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An economic evaluation of the randomised controlled trial of topical corticosteroid and home-based narrowband UVB for active and limited vitiligo (The HI-Light Trial)

Short title: Economic evaluation of the HI-Light vitiligo trial

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What's already known about this topic?

- Vitiligo is a common skin condition with significant psychological impact.
- Topical corticosteroids (TCS) are standard care for vitiligo. Narrowband UVB (NB-UVB) is only available in secondary care as full-body treatment.
- Economic evidence for hand-held NB-UVB in combination with topical corticosteroid (TCs) is absent.

What does this study add?

- Combination treatment, compared to TCS alone, has the lowest incremental cost per successful treatment. Whether this is considered cost-effective depends on decision makers' judgement on how much they are willing to pay to achieve a successful treatment.
- Generic utility instruments, such as the EQ-5D-5L, may not be appropriate for vitiligo studies due to high ceiling effects. Measurement of quality of life for this condition warrants further research.
- This study provides results that can be compared with new emerging vitiligo treatments.

Summary

Background: Economic evidence for vitiligo treatments is absent.

Objective: To determine the cost-effectiveness of (a) hand-held narrowband-UVB (NB-UVB) and (b) combination of topical corticosteroid (TCS) and NB-UVB compared to TCS for localised vitiligo.

Methods: Cost-effectiveness analysis alongside a pragmatic, 3-arm, placebo-controlled RCT with 9 months' treatment. 517 Adults and children (aged ≥5 years) with active vitiligo affecting <10% of skin recruited from secondary care and community were randomised 1:1:1 to receive: TCS; NB-UVB; or both. Cost per successful treatment (measured on the Vitiligo Noticeability Scale) was estimated. Secondary cost-utility analyses measured QALYs using the EQ-5D-5L for those aged 11+ and CHU-9D for those aged 5 to <18.

Results: Mean (SD) cost per participant was £774.4 (83.71) for NB-UVB, £813.38 (111.39) for combination treatment and £599.98 (96.18) for TCS. In analyses adjusted for age and target patch location, incremental difference in cost for combination treatment compared to TCS was £211.46 (95% CI 188.10 to 234.81), corresponding to a risk difference of 10.94% (Number-Needed-To-Treat (NNT= 9). Incremental cost was £1,932.35 per successful treatment. The incremental difference in cost for NB-UVB compared to TCS was £173.44 (95% CI 150.55 to 196.32) with a risk difference of 5.20% (NNT=19). Incremental cost was £3,335.74 per successful treatment.

Conclusion: Combination treatment, compared to TCS alone, has a lower incremental cost per additional successful treatment than NB-UVB only. Combination treatment would be considered cost effective if decision makers are willing to pay £1,932 per additional treatment success.

Trial registration: ISRCTN17160087. 8th Jan 2015

Introduction

A 2018 systematic review showed that the economic evidence for vitiligo treatment is virtually non-existent[1]. One of two studies identified in this review estimated the annual direct cost of treating vitiligo in the USA to be $15,000,000 for the price year 2004[2]. The other study demonstrated that 32.5% of people with vitiligo would be willing to make a one-off payment of €5000 for a cure (2006 price year)[3], allowing an estimate of the maximum potential for benefit should a "cure" be found. Although these papers indicate the cost to an affected person and health care system, they do not provide evidence to inform resource allocation decisions. No papers were identified that undertook full economic evaluations (those which compare costs and benefits of two or more interventions[4]) of vitiligo treatments alongside clinical trials or as economic modelling. This paper reports the first full economic evaluation of treatment for localised, non-segmental vitiligo, including current standard treatment Topical Corticosteroids (TCS) and new treatment (home-based NB-UVB light therapy), alone and in combination with TCS, with the aim of estimating the cost effectiveness of these treatments for the UK NHS.

Methods

This health economic evaluation estimated the within-trial cost-effectiveness of

i) active hand-held NB-UVB light compared to TCS (standard care) and
ii) combination of active hand-held NB-UVB plus TCS compared to TCS (standard care)

in terms of cost per additional treatment success (henceforth referred to as treatment success) at the end of the treatment period (9 months) for the treatment of limited, non-segmental vitiligo, using individual level data collected within the trial. A treatment period of 9 months was chosen to reflect clinical practice where clinical experience and clinical guidelines suggest that treatment should be initiated for a minimum of 3-4 months, but that treatment would normally be required for a longer period in order to achieve a clinically meaningful treatment response.

