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REVIEW ARTICLE

Adherence to Discounting Guidelines: Evidence from Over 2000 Published Cost-Effectiveness Analyses

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Abstract

Previous studies have shown that not all cost-effectiveness analyses (CEAs) adhere to recommended guidelines on intertemporal discounting. This analysis investigates adherence in a sample of over 2000 CEAs from seven countries. Guideline discount rates were retrieved for Australia, Belgium, Canada, Ireland, The Netherlands, New Zealand and the UK. Data on the rates applied in published CEAs were retrieved from the Tufts CEA Registry from the sample countries within the periods covered by the discounting guidelines. The relationship between adherence and candidate explanatory factors were assessed using logistic regression. The analysis appraised 2270 CEAs. The overall rate of adherence to discounting recommendations was 79%. Country-specific adherence ranged from 28% in New Zealand to 87% in Belgium and the UK. Adherence in Australia and Canada was 73% and 66%, respectively. Adherence is statistically significantly higher in more recent studies, countries currently applying differential discounting and manufacturer-sponsored studies. Relative to the reference case of Australia, adherence is statistically significantly higher in the UK and lower in Canada and New Zealand. There is notable variation in the rates of adherence to discounting recommendations between countries and over time. Incomplete adherence raises concerns regarding the comparability of evidence between studies. In turn, this raises concerns regarding equity of access to scarce healthcare resources. Journal editors should ensure that adherence to discounting recommendations is assessed as part of the peer review process.

1 Introduction

Cost-effectiveness analysis (CEA) is used to guide decisions on the allocation of scarce healthcare resources over multiple competing health needs [1]. Discounting is applied to account for time preference when calculating the present value of future costs and health effects. The discount rate can be highly influential on the cost-effectiveness estimates of many interventions, especially those in which a greater proportion of outcomes occur in future periods rather than the present [2, 3]. For example, the application of higher discounting rates reduces the estimated cost effectiveness of preventative interventions.

Key Points for Decision Makers

Adherence to discounting recommendations within cost-effectiveness analysis is known to be imperfect. This analysis examines a large sample of non-US cost-effectiveness analyses to show how adherence varies with factors including country setting, study sponsorship and intervention type.

Results show that adherence is particularly low in New Zealand, is high in the UK and appears to have improved recently in Canada. Relative to other intervention types and sources of funding, adherence appears stronger in analyses of drugs and in studies sponsored by manufacturers.

Decision makers need to carefully examine whether the cost-effectiveness evidence presented to them correctly adheres to national discounting recommendations. Otherwise, the decision-making process may be unjustifiably biased in favour of certain interventions and their recipients.

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Reducing the discount rate will often lead to a lower cost-effectiveness ratio for a given intervention, thereby apparently enhancing its cost effectiveness. In order to ensure parity when allocating scarce resources across competing interventions, the base case discount rate is typically subject to CEA methods guidelines. The recommended rates within these guidelines vary between countries and can be subject to revision over time. Most countries recommend equal discounting of costs and health effects, commonly at rates between 3 and 5% [2]. A minority of countries recommend differential discounting, whereby typically a lower discount rate is applied to health effects than costs [2]. The rationale for differential discounting is to account for anticipated growth in the value of health effects over time [2].

Previous assessments of the CEA literature show that adherence to recommended discount rates is imperfect [4–6]. Adherence to recommended discount rates is one of a number of markers of methodological quality recorded by the Tufts CEA Registry [5, 7]. A survey of CEAs by the Tufts Registry found that the proportion of studies adhering to discounting guidelines increased from 76% to 88% in time periods between 1976 and 2006 [4]. While that previous assessment of discounting adherence did include CEAs from multiple countries, the reported analysis did not disaggregate adherence by country. The single largest country of origin within the Tufts analysis was the US, which represented 51% of the reviewed CEAs [4].

The purpose of our analysis is to investigate if adherence varies systematically between studies and to establish what factors influence adherence and how. Our analysis is novel in that it assesses difference in adherence rates between countries and between periods over which discounting guidelines changed.

