Development and evaluation of a personalised psychological intervention to improve adherence to photoprotection in adults with Xeroderma Pigmentosum (XP)

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Scientific summary

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Scientific summary

Background

The aim was to understand the factors involved in adherence to rigorous ultraviolet radiation (UVR) photoprotection in the rare disease, xeroderma pigmentosum (XP; *N* = ~100 in the UK), and to develop and evaluate a personalised intervention to improve photoprotection behaviour and clinical outcomes. 'Usual care' in the UK comprises being cared for by the National Clinical Xeroderma Pigmentosum Service, based in London, which provides the following components of care: photoprotection advice and instruction from XP specialist nurses including NHS prescription of sunscreens and provision of ultraviolet (UV) meters for home use; multidisciplinary clinic appointments with dermatologist, ophthalmologist, neurologist, geneticist, neuropsychologist and paediatrician; outreach visits by specialist nurses.

PHASE I

Objectives

The overall aim was to determine the extent and determinants of non-adherence to photoprotection recommendations in XP patients.

Workstream 1

- Objectively measure UVR exposure to calculate the UVR dose to the face.
- Determine the feasibility of 'UVR dose-to-face' as the primary outcome for the Phase II intervention.
- Qualitatively explore individuals' experiences of XP and influences on photoprotection behaviours.
- Identify the psychological, social, disease-specific and sociodemographic factors associated with poor adherence to photoprotection.

Workstream 2

- Test the relevance of the factors identified in Workstream 1 in a larger questionnaire study of international XP patients.
- Examine differences between three regions to assess psychosocial, cultural and climatic effects on photoprotection behaviour in XP.
- Identify the predictors of the service use and costs associated with XP in each country.

Design

Workstream 1

Qualitative study employed semistructured interviews to understand the meaning and impact of XP on everyday life and factors that influence photoprotection behaviour. Interviews were recorded, transcribed and entered in NVivo11 for analysis. Thematic framework analysis was used to examine themes and patterns between cases and across groups; analyses were conducted separately for adults and children.

The *n*-of-1 study involved completion of a Short Message Service-based electronic daily diary for 50 consecutive days. Questions assessed a range of factors (e.g. motivation, confidence, effort, planning, goal priority and conflict). A paper-based daily UVR protection diary was used concurrently to record outdoor time and facial protection. This was used for the *n*-of-1 study (primary outcome: photoprotection behaviour used when outside) and to calculate UVR dose-to-face, using dynamic logistic regression, controlling for time trends.

Dosimeter study involved a wrist-worn dosimeter, which measured environmental UVR throughout a 3-week period. Dosimeter data were combined with the daily UVR protection diary to calculate the UVR dose-to-face, which was combined with cross-sectional data derived from the international survey (Workstream 2) to determine the predictors of UVR dose-to-face (UK sample only). Mixed-effects longitudinal models examined the association of clinical and psychosocial factors with the average daily UVR dose-to-face.

Workstream 2

International cross-sectional survey.

Setting and participants

Workstream 1

Participants were identified from the database at the National Xeroderma Pigmentosum Service at St Thomas' Hospital.

Inclusion criteria

- Patients > 16 years with a confirmed diagnosis of XP, sufficient English language comprehension and no cognitive impairment completed the measures themselves.
- Parents/caregivers of children (< 16 years) and adults with cognitive impairment completed the measures on behalf of the patient.

Workstream 2

Participants were recruited from four Western countries (UK, France, Germany and the USA) and two non-Western countries (Tunisia and Japan).

Main outcome measures

Workstream 1

See Design.

Workstream 2

The primary outcome was a self-reported measure of adherence to photoprotection, which included separate subscales for face and body photoprotection, for sunny and cloudy days, and avoidance of going outside during daylight. There were two versions: the adult self-completed version and the 'cared for' version.

Additional questionnaires assessed beliefs about photoprotection and XP, intention and self-efficacy for photoprotection, automaticity and social support. Clinical characteristics included age at diagnosis, skin cancer history and sunburn response.

Data synthesis

Univariate and hierarchical ordinal logistic regression were used to identify psychosocial predictors of photoprotection, controlling for demographic and disease-related factors.

