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Title: The Modelled Cost-Effectiveness of Cognitive Dissonance for the Prevention of Anorexia Nervosa and Bulimia Nervosa in Adolescent Girls in Australia

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Abstract

Background

Eating disorders (EDs), including Anorexia Nervosa (AN) and Bulimia Nervosa (BN), are prevalent disorders that carry substantial economic and social burden. The aim of the current study was to evaluate the modelled population cost-effectiveness of cognitive dissonance (CD), a school-based selective intervention demonstrated to prevent EDs, in the Australian health care context.

Method

A population-based Markov model was developed to estimate the cost per disability adjusted life-year (DALY) averted by CD relative to no intervention. We modelled the cases of AN and BN that could be prevented over a 10-year horizon in each study arm and the subsequent reduction in DALYs associated with this. The target population was 15-18 year old secondary school girls with high body-image concerns. This study only considered costs of the health sector providing services and not costs to individuals. Multivariate probabilistic and one-way sensitivity analyses were conducted to test model assumptions.

Results

Findings showed that the mean incremental cost-effectiveness ratio at base-case for the intervention was $103,980 per DALY averted with none of the uncertainty iterations falling below the threshold of AUD$50,000 per DALY averted. The evaluation was most sensitive to estimates of participant rates with higher rates associated with more favourable results. The intervention would become cost-effective (84% chance) if the effect of the intervention lasted up to 5 years.

Conclusion

As modelled, school-based CD intervention is not a cost-effective preventive intervention for AN and BN. Given the burden of EDs, understanding how to improve participation rates is an important opportunity for future research.

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INTRODUCTION

Eating Disorders (EDs), including Anorexia Nervosa (AN) and Bulimia Nervosa (BN), are common and are associated with significant impairment of health related quality of life (HRQoL).[1, 2] EDs are also associated with substantial economic and social burden.[1] The global burden of disease study (GBD) (2013) estimated that BN and AN respectively are the 5th and 8th major causes of disease burden in Australian females aged 10 to 24 years, calculated in disability-adjusted life years (DALYs).[3, 4] EDs were the 12th major cause of mental health hospitalisation costs within Australia.[5] Moreover, the annual costs of AN treatment in Australia (based on a broader societal perspective) were estimated to be up to $20,000, of which health care costs accounted for 10-15%.[6] In the private hospital sector, the cost of treatment of an episode of AN was estimated to be the second most costly treatment after the cost of cardiac artery bypass surgery.[7]

A number of risk factors (e.g., dieting, body dissatisfaction) are associated with the development of EDs including AN and BN.[8] Of note, recent research studies have highlighted that adolescents engaging in dieting and disordered eating behaviours continue to have an increased risk for these behaviours into young adulthood.[9] A number of interventions have been developed to try and prevent the development of disordered eating problems.[10-15] Amongst these interventions, two recent systematic reviews found that a cognitive dissonance (CD) based intervention known as *The Body Project* is the only intervention with strong evidence of reducing ED risk factors as well as ED diagnostic symptoms as measured by the Eating Disorder Diagnostic Survey/Interview (EDDS/EDDI).[10, 11] This intervention has been broadly implemented in high schools, colleges and universities in the United States (US), Iceland, and Mexico.[16]

To our knowledge, economic evaluations of preventive interventions targeting EDs are relatively rare in the academic literature. However, such evaluations are an important tool to aid decision-makers in determining which interventions are value-for-money.[17] There have been two modelled cost-utility analyses (CUAs) of preventive interventions for ED.[18, 19] In one of these studies, Wang and colleagues[18] evaluated the cost-effectiveness of "Planet Health", an obesity preventive intervention targeting the prevention of BN, while in the other study Wright and Austin[19] evaluated the cost-effectiveness of annual screening interventions for EDs. Wang and colleagues[18] estimated that averting one case of BN would result in an estimated cost-saving of US$33,999 and a gain of 0.7 quality-adjusted life years (QALYs) at an intervention cost of US$46,803. Wright and Austin[19] found that the evaluated screening program was 41% likely to be cost-effective at the commonly accepted[20] willingness-to-pay threshold of US$50,000 per QALY.

The goal of the current study was to evaluate the modelled population cost-effectiveness analysis of a cognitive dissonance intervention relative to no intervention to answer the question of whether CD provides value-for-money within the Australian health care system.

