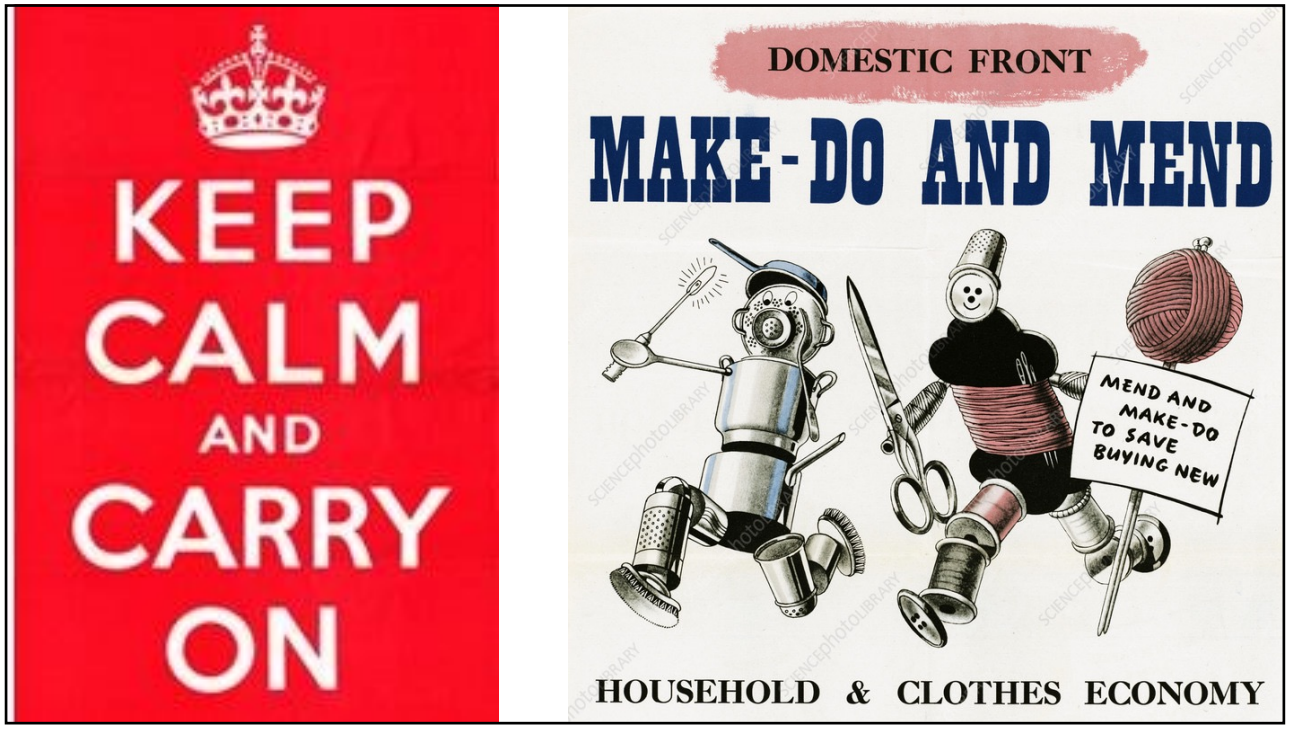

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‘Keep Calm & Carry On’ or ‘Make Do and Mend’?

Review NICE’s Task & Finish Group Report on ATMPs

Review Towse & Fenwick’s ‘Uncertainty & Cures’

Propose an additional solution

Concluding statement

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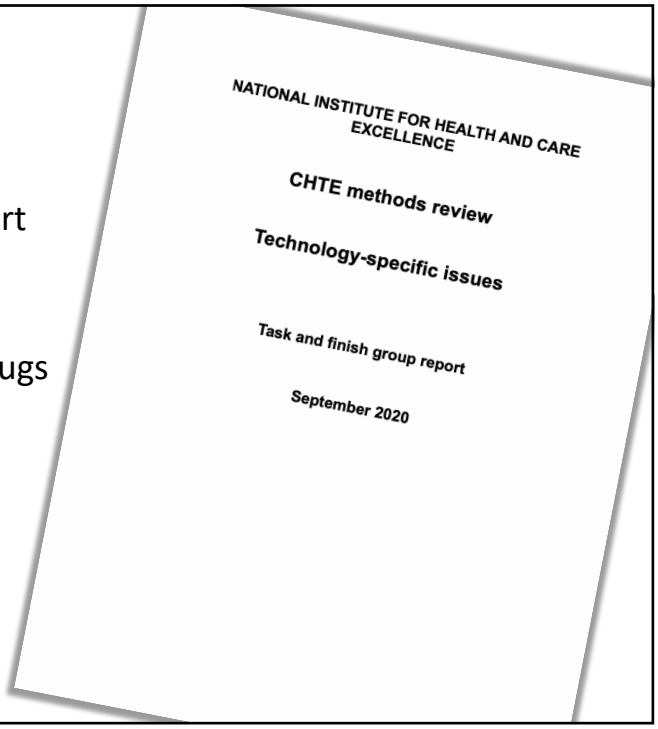
NICE 2020

