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**University College Cork, Ireland**  
Coláiste na hOllscoile Corcaigh

## **A cost-effectiveness analysis of school-based suicide prevention programmes**

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## **Abstract**

Suicide is one of the leading causes of death among young people globally. In light of emerging evidence supporting the effectiveness of school-based suicide prevention programmes, an analysis of cost-effectiveness is required. We aimed to conduct a full cost-effectiveness analysis (CEA) of the large pan-European school-based RCT, Saving and Empowering Young Lives in Europe (SEYLE). The health outcomes of interest were suicide attempt and severe suicidal ideation with suicide plans. Adopting a payer's perspective, three suicide prevention interventions were modelled with a Control over a 12-month time period. Incremental cost-effectiveness ratios (ICERs) indicate that the Youth Aware of Mental Health (YAM) programme has the lowest incremental cost per 1% point reduction in incident for both outcomes and per quality adjusted life year (QALY) gained versus the Control. The ICERs reported for YAM were €34.83 and €45.42 per 1% point reduction in incident suicide attempt and incident severe suicidal ideation respectively and a cost per QALY gained of €47,017 for suicide attempt and €48,216 for severe suicidal ideation. Cost-effectiveness acceptability curves were used to examine uncertainty in the QALY analysis, where cost-effectiveness probabilities were calculated using net monetary benefit analysis incorporating a two-stage bootstrapping technique. For suicide attempt, the probability that YAM was cost-effective at a willingness to pay of €47,000 was 39%. For severe suicidal ideation, the probability that YAM was cost-effective at a willingness to pay of €48,000 was 43%. This CEA supports YAM as the most cost-effective of the SEYLE interventions in preventing both a suicide attempt and severe suicidal ideation.

**Key words:** Suicide attempt; Suicidal ideation; Prevention; Intervention; Adolescents; School; Cost-effectiveness

**Trial registration number** DRKS00000214

## **Introduction**

Suicide is the second leading cause of death among 10-24 year olds globally [1]. Young people are one of the groups most susceptible to suicidal ideation and self-harm [2] and the WHO has highlighted that a multi-sectoral approach is required to address suicide prevention [3]. There is evidence from the United States where school-based suicide preventive intervention programmes have been implemented - Signs of Suicide [4], Garrett Lee Smith Memorial Suicide Prevention Program [5], and Good Behaviour Game [6] - that attempted suicide can be significantly reduced. In Europe, the large-scale *Saving and Empowering Young Lives in Europe* (SEYLE) study reported a significant effect of a universal school-based mental health awareness programme - Youth Aware of Mental Health (YAM) - in reducing incident suicide attempt and severe suicidal ideation [7].

The need for economic evaluations in the area of adolescent and children's mental health has long been recognised. A 2005 systematic review of economic evaluations of child and adolescent mental health interventions reports that few economic evaluations, of generally poor quality, have been undertaken [8]. In light of emerging evidence supporting the effectiveness of school-based suicide prevention programmes, the estimated societal lifetime cost of one suicide death in people aged 10yrs and over in the United States which stands at \$1.2 million (2010 Prices) [9], and growing demands on scarce health resources, an analysis of cost-effectiveness is now a necessity.

Against this backdrop, we undertook an economic evaluation of the school-based SEYLE cluster randomised controlled trial (RCT) [10]. The authors have made no assumptions regarding the clinical effectiveness of the interventions implemented in SEYLE. Therefore, all three of the active interventions described below are compared with the Control.

## **Methods**

### **Randomised controlled trial**

The SEYLE RCT, coordinated by the Karolinska Institute in Sweden, was the first randomised controlled trial comparing the efficacy, cost-effectiveness and cultural adaptability of suicide prevention strategies in schools [10]. In total, 11,110 students from 168 schools in 10 European Union (EU) countries - Austria, Estonia, France, Germany, Hungary, Ireland, Italy, Romania, Slovenia, and Spain - were recruited to SEYLE. Each participating school was randomly assigned to one of three active intervention groups or a Control group between November

2009 and December 2010 [7].