2 Methods

2.1 Data Retrieval and Cleaning

We consulted the cost-effectiveness guidelines for Australia, Belgium, Canada, Ireland, The Netherlands, New Zealand and the UK to determine what the recommended discount rates were. We chose countries with clear national CEA guidelines that offered a variety of discount rates for investigation, including the application of equal and differential discounting. We deliberately excluded US studies, as such CEAs represent the majority of analyses reviewed in previous assessments of adherence to discounting recommendations [4, 5]. We consulted both current and previous CEA guidelines to determine the longest period over which discounting recommendations prevailed for each country. In cases in which previous guidelines were not available from the national CEA authority websites, we contacted the agencies to retrieve the previous documents. We were unable to retrieve the original 1992 and 1994 Australian and Canadian guidelines, respectively. In these cases, we inferred the recommended discount rates from studies citing them [8–10].

We used the Tufts Medical Centre CEA Registry (the Registry) as the primary data source for this analysis [7]. The Registry is an online database that reports reviews of CEAs published in the international academic literature that feature cost per quality-adjusted life-year (QALY) estimates of cost effectiveness. The Registry publishes brief, publicly available summaries of each CEA reviewed, which includes data on what discount rates were applied to costs and QALYs. The majority of reviews available on the Registry are listed as 'full review' and contain a detailed list of summary information. Other reviews are described as 'partial review' and do not contain a complete record of information.

We interrogated the Registry using date search terms corresponding to the period from 1993 onwards to retrieve CEA summary records from the registry. We retrieved the article title, publication year, journal title, country setting, research funding source, intervention type, analysis time horizon and the discount rates applied. The Registry compiles a quality score of between 1 and 7 (low to high) in increments of 0.5. This score was retrieved for each record. We then searched through the retrieved records for studies listed as being in the countries of interest. We excluded records for which the Registry has only recorded a partial review. The final iteration of our search was conducted in February 2020.

We removed duplicate entries and those that did not correspond to the country setting recorded in the Registry. Studies that reported analyses for multiple countries were disaggregated into separate records for each relevant country. We limited the selection of CEAs to the time periods covered by the CEA guidelines for each country. We included CEAs from the year following the publication of the first CEA guidelines in each country of interest. For example, since the first Australian guidelines were published in 1992, we included Australian CEAs published from 1993 onwards. In cases in which the Registry did not record the discount rates applied, we then attempted to retrieve the rates applied from the original study. In cases in which studies mentioned that discounting was applied but did not specify the rate, we made the assumption that discounting was conducted correctly. In cases in which studies did not mention discounting, we assumed it was not applied. This resulted in 2270 unique CEAs following disaggregation for multiple country analyses within single publications. In total, we included 2251 unique publications, the PubMed identification numbers of which are provided in Appendix A [see Electronic Supplementary material (ESM)].

We used the source of funding reported by the Registry to classify CEAs as either manufacturer or non-manufacturer

sponsored. The non-manufacturer classification included government, foundations and pro-member funders. We classified studies recorded by the Registry as joint funded and by a manufacturer as manufacturer-funded. The Registry reports a broad number of intervention types, which we classified into three categories. We classified those involving screening or immunisation as 'prevention'. Those involving a pharmaceutical intervention were classified as 'pharmaceutical'. All other intervention types were classified as 'other therapeutic'. Similarly, analytical time horizons of 2 years or less were classified as 'short', those of between 2 and 5 years were classified as 'medium' and those of 5 years or longer were classified as 'long'. We aggregated the quality scores into three categories of low, medium and high using scores of 1–4, 4.5–5 and 5.5–7, which roughly divided the sample into tertiles.

2.2 Analysis

We compared the discount rates for costs and effects applied in the CEAs to the guideline rates. We recorded studies applying recommended rates as being adherent. In the cases in which discounting guidelines changed, CEAs found to be applying the previously recommended discount rate in the 2 years following the year of revision were still classified as adherent. NICE accepts CEAs that apply lower discount rates in special cases [11]. None of the UK studies in our sample corresponded to such special cases. NICE also issues specific methods guidelines for public health interventions, which recommend the application of a discount rate of 1.5% to costs and health effects [11]. One study in our sample corresponded to such an intervention and applied discounting of 1.5% and so was recorded as being adherent. Some studies did not apply discounting, citing a short time horizon for the appraisal of outcomes as the reason for omitting discounting. We checked these studies to assess if they did indeed only include outcomes within 1 year, then we considered the non-application of discounting in accordance with guidelines. We did not appraise whether the short horizon of analysis was itself appropriate or not.