A secondary objective was to undertake cost utility analyses for those aged 11 and over using the EQ-5D-5L and separately for participants aged under 18 years using the CHU-9D. Typically, a cost-utility analysis would form the primary analysis as it enables decision makers to compare the cost effectiveness of a range of interventions for different conditions on a common scale. As utility is measured differently in adults and children a common cost-utility analysis was not possible, so a clinical outcome was used. Also cost-utility instruments are considered less effective at capturing the psychological impact on quality of life, which is considered to be more important than physical impacts in vitiligo. *A-priori* we were also sceptical that available generic utility instruments would capture the health-related quality of life aspects that people living with vitiligo experience.

The evaluation was undertaken in line with published guidelines for the economic evaluation of health care interventions [4-8]. A health economics analysis plan was written and approved before the trial database was locked. A full trial report will be available through the NIHR Journal series[9] and the clinical results paper is available in this journal[10].

The trial was conducted in the UK National Health Service (the NHS) - a publicly-funded healthcare that is largely free of charge at the point of use. Therefore, the analysis was primarily from an NHS perspective, in keeping with the NICE reference case[8]. In a sensitivity analysis, out of pocket costs incurred by participants (or parents/guardians) are presented reflecting a personal perspective.

Resources use and costs

The primary analysis captured the intervention costs (including any side-effect costs) to the NHS and the participant's wider use of the NHS (including primary care visits; secondary care outpatient, inpatient and A&E visits; and prescriptions) as a result of vitiligo. Participants' personal out of pocket expenses (for example, camouflage/ makeup, sun cream and sun care) incurred from vitiligo were also captured in a separate sensitivity analysis taking a broader perspective. Participant time burden for home treatment was not costed, but is reported elsewhere [9, 10].

Resource use for the intervention phase was collected at 3, 6, and 9 months using information recorded by participants in daily diaries and collated by the researcher at follow-up visits. Intervention and side effect related resource use was recorded in Clinical Reports Forms. Further questionnaires collected resource use data at 12, 15, 18 and 21 months for the follow-up phase.

Intervention cost was estimated at the individual level. Participants randomised to NB-UVB alone were also given a placebo ointment whilst those in the TCS alone group received a dummy NB-UVB device. The dummy devices and placebo ointment were not costed.

NB-UVB Device:

The hand-held device cost was estimated using manufacturer's purchase price divided by an annuity factor (interest rate 3.5%, 5 years) to give an equivalent annual cost (EAC). EAC was divided by 12 months and multiplied by 9 to reflect the 9-month timeframe. The purchase price of personal protective equipment (goggles and glasses) were included at full cost since these are unlikely to be as durable as the devices. Costs of quality assurance process for the devices were included. Device repair and replacement costs were not included in the analysis faulty devices were replaced in the study: though in practice some might be repaired.

Time spent by investigators training participants on using the device was recorded and costed.

Topical Corticosteroid

Participants in the TCS intervention group were supplied with two 90g tubes of mometasone furoate 0.1% ointment (Elocon® 0.1% Ointment, Merck Sharp & Dohme, Hertford). TCS costs were was sourced from the Prescription Cost Analysis for 2017[11] and had the National Average Discount Percentage of 7.37% (https://www.nhsbsa.nhs.uk/prescription-data/understanding-our-data/financial-forecasting) deducted. The professional pharmacist fee of £1.29 was added, assuming that a single tube would be prescribed at any one time. Additional ointment requested by participants was recorded and costed.

Trial participants in all treatment groups were offered appointments with a dermatologist at 0, 3, 6, and 9 months, we assumed in the analysis that this would happen in routine care . These were costed even though they cancel each other out between treatment groups.

Side effects requiring medical attention from either treatment were recorded as one type of unscheduled contact.

Unit costs were identified from published sources, see Table 1, and valued in UK£Sterling 2017. Patient-reported estimates of out of pocket costs resulting from vitiligo were captured.

Clinical outcome: Treatment success

The primary clinical outcome measure in the HI-LIGHT trial was participant-reported treatment success, measured at 9 months, using the Vitiligo Noticeability Scale (VNS)[14]. Treatment success, a binary outcome, was defined by whether the participant responded that their target vitiligo patch was “a lot less noticeable” or “no longer noticeable” in response to the question: "Compared to the start of the study, how noticeable is the vitiligo now?". Because no previous studies have compared the treatments or outcome used in this study, we used a single study-based estimate of effectiveness in the cost-effectiveness analysis.

