Investigating the long-term impact of a childhood sun-exposure intervention, with a focus on eye health: protocol for the Kidskin-Young Adult Myopia Study

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ABSTRACT

Introduction Excessive and insufficient sun exposure during childhood have been linked to serious diseases in later life; for example, insufficient sun exposure during childhood may increase the risk of developing myopia. The Kidskin-Young Adult Myopia Study (K-YAMS) is a follow-up of participants in the Kidskin Study, a non-randomised controlled trial that evaluated the effect of a 4-year educational intervention on sun-protection behaviours among primary school children in the late 1990s. Children who received the Kidskin intervention had lower levels of sun exposure compared with peers in the control group after 2 and 4 years of the intervention, but this was not maintained 2 years after the intervention had ceased. Thus, a follow-up of Kidskin Study participants provides a novel opportunity to investigate the associations between a childhood sun-exposure intervention and potentially related conditions in adulthood.

Methods and analysis The K-YAMS contacts Kidskin Study participants and invites them to participate using a variety of methods, such as prior contact details, the Australian Electoral Roll and social media. Self-reported and objective measures of sun-exposure and sun-protection behaviours are collected as well as a number of eye measurements including cycloplegic autorefraction and ocular biometry. Data will be analysed to investigate a possible association between myopic refractive error and Kidskin intervention group or measured sun exposure.

Ethics and dissemination The K-YAMS is approved by the Human Research Ethics Committee of the University of Western Australia (RA/4/1/6807). Findings will be disseminated via scientific journals and conferences. Trial registration number ACTRN12616000812392; Pre-results.

INTRODUCTION

High levels of sun exposure during childhood increase the risk of melanoma in later life.1 However, a lack of sun exposure during childhood has been linked to the development of diseases such as myopia,2 3 multiple sclerosis4 and type 1 diabetes mellitus.5 Myopia (near-sightedness) is a common condition affecting approximately 24% of 20-year olds in Australia.6 The prevalence of myopia is increasing in many parts of the world, and current research aims to prevent the onset or progression of myopia and the potentially blinding diseases associated with myopia.6 7 Recent randomised clinical trials in Chinese school children have shown that spending extra time outside during the day prevented the onset of myopia in some children,8 9; however, it is unknown whether sun exposure, increased retinal illumination or viewing of distant objects is responsible for this beneficial effect.

Between 1995 and 2001, Western Australian researchers conducted the Kidskin Study, a 6-year non-randomised controlled trial that aimed to ‘design, implement and evaluate an intervention to reduce sun exposure in children’10 and thus reduce the risk of melanoma in later life.10 11 Eligible participants were those attending their first year of schooling in 1995 at a participating school, all of which were located within 30 km of Perth. Of the 2528 children invited to participate in the Kidskin Study, consent was provided by a parent or
The primary outcome was change in number of melanocytic naevi on the back at the 4-year follow-up. This was not significantly different between the high, moderate and control groups with the exception of the high group had significantly lower reported time spent outdoors between 11:00 and 14:00 at the 2-year follow-up, but at the 4-year follow-up, only children in the high group had significantly lower reported time spent outdoors between 11:00 and 14:00 compared with the control group. Measurement of suntan using skin spectrophotometry showed that children in the high and moderate groups had a significantly lower level of suntan at the end of summer than the control group at the 2-year follow-up. However, there was no significant difference at the 4-year and postintervention follow-ups. The skin spectrophotometer had to be changed between the 2-year and 4-year follow-ups as it became unserviceable, and this change in measurement instrument may be a factor in the lack of an association between measured suntan and intervention group at the later follow-ups. At the final Kidskin Study follow-up in 2001, 2 years after the intervention had ceased, there was no significant difference in suntan or sun exposure between children in the high, moderate and control groups with the exception of applying sunscreen to the back, which was more common in the moderate and high groups.

The size, quality and length of intervention and follow-up of the Kidskin Study make it unique among studies of child and adolescent sun protection. Other sun-protection intervention studies have had mixed results in reducing sun exposure in participants. Studies finding no effect of an intervention, lacking a control group or not longitudinally following the same participants have limited usefulness when investigating the impacts of sun exposure during childhood. Of the studies that have successfully reduced sun exposure in the intervention group compared with the control group, all have had shorter intervention and follow-up periods than the Kidskin Study.

Hence, the Kidskin Study provides a novel opportunity to investigate the association between sun exposure during childhood and the development of potentially related conditions in adulthood. The intervention study formed a cohort in which particular groups of participants had different levels of sun exposure during a well-defined period in primary school. Additionally, participants had both subjective and objective measurements of sun exposure recorded at multiple time points throughout childhood.