Task & Finish Group Methods Report covering:

- AMTPs
- Histology Independent Cancer Drugs
- Horizon Scanning
- Devices & Diagnostics Regulation



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Task & Finish Group Conclusions: ATMPs

- Uncertainty of the evidence
  - absence of evidence of long-term benefits
  - use of single-arm studies
  - small patient numbers
  - lack of reliable utility values
  - difficulty in identifying the appropriate comparator
- High costs of the treatment
- sensitivity of the ICERs to the discounting rate

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Histology Independent Cancer Drugs

- Explore assumptions of homogeneity of treatment effects across histologies (consider Bayesian hierarchical models)
- No single approach to constructing the counterfactual will provide robust estimates of relative effectiveness … consider several alternatives
- Exploration of the cost effectiveness of the drug in histologies not included in the clinical trial
- Consistent approach to the inclusion of genomic testing costs
- Use of net health benefits rather than only an ICER for decision uncertainty because they take the size of different subgroups into account.

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Themed Section: Curative Therapies

Uncertainty and Cures: Discontinuation, Irreversibility, and Outcomes-Based Payments: What Is Different About a One-Off Treatment?

Adrian Towse, MA, MPhil[1,*] Elisabeth Fenwick, PhD[2]

[1]Office of Health Economics, London, England, UK; [2]Pharmerit International, Oxford, England, UK.

ABSTRACT

Payers are concerned that one-off "cures" bring great uncertainty with the consequential risk of incorrect adoption decisions, and significant budget impact from large one-off payments. Innovators worry about bias against "cures" in favor of repeat treatment, which is not in patients' interests. We find that even in the absence of a difference in uncertainty of outcomes, adverse pay-offs differ. The greater financial risk associated with a cure is related to the issue of treatment discontinuation, driven by irreversibility. This paper uses a stylized example to illustrate the need to separate three different elements of the issue: (i) one-off versus repeat or ongoing treatment, (ii) duration of treatment effect, and (iii) the potential role of financial arrangements or risk sharing to mitigate the financial risk to the payer. It concludes that: (i) prevalence and discontinuation issues mean that the impact on the payer of an incorrect decision is greater with a one-off treatment than a repeat therapy; (ii) with evidence collection this risk diminishes over time (a form of CED or OWR); and (iii) financial arrangements or risk sharing can eliminate differences for the payer as between one-off and repeat therapy. The impact of (iii) also addresses payer concerns about budget impact.

Keywords: curative therapies, economic evaluation, treatment discontinuation, uncertainty.

VALUE HEALTH. 2019; 22(6):677–683

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Table 1. Parameters in the stylized example.

Parameter	Current treatment	One-off cure	Repeat-dose cure
Prevalence		8000 patients	
Discount rate for costs		5%	
Discount rate for effects		5%	
Background mortality		0.05%/mo	
Disease mortality	0.5%/mo	0%/mo*	0%/mo*
Utility	0.0025	1*	1*
Treatment cost	$740/mo	$296 741	$4502/mo
Annual monitoring cost	NA	$120	$120
Probability of cure	0%	100%†	100%†

NA indicates not applicable.
*Only apply while treatment remains effective. Once treatment stops being effective, mortality and utility revert to values for current treatment.
†Probability of cure associated with both one-off and repeat-dose treatments is assumed to decline to 92% by 30 y.

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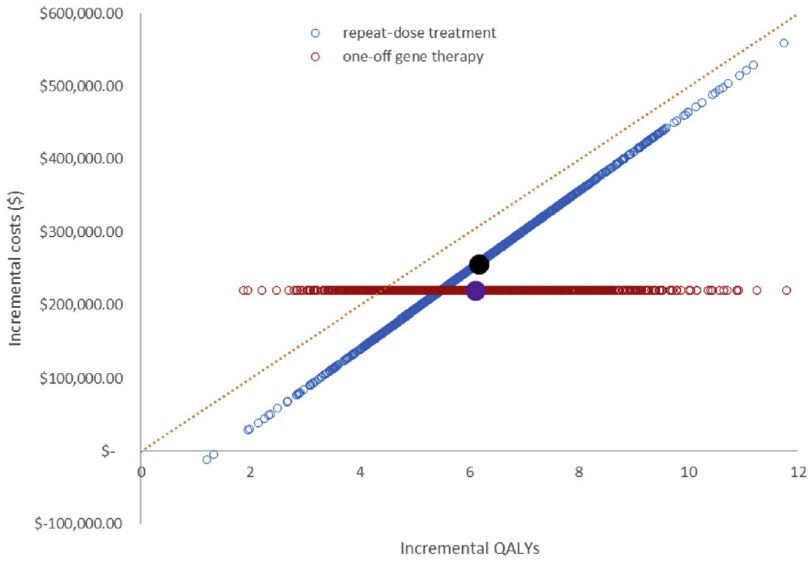
Figure 1. Comparison of one-off treatment and repeat-dose treatment in the cost-effectiveness plane.



QALY indicates quality-adjusted life-year.

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Inverse Discounting: an alternative mechanism to reimburse 'one-and-done' treatments?