Quality of Life

Quality Adjusted Life Years (QALYs) were estimated in secondary analyses using utility scores obtained from the EQ-5D-5L instrument for participants aged 11+ years[18], and the CHU-9D in the analysis focussed on children <18 years.[15-17] For participants aged 5-6 years old, the CHU-9D was completed by parental proxy. For all other ages these instruments were self-completed. We chose to use just one version of the EQ-5D-5L in the study for consistency. We chose the CHU-9D for the youngest participants because the EQ-5D-Y does not currently have a UK valuation set. .

Utility measurements were collected in clinic at baseline, 9, and 21 months to reflect the likely timeframe for observing a clinically meaningful treatment response and in order to observe if any response found was sustained longer term.

In the cost utility analysis, quality of life instrument responses were converted to utility scores using the EQ-5D-5L Crosswalk[19] UK preference weights in line with current recommendations[20, 21]. The CHU-9D was valued using the UK value set[15]. Following this, the utility values were used to calculate quality adjusted life years (QALYs) generated over the trial treatment period of 9 months, using both linear interpolation and area under the curve analysis with baseline adjustment[24].

Economic analysis

The economic primary analysis was performed on the full analysis set. In line with the primary statistical analysis[10], multiple imputation was used to account for missing primary outcome data at 9 months. Cost analyses employed multiple imputation with chained equations using MI impute in STATA generating 60 (m=60) datasets using predictive mean matching and separately by treatment allocation as reported by Faria *et al*[23]. Given the 9-month time horizon, costs and benefits were not discounted.

Mean (SD) resource use and cost per participant was estimated for each randomised group. Mean difference (95% CI) in resource use and cost between arms (NB-UVB compared to TCS; and combination treatment compared with TCS) is presented.

Costs and QALYs were adjusted for age and location of target patch as well as baseline utility using seemingly unrelated regression (SUR)[24].

Non-parametric bootstrapping was used to determine sampling uncertainty surrounding the mean Incremental Cost Effectiveness Ratios (ICERs) by generating 10,000 estimates of incremental costs and benefits. These estimates were used to produce Cost-Effectiveness Acceptability Curves to show the probability each intervention arm is cost effective at different values of willingness to pay.

Other than pre-planned secondary analysis based on the different utility instruments used (EQ-5D-5L and CHU-9D), no subgroup analyses were undertaken. The secondary outcome for the economic evaluation is quality-adjusted life years (QALYs) of participants over 9 months. Mean (SD) utility and mean (SD) QALYs per participant per randomised group is estimated, as is mean difference (95% CI) in QALYs between arms (NB-UVB to TCS; and combination treatment compared with TCS) adjusted for age and location of target patch. In secondary analyses, the reported economic analysis used a cost-effectiveness threshold of £20,000 per QALY[8].

All analyses were conducted in Stata MP4 version 15.

Sensitivity analyses were undertaken to explore key uncertainties including (i) comparing multiple imputation analysis to a complete case analysis, (ii) varying NB-UVB device costs (zero and double the price in the primary analysis), (iii) wider cost perspective including vitiligo out-of-pocket costs, (iv) limiting analysis to participants with good adherence (defined as greater than 75% adherence), and (v) extending the time horizon to 21 months to include the 12 months follow-up period.

It was expected that the majority of costs and benefits would be captured in the treatment period such that *a priori* it was not considered necessary to develop a decision-analytic model for a longer timeframe. This proved appropriate, as quality of life scores were similar between treatment arms at 21 months (see supplementary Table 6 in the clinical paper[10]).

Results

Baseline characteristics of the participants included in the cost effectiveness analysis are described in Table 1 of Thomas *et al* (submitted)[10]. With imputation 517 participants (398 adults, 119 children; 173 TCS, 169 NB-UVB, and 175 Combined treatment) were included.

Intervention costs

Mean number of devices, googles, glasses, drug costs, dermatology appointments, training and unscheduled visit/telephone by group (Table 2) and mean costs (Table 3)

are reported. The mean cost of the intervention per participant for TCS (standard care) was £583.42 (SD 29.59), £753.06 (SD 59.16) for NB-UVB, and £792.06 (SD 94.61) for combination treatment. Details of the time and cost of quality assurance processes are shown in Supplementary Table 1.

Training time was a mean of 73.08 minutes for NB-UVB and 69.17 minutes for combination treatment, noting that all participants received both a device and ointment (dummy devices and placebo ointment were not costed).