## Participants

Of the 11,110 participants who completed the baseline assessment, 636 reported ever making a suicide attempt prior to baseline and/or reported experiencing severe suicidal ideation in the previous two weeks prior to baseline. As SEYLE is a preventive trial, only incident cases of attempted suicide and severe suicidal ideation were analysed. Prevalent cases, where pupils reported lifetime suicide attempts and severe suicidal ideation in the two weeks prior to baseline measurements, were given qualified psychological or psychiatric treatment after thorough assessment. However they were not randomised to treatment due to different healthcare systems in the participating 10 EU countries [11]. We therefore excluded prevalent cases from this CEA, a decision informed by and consistent with the SEYLE RCT [7]. A further 321 participants were excluded due to missing data at baseline for questions on suicide attempt and severe suicidal ideation. Table 1 provides detail of baseline characteristics and participant numbers from study recruitment to inclusion in the CEA.

**Table 1** Baseline characteristics & participant numbers from study enrolment to inclusion in CEA

<b>Baseline characteristics</b>	<b>QPR</b>	<b>YAM</b>	<b>ProfScreen</b>	<b>Control</b>	
Mean Age in Years (SD)	14.80 (0.82)	14.80 (0.85)	14.81 (0.80)	14.78 (0.89)	
Gender (male %/female %)	37/63	40/60	42/58	44/56	
<b>Participant Numbers (n)</b>	<b>QPR</b>	<b>YAM</b>	<b>ProfScreen</b>	<b>Control</b>	<b>Total</b>
<b>Baseline<sup>1</sup></b>					
Participants	2,692	2,721	2,764	2,933	11,110
Participants (%)	24.2%	24.5%	24.9%	26.4%	100%
Baseline exclusions <sup>2</sup>	146	175	165	150	636
Baseline missing data	75	24	141	81	321
Pupils eligible for inclusion in CEA	2,471	2,522	2,458	2,702	10,153
Responded to Suicide Attempt question	2,632	2,705	2,628	2,867	10,832
Suicide Attempt	83	115	102	86	386
Prevalence of Suicide Attempt	3.2%	4.3%	3.9%	3.0%	3.6%
Responded to Severe Suicidal Ideation question	2,663	2,697	2,735	2,898	10,993
Severe Suicidal Ideation	99	106	96	103	404
Prevalence of Severe Suicidal Ideation	3.7%	3.9%	3.5%	3.6%	3.7%
<b>12 month follow-up</b>					
Missing Suicide Attempt data	8	16	8	17	49
Absent from school on day of survey	485	519	489	429	1,922
Included in Suicide Attempt CEA	1,978	1,987	1,961	2,256	8,182
Missing Severe Suicidal Ideation data	9	12	7	12	40
Absent from school on day of survey	485	519	489	429	1,922
Included in Severe Suicidal Ideation CEA	1,977	1,991	1,962	2,261	8,191

<sup>1</sup> Before excluding those with severe suicidal ideation in the past 2 weeks and/or those who have ever made a suicide attempt

<sup>2</sup> Those with severe suicidal ideation in the past 2 weeks and/or those who have ever made a suicide attempt

## **Interventions**

We compared three active interventions; Question, Persuade, Refer (QPR), Youth Aware of Mental Health programme (YAM) and Screening by Professionals (ProfScreen) to a Control. The interventions took place during a 4-week period following the baseline assessment [12]. The QPR program focuses primarily on training gatekeepers within the school setting to identify and intervene when individuals are engaged in risky behaviours. Gatekeepers included teachers, guidance counsellors, administrators, special needs assistants, and security and maintenance staff. The YAM intervention is designed to promote knowledge of mental health, healthy lifestyles and behaviours. It was developed for SEYLE [10,12] and is a manualised, universal intervention, targeting all pupils. It comprises two 1 hour interactive lectures about mental health, 3 hours of role-play sessions on life dilemmas, stress and crisis situations, depression and suicide, all combined with six educational posters and a 32-page booklet that pupils could take home. ProfScreen is designed as a two-stage screening tool to help health professionals to identify at-risk adolescents based on mental health responses in a self-report questionnaire; pupils are then referred for clinical assessment (second stage) and onwards for professional treatment or to an appropriate non-clinical healthy-lifestyle group [13]. For ethical reasons the Control group could not be completely excluded from an intervention and therefore were exposed to the same six educational posters as those utilised in YAM. The posters constituted just one minor component of several components utilised in the YAM programme and were displayed in the classrooms with no other form of intercession. A detailed description of the interventions has been previously published [10] [12,13].