Our data were recorded in Microsoft Excel 2016 and our analysis was conducted in R Version 3.5.3. We compiled summary statistics to provide an overview of how adherence varied between countries, the year of publication, source of sponsorship, the intervention type, the intervention time horizon class, the quality class and between the top five journals by volume of publication within the sample. Our primary statistical analysis used binary logistic regression analysis using the GLM function from the ISLR package (Version 1.2) to assess if rates of non-adherence varied significantly by country of study setting, publication year, source of funding and discounting type (equal discounting or differential discounting). We used three specific dummy variables. The first two control for differential discounting: one for differential discounting currently applied in both The Netherlands and Belgium, and the second for differential discounting applied in the UK between 2002 and 2004. The third dummy was for Canada for years 2018 and 2019, corresponding to the period following a large reduction in the recommended discount rate made in 2017.

3 Results

Table 1 details the official discounting guidelines over the relevant periods for the selected countries. The discount rates ranged from 1.5 to 10%. The rate of 10% was recommended in New Zealand from 1998 [12], which is particularly high relative to the other recommendations. However, this rate was since revised to 8% and then 3.5% in 2005 and 2007, respectively [13, 14]. Another notable revision is the substantial reduction of the Canadian discount rate from 5 to 1.5% in 2017 [15]. Ireland was the only country to revise its discounting rates upwards. It increased the recommended rate on both costs and health effects from 4 to 5% in 2014 [16, 17], before revising down again to 4% in 2019 [18]. There were also changes in the type of discounting applied. The UK stopped recommending differential discounting in 2004 [19, 20], whereas The Netherlands adopted differential discounting in 2006 [21].

The observed rates of adherence by country and specific guideline period are reported in Table 2. No confidence intervals are reported in cases in which the number of observations is small (<25). The overall rate of adherence observed within our sample is 79%. This rate varies substantially between the countries studied. The lowest rate of adherence found was 28% for New Zealand. This contrasts with New Zealand's geographical neighbour, Australia, which exhibited a rate of 73%, which is not statistically significantly different from the overall average when assessed with a 95% confidence interval. Ireland exhibited a rate of 68%. Canada's adherence rate of 66% is statistically significantly below the overall average.

The UK's overall adherence rate is 87% for the complete period from 2002 to present, which is statistically significantly higher than average over all countries. The UK employed differential discounting from 2001 to 2004 and exhibited a somewhat lower rate of adherence of 70% during that period. Since the adoption of equal discounting, the percentage of adherent UK studies increased markedly to 88%, above the overall average. The converse is observed with The Netherlands, as adherence increased from 62 to 82% following its adoption of differential discounting in 2006. Belgium has applied differential discounting since its first guidelines were published in 2006 and also exhibits a high rate of adherence at 87%, although the confidence interval of this estimate does not lie above the overall average.

Further univariate analysis is shown in Table 3. It examines how the rate of adherence varies according to a number of factors. The rate of adherence generally increased over time. Adherence has increased from a low of 63% in the second 5-year period to over 80% in the most recent period.

Table 3 also reports the rates of adherence for the top five journals in the sample according to the number of publications. Approximately a fifth ($n = 465$) of all the reviewed CEAs are accounted for by these five journals. Four of the five journals have adherence rates that are statistically significantly above the overall average.

The univariate analysis shows the mean adherence rate was highest among manufacturer-sponsored studies and the confidence interval lay above the overall mean. Adherence was lower in non-manufacturer sponsored studies and in those in which the source of funding could not be determined, with the confidence interval of the latter lying below the overall average adherence rate. Adherence was higher in analyses of pharmaceutical interventions and lower in preventative and other therapeutic interventions relative to the overall adherence rate. Analyses with the shortest time horizons of 2 years or less had the highest adherence rate of any of the time horizon classes of 92%. This likely owes to the fact that interventions of 1 year or less did not need to apply discounting to be adherent. Analyses with a time horizon of 2–5 years had the lowest rate of non-adherence, while those with a horizon of 5 years or more had adherence close to the overall rate. According to our categorisation of the Tufts quality score, adherence increased from low to medium to high quality categories. The confidence intervals for low and high quality categories lie below and above the overall adherence rate, respectively, while the medium category lies approximately on the overall average.