Wider resource use and costs

Wider health care resource use (primary care, secondary care and medicines) for vitiligo beyond those required for the intervention were not significantly different between groups (Table 2). Vitiligo patients reported low NHS healthcare usage. Table 3 displays mean costs per participant by treatment group using available case data. The overall mean cost per participant for NB-UVB was £774.64 (SD 83.71) compared to £599.98 (SD 96.18) for TCS - an unadjusted mean difference in cost of £174.66 (95% CI 152.75 to 196.66). Combination treatment had overall mean costs per participant of £813.38 (SD 111.39); compared to TCS this gave an unadjusted mean difference of £213.40 (95% CI 188.33 to 238.46) per participant. These figures suggest that the costs of the interventions were not offset by reductions in wider healthcare resource use related to vitiligo.

Primary Economic Analysis

Cost effectiveness analysis of NB-UVB compared to TCS (standard care)

The adjusted incremental difference in cost was £173.44 (95% CI 150.55 to 196.32). The adjusted risk difference for NB-UVB compared to TCS was 5.20%, this equates to a number needed to treat (NNT) of 19; in other words, 19 participants would need to be treated for one of them to gain treatment success. The adjusted incremental cost was £3,335.74 per additional successful treatment (estimated by dividing the adjusted incremental difference in cost, £173.44, by the adjusted risk difference, 0.052).

Figure 1a shows the probability that NB-UVB is cost-effective at different possible levels of willingness to pay for an additional treatment success; probability increases as willingness to pay increases. Figure 1a shows considerable uncertainty surrounding the decision as to whether NB-UVB, compared to TCS, represents value for money as there is always at least 40% probability of making the wrong decision if choosing to fund NV-UVB alone below a threshold value of willingness to pay of £10,000 per additional treatment success.

Cost effectiveness analysis of combination treatment compared to TCS (standard care)

The adjusted incremental difference in cost was £211.46 (95% CI 188.10 to 234.81). The adjusted risk difference for combination treatment compared to TCS was 10.94%. This equates to a NNT of 9. The adjusted incremental cost was £1,932.35 per additional successful treatment.

Figure 1b shows the probability that combination treatment is cost-effective at different possible levels of willingness to pay for an additional treatment success and shows that combination treatment is likely to be cost effective if decision makers are willing to pay more than £3,000 per additional treatment success as the probability of making the wrong decision is less than 50%.

Sensitivity analyses exploring key uncertainties in the economic evaluation are summarised in Supplementary Table 2. Limiting analysis to only adherent participants made the most difference to the incremental cost effectiveness ratio (£1,836.31 for combination treatment compared to TCS and £3,152.30 for NB-UVB compared to TCS), with those adherent to treatment being more likely to be cost effective to treat.

Secondary Economic Analysis

248 (55%) trial participants reported having no problems on any of the five domains of the EQ-5D-5L at baseline, suggesting that over half of the sample started the study in

perfect health as defined by EQ-5D-5L. To put this value into perspective, in a general population sample from England the number of participants reporting no limitations on any dimension of the EQ-5D-5L was 43.87%[25]. Thus, the ceiling effect in this study can be considered large and of an order such as to limit the discriminatory power of the instrument for this patient population. Similar levels of ceiling effect were observed at subsequent follow-up. Similarly, for the CHU-9D 30% of participants aged under 18 years had no problems according to any of the nine dimensions on the CHU-9D at baseline. Anxiety and depression on the EQ-5D-5L and Worry, tiredness and sleeping on the CHU-9D were the domains for which problems were reported most commonly. No floor effect was observed at any time point on either instrument. As these high ceiling ratios suggests these instruments are unlikely to be able to detect change, we report the mean utility estimates in supplementary Tables 3 and 4 and the cost utility analyses in supplementary Table 5. With this limitation in mind, both NB-UVB and combination treatment compared to TCS (standard care) had cost utility ratios within accepted thresholds (<£20,000 per QALY) for the sample aged 11 + years (NB-UVB was superior compared to TCS than combination treatment in contrast to the cost-effectiveness analysis). Neither treatment was cost-effective in the analyses of those participants aged<18 years but this may reflect the small sample size (n = 119).