METHODS

The current study was conducted within the context of a larger study. This larger study has the overall aim of using economic evidence to inform mental health interventions and service delivery within the Australian context. A standardised economic evaluation protocol has been developed to ensure that the methods across the different evaluations are as similar as possible in order to improve the comparability of cost-effectiveness of different interventions across different mental disorders.[21-23] As a first step, the effectiveness and characteristics of preventive interventions of ED were retrieved from the published literature. The intervention was chosen based on the strength of evidence of effectiveness as well as generalisability of

the setting/population to the Australian context. The effect size of the chosen interventions were based on a meta-analysis of multiple randomised controlled trial studies of that intervention.[10] The decision-analytic model was then developed to estimate the costs and benefits of implementing the chosen intervention among adolescent girls in the Australian context.

The current study employed a cost-utility analysis framework, expressing outcomes as DALYs. As the context of the study is the global burden of disease estimates for Australia, the disability weights of AN and BN was sourced from the GBD 2013.[24] A health sector perspective was adopted that focussed on costs and benefits accruing to students, health care providers, school staff and third-party payers. All costs and cost offsets were measured in Australian dollars and expressed in 2013 dollar values (using published health price deflators from the Australian Institute of Health and Welfare (AIHW), if appropriate).[25] Students' time and travel costs were not included since the intervention occurs in school settings. The costs of unrelated diseases resulting from increased life expectancy were also excluded. A discount rate of 3% per annum was applied to all costs and benefits. Results (with and without cost-offsets) are reported as the incremental cost-effectiveness ratio (ICER) (an ICER is calculated as the difference in total costs between the intervention and comparator divided by the difference in DALYs averted between the intervention and comparator). The ICER was examined in relation to a cost-effectiveness value-for-money threshold of AU$50,000 per DALY averted (primary threshold) or AU$100,000 per DALY averted (secondary threshold) which have been used in previous Australian economic evaluation studies.[22, 26] This study adheres to the guidelines in Consolidated Health Economic Evaluation Reporting Standards (CHEERS).[27]

Intervention description

The CD intervention is characterised as a psychological intervention based on interactive verbal, written and behavioural exercises that guide participants toward taking a stance against the thin-ideal. The intervention is delivered in group format (six to ten participants),[13] with session numbers and duration ranging from six sessions of 45 minutes to four sessions of 60 minutes.[13, 16, 28] If a participant misses a session, brief (10-15 minute) individual make-up sessions are conducted to review missed material when possible.[13] For the current modelled evaluation, we assumed the intervention was delivered by school counsellors.

Eligible population for the intervention

We modelled the intervention pathway based on how studies of preventive CD interventions were undertaken. The technical advisory panel constituted for this study suggested that this was likely to be realistic of routine roll-out. All females aged 15-18 years enrolled in Australian secondary schools are recruited using emails, flyers, and leaflets inviting females with body image concerns to participate in the CD intervention. The proportion of participants who respond to these recruitment materials is 9.2% (sourced from clinical trials).[13] Students who verbally affirm that they have high body image concerns through phone screening with staff are offered the intervention. The proportion of Australian female students who self-identify as having high body image concern (68.9%) was sourced from the 2013 Mission Australia Youth Survey of young women.[29] Data from RCT studies (n = 12) indicate that 83% (range: 64% – 95%) of students agree to participate in the intervention after such initial screening. We assumed a much lower participation rate of 30% in the real world setting given that financial incentives would not be provided to participants and the staging of these interventions during the later years of secondary school coincides with a heavy student assessment load.[30]

Effectiveness of intervention

Based on a meta-analysis undertaken in 2016[10], CD interventions were effective in reducing ED symptoms (measured by EDDS/EDDI) compared to waitlist control at post-test (Hedges' g = -0.30, 95% confidence interval (CI) -0.47 to -0.13) with substantial heterogeneity (I^2 = 51%, Q = 16.49, p = 0.04). The exclusion of one outlier[31] decreased the effect size to g = -0.25 (95% CI -0.37 to -0.14) and the heterogeneity became insignificant. Therefore, this effect size (after removal of the outlier) was chosen as the estimate of intervention effectiveness for use in the economic evaluation. Although the effect on ED symptoms at 1-year follow up still favoured CD interventions compared to control, this effect size became non-significant (Hedges' g = -0.06, 95% CI -0.19 to 0.06, I^2=0%, Q=4.76, 0.45)).[28] Therefore, statistically significant effect sizes (i.e., post-intervention) have been modelled in the baseline cost-effectiveness models.