An assessment of the frequency of the deviations from guideline rates finds the overall most frequent was the unjustified application of no discounting (162 cases; 7.1% of the total sample). The single most common deviation from guideline rates was found to be the application of 3% when the recommended rate is 5% (148 cases: 119 from Canada, 29 from Australia). The second most common single deviation was the application of 3% in the context of a recommended rate of 3.5% (37 cases: 22 from the UK, 15 from New Zealand). The third most common error (32 cases) was the application of 3% in The Netherlands when the recommended rates are 4% and 1.5% for costs and health effects, respectively. Where errors did occur, lower rates than the recommended (including no discounting) were applied to outcomes in 88% of cases. Of the total errors, 35% were the application of no discounting.

When we assessed the mean quality scores by intervention type using analysis of variance, we find those for CEAs of pharmaceutical interventions statistically significantly exceed those of preventative interventions (4.95 vs 4.77, respectively, $p = 0.025$). Similar differences in the quality scores are found when comparing study sponsorship categories. The mean score for manufacturer-sponsored studies statistically significantly exceeds that of the non-manufacturer-sponsored studies (4.96 vs 4.76, respectively, $p = 0.0001$). An examination of the study sponsorship by funding type revealed a higher proportion of manufacturer-sponsored studies in pharmaceuticals than in preventative interventions (70% vs 9%, respectively).

The multivariate logistic regression analysis reported in Table 4 broadly reflects the descriptive statistics. The publication year demonstrated a statistically significant relationship with adherence. The odds ratio (OR) of 1.04 (CI

Table 1 Guideline discount rates by country and period

Country	Year	Costs discount rate (%)	Effects discount rate (%)
Australia	1992–current [8, 22]	5	5
Belgium	2006–current [23–25]	3	1.5
Canada	1994–2017 [9, 10, 26]	5	5
	2017–current [15]	1.5	1.5
Ireland	2010–2014 [16]	4	4
	2014–2019 [17]	5	5
	2019–current [18]	4	4
The Netherlands	1999–2006 [27]	4	4
	2006–current [21, 28]	4	1.5
New Zealand	1999–2005 [12]	10	10
	2005–2007 [14]	8	8
	2007–current [13, 29, 30]	3.5	3.5
The United Kingdom	2001–2004 [19]	6	1.5
	2004–current [20, 31]	3.5	3.5

Table 2 Descriptive statistics of adherence rates by country

Study country and period	Number of studies	Adherent studies		
		Number	Percentage (%)	Confidence interval* (%)
Australia	169	124	73	66–80
Belgium	76	66	87	77–93
Canada	491	324	66	62–70
1995–2017	464	300	65	60–69
2017–current	27	24	89	70–97
Ireland	22	15	68	†
2011–2014	17	11	65	†
2014–current	5	4	80	†
The Netherlands	424	337	79	75–83
2000–2006	60	37	62	48–74
2006–current	364	300	82	78–86
New Zealand	29	8	28	13–47
2000–2006	1	1	100	†
2006–2007	4	2	50	†
2007–current	24	5	21	†
UK	1059	921	87	85–89
2002–2004	74	52	70	58–80
2004–current	985	869	88	86–90
Total	2270	1795	79	

*Two-tailed confidence intervals assessed at significance level of 5%

†Confidence intervals omitted in cases where the number of observations is small ($n < 25$)

1.01–1.07) indicates the probability of adherence rose modestly over time. When compared against Australia as a reference country, studies from Canada (OR 0.58, CI 0.38–0.88), and New Zealand (OR 0.08, CI 0.03–0.20) were significantly less likely to adhere to guidelines, with the magnitude and statistical significance being the most pronounced for New Zealand. While neither The Netherlands nor Belgium independently demonstrate a statistically significant difference in adherence, both apply differential discounting, which does lead to a statistically significant level of improved adherence relative to a reference case of equal discounting (OR 2.22, CI 1.13–4.31). The UK is statistically significantly more likely to apply discounting correctly relative to the reference case of Australia (OR 2.47, CI 1.61–3.74). The UK's application of differential discounting between 2002 and 2004 is associated with a very low odds ratio of applying discounting correctly that is highly statistically significant (OR 0.24, CI 0.14–0.41).