## **Costs**

We required data on the direct costs of each of the three interventions and the Control. In order to identify, measure and value all relevant costs, four separate costing questionnaires, one for each arm of the study, were designed and distributed to the SEYLE site leaders in each country after the interventions had taken place (Fig. 3 - 6 Appendix). The questionnaires were generated online and a link to the questionnaires was sent to all SEYLE centres. Respondents also had the opportunity to note any additional costs incurred by their centre in the implementation of each of the interventions. Costs were collected in the currency of each country. Costs are presented in 2010 Euro and were equivalised using GDP

purchasing power parities (Eurostat EU27=1).

Costs for the Control arm included cultural adaptation, translation and printing of the posters, travel, and implementation in the schools. The occupations of those responsible for implementing the intervention and the duration of the task were captured in the questionnaire. Occupations varied between countries and included psychology researchers, a social worker, teachers, psychologists, a psychiatrist and a guidance counsellor.

The QPR arm focuses on the role of gatekeepers and valued costs mostly related to training the gatekeepers who were then effectively responsible for implementing the intervention. The occupations of both the professionals who facilitated gatekeeper training and the teachers and other school personnel who received gatekeeper training, as well as training duration were recorded in the QPR questionnaire. Other costs collected included travel, printing of booklets and business cards containing contact information for local healthcare services and non-clinical healthy lifestyle groups, translation, and content modification (for cultural differences).

The YAM facilitators play a key role in the delivery of the intervention. The facilitators are trained in the methodology and then implement the intervention at each site to youths that they are not currently working with. The occupations of both those conducting the training and of the YAM facilitators were recorded in the questionnaire. The duration of the training and intervention implementation were also captured in order to value the associated costs. Additional costs included travel, translation and cultural adaptation of the awareness material, and printing of YAM programme booklets.

Lastly, the costs associated with the ProfScreen arm were primarily professional costs associated with training the clinical interviewers and conducting the clinical interviews which were aimed at evaluating mental health problems of those referred for professional clinical assessment based on scoring in the SEYLE questionnaires. The occupations of the trainers and clinical interviewers were collected along with the duration of both training and the clinical interviews. Other costs included cultural adaptation of the guidelines for the clinical interview and translation of the ProfScreen material.

Hourly wage rates for those involved in implementing each intervention were provided by respondents in France, Italy, Slovenia and Hungary only. Unit values for pay costs for the other six centres were either not reported or reported in a non-usable form. Irish values were sourced from published payscales of the Health Service Executive [14]. As there is no public

repository of such unit values (either from Eurostat or the OECD), unit values for the remaining five centres were calculated by adjusting Irish unit values by the ratio of Irish GDP per capita (2010 Eurostat) to the GDP per capita of the other participating countries. Total pay costs comprise direct hourly wage costs and indirect labour costs, including social security/national insurance, imputed pension costs and overheads. An average social security rate of 21.22% was calculated from individual SEYLE country rates [15] and applied to hourly wage rates. Additionally, in line with Irish guidelines for the economic evaluation of health technologies [16], an imputed pension cost of 4% and overhead cost of 25% were also applied to direct hourly wage costs to calculate total staff costs.

Intervention costs were collected at country level, so the cost of an intervention in SEYLE doesn't differ between schools in the same country. The mean cost of each intervention was calculated based on the total cost of each intervention and the total number of participants in that intervention across the 10 participating countries.

## **Outcomes**

A baseline assessment of SEYLE participants was initially completed by means of a number of questionnaires. The two clinical outcome measures chosen for our study, (i) incident suicide attempt and (ii) incident severe suicidal ideation with suicide plans, were collected at both 3 months and 12 months via post-intervention questionnaires [10]. In this CEA we measured both health outcomes at 12 months in two different ways.

First, we measured condition-specific outcomes, that is, incident suicide attempt and incident severe suicidal ideation. Pupils were identified as having made a suicide attempt if they answered 'Yes' to the question 'Have you ever tried to take your own life?' [10]. Pupils were identified as having severe suicidal ideation if they answered: 'Sometimes', 'Often', 'Very often', or 'Always' to the following question in the Paykel Hierarchical Suicide Ladder [17] – 'During the past 2 weeks, have you reached the point where you seriously considered taking your life, or perhaps made plans how you would go about doing it?' [10].