A new method has been developed by the research team which re-weights Hedges' g formulation to transform the effect size on ED symptoms to reduced ED incidence.[28] The ED incidence outcome is important as the burden of disease studies only included diagnosed prevalent cases (including new incident and existing cases) of mental disorders in the estimates. Applying this method, we estimated that the intervention can reduce 15% of the incidence of ED post-intervention (relative risk (RR) = 0.85, 95% CI: 0.79 to 0.92). A 50% decay rate of benefit was modelled for interventions from 1-year to 4-year follow up and by year 5 the intervention effect reduces to almost zero. This decay effect is consistent with the results of the meta-analysis of preventive interventions for mental health (e.g., depression) which found that intervention effects reduce over time.[32]

Costs

Cost of the intervention includes the cost of recruitment and screening, cost of training intervention for school-counsellors and the cost of school counsellors who deliver the CD

sessions. We assumed that these will all be publicly provided services. The unit cost of school-counsellors was sourced from The Australian Psychologist and Counsellors in School Association's Report 2013.[33] The cost of training school counsellors was sourced from the Body Project expert training website.[34] We assumed that the intervention is in "steady state" operation, i.e., trained staff and necessary infrastructure are available to scale up the interventions, which is assumed to be working in accordance with their efficacy potential.[22, 26, 35] The cost offsets (that is, averted treatment costs) were the mean cost of treating each ED case (weighted by AN & BN prevalence) valued at $788 (sourced from AIHW for the year 2008-2009, and inflated to 2013 prices).[6] Cost offset included hospital costs, out-of-hospital costs (including GP services, imaging, pathology, psychologists and medical specialists) and medication costs. Key assumptions which have been made in costing the intervention pathway are detailed in Table 1.

[INSERT TABLE 1]

Modelling health outcomes

A decision-analytic multiple cohort Markov model developed in Microsoft Excel 2010 was designed using a 10-year time horizon to estimate the cost effectiveness of CD interventions compared to no intervention controls. The DisMod-II model was adapted to simulate how a population cohort moves between three health states over time having body image concerns, having a specified ED (AN and/or BN) and being dead (Figure 1). More complicated models (e.g. microsimulations) were not appropriate to the current context as we have no evidence of individual heterogeneity of intervention outcomes.

[INSERT FIGURE 1]

Transitions between health states were governed by epidemiological data (from the GBD 2013 study) including adjusted ED incidence, remission rates, and adjusted mortality rates.[3]

The incidence of ED was the sum of the incidence of AN and BN with the assumption that comorbid cases are assigned to one of each (e.g. female adolescent who developed AN could never develop BN). The ED remission rate and mortality rate was, respectively the average of remission rate and mortality rate of AN & BN, weighted by AN and BN prevalence. The ED incidence rate from GBD 2013 was adjusted for age and body dissatisfaction risk factors in the model. According to Rohde and Stice 2014[8], elevated body dissatisfaction is associated with an elevated odds ratio of 1.51 and 1.67 at age 15 and 16 of developing an ED (these odds were converted to relative risks of 1.44 and 1.57, respectively).[36] The assumption was made that the relative risk of 1.57 would be applied to adjust the incidence of ED for age 17 and so on. The mortality was adjusted by standardized mortality ratios of (SMRs) of 5.86 for AN and 1.93 for BN.[37]

Uncertainty and sensitivity analysis

To test how robust the results are to the assumptions made in the analysis, a probabilistic multivariate uncertainty analysis was undertaken using Monte Carlo simulation methods. For the Monte Carlo simulation, probability distributions related to natural history parameters, relative risks, disability weighs and costs were incorporated into the analysis. Estimates of incremental costs and DALYs were obtained by re-running the model which draws values from the distribution parameters in 5000 replications. Details of the parameters varied in the uncertainty analysis are presented in Table 2.

[INSERT TABLE 2]

The uncertainty simulations are presented on a cost-effectiveness plane. A cost-effectiveness plane is a quadrant of cost differences plotted against benefit differences. The area above the horizontal axis indicates that the intervention is more costly while the area to the right of the vertical axis indicates that the intervention is more effective (than the comparator).