Our results show that manufacturer sponsorship is statistically significantly associated with a large increased probability of adherence compared with non-manufacturer funding (OR 1.57, CI 1.18–2.10). We found no statistically significant relationship for studies in which the source of funding could not be determined. Relative to other therapeutic interventions, pharmaceutical interventions had a highly statistically significant increased probability of adhering to discounting guidelines (OR 1.74, CI 1.32–2.28). While the univariate analysis found preventative interventions had a lower than average adherence rate, the multivariate analysis did not find a statistically significant reduced probability of adherence for such interventions relative to the reference case of other therapeutic interventions. The multivariate analysis shows that relative to a reference case of a time horizon of 2–5 years, studies with short and longer time horizons both have highly statistically significant increased probability of adherence to discounting guidelines.

4 Discussion

This study examined adherence to guideline discounting rates in published CEAs. We find highly statistically significant relationships between the source of funding, the type of discounting and, in some cases, the country of origin with adherence to discounting guidelines. Studies funded by manufacturers and published more recently are more likely to apply discounting correctly, as are studies from countries that currently apply differential discounting. The UK demonstrates better adherence when other

Table 3 Descriptive statistics of adherence rates by period

Co-factor	Number of studies	Adherent studies		
		Number	Percentage (%)	Confidence interval* (%)
Period of publication				
1994–1998	22	15	68	**
1999–2003	124	78	63	54–71
2004–2008	472	347	74	69–77
2009–2013	805	640	80	77–82
2014–2019	847	715	84	82–87
Journal (top 5 by volume)				
PharmacoEconomics	124	110	89	81–93
Value Health	118	107	91	84–95
J Med Econ	85	79	93	85–97
PLoS One	76	60	79	68–87
BMJ	62	58	94	84–98
Study sponsor				
Manufacturer	742	639	86	83–88
Non-manufacturer	1175	909	77	75–80
Could not be determined	353	247	70	65–75
Intervention type				
Pharmaceutical	918	779	85	82–87
Prevention	289	204	71	65–76
Other therapeutic	1063	812	76	74–79
Analysis time horizon				
Short (< 2 years)	553	506	92	89–94
Medium (2–5 years)	156	98	63	55–70
Long (> 5 years)	1473	1138	77	75–79
Not reported	88	53	60	49–70
Tufts Quality Score				
Low (1–4)	692	495	72	68–75
Medium (4.5–5)	821	649	79	76–82
High (5.5–7)	757	651	86	83–88
Total	2270	1795	79	

*Two-tailed confidence intervals assessed at significance level of 5%

**Confidence interval for 1994–1998 omitted due to a small sample for this period

Table 4 Binary logistic regression examining the influence of variables on adherence to recommended discount rates

	Odds ratio	Confidence interval	
Publication year	1.04	1.01–1.07	**
Sponsor			
Non-manufacturer	Reference		
Could not be determined	0.83	0.62–1.12	
Manufacturer	1.57	1.18–2.10	**
Discounting type			
Equal	Reference		
Differential	2.22	1.13–4.31	*
Country			
Australia	Reference		
Belgium	0.80	0.30–2.29	
Canada	0.58	0.38–0.88	*
Canada, 2018–2019	4.30	1.41–18.76	*
Ireland	0.70	0.25–2.07	
The Netherlands	0.66	0.33–1.32	
New Zealand	0.08	0.03–0.20	***
UK	2.47	1.61–3.74	***
UK, 2002–2004	0.24	0.14–0.41	***
Intervention class			
Other therapeutic	Reference		
Pharmaceutical	1.74	1.32–2.28	***
Prevention	0.91	0.66–1.26	
Time horizon			
Medium (2–5 years)	Reference		
Long (> 5 years)	2.46	1.68–3.60	***
Short (< 2 years)	8.44	5.29–13.59	***
Not reported	1.79	0.97–3.34	

*, **, ***Significant at 5%, 1% and 0.1% levels, respectively

factors are controlled for, while Canada and, most particularly, New Zealand demonstrate worse adherence.

The very low rate of adherence for New Zealand is the most obvious finding within our review. Many studies from New Zealand applied a discount rate of 3%, even following the revision of the guideline rate to 3.5% in 2007. We speculate that the high discount rates of 10% and 8% that were recommended until 2005 and 2007, respectively, led to a practice of non-adherence that has not subsided following the revision to 3.5%. The low rate of adherence in New Zealand is likely to be of only limited policy significance, however. The difference of 0.5% between the recommended and most commonly applied rate means that any distortion to optimal intervention choice is likely to be very modest.