Discussion

We present the first full economic evaluation of treatments for vitiligo using standard care TCS as the comparator. The additional cost of the combination treatment was not offset by NHS cost savings but did result in significant treatment success over the 9 month treatment period which could be gained if decision makers were willing to pay more than the adjusted incremental cost of £1,932.35 per additional successful treatment. NB-UVB was less costly than combination treatment but also less effective, such that the incremental cost per successful treatment was higher than for combination treatment, suggesting that the NHS would get better value for money from combination treatment than light therapy alone. There is currently no evidence to indicate how much a decision maker would be willing to pay for an additional treatment success as defined in this study.

Should the decision makers' willingness to pay per additional treatment success be low then uncertainty surrounding the decision to fund combination treatment is high.

Treatment options are limited for vitiligo and existing treatments are used little in the NHS which may be due to treatments not being offered rather than absence of need.[26]

Cost effectiveness analysis was undertaken as the primary analysis because it enabled us to analyse all participants together, irrespective of age. We had a prior belief that generic utility instruments may not fully capture the health-related quality of life impairment of people living with vitiligo. This was supported by a high ceiling effect on the EQ-5D-5L and CHU-9D at baseline such that there was no capacity to measure any gain using these instruments for many participants. The cost utility analysis gave different results to the clinical and cost effectiveness results, in that NB-UVB appeared more cost effective than combination treatment, compared to TCS for those aged 11 and over. There was also a difference in results between the cost utility analyses undertaken by age, the new interventions were estimated as cost-effective in those aged 11 and over but not in those aged <18 years. This could reflect the different utility instrument used but more likely reflects the small sample size of the <18 years analysis and the fact that there was a lot of uncertainty around the QALYs gained as the gain between groups was very close to zero in all comparisons. Therefore, more weight should be attached to the clinical effectiveness results and further work to explore the validity of the EQ-5D-5L and CHU-9D in this patient group is warranted, given the high ceiling effect observed in this study. It may be that a disease specific utility instrument needs to be developed for vitiligo.

Sensitivity analyses suggested that a wider perspective, cost of the NB-UVB light device, and method of dealing with missing data did not change the conclusions reached. Incremental cost per treatment success was lowest for those with greatest adherence.

New treatments such as Janus Kinase (JAK) inhibitors are being developed for vitiligo and are likely to be costly. The relatively low cost of the interventions assessed in this trial may make them affordable when resources are limited. The trial has yielded useful cost-effectiveness data which can be used for future comparisons with novel treatments.

A strength of the study was that the HI-Light trial was a large, pragmatic trial of home interventions for people with active, limited vitiligo that controlled for common causes of bias. Retention throughout the trial was challenging, and the treatments placed considerable time burden on participants. Because less than 50% responded to secondary outcomes at 21 months, a longer term economic evaluation to 21 months was not undertaken, which is a limitation of the present study. However, given treatment effects beyond the 9-month period were not sustained one can assume that the cost-effectiveness of the interventions would likely decline over time if treatments were not continued.

Conclusion

Combination treatment, compared to TCS alone, has a lower incremental cost per successful treatment than NB-UVB but whether this is considered cost-effective will depend on how much healthcare decision makers are willing to pay to achieve a successful treatment. The fact that vitiligo has few treatment options available, and the likely high cost of newer treatments being developed, may influence these decisions.

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Data sharing

Anonymised patient level data are available from Dr Jonathan Batchelor (jonathan.batchelor@nottingham.ac.uk) upon reasonable request.

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Table 1 Unit Costs Table (UK£ sterling, 2017)

Resource Item	Unit Cost (£2017)	Source (notes)
Intervention resources		
Annuity factor	4.515 based on r = 3.5% and n = 5	Drummond et al.[4]
Purchase price	149.00	Dermfix Ltd website
Annuitised 9-month purchase price[a]	24.75	(Purchase price divided by annuity factor to give equivalent annual cost (EAC). EAC divided by 12 months and multiplied by 9.)
Annuitised 9-month quality assurance (£17.83 multiplied by annuity factor)	2.96	Quality assurance: Medical Physics, Nottingham University Hospitals
Glasses (per set)	15.00	Dermfix Ltd website
Goggles (per set)	7.00	Dermfix Ltd website
TCS (per 90g tube of mometasone furoate 0.1%)	12.13	Health and Social Care Information Centre Prescription Cost Analysis[11]
Investigator face to face and telephone support (per minute, assumed band 7 £54 per hour)	0.90	PSSRU 2017[12]
Dermatologist Face to face first appointment	159.00	NHS Schedule of Reference Costs[13]