In addition to multivariate probabilistic uncertainty analysis described above, we also employed a series of one-way sensitivity analyses to explore how different assumptions and parameters, such as incidence and participation rate, affect the results. The following scenarios were modelled:

- Scenario 1: Decay rates range from 0% (full benefit lasts for the entire 5 years) to 100% (one year benefit)
- Scenario 2: Incidence rates range from normal incidence without adjusting for body dissatisfaction to double normal incidence with adjusting for body dissatisfaction.
- Scenario 3: Time horizon of model ranges from 5 years to 15 years.
- Scenario 4: Proportion of participants who respond to recruitment material ranges from 5% to 30%.
- Scenario 5: Proportion of participants who have high body-image concerns ranges from 46.8% to 84%.
- Scenario 6: Participant rates of receiving the intervention ranges from 10% to 90%.
- Scenario 7: Cost offsets range from $0 (no cost offset) to $5841.

RESULTS

Table 3 contains a detailed breakdown of the economic evaluation results of the CD intervention. The mean of total intervention costs was $1,565,676 (without cost off-sets) (95% CI: $1,336,190 to $1,803,168) or $1,509,932 (with cost off-sets) (95% CI: $1,278,657 to $1,748,913). The mean of total DALYs averted by the intervention was 16 (95% CI: 9 to 24). In the cost-effectiveness plane, the uncertainty iterations fell in the north-east corner which means that the intervention was more effective and more costly than no intervention (Figure 2). Without cost-offsets, the mean ICER for this intervention was $103,980 per DALY averted (95% CI: $62,273 to $168,814) and none of the iterations fell below the

willingness-to-pay (WTP) threshold of AUD$50,000 per DALY. In relation to a secondary WTP threshold of AU$100,000 per DALY averted, the ICER without cost-offset was still slightly higher but 50% of the iterations fell below this threshold. Including cost-offsets (i.e. $788 per case per year) made very little difference to both primary and secondary results.

[INSERT TABLE 3]

[INSERT FIGURE 2]

Sensitivity analysis

Generally, the evaluation was most sensitive to intervention effect decay rate (scenario 1), ED incidence rate (scenario 2) and the proportion of participants who receive the intervention (scenario 6). In scenario 1, the ICER was $40,033 (95% CI: $24,136 to $65,771) per DALY if there was no decay of intervention effect. The intervention was also 84% likely to be cost-effective at WTP threshold of $50,000 per DALY. In scenario 2, doubling the incidence rates of EDs led to a lower ICER ($53,865, 95% CI: $32,220 to $88,536) but this ICER was still slightly higher than the WTP threshold of $50,000 per DALY. Variation in time horizon in scenario 3 did not significantly alter the ICER except a shorter time horizon led to an increase in the ICER. In scenario 4, the ICER was $92,114 (95% CI: $56,041 to $148,831) per DALY and the intervention was not cost-effective at the examined threshold when 30% participants who responded to recruitment materials was used. Scenario 5 indicated an ICER of $87,879 (95% CI: $52,540 to $143,631) per DALY when a high proportion of participants who have high-body image concerns was employed. Regarding the proportion who would take up the intervention (scenario 6), the ICER decreased to $46,427 (95% CI: $27,568 to $75,904) per DALY and the intervention was 68% likely to be cost effective at WTP threshold of $50,000 per DALY when a tripled participation rate was considered. The sensitivity analysis that refers to the higher cost-offset (scenario 7) led to a decrease of the ICER to $76,724 (95% CI:

$41,487 to $132,538) with nine percent of iterations falling under the WTP threshold of $50,000 per DALY. Further details of sensitivity analysis were presented at Figure 3.

[INSERT FIGURE 3]

DISCUSION

In this study, a population-based Markov model was developed to estimate the cost-effectiveness of a CD intervention relative to no intervention for the prevention of EDs. To our knowledge, this is the first study to assess the cost-effectiveness of an evidence-based selective preventive intervention of ED from a population cost-effectiveness perspective. This study demonstrated that CD is likely to result in very few DALYs averted, although the costs of the intervention are also not prohibitive. The cost-effectiveness ratio was above commonly accepted value-for-money thresholds of $50,000 per DALY in an Australian setting. Although such thresholds are somewhat arbitrary, $50,000 per DALY appears an acceptable threshold to Australian decision-makers and has been used in a number of previous health economic evaluations, including mental health interventions.[22, 23] Having said that, the sensitivity analysis demonstrated that variations in some of the modelling parameters could change this conclusion.