Second, we measured health outcomes in terms of health-related quality of life and calculated quality adjusted life years (QALYs). Although quality of life was not measured in SEYLE, participants completed the Strengths and Difficulties Questionnaire (SDQ) [18] which enabled mapping to utility weights. The SDQ is a 25-item behavioural screening tool for children that consists of 5 symptom subscales: emotional, conduct problems,

hyperactivity/inattention, peer relationship problems and prosocial behaviour. Furber et al. [19] generated an algorithm, using the five SDQ subscales, to map scores from the SDQ to utility values obtained using the preference-based Child Health Utility (CHU9D) instrument [20]. Evidence from a 2016 study suggest that this mapping algorithm can be used to accurately predict mean utility [21] in school-going adolescents. We applied the algorithm to the individual SDQ scores at 12-month follow-up and calculated a mean utility value for both those who had and those who did not have a suicide attempt and for those with and without severe suicidal ideation. Expected outcomes for each of the interventions, expressed as QALYs, were calculated using these utility values and trial values for incident suicide attempt and incident severe suicidal ideation.

### **Cost-effectiveness analysis**

The economic evaluation consisted of a trial-based analysis at 12 month follow up, conducted and reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [22]. We undertook this CEA from the payer's perspective, so although a large proportion of the costs were incurred within the education system, we assumed that costs were paid by the health and social care system. Costs and outcomes were not discounted as the analysis did not extend beyond a 12-month period. Incremental cost-effectiveness ratios have been calculated and reported using incident suicide attempt and severe suicidal ideation and point estimates of mean costs and QALYs. The analysis was undertaken in Stata 12 (StataCorp LLC, College Station, TX, USA), SPSS Statistics 22 (IBM Co., Armonk, NY, USA) and Microsoft Excel (Microsoft, Redmond, WA, USA).

### **Uncertainty analysis**

The uncertainty analysis was conducted in accordance with current guidelines for cluster RCTs, adopting techniques that recognise both correlation and clustering in the data by resampling clusters and then individuals within clusters [23-25]. Uncertainty around point estimates of mean costs, incident rates and QALYs was examined using 95% confidence intervals derived from a two-stage non-parametric bootstrapping technique, recognising clustering at country level for costs and school level for outcomes. Overall uncertainty with the cost utility model results, including the known difficulties assessing uncertainty with ICERs [26], was also explored by employing a two-stage non-parametric bootstrapping technique. We performed a technique

using net benefit analysis and the *tsbceprob* command in Stata 12, a method which explicitly accounts for the correlation and clustering of the data [24]. All four options, (three interventions and the Control), were included in the net benefit analysis, with no need to specify the comparator [26]. In each of the 1,000 bootstrap replicates, the total cost (C) and total effect (E) for the four options at different levels of willingness to pay ( $\lambda$ ) from €0 to €100,000 were estimated. Net monetary benefit (NMB) was calculated as:  $NMB = (E \times \lambda) - C$ . A positive NMB indicates cost-effectiveness, that is, the benefit outweighs the cost [27]. The option with the highest NMB is identified for each of the 1,000 iterations, at each level of willingness to pay, and the probability of being cost-effective is the proportion of iterations for which that option has the highest NMB. The probability of cost-effectiveness as a function of the different values of willingness to pay is plotted using cost-effectiveness acceptability curves (CEACs). The CEAC then enables a decision maker, who knows their maximum willingness to pay for health gain, to establish the strength of the evidence in support of cost-effectiveness [27].

We identified clinical interview time in the ProfScreen intervention as the only resource use parameter across all arms that displayed potential variation. This is owing to the fact that all other resources used were determined by the study protocol. We conducted a one-way sensitivity analysis varying clinical interview time +/-15%, +/-30% and +/-50%. We also conducted a threshold analysis to establish the level of reduction in clinical interview time at which the ICER for Profscreen is the lowest of all three interventions.

## **Results**

### **Costs**

The cost point estimates were calculated as the cost per participant of each intervention across the 10 participating countries. The point estimates for each intervention and a breakdown of same, by resource item, are provided in Table 2. When compared with the Control, all three interventions had a higher mean cost for both outcome measures. Detailed cost spreadsheets for each intervention in each country are provided in the Appendix (Tables 6 – 41).