The Kidskin Study participants are 27–28 years old in 2017—an age when the prevalence of myopia, a disorder that predominantly develops in younger life—has generally stabilised. The Kidskin Young Adult Myopia Study

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**Table 1** Schedule of Kidskin study intervention and data collection

<table>
<thead>
<tr>
<th>Year</th>
<th>Intervention</th>
<th>Questionnaire</th>
<th>Constitutional†§</th>
<th>Naevus counts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>Spring*</td>
<td>Spring</td>
<td>Winter*</td>
<td>Winter</td>
</tr>
<tr>
<td>1996</td>
<td>Spring</td>
<td>Summer†</td>
<td>Winter</td>
<td>Winter</td>
</tr>
<tr>
<td>1997</td>
<td>Spring</td>
<td>Summer‡</td>
<td>Winter</td>
<td>Winter</td>
</tr>
<tr>
<td>1998</td>
<td>Spring</td>
<td>Summer‡</td>
<td>Winter</td>
<td>Winter</td>
</tr>
<tr>
<td>1999</td>
<td>Summer‡</td>
<td>Summer‡</td>
<td>Winter</td>
<td>Winter</td>
</tr>
<tr>
<td>2000</td>
<td>Summer‡</td>
<td>Summer‡</td>
<td>Winter</td>
<td>Winter</td>
</tr>
<tr>
<td>2001</td>
<td>Summer‡</td>
<td>Summer‡</td>
<td>Winter</td>
<td>Winter</td>
</tr>
</tbody>
</table>

Adapted from Milne. In Australia, summer is from December to February, autumn from March to May, winter from June to August and spring from September to November. "Measured by skin spectrophotometry. †Measured at the end of summer immediately after school holidays. §Constitutional skin colour measured from inner arm.

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(KYAMS) will follow-up participants in the Kidskin Study, to determine the long-term effects on health—particularly eye health—of a sun-protection intervention during childhood.

**METHODS AND ANALYSIS**

**Recruitment**

The K-YAMS aims to use the established Kidskin Study cohort to investigate the association between the Kidskin intervention and the prevalence of myopia in participants of the Kidskin Study, who are now young adults. Recruitment for the K-YAMS began in May 2015 and will be completed by the end of 2018. All participants of the Kidskin Study are eligible to participate. The expected follow-up sample size (~800) is likely to be too small to investigate rarer outcomes such as type 1 diabetes mellitus, but will be large enough to detect differences in relatively common disorders such as myopia.

While a significant amount of time has passed since the Kidskin participants were last contacted, approximately one-third (n=547) of participants responded to a mail out invitation to provide a saliva sample in 2005; however, since 2001, the majority of the Kidskin participants have not been contacted. We are therefore using a variety of approaches to contact participants including previous address and telephone or mobile phone details from the Kidskin Study, Facebook, the Australian Electoral Roll and snowball recruiting from participants we have been able to contact, asking them to help spread awareness of the K-YAMS to their schoolmates.

**Data collection**

An overview of the measures being collected in the K-YAMS is given in table 2. The K-YAMS focuses on myopia and eye health; however, a number of other broader health measures are also being collected. Participants are required to attend a study examination at the Lions Eye Institute in Perth, Western Australia. Written informed consent is obtained from all participants prior to the study examination.

**Self-reported data**

Participants are asked to complete a questionnaire as well as a sun calendar at home or during the study visit. Questionnaire data include current demographics, medical and ophthalmic history, recent and past sun exposure, natural hair colour, skin type and skin reaction after sun exposure. The sun calendar asks participants to report city of residence and sun-exposure (summer and winter in categories of ‘less than half an hour per day’, ‘half to 1 hour’, ‘1–2 hours’, ‘2–3 hours’, ‘3–4 hours’ and ‘more than 4 hours’) and sun-protection behaviours (hat, sunglasses and sunscreen in categories of ‘never’, ‘less than half of the time’, ‘half of the time’, ‘more than half of the time’ and ‘all of the time’) for each year of life from 5 years of age onward. The self-reported calendar data for the period of the intervention will be compared with the self-reported and measured data on sun exposure and sun protection for the intervention period.

**Exposure measurements**

A variety of objective measures of sun exposure are being collected to gain a better understanding of each individual’s past and recent exposure to sun. Skin photodamage is measured using silicone skin casts taken from the back of participants’ right hands and graded on a scale of 1 to 6, as previously described by Holman et al., where grade 1 represents no or little sun-related skin damage and grade 6 represents severe skin damage. Participants will have their back photographed and the number of naevi counted by a trained examiner. Conjunctival ultraviolet autofluorescence photographs to measure past sun exposure of the eye are captured using a Nikon D100 camera (Nikon, Melville, New York, USA) with a B+W 486 UV filter (Schneider Kreuznach, Bad Kreuznach, Rhineland-Palatinate, Germany) fitted to a 105 mm f/2.8 Micro Nikkor lens (Nikon). Two Metz 36 C-2 flashes (Metz, Zirndorf, Middle Franconia, Germany) with 18 A Wratten glass filters fitted over the flash heads are used as the excitation source. Blood is taken by venepuncture into serum separator tubes. One millilitre aliquots of serum are frozen at ~40°C until the completion of the study. Liquid chromatography tandem–mass spectrometry will then be used to measure serum 25-hydroxy vitamin D concentration, as a marker of recent sun exposure, after completion of data collection.