Results

Workstream 1

Forty-seven participants with XP were recruited to the mixed-methods study (25 adults; 12 children without cognitive impairment; 5 adults and 5 children with cognitive impairment). Children and those with cognitive impairment are referred to as the 'cared for' sample. Forty seven were interviewed

(themselves or with parent/caregiver present), 41 wore the dosimeter and 20 adults without cognitive impairment completed the *n*-of-1 study.

Qualitative analysis (*n* = 25 adults) revealed three modes of adjustment to photoprotection:

- *Dominated by photoprotection:* achieved very good photoprotection which dominated their lives. Drivers included: immediate effects of UVR (e.g. skin reddening, sunburn); concerns about pigmentation; risks of cancerous lesions and treatment scars to face; and recognition of the risks of a reduced life expectancy. This group described considerable social and psychological costs of photoprotection.
- *Resistant to photoprotection:* few photoprotection practices, reluctance to disclose XP to friends and responded negatively to reminders to protect. Drivers included: desire to resist the self-identity associated with a chronic condition, the visibility and demands of photoprotection, or a view that XP was one of many risks and they preferred to 'live for today'. They justified their low photoprotection by explaining that lesions still occurred despite photoprotection and regarded sunscreen as greasy/uncomfortable.
- *Integrating photoprotection:* had generally accommodated photoprotection requirements as habits without major practical/emotional burdens. Two forms of adaptation were identified: largely staying indoors; and accommodating photoprotection into normal life, facilitated by social support and, for older people, by their changing expectations and circumstances.

Key findings from the *n*-of-1 study:

- Most participants failed to protect their face from UVR; 13/20 were using 'very poor' or no protection during at least 20% of all outdoor time (40–100% in some participants).
- Despite reasonable protection when they first went outside, this was not always maintained.
- Fluctuations in behaviour were associated with time of day (better protection 11 a.m. to 3 p.m.; weekday vs. weekend); risk perception; weather; and attribution of symptoms to UVR exposure and psychological factors such as planning and cognitions. Stress, negative mood and feeling self-conscious showed different relationships with protection across individuals and are likely to be bidirectional.

Key findings from the dose-to-face study included:

- Across 509 useable days the mean daily UVR dose for was 0.24 Standard Erythemal Dose (SED) in adults and 0.50 in the 'cared for' sample as compared with 0.58 in a healthy sample.
- Adjusting for photoprotection, mean daily UVR dose-to-face was similar for adults (0.13) and the 'cared for' sample (0.12). Although the latter were exposed to a higher level of environmental UVR, their photoprotection was also higher, shielding them from 66% of UVR reaching the face, compared to 43% for adults.
- Cross-sectional predictors of lower UVR dose-to-face included:
  - greater perceived necessity of photoprotection [risk ratio (RR) 0.86, 90% confidence interval (CI) 0.65 to 1.13]
  - stronger concerns about photoprotection (RR 0.84, CI 0.59 to 1.19)
  - greater automaticity of photoprotection (RR 0.72, CI 0.55 to 0.95)
  - greater self-efficacy (RR 0.67, CI 0.53 to 0.84)
  - lower satisfaction with social support (RR 1.26, CI 0.92 to 1.72)
  - greater negative emotional impact of XP (RR 0.76, CI 0.58 to 0.99).

Workstream 2

There were 156 participants in the Western sample (UK, France, Germany and USA), representing ~50% of known cases. Recruitment issues in Japan and Tunisia precluded analysis of these data and completion of the cross-cultural comparison.

Key findings included:

- Level of adherence to photoprotection varied; 'cared for' sample reported better face [*M* = 4.2, standard deviation (SD) = 0.7] and body protection (*M* = 4.7, SD = 0.6) than the adults (*M* = 2.9, SD = 1.2; *M* = 3.7, SD = 1.1).
- Older participants reported lower adherence to photoprotection [odds ratio (OR) 0.61, 95% CI 0.44 to 0.83], as did those older at diagnosis (OR 0.59, CI 0.43 to 0.81).
- Variables associated with better facial photoprotection were:
  - greater perceptions of personal control over XP (OR 1.57, CI 1.02 to 2.41)
  - greater perceptions of effectiveness of photoprotection (OR 1.54, CI 1.07 to 2.19)
  - stronger belief that photoprotection is effective at protecting against UVR (OR 1.70, CI 1.11 to 2.60)
  - stronger necessity beliefs (OR 1.62, CI 1.08 to 2.41)
  - greater automaticity (OR 1.95, CI 1.20 to 3.16).