**Table 2** Intervention costs by resource item and outcome measure (per participant, €)

Resource Item	Control		QPR		YAM		ProfScreen <sup>3</sup>	
	SA	SSI	SA	SSI	SA	SSI	SA	SSI
Training of gatekeepers and facilitators	0.00	0.00	28.90	28.92	1.52	1.51	4.52	4.52
Cultural adaptation & translation of intervention material	3.28	3.27	5.29	5.30	17.02	16.98	10.57	10.56
Clinical interviews	0.00	0.00	0.00	0.00	0.00	0.00	15.07	15.06
Intervention implementation in classrooms	0.71	0.71	0.00	0.00	8.32	8.30	0.00	0.00
Printing of intervention material	0.45	0.45	4.88	4.89	2.39	2.38	0.00	0.00
Travel	0.28	0.28	1.80	1.80	3.69	3.68	0.17	0.17
<b>Total Cost</b>	<b>€4.71</b>	<b>€4.70</b>	<b>€40.88</b>	<b>€40.90</b>	<b>€32.92</b>	<b>€32.86</b>	<b>€30.33</b>	<b>€30.32</b>

SA suicide attempt; SSI severe suicidal ideation

<sup>3</sup> Cost data for ProfScreen in Romania were missing. Values were imputed from data from Ireland, Estonia, Germany, Hungary, Italy, Slovenia & Spain

## Outcomes

A first-ever suicide attempt during the 12-month follow-up was least often reported in the YAM group (0.70%, n=14). It was more common in the ProfScreen (1.02%, n=20) and QPR groups (1.11%, n=22) and most common in the Control group (1.51%, n=34). Severe suicidal ideation in the two weeks prior to the 12-month follow-up was also lowest in the YAM group (0.75%, n=15) and more common in the ProfScreen (1.12%, n=22), Control (1.37%, n=31) and QPR groups (1.47%, n=29). Mean utility values for those who reported and did not report a suicide attempt were 0.7689 and 0.8392 respectively. Mean utility values for those who reported and did not report severe suicidal ideation were 0.7453 and 0.8395 respectively. The QALY point estimates for each of the interventions are displayed in Table 3. When compared with the Control, all three interventions were associated with an increase in mean QALYs for suicide attempt. For severe suicidal ideation, mean QALYs for YAM and ProfScreen were greater than the Control but those for QPR were lower.

## Cost-effectiveness analysis

Using the Control as comparator, ICER analysis indicates that YAM is the most cost-effective intervention. When we measured health outcomes in terms of the cost per 1 percentage point reduction in both incident suicide attempt and incident severe suicidal ideation, ICERs for YAM were lowest at €34.83 per participant for suicide attempt and €45.42 per participant for severe suicidal ideation.

The ICER analysis also indicates that the incremental cost per QALY gained for YAM <sup>Suicide Attempt</sup>

(€47,017) and YAM Severe Suicidal Ideation (€48,216) were both lower than those for QPR and Profscreen. YAM is therefore deemed the most cost-effective of the three interventions in preventing a suicide attempt and preventing severe suicidal ideation. The results from the incremental cost-effectiveness analysis are presented in Table 3.