consultant-led		
Dermatologist Face to face follow-up appointment consultant-led	129.00	NHS Schedule of Reference Costs[13]
Dermatologist telephone appointment consultant-led	100.00	NHS Schedule of Reference Costs[13]
Training time (per minute, assumed band 7 £54 per hour)	0.90	PSSRU 2017[12]
Primary Care resources (per visit)		
GP	37.00	PSSRU 2017[12]
Practice Nurse	10.85	PSSRU 2017[12]
Pharmacist (assumed to be a community pharmacist)	11.11	PSSRU 2017[12]
Hospital Doctor	53.33	PSSRU 2017[12]
Hospital Nurse	15.00	PSSRU 2017[12]
Therapist	27.00	PSSRU 2017[12]
Other (reported by participants)	Range from 15.00 to 86.00	PSSRU 2017[12] and NHS Schedule of Reference Costs[13]
Other Resources		
Medication (Various, NIC per item less NADP plus professional fee)	Range from 3.37 to 36.92	PCA 2017[11]
Participant and family out of pocket costs	Various	Estimates reported by participants

Acronyms: NADP = National Average Discount Percentage; NIC = Net Ingredient Costs; TCS = Topical Corticosteroids.

Table 2 Mean (Standard Deviation) resource use according to intervention arm over the 9-month treatment phase for all participants (based on available data)

	TCS (Standard Care) (n=173)		NB-UVB (n=169)		Mean difference (NB-UVB minus TCS)	Combination treatment (n=175)		Mean difference (Combination minus TCS)
	Mean	**Std dev (n)**	**Mean**	**Std dev (n)**	**(95% CI)**	**Mean**	**Std dev (n)**	**(95% CI)**
Intervention								
NB-UVB intervention*	0.00	0.00 (173)	1.08	0.30 (169)	1.083 (1.04 to 1.13)	1.07	0.30 (175)	1.07 (1.03 to 1.12)
Glasses^	0.00	0.00 (173)	1.41	0.58 (169)	1.41 (1.33 to 1.50)	1.50	0.56 (175)	1.50 (1.41 to 1.58)
Goggles^	0.00	0.00 (173)	0.46	0.60 (169)	0.46 (0.37 to 0.54)	0.40	0.56 (175)	0.40 (0.32 to 0.48)
TCS	2.15	0.55 (173)	0.00	0.00 (169)	-2.15 (-2.23 to -2.07)	2.12	0.49 (175)	-0.03 (-0.14 to 0.08)
Training time (mins)	0.00	0.00 (173)	73.08	40.47 (169)	73.08 (67.03 to 79.13)	69.17	34.51 (175)	69.17 (64.01 to 74.33)
Dermatologist time (clinic +	4.00	0.00 (173)	4.00	0.00 (169)	0.00 (0.00 to 0.00)	4.00	0.00 (175)	4.00 (4.00 to 4.00)

telephone)								
Nurse time (clinic + telephone)	0.00	0.00 (173)	2.00	0.00 (169)	2.00 (2.00 to 2.00)	2.00	0.00 (175)	2.00 (2.00 to 2.00)
Unscheduled clinic with Nurse	0.01	0.11 (173)	0.03	0.20 (169)	0.02 (-0.02 to 0.05)	0.13	0.51 (175)	0.12 (0.04 to 0.20)
Unscheduled telephone with Nurse	0.39	0.87 (173)	0.46	0.95 (169)	0.07 (-0.13 to 0.26)	0.66	1.29 (175)	0.28 (0.04 to 0.51)
Unscheduled clinic with dermatologist	0.02	0.13 (173)	0.04	0.20 (169)	0.02 (-0.01 to 0.06)	0.10	0.43 (175)	0.09 (0.02 to 0.15)
Unscheduled telephone with dermatologist	0.02	0.17 (173)	0.03	0.20 (169)	0.01 (-0.03 to 0.05)	0.05	0.27 (175)	0.03 (-0.01 to 0.08)
Primary Care and Community								
Number	0.12	0.44 (136)	0.17	0.64 (132)	0.06 (-0.07 to 0.19)	0.12	0.55 (142)	.002 (-0.12 to 0.12)
Secondary Care								

Number	0.48	4.47 (136)	0.20	0.61 (132)	-0.28 (-1.05 to 0.49)	0.20	0.63 (142)	-0.28 (-1.03 to 0.46)
Other								
Medication	0.12	0.50 (138)	0.08	0.35 (133)	-0.04 (-0.14 to 0.06)	0.09	0.34 (141)	-0.03 (-0.13 to 0.07)
Out of pocket purchases	0.40	1.44 (141)	0.28	0.88 (137)	-0.12 (-0.40 to 0.16)	0.31	1.27 (144)	-0.09 (-0.41 to 0.23)

* Includes number of NB-UVB devices only.^ participants could choose to have more than one set, for instance if they needed a parent or partner to help them deliver the treatment.