- Variables associated with avoidance of going outside were:
  - higher XP-related distress (OR 2.11, CI 1.54 to 2.89) and concern (OR 1.65, CI 1.20 to 2.25)
  - stronger belief about serious consequences of XP (OR 1.47, CI 1.09 to 1.99)
  - greater concerns about photoprotection (OR 1.80, CI 1.32 to 2.46).

Key findings from the service use associated with XP:

- There were similarities between countries with generally relatively high use of dermatology and ophthalmology except in the USA.

PHASE II

Consensus conference to select modifiable targets for intervention; development of a personalised intervention to improve photoprotection Enhancing Xeroderma Pigmentosum Photoprotection Activities – New Directions (XPAND) (Workstream 3); randomised controlled trial (RCT) to test the efficacy and potential mechanisms of impact of the intervention (Workstream 4); cost-effectiveness analysis (Workstream 5).

Objectives

Workstream 3

- To synthesise the findings from Phase I.
- To identify potentially modifiable psychosocial factors associated with poor photoprotection adherence.
- To agree the targets for intervention in Phase II.
- To design an evidence-based intervention for delivery and evaluation.

Workstream 4

- To determine the efficacy of 'XPAND' to reduce daily UVR dose-to-face and improve photoprotection behaviour.
- To explore the acceptability of XPAND to patients.
- To examine the mechanisms of impact of any observed improvements from participation in XPAND.

Workstream 5

- To assess the cost-effectiveness of XPAND.

Design

Workstream 3

Consensus conference

Research teams submitted a series of 'evidence statements' which were synthesised and grouped into 'intervention recommendation statements' by the core intervention team.

Evidence statements were presented, and recommendations discussed and approved, rejected or amended. The day was attended by researchers (*n* = 10), patient and public involvement (PPI) panel (*n* = 3) and XP clinical team (*n* = 5). PPI and clinical teams defined their priorities for intervention.

Intervention development

The design process took 12 months and used using an intervention mapping framework. This specified the 'behavioural objectives' for and 'change objectives' needed to achieve these, using behaviour change methods derived from several taxonomies and clinical approaches. Intervention piloting was not possible due to small numbers; the intervention was reviewed by the PPI team and patients with excellent photoprotection who were ineligible for participation.

Workstream 4 (randomised controlled trial and process evaluation)

Two-armed parallel-group RCT with assessments at baseline (April 2018), post intervention (June 2018), late summer (August 2018), winter (December 2018), spring (2019) and early summer (2019)

Workstream 5

A decision model was used to assess the cost-effectiveness of XPAND.

Hypothesis

The intervention group will have a lower mean daily UVR dose-to-face (SED) compared to the control group at the post-intervention (June 2018) and late summer follow-up (August 2018).

Procedure

Participants were randomised to the immediate or delayed intervention control condition. All participants completed the daily UVR photoprotection diary for 3 weeks at baseline (April 2018), post-intervention (June 2018) and late summer follow-up (August 2018). The diary included measures of automaticity, self-efficacy, importance and mood. Participants used the wrist-worn dosimeter for the entire assessment/intervention/follow-up period. Self-report measures of quality of life (QoL), automaticity and self-efficacy despite barriers were completed at each measurement point. Intervention participants received 'XPAND' over 12 weeks in spring to summer 2018. The same procedure was followed in spring to summer 2019 for those who had been the control group in 2018.

Setting and participants

Workstream 3

See Design.

Workstreams 4 and 5

Adults with XP, no cognitive impairment, sufficient English language skills and suboptimal adherence to photoprotection, as identified by the XP clinical team, National Xeroderma Pigmentosum 'Service at St Thomas' Hospital, from data held in medical notes, or from data collected during Phase I.