**Table 2** Outcome measures in the K-YAMS

<table>
<thead>
<tr>
<th>Eye and vision measures</th>
<th>Sun-exposure measures</th>
<th>Other health measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive error</td>
<td>Sun damage measured from silicone skin cast of back of right hand</td>
<td>Height</td>
</tr>
<tr>
<td>Strength of current prescribed glasses</td>
<td>Serum 25(OH)D concentration</td>
<td>Weight</td>
</tr>
<tr>
<td>Visual acuity</td>
<td>Ocular sun exposure (CUVAF)</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>Corneal endothelial cell count</td>
<td>Self-reported history of sun exposure</td>
<td>Naevi count on back</td>
</tr>
<tr>
<td>Ocular motility and stereocytosis status</td>
<td></td>
<td>Naevi count on right arm</td>
</tr>
<tr>
<td>Eye colour photography</td>
<td></td>
<td>DNA</td>
</tr>
<tr>
<td>Ocular biometry</td>
<td></td>
<td>Self-reported skin and hair phenotypes</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macular and optic disc parameters measured using HRT and OCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinal photography</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

25(OH)D, 25-hydroxy vitamin D; CUVAF, conjunctival ultraviolet autofluorescence; HRT, Heidelberg retina tomography; K-YAMS, Kidskin-Young Adult Myopia Study; OCT, optical coherence tomography.
equivalent ≤0.50 dioptres (D) (calculated as sphere+½ cylinder). A variety of other eye and vision measurements are collected including visual acuity (ETDRS chart R; Precision Vision, Woodstock, Illinois, USA), ocular biometry (IOL master 500; Carl Zeiss Meditec, Jena, Germany), intraocular pressure (icare TA01i; icare, Vantaa, Finland), optical coherence tomography (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) and fundus photography (CF-60DSi; Canon, USA).

Data analysis
The primary analysis of the K-YAMS will test the association between spherical equivalent/prevalence of myopia and intervention group of the Kidskin Study. Linear and logistic regression models will be constructed to investigate the impacts of the Kidskin Study intervention on continuous and categorical outcomes, respectively, while adjusting for covariates such as age and education. Secondary analysis will involve the construction of further linear and logistic regression models to investigate the associations between past sun exposure, irrespective of Kidskin Study intervention arm, and ocular parameters such as spherical equivalent and axial length, while adjusting for confounding variables.

We will have 99.63% power to detect a difference of 0.50 D of spherical equivalent between the high intervention and control groups with a sample size of 800. However, if we are unable to meet our recruitment target, we will still have 96.7% and 87.5% power to detect a difference of 0.50 D between the high and control groups with sample sizes of 600 and 400, respectively.

Implications
Australia has the highest skin cancer incidence in the world; melanoma is the deadliest of the skin cancers and is particularly associated with childhood sun exposure. Incidence rates of melanoma were rapidly rising in the late 20th century. In the face of this, Australia led the world in developing sun-protection programmes to reduce childhood sun exposure. Encouragingly, the incidence of melanoma in Australia has remained stable since 2006. However, recent evidence suggests that there may be beneficial effects of sun exposure, such as preventing onset of myopia, and it is now accepted that there may be beneficial effects of sun exposure, specifically to sun exposure, due to other confounding factors that often accompany sun exposure, such as physical activity. Randomised controlled trials can overcome this issue, but are difficult and costly to run, and can pose ethical dilemmas, for example, where the full effects of an intervention have potential adverse effects on health. In addition, in an intervention study, it may be a long time before the harmful or beneficial effects of the intervention are fully appreciated. The Kidskin Study was a thorough controlled trial that was completed in 1999 and presents a truly unique opportunity to immediately begin studying the effects of an intervention which successfully reduced sun exposure compared with controls. A difference in myopia prevalence across the intervention groups may suggest that the age period over which Kidskin participants received the intervention is a key period in the development of myopia. This age group could then be targeted by public health campaigns aimed at preventing the onset of myopia in at-risk children through a controlled increase in time spent outside. However, the utility of the Kidskin Study cohort is not limited to myopia, and further follow-ups could provide crucial information in examining the effects of reducing childhood sun exposure.

ETHICS AND DISSEMINATION
Findings from the K-YAMS will be disseminated via publication in scientific peer-reviewed journals and presentation at national and international conferences. K-YAMS participants will also be notified of publications and provided with a copy where possible. All subjects provide written informed consent prior to participating in the study and are made aware that they may withdraw their consent at any time or refuse any procedure such as venepuncture or administration of cycloplegic eye-drops. A trained medical doctor is present during study examinations in the unlikely event of an adverse event occurring.

Contributors GL, DAM, SY and RML were involved in the conception and design of this manuscript. EM, DRE, DC and RSJ were involved in the conception, design, implementation, data collection and analysis of the Kidskin Study between 1995 and 2001. DAM, SY, RML and EM were involved in the conception and design of the K-YAMS. GL was responsible for the initial drafting of the manuscript. All authors critically reviewed, revised and contributed to the manuscript.

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Competing interests None declared.

Patient consent Parental/guardian consent obtained.

Ethics approval K-YAMS is approved by the Human Research Ethics Committee of the University of Western Australia (RA/4/1/6807).

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

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