The largest component of the intervention costs was the screening costs which accounted for 50% of the total costs. With a low participation rate for the actual CD intervention (which is what reduces the burden) it is therefore unsurprising that the results of the current analysis were not favourable. Our resultant ICER was higher than that observed in previous studies. Previous US research by Wright and colleagues[19], which evaluated a screening intervention, found an ICER of AUD$87,010 per QALY (convert to AUD$ using purchasing power parities of 1.54 in 2012[38]) while Wang et al.[18] evaluated the cost-effectiveness of an obesity – ED prevention program and reported an ICER of AUD$27,437 per QALY (self-calculated

and converted to AUD$ using purchasing power parties of 1.50 in 2010[39]). The differences between these results and our results is likely to be because of the low participant rates and the screening costs (e.g. recruitment cost) that were included in this study.

A strength of the current study is the use of plausible assumptions based on the latest available literature to develop the economic model. However, it is important to note that many of these have their own limitations. For example, while we used health-sector related cost-offsets from the AIHW, it is known that EDs are associated with higher costs, ones that often lie outside the health sector.[40, 41] For example, Stuhldreher and colleagues[40] found that up to 40% of the costs associated with EDs are attributable to indirect (or productivity costs). We may therefore have underestimated the potential cost-savings associated even with a delay in ED onset, particularly as the intervention girls enter adulthood.[40] Future intervention-based research needs to consider adding economic dimensions so that a more accurate estimations of any costs, cost-offsets as well as health impacts from various interventions can be obtained.

Another strength (that is also a limitation) of the current study is the background context of the burden of disease studies for Australia. Any health benefits associated with interventions for ED have to impact either the prevalence or incidence of existing disease since the health benefit was based on a single disability weight. This does not include sub-syndromal disease, which is common in ED[42] or even disease severity[43]. It must therefore be appreciated that the current health burden averted by such interventions has been conservatively estimated in this study. The epidemiological data from the GBD 2013 study pooled all data available for a given disorder into a weighted average, while simultaneously adjusting for known sources of variability in estimates reported across studies.[43] The current simulation model, as with all similar simulation models, used many assumptions that limit conclusions. However, our approach in the use of both uncertainty analysis and sensitivity analysis helped to ascertain

which variables had the largest impact on the conclusions. For example, the current study used the assumption that a female adolescent with AN could never develop BN given that the transition between AN & BN is difficult to address in the current model. While the cross-over rates might impact on the incidence rates, the sensitivity analysis of lower or higher incidence rate of EDs (i.e. scenario 2) showed that the overall study conclusion was unchanged although the ICER was substantially altered.

One issue highlighted by the sensitivity analysis as being significantly important is the low participation rate for actual engagement with the CD intervention. This study estimated that only 30% of female adolescents with high-body image concerns (equivalent to 2% of the female population in this age range) agreed to participate in the intervention under non-financial incentive circumstances. The sensitivity analysis demonstrated that if this participant rate was doubled or tripled, the ICER would reduce to AUD$58,642 or $44,716 per DALY averted and the intervention would be between 27% and 68% likely to be cost-effective at willingness-to-pay threshold of AUD$50,000 per DALY averted, respectively. Enhancing dissemination of a preventive intervention for EDs is an important challenge since individuals have been found to have a low interest in ED prevention[44], especially teenagers, where "there is not always an easy avenue for mandatory participation as for school programmes".[30] It is important that future research considers how such interventions can appropriately engage more people who are most likely to benefit from the interventions, including the role of financial drivers.

Lastly, the current study was developed to assess the cost-effectiveness of screening and treatment interventions from an Australian perspective. The proportion of female adolescents who have high-body image concerns and the proportion of those who receive the intervention may differ across countries. Therefore, extrapolation of the results to different contexts needs to be undertaken with caution. In particular, even though the CD intervention has been found

to be effective for female undergraduate or college students in the US, this would require a different screening pathway which was not evaluated in this study and may incur different costs in Australia.

CONCLUSION

This analysis suggests that the CD intervention delivered to Australian female adolescents with high body dissatisfaction to prevent diagnosable case of ED is more effective and more costly relative to the "no intervention" control, with the ICER falling above commonly accepted value-for-money thresholds in Australia. However, extensive sensitivity analysis around this result suggested that important model assumptions impacted the ICER. Approaches that increase the participation rate of the CD intervention might render the intervention to be cost-effective at such thresholds. Future research needs to consider the economic credentials of such interventions along with their ability to reliably impact cases of ED.