It is notable that only two-thirds of Canadian studies applied the correct rate. We believe it likely that the US recommendation of 3% made by both the first and second Washington Panels on cost-effectiveness in health and medicine may be highly influential in a North American context [1, 32]. Indeed, this is in accordance with anecdotal observation when acting as journal reviewers on Canadian manuscripts that often used the 3% rate rather than the rate of 5% recommended until recently. While our sample only includes a small number of observations from Canada following the 2017 reduction in the recommended

discount rate to 1.5%, there is already an indication within our results that adherence has improved since a more favourable rate has been adopted.

A possible explanation for the high rates of adherence observed within Belgium and The Netherlands, and the increase in Dutch adherence since the adoption of differential discounting in 2006, is that the application of differential discounting tends to lead to more favourable cost-effectiveness ratios. Despite this, the period in which differential discounting applied in the UK between 2001 and 2004 was marked by low adherence in our sample. We believe NICE's initial recommendation of 6% and 1.5% for costs and health effects, respectively, was not considered credible and often ignored. We think this is likely as the recommended rates were markedly different from other guidelines. Furthermore, the differential between the rates implies an annual rate of growth in the value of health of approximately 4.5% [33], which is larger than a recent Canadian study considered reasonable, and was not supported by clear empirical evidence with the 2001 NICE guidance [19].

Within our sample, only Australia and Belgium have not revised their guideline discount rates. In principle, frequency of revision should not necessarily impact on adherence, as analysts should be able to apply the prevailing guideline rates at the time of assessment. In practice, more frequent revision may leave more room for confusion or gaming of regulatory processes, especially if rates are revised upwards and analysts choose to apply older, lower rates. However, such guideline revisions are likely to remain sufficiently infrequent that any such effect would be small at best.

One common deviation from recommended rates is the application of 3% instead of 4% and 1.5% in Dutch studies, despite the fact that The Netherlands has a high rate of adherence overall. In part, this may reflect debate within the Dutch CEA community on whether the implications of differential discounting are fully appreciated and if the recommended rates are appropriate [34]. In light of this debate, some Dutch analysts have applied a 3% discount rate instead [35].

Compared with a previous study conducted by the Tufts Registry, we found lower rates of adherence to guidelines. The previous analysis found 83% adherence over 1393 studies published between 1976 and 2006 [4]. The largest single country of origin in that sample was the US. The dominance of US analyses probably explains the high adherence observed in that study. That analysis, however, assessed an earlier period of research, during which we might expect lower adherence. Another previous review by Smith and Gravelle noted concern at the high proportion (28%) of studies they found that did not apply discounting [6]. Although we also found a large proportion of studies did not apply discounting, in most cases this was justified, as the analyses did not appraise outcomes over a period longer than 1 year. Accordingly, the absence of discounting should not necessarily be construed as a deviation from guideline practice.

The statistically significant increase in adherence observed over time was as expected and in accordance with other findings from data from the Registry. This may be due to a general improvement of understanding of CEA methods over time and increasing familiarity with guidelines among authors, editors and reviewers.

We found greater adherence in studies funded by manufacturers. No such difference was found by Neumann et al. in their previous analysis of the Tufts Registry data [4]. It is possible that the CEA literature has changed composition since the earlier Tufts study. The finding that adherence is higher in studies with a clear sponsor interest is possibly counterintuitive, as we might expect manufacturers to attempt to game the appraisal process. While our analysis cannot examine causation, a possible explanation for the higher adherence in manufacturer-sponsored studies may be because the quality of CEAs as appraised by the Tufts quality score is higher in pharmaceutical studies and manufacturer sponsorship is the most common funding source within this type of intervention.

We found that the overwhelming majority of deviations from discounting recommendations involved the application of lower discount rates or no discounting. This, coupled with the increase in adherence in Canada since 2017, indicates that deviation from guidelines is not random. We believe it likely that analysts are biased towards applying rates that lead to more favourable cost-effectiveness ratios. While our results do not point towards gaming by manufacturer-sponsored studies, we speculate that it may be the case that unsponsored analysts are subject to a degree of 'intervention capture', meaning that they may be biased towards an intervention in their field of research and attempt to find results that favour provision.

In principle, cost-effectiveness evidence can determine which patients will receive access to certain interventions and which will not. Accordingly, it is important that the correct discount rates are applied in all studies, both for reasons of technical efficiency and ethical concerns of fairness. No patient group or particular intervention should be unfairly advantaged by being subject to more favourable discount rates than are applied to others.