Interventions

Workstream 3
Not applicable.

Workstreams 4 and 5
Immediate receipt of 'XPAND' (2018) versus delayed intervention control.

Main outcome measures

Workstream 3
Not applicable.

Workstream 4

- Primary outcome was average daily UVR dose-to-face. Data were analysed using a mixed-effects model with patient ID as a random effect and with fixed treatment and time effects.
- Secondary outcomes were time spent outside, photoprotection behaviour, sunscreen application, automaticity, self-efficacy, importance, mood, automaticity and QoL.
- These measures were used in the quantitative process evaluation to determine mechanisms of impact.
- Semistructured interviews following delivery in 2018 or 2019 to assess acceptability and possible change mechanisms.

Workstream 5
Service use was measured via completion of the Client Service Receipt Inventory, which retrospectively assesses use of primary and secondary healthcare services, social care, tests/investigations and aids/adaptations. Costs were calculated by combining service use data with appropriate unit cost information. Other XP-related costs include patient costs (e.g. sunscreen) and time lost from work/education. These were calculated, using average wage rates and return to education information, and combined with quality-adjusted life-years (QALYs) derived from the EuroQol-5 Dimensions, five-level version (EQ-5D-5L). The estimated cost of the intervention was based on staff time required to deliver it plus additional training and materials.

Results

Workstream 3
Phase I studies produced 64 evidence statements and 21 intervention recommendation statements, of which 19 were accepted by the consensus conference. This included 3 recommendations concerning behaviour and 16 relating to determinants of protection.

XPAND is a seven-session behaviour change programme, containing core and personalised elements. Sessions 1, 6 and 7 contain core content focused on motivational and habit formation processes, and relapse prevention strategies. Sessions 2–5 can be personalised, depending on preferences and identification of individual-level determinants. Delivery was guided by the facilitator manual, and aided by the XPAND magazine, purpose-designed worksheets and a video demonstrating correct sunscreen application.

Workstream 4
Sixteen adult XP patients were recruited; one withdrew, and dosimeter data loss resulted in the exclusion of two cases from analysis. The XPAND group (n = 8; six included in primary outcome analysis) had lower average daily UVR D-to-F during the June to July 2018 assessment period [0.03 (SD 0.02)

SED] compared to control (n = 8; seven included in primary outcome analysis) [0.36 SED (SD 0.16)] (adjusted difference = −0.25, $p < 0.001$). Interpretation of these findings was constrained by the failure of randomisation to balance baseline group differences in UVR protection.

Qualitative process evaluation analysis found that participants felt supported by XPAND and identified the importance of automatic processes for improving photoprotection, especially sunscreen application, reinforced by improvements in confidence in daily managing of XP.

Workstream 5

The economic analysis indicated that QALYs were similar between the intervention and control group, and the intervention was associated with lower costs. The magnitude, duration, cost-effectiveness and generalisability of the intervention are difficult to evaluate.

Conclusions

There were a number of important limitations across the different aspects of the programme. The small sample size means we have to be cautious about both costs and QALYs, and in the short term we probably would not expect QALY differences given the long-term aims of photoprotection. Many arose from the rarity of XP and the very small pool of potential participants for each aspect of the programme, particularly the RCT. The key limitations were lack of direct measure of UVR dose-to-face; low recruitment in Workstream 2; dosimeter failure; imbalance in baseline measures of UVR protection between the interventions and control groups; and lack of blinding.

The XP programme grant fulfilled its primary objective to develop an adherence intervention that improved photoprotection and reduced the dose of UVR reaching the face in patients with XP. It was cost-effective, valued, accepted by participants and did not reduce emotional well-being. We identified the psychological drivers of rigorous photoprotection, provided comprehensive understanding of the impact of this regime on patients and developed a novel approach to measuring the dose of UVR reaching the face. Future research needs to adapt and evaluate the XPAND intervention for use with other groups of adults at higher risk of non-malignant skin cancers.

Work is ongoing to train clinical staff to integrate XPAND into standard care.

Trial registration

This trial is registered as ClinicalTrials.gov NCT03445052.

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