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Table 1: Assumption and cost items for the CD intervention

Parameters	Assumption/Unit cost	Sourced
Screening staff	A school counsellor spent 10 mins to deliver flyers to 25 students (equivalent to one secondary-school class size)	Expert Opinion
Screening process	A school counsellor spent 10 mins (5 mins preparation + 5 mins of a phone call) to do a phone screening per student. At least three phone calls were undertaken.	Expert Opinion
Training	Each school receives formal training for one school counsellor from Body Project experts plus 15 minutes of technical support.	Expert Opinion
School counselors (Average salary of school counselors)	$ 80,467 per year $ 41.3 per hour	The Australian Psychologist and Counsellors in School Association, 2013 [33]
Training cost		Body Project Training Team & Estimation.[34] Converted to AUD$ using purchasing power parties of 1.48 in 2013.
Onsite training	$1850 per training (16 participants)	
Trainer travel expense	$1480 per training (16 participants)	
Technical Assistance (4 hours)	$185 per hour (4 participants)	

Oncosts	30%	Expert Opinion

Table 2: Input parameters and uncertainty ranges used in the simulation analysis

Parameters	**Values**	**Uncertainty Distributions**	**Source**
Efficacy (RR of developing ED) – post test	0.85 (0.79, 0.92)	Lognormal	From 9 RCTs comprising meta-analysis [10]
Body dissatisfaction adjusted for incidence (RR) - Age 15 - Age 16 to 30	 1.44 (1.00, 2.05) 1.58 (1.17, 2.13)	Lognormal	Rohde, Stice 2014 [8]
Standardized mortality ratios - Anorexia Nervosa - Bulimia Nervosa	 5.86 (4.17, 8.26) 1.93 (1.44, 2.59)	Lognormal	Arcelus, Mitchell 2011 [37]
Disability weight of ED (Average AN & BN disability weight, weighted by AN & BN prevalence)	0.22 (0.15, 0.31)	Beta	GBD 2013 study[45]
Private costs (including unit costs of school counsellors, screening materials and training costs)	±20%	Pert	Own assumption
Number of sessions	4	Discrete	From 8 RCTs
Make-up session duration (hour)	0.2 (0.15, 0.25)	Pert	From 8 RCTs

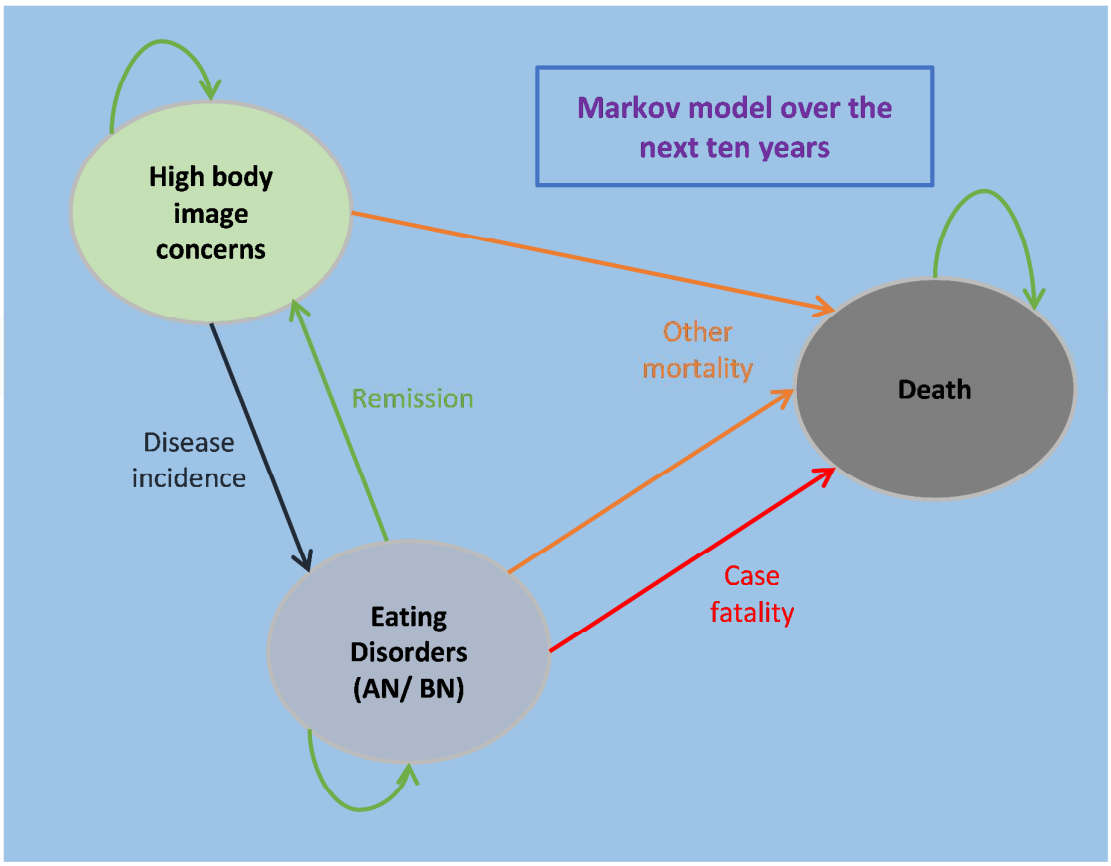
RR: relative risk; RCTs: randomized controlled trials; ED: eating disorder; AN: anorexia nervosa; BN: bulimia nervosa.