**Table 3** Incremental cost-effectiveness analysis

<b>Suicide Attempt</b>	<b>Control</b>	<b>QPR</b>	<b>YAM</b>	<b>ProfScreen</b>
<b>Cost analysis</b>				
Total Cost (€)				
Mean	4.71	40.88	32.92	30.33
95% CIs (BCa)	3.63, 6.01	31.40, 50.12	24.42, 41.76	16.23, 55.31
Mean difference	-	36.17	28.21	25.62
<b>Effectiveness analysis</b>				
Incident				
Mean	1.51%	1.11%	0.70%	1.02%
95% CIs (BCa)	0.89%, 2.18%	0.55%, 1.66%	0.37%, 1.31%	0.57%, 1.53%
Mean difference	-	-0.40%	-0.81%	-0.49%
QALYs				
Mean	0.8381	0.8384	0.8387	0.8385
95% CIs (BCa)	0.8376, 0.8386	0.8380, 0.8387	0.8383, 0.8390	0.8381, 0.8388
Mean difference	-	0.0003	0.0006	0.0004
<b>Cost-effectiveness analysis</b>				
ICER (€/1% point reduction in incident)	-	€90.43	€34.83	€52.29
ICER (€/QALY gained)	-	€120,567	€47,017	€64,050
<b>Severe Suicidal Ideation</b>	<b>Control</b>	<b>QPR</b>	<b>YAM</b>	<b>ProfScreen</b>
<b>Cost analysis</b>				
Total Cost (€)				
Mean	4.70	40.90	32.86	30.32
95% CIs (BCa)	3.88, 5.82	30.95, 50.96	23.65, 41.55	19.89, 48.42
Mean difference	-	36.20	28.16	25.62
<b>Effectiveness analysis</b>				
Incident				
Mean	1.37%	1.47%	0.75%	1.12%
95% CIs (BCa)	0.75%, 1.98%	0.50%, 2.59%	0.41%, 1.17%	0.51%, 1.74%
Difference	-	0.10%	-0.62%	-0.25%
QALYs				
Mean	0.8382	0.8381	0.8388	0.8384
95% CIs (BCa)	0.8376, 0.8387	0.8373, 0.8387	0.8383, 0.8391	0.8379, 0.8389
Mean difference	-	-0.0001	0.0006	0.0002
<b>Cost-effectiveness analysis</b>				
ICER (€/1% point reduction in incident)	-	dominated	€45.42	€102.48
ICER (€/QALY gained)	-	dominated	€48,216	€108,790

## Uncertainty analysis

95% confidence intervals for the cost and outcome point estimates used to calculate ICERS, are reported in Table 3. As it is not possible to calculate 95% confidence intervals for an ICER (as it is a ratio), we characterised uncertainty in the cost utility model results by using net monetary benefit analysis to present CEACs. CEACs associated with suicide attempt and severe suicidal

ideation are displayed in Figures 1 and 2. At willingness to pay levels of €52,000 per gained QALY and greater, YAM had the greatest probability (44%) of being cost-effective in preventing a suicide attempt. For severe suicidal ideation, YAM had the greatest probability of being cost-effective (45%) at willingness to pay levels of €50,000 and greater.

The cost of clinical interviews comprised almost 50% of the cost of the ProfScreen intervention. Clinical interview time in the study ranged from 30 to 90 minutes with a mean value of 45 minutes. The impact of varying clinical interview time by +/-15%, +/-30% and +/-50% are provided in Table 4 of the appendix. Where interview time was reduced by 50%, the cost per QALY gained for ProfScreen was lower than that of YAM for suicide attempt. In all other instances, the YAM ICER remained lower than that of ProfScreen. The results of the threshold analysis are presented in Table 5 of the appendix.