Table 3 Mean (Standard Deviation) costs and outcomes according to intervention arm over 9-month treatment phase (UK£Sterling, 2017) for all participants (based on available data)

	TCS (Standard Care) (n=173)		NB-UVB (n=169)		Mean difference (NB-UVB minus TCS)	Combination treatment (n=175)		Mean difference (Combination minus TCS)
	Mean	Std dev (n)	Mean	Std dev (n)	(95% CI)	Mean	Std dev (n)	(95% CI)
Intervention								
NB-UVB Device	0.00	0.00 (173)	24.75	0.00 (169)	24.75 (24.75 to 24.75)	24.75	0.00 (175)	24.75 (24.75 to 24.75)
Quality assurance for device	0.00	0.00 (173)	2.96	0.00 (169)	2.96 (2.96 to 2.96)	2.96	0.00 (175)	2.96 (2.96 to 2.96)
Glasses	0.00	0.00 (173)	21.21	8.74 (169)	21.21 (19.91 to 22.52)	22.46	8.34 (175)	22.46 (21.21 to 23.70)
Goggles	0.00	0.00 (173)	3.19	4.18 (169)	3.19 (2.56 to 3.81)	2.80	3.90 (175)	2.80 (2.22 to 3.38)
TCS	26.08	6.67 (173)	0.00	0.00 (169)	-26.08 (-27.09 to -25.07)	25.71	5.99 (175)	-0.37 (-1.70 to 0.97)
Training time	0.00	0.00 (173)	65.77	36.42 (169)	65.77 (60.32 to 71.22)	62.25	31.06 (175)	62.25 (57.61 to 66.90)

Dermatologist (clinic + telephone)	546.00	0.00 (173)	546.00	0.00 (169)	0.00 (0.00 to 0.00)	546.00	0.00 (175)	546 (546.00 to 546.00)
Nurse (clinic + telephone)	0.00	0.00 (173)	72.00	0.00 (169)	72.00 (72.00 to 72.00)	72.00	0.00 (175)	72.00 (72.00 to 72.00)
Unscheduled clinic with Nurse	0.21	1.93 (173)	0.53	3.64 (169)	0.32 (-0.29 to 0.94)	2.41	9.53 (175)	2.20 (0.75 to 3.66)
Unscheduled telephone with Nurse	7.16	16.30 (173)	8.34	17.53 (169)	1.19 (-2.41 to4.79)	12.30	23.92 (175)	5.14 (0.82 to 9.46)
Unscheduled clinic with dermatologist	2.24	16.89 (173)	5.34	25.78 (169)	3.11 (-1.52 to 7.73)	13.27	55.45 (175)	11.03 (2.37 to 19.70)
Unscheduled telephone with dermatologist	1.73	16.96 (173)	2.96	20.20 (169)	1.22 (-2.74 to 5.19)	5.14	26.84 (175)	3.41 (-1.33 to 8.15)
Total cost of intervention	**583.42**	**29.59 (173)**	**753.06**	**59.16 (169)**	**169.64 (159.73 to 179.56)**	**792.06**	**94.61 (175)**	**208.64 (193.82 to 223.46)**

Primary Care and Community								
Cost	3.90	15.21 (136)	5.90	22.20 (132)	2.00 (-2.56 to 6.57)	2.84	14.09 (142)	-1.06 (-4.52 to 2.40)
Secondary Care								
Cost	11.05	77.14 (136)	9.30	30.05 (132)	-1.74 (-15.90 to 12.42)	8.52	26.87 (142)	-2.53 (-16.05 to 11.00)
Other								
Medication	2.48	10.52 (138)	1.49	7.06 (133)	-0.99 (-3.14 to 1.16)	1.20	6.09 (140)	-1.28 (-3.30 to 0.75)
Total mean cost per participant	**599.98**	**96.18 (132)**	**774.64**	**83.71 (131)**	**174.66 (152.75 to 196.56)**	**813.38**	**111.39 (136)**	**213.40 (188.33 to 238.46)**
Out of pocket costs	14.44	96.78 (141)	4.94	20.09 (137)	-9.49 (-26.11 to 7.12)	6.62	28.45 (144)	-7.81 (-24.37 to 8.75)
Primary outcome								
VNS*	20/119 (16.81%)		27/123 (21.95%)		7 (5.14%)^	34/128 (26.56%)		14 (9.75%)

*The number (the percentage) of participants who reported a treatment success (VNS) (a lot less noticeable or no longer noticeable) at 9 months divided by the number of participants with primary outcome recorded at 9 months. ^ Between group difference is number of participants experiencing a treatment success (between group risk difference %).