Table 3: Results of cost-effectiveness analysis for Cognitive Dissonance intervention.

	Mean	95% CI	Probability to be cost-effective at $50,000 per DALY averted	Probability to be cost-effective at $100,000 per DALY averted
DALYs averted	16	9 to 24		
Cost (exclude cost-offsets)	1,565,676	$1,336,190 to $1,803,168		
Cost (Include cost offsets)	1,509,932	$1,278,657 to $1,748,913		
ICER (exclude cost offsets) – per DALY averted	$103,980	$62,273 to $168,814	0%	50%
ICER (include cost offsets) – per DALY averted	$100,363	$59,417 to $164,021	0%	56%

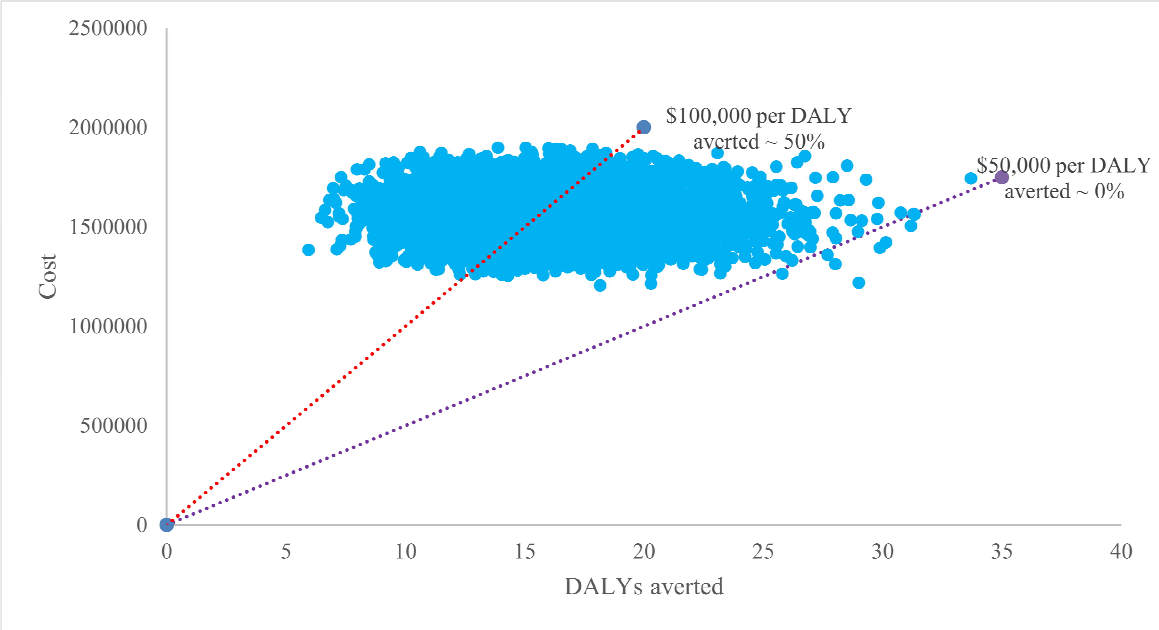
DALY: Disability averted life year; ICER: incremental cost effectiveness ratio.

Figure 1: State transition diagram used to estimate health benefit of cognitive dissonance intervention for eating disorder prevention.