Figure 1 Cost-Effectiveness Acceptability Curve (CEAC) for Suicide Attempt

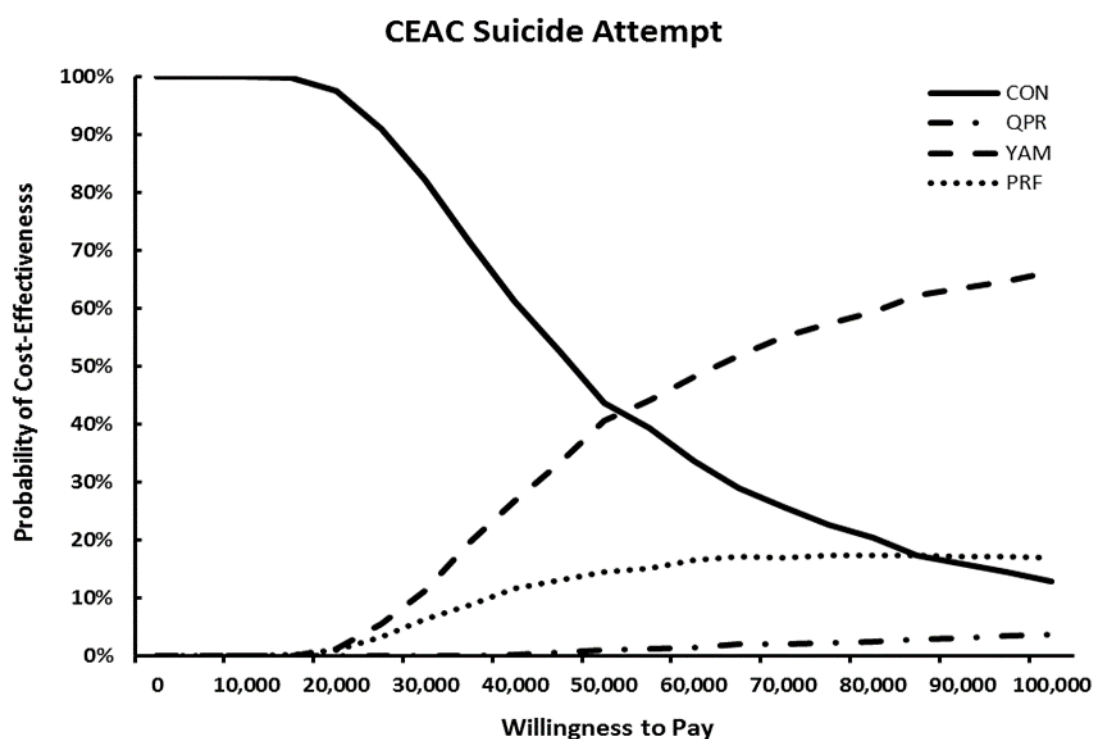
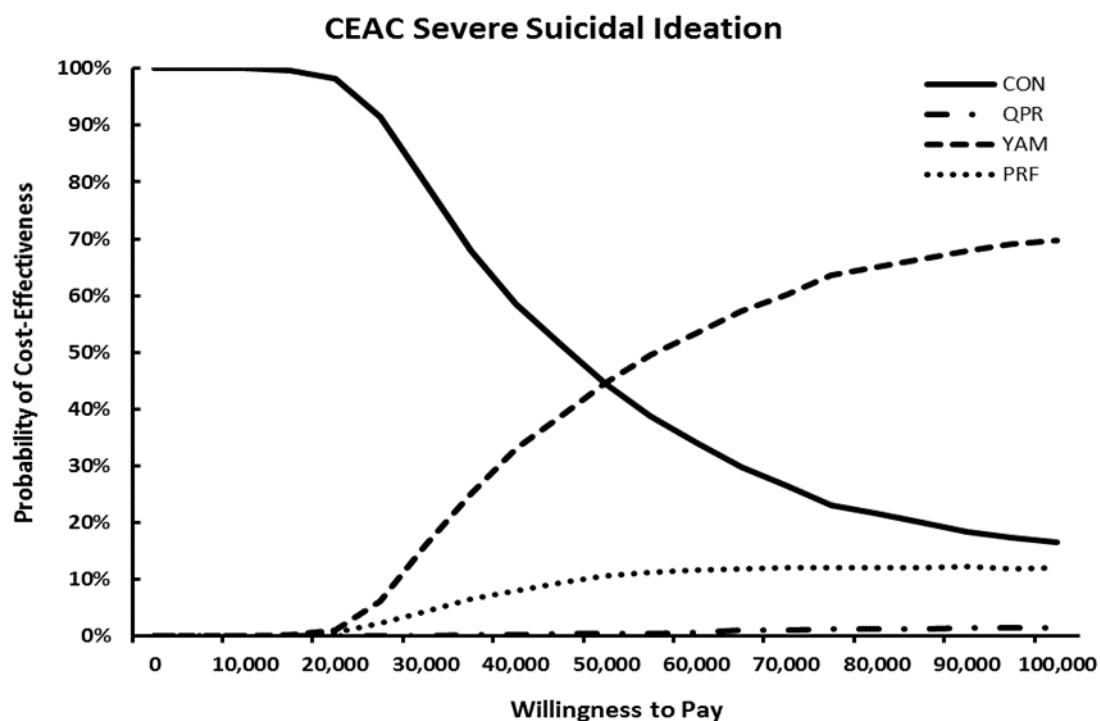


Figure 2 Cost-Effectiveness Acceptability Curve (CEAC) for Severe Suicidal Ideation



## Discussion

The results demonstrate that the YAM programme is the most cost-effective intervention versus the Control in preventing both a suicide attempt and severe suicidal ideation, at a cost per 1% point reduction of €34.83 and €45.42 respectively and willingness to pay levels of €47,017 and €48,216 per QALY gained respectively. The results add to the findings, reported elsewhere, which demonstrate that YAM is the most effective of the three interventions. The following discussion points emerge from the analysis.