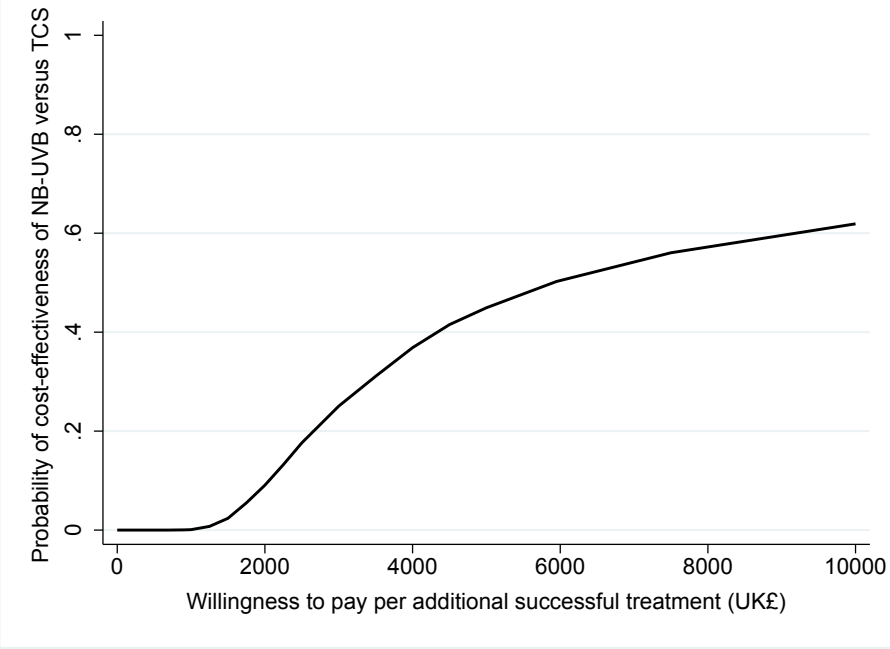

Figure 1a: Cost effectiveness Acceptability curve for NB-UVB versus TCS

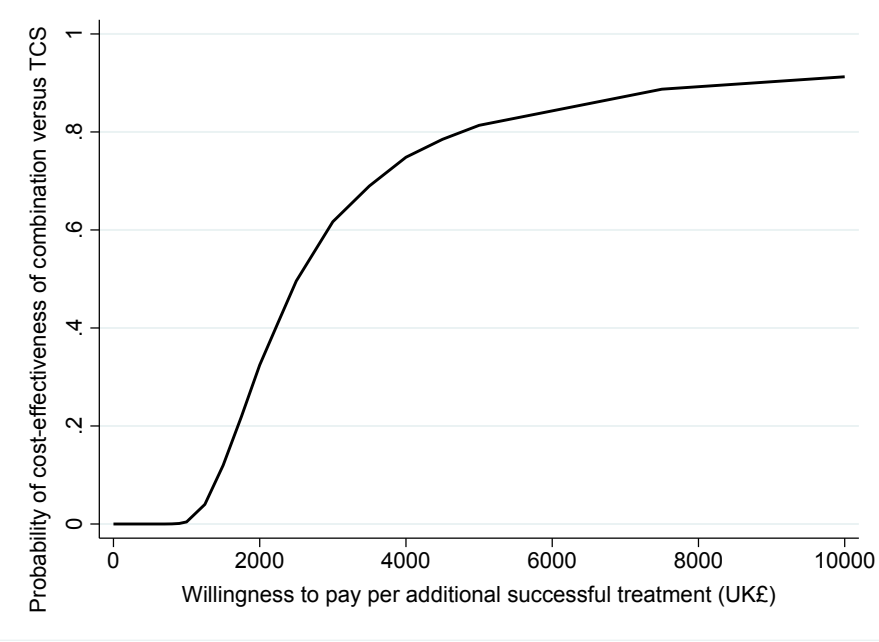

Figure 1b: Cost effectiveness Acceptability curve for NB-UVB versus TCS