4.1 Recommendations Regarding Discounting Practice

We recommend that researchers and journal editors ensure clear reporting of the discount rates applied. This

permits greater transparency regarding the comparability of cost-effectiveness estimates against other studies and cost-effectiveness thresholds. We recognise that academic research may be justified in deviating from national CEA guidelines, possibly for reasons of comparability with international evidence or for methodological purposes. In these cases, researchers and journal editors should ensure that the deviations from national guidelines be explicitly stated, and, as is often practiced, that results also include estimates according with national guidelines. At present, it is unclear if journal editors and reviewers are aware that deviations from national guidelines are acknowledged or not. We support the existing recommendations of the Washington Panel and the International Decision Support Initiative (iDSI) that cost-effectiveness analyses report results for both a common reference rate of 3% and national guidelines [32, 36].

4.2 Limitations

We used data from the Tufts Registry under the assumption that it is accurate. In a very small proportion of cases ($n = 66$, 2.9%), however, we found that the Registry had recorded data incompletely, which then required the interrogation of the original studies. Similarly, our use of the intervention types and time horizons recorded in the Tufts registry depends on the accuracy of the initial data capture by the registry. Moreover, we used the Tufts quality scores, which clearly depend on the weightings used within that system. A natural limitation of relying on one single database is that any constraints on the scope of the Registry will therefore limit our sample. For instance, as the Registry does not capture grey literature CEAs, our analysis omits assessments conducted by government agencies explicitly for the purposes of determining cost effectiveness in given jurisdictions. It seems plausible that such analyses might demonstrate better adherence than analyses published within academic journals. Accordingly, the conclusions from our analysis clearly can only apply to the academic literature. Another potential limitation of relying on the Registry data is that it only indexes studies reporting health effects in QALYs. Our analysis therefore omits CEAs reporting health effects in life-years gained, which may still be common within certain portions of the CEA literature such as cancer screening. However, limiting the analysis to studies reporting QALYs ensures our sample corresponds to the outcome measures recommended by the current national CEA guidelines within our sample, which all state that the QALY is the preferred measure of effects.

Despite the possible sample limitations given above, the use of the Registry permitted a single, consistent data source that allowed us to assess a large volume of CEAs quickly and efficiently. A potential limitation of our analysis is that we used the discount rates reported in the base-case analysis to assess adherence. We did not consider secondary results presented for other discount rates elsewhere within the CEAs that may have accorded with national guidelines. Nevertheless, we consider using the results presented in the base case to be a fair test of adherence.

A caveat to our analysis is that we have focused on adherence to recommended guidelines but have not given explicit consideration to the separate question of adequate reporting of discounting practice. Many analyses may report clearly, but do not adhere to guidelines. Conversely, some may adhere to guidelines but not report clearly. A recent review of methodological adherence in CEAs in low- and middle-income countries did give consideration to that distinction [37]. Accordingly, it is important that readers bear this distinction in mind when considering our results.

5 Conclusion

There is evident scope for improvement in adherence to official CEA discounting guidelines, despite the trend for improvement over time. Manufacturer-sponsored CEAs appear to demonstrate better adherence. Adherence appears better in countries currently applying differential discounting. The substantial differences in adherence between countries indicates that certain jurisdictions need to make particular efforts. We echo the call of a similar review from almost two decades ago that then appealed for journal editors and reviewers to show greater diligence in insisting that discounting guidelines are adhered to [6]. The question of appropriate guideline adherence represents more than a simple issue of technical consistency, but relates to important ethical questions of fairness regarding access to scarce healthcare resources.

Author Contributions The study design was conceived by JOM. The data was gathered and analysed by MQTK, MAM, MJC, FL. KT reviewed the statistical methods applied. The manuscript text was drafted by MQTK, MAM, MJC and FL. The manuscript text was edited and revised by MQTK, MAM and MJC under the guidance of JOM. Final production and submission of the manuscript was led by MQTK.

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Compliance with Ethical Standards

Conflict of interest The authors, Michelle Q.T. Kwok, Mistura A. Kareen, Michael J. Cash, Fiona Lafferty, Katy Tobin and James F. O'Mahony have no conflicts of interest to declare. There are no direct proprietorial or professional interests at stake with respect to this manuscript. Furthermore, the authors have no indirect proprietorial or

professional interests that will be enhanced by improved adherence to discounting.

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