With regard to outcomes, there is a possibility that the incremental effects of the YAM intervention are in fact underestimated, with implications for the results. For ethical reasons, the Control group could not be excluded completely from an intervention and were exposed to the YAM educational posters. In effect then, the health outcomes associated with the Control may not reflect the health outcomes associated with a strictly 'do nothing' comparator.

An analysis of the intervention costs demonstrates that a high proportion of the costs are non-recurring start-up costs that would not be incurred again if the interventions were to be rolled out. The highest cost items for both QPR and YAM are non-recurring; 'training' for QPR constituted >70% of the average cost per participant and 'cultural adaptation and

translation' of content for YAM constituted >50% of the average cost per participant. Going forward, these intervention costs may potentially be lower than those used in the CEA, thus improving the cost-effectiveness of the interventions.

Notwithstanding the potential for lower intervention costs, costs were restricted to direct intervention costs only and did not incorporate downstream costs such as the cost of referrals. When measuring suicide attempts, our analysis at 12-month follow-up indicates referral rates over the duration of the RCT of 4.5% in the Control, 4.9% in YAM, 5.1% in ProfScreen and 6.3% in QPR. Referral rates, when measuring severe suicidal ideation, were 4.6% in the Control, 4.9% in YAM and ProfScreen and 6.3% in QPR. Given this variation in referral rates amongst intervention groups, incorporating the cost of referrals could potentially impact the ICER results. However, referral rates (and therefore referral costs) for YAM are equal to or lower than both ProfScreen and QPR for both outcome measures.

There are a number of limitations to this study. Firstly, health related utility was not measured as part of the SEYLE study. Furthermore, to the authors' knowledge there has been no publication of utility weights for suicide attempt and/or severe suicidal ideation in the adolescent population. To enable QALY analysis, the authors reviewed all questionnaires administered during the RCT and identified the SDQ as the most appropriate measure available to establish utility values. This gives rise to uncertainty which the authors have sought to address by quantifying uncertainty around the point estimates used to calculate the QALY ICERs. Additionally, the presentation of CEACs helps to characterise the uncertainty with the ICERs and seeks to further inform the overall decision-making process. Secondly, the CEA was conducted by pooling cost and outcome data from 10 European countries. At a high level, cultural and social differences between countries were recognised at the outset of the SEYLE study and the intervention material was adapted accordingly. However, sample size limitation in costing prevented us from accounting for country level variation. Consequently, data were pooled which has potential implications for the use of one cost-effectiveness ratio in informing an individual country's resource allocation decisions. The CEA is also set against a challenging backdrop with regard to previous relevant research. There is an extremely limited body of research in the area of cost-effectiveness of suicide prevention programmes and a complete absence relating specifically to adolescents in a school-based setting. There is therefore limited scope to compare the results with previous research.

Suicide prevention is regarded by the WHO as an important global priority [1] and it has been

found that the intensity of suicidal ideation predicts suicide attempts and that suicide attempt is the strongest predictor of completed suicide [28]. As an increasing number of health interventions compete for scarce resources, demonstrated cost-effectiveness of interventions is also required to inform resource allocation decisions. With a dearth of evidence on the cost-effectiveness of suicide prevention interventions, the presentation of this CEA is an important and valuable contribution to the development of reliable and valid results for the cost-effectiveness of school-based suicide prevention interventions.

Future research should consider a broadening of the study to capture the effects of the interventions over a longer time horizon. This would ensure the capture of downstream costs, longer-term costs and outcomes associated with the duration of the intervention 'dose' and possibly combinations of interventions. Given the age profile of the SEYLE cohort, and in light of the long term effectiveness of a suicide prevention intervention demonstrated in an RCT in the United States [6], an assessment of the longer-term cost-effectiveness of the SEYLE interventions is recommended.

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### **Conflict of Interest**

On behalf of all authors, the corresponding author states that there is no conflict of interest.

### **Ethics Approval**

The SEYLE study was approved ethically by the European Commission as a precondition of funding approval for the project. Ethical permission for the project, including permission to follow up individual pupils was obtained in each participating country by the Research Ethics Committees. All requirements of obtaining Informed Consent from pupils and parents were followed carefully

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