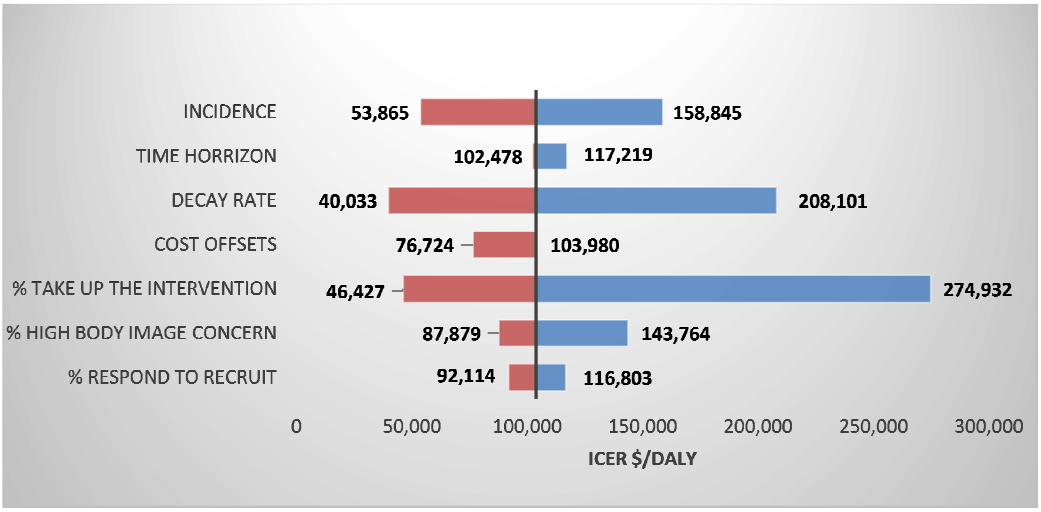
AN: anorexia nervosa; BN: bulimia nervosa.

Figure 2: Cost-effectiveness plane of base case analysis with willingness to pay threshold of $50,000 and $100,000 per DALY



DALYs: Disability Adjusted Life Years

Figure 3 – One-way sensitivity analyses of the potential cost-effectiveness of cognitive dissonance intervention.



ICER = incremental cost-effectiveness ratio; DALY = disability-adjusted life-year.

AUTHOR DISCLOSURE

ROLE OF FUNDING SOURCES

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CONFLICT OF INTEREST

J. J. B. owns Epigear International, which sells the Ersatz software used in the analysis.

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The other authors declare no conflicts of interest.

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Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/Item	Item no.	Recommendation	Reported on page no. / line no.
Title and abstract			
Title	1	Identify the study as an economic evaluation, or use more specific terms such as ‘‘cost-effectiveness analysis’’ and describe the interventions compared.	Page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base-case and uncertainty analyses), and conclusions.	Page 2-3
Introduction			
Back ground and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Line 4-25 Line 26-40
Methods			
Target population and subgroups	4	Describe characteristics of the base-case population and subgroups analyzed including why they were chosen.	Line 84-97
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made	Line 45-56
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Line 60-61
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen	Line 137-139
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Line 137-139
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Line 66
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Line 57-60
Measurement of effectiveness	11a	*Single study–based estimates*: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Not applicable

	11b	*Synthesis-based estimates*: Describe fully the methods used for the identification of included studies and synthesis of clinical effectiveness data.	Line 99-109
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study–based economic evaluation*: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs	Not applicable
	13b	*Model-based economic evaluation*: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Line 121-134
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate	Line 61-66 Line 121-134
Choice of model	15	Describe and give reasons for the specific type of decision-analytic model used. Providing a figure to show model structure is strongly recommended.	Line 137-143 Figure 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytic model.	Line 145-157
Analytic methods	17	Describe all analytic methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (e.g., half-cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Line 110-119 Line 145-157
Results			
Study parameters	18	Report the values, ranges, references, and if used,	Table 1-2

		probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Line 188-200
Characterizing uncertainty	20a	*Single study–based economic evaluation*: Describe the effects of sampling uncertainty for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation*: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Line 191-213 Table 1-2
Characterizing heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Not applicable
Discussion			
Study findings, limitations, generalizability, and current knowledge	22	Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.	Line 216-284
Others			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other nonmonetary sources of support	Role of funding sources (page 26)
Conflict of interest	24	Describe any potential for conflict of interest among study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors' recommendations.	Conflict of interest (page 26)