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Q: Why should one-and-done treatments be reimbursed at one-and-done prices?

Inverse discounting in three easy steps:

1. Calculate the net-present value of treatment
2. Annualise over the expected lifetime
3. Inverse discount to give the original NPV over the lifetime

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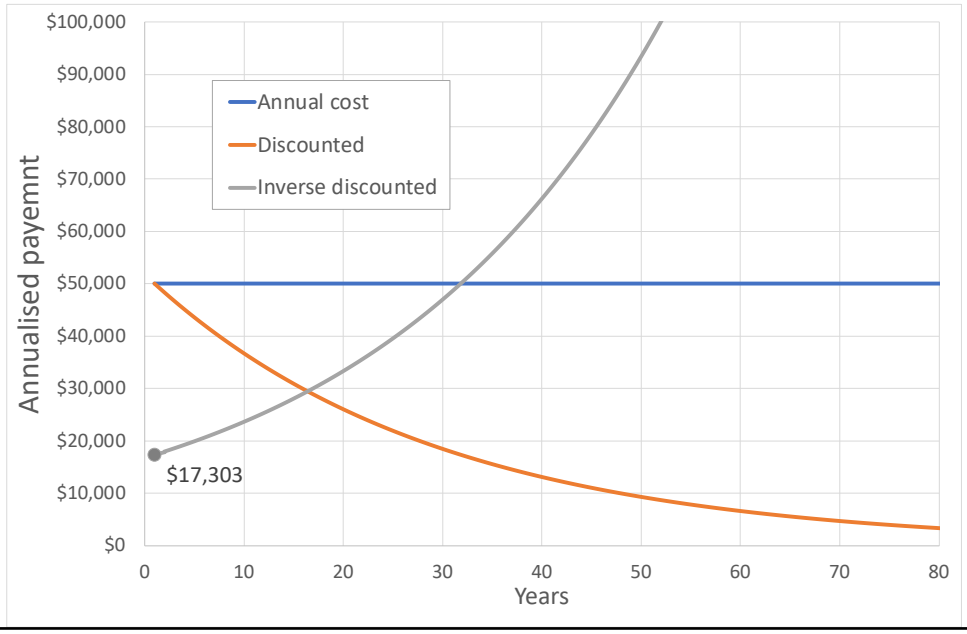
Inverse discounting: an illustration (3.5%)



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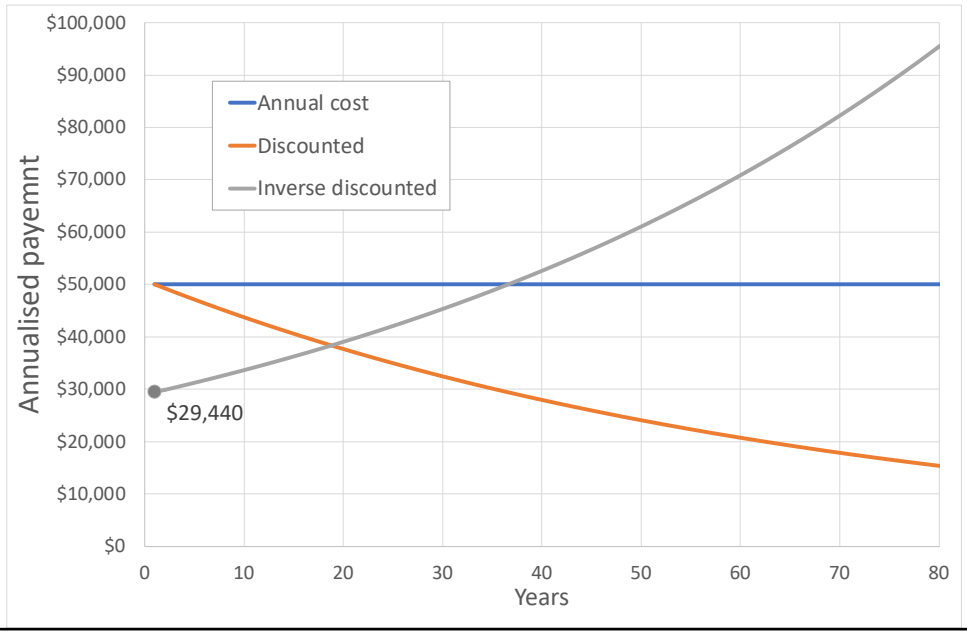
Inverse discounting: an illustration (1.5%)



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'Keep Calm & Carry On' or 'Make Do and Mend'?

- No evidence that we need to 'amend' the methods of HTA/Cost-effectiveness to accommodate ATMPs
- Nevertheless: there is a challenge if 'one and done treatments' are only offered with 'one-and-done' payments
- Paying for 'one-and-done' treatments as if they are 'repeat dose' cures
- Reduces the uncertainty for the decision maker
- Effectively a simple 'outcomes-based risk sharing agreement'
  - (a little less simple if failure of cure is not immediately life threatening)
- Inverse discounting would allow skew towards more distal outcomes further reducing risk while maintaining NPV for manufacturer

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Thank you for listening

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