3 Methods

3.1 Topics for research

To meet the requirements of the brief, we developed a search strategy based on the following questions relating to eye health:

1. Risk factors for eye disease and injury
   What is the relationship between the following factors and conditions?

- Factors
  - tobacco use
  - alcohol consumption
  - diet and diet-related issues (obesity, supplements, fatty acids)
  - eye infections
  - age or ageing[1]
  - heredity
  - UV damage
  - injuries and accidents
  - medication side effects
- Conditions
  - macular degeneration
  - cataract
  - glaucoma
  - diabetic retinopathy
  - retinitis pigmentosa
  - trachoma
  - amblyopia
  - injury
  - refractive errors (myopia, hyperopia, presbyopia, astigmatism)
  - pterygium[2]
  - ocular surface neoplasia[2]

2. Eye infections
   Do infection control methods reduce the incidence of eye infections?
   What impact does use of contact lenses have on incidence of eye infections?
   Does education on use and misuse of contact lens affect incidence of eye infections?

3. Eye tests
   Do regular eye tests reduce the incidence of eye disease?
   What is the optimal frequency of eye tests for each age group?
   What are the risks and benefits of different frequencies of eye tests?

Where interventions were identified (eg use of sunglasses, eye tests and nutritional supplements), we attempted to look at both the beneficial effects and any possible adverse consequences of the intervention.

[1] In this literature review, a distinction is made between 'age', which refers to onset of a condition at a specific age (eg amblyopia in children), and 'ageing', which refers to progressive onset as a result of increasing age (eg cataract, age-related macular degeneration) .

[2] The only risk factor reviewed for pterygium, and ocular surface neoplasia was UV damage. These two reviews were added to the report in November 2008.

3.2 Literature review methods

We followed the systematic literature review methods set out in the NHMRC booklet, *How to Review the Evidence: Systematic Identification and Review if the Scientific Literature* (NHMRC 2001). This involved four main stages:

- developing focused questions based on 'PICO' components (population, intervention or indicator, control, outcome)
- using the PICO questions to identify search terms and searching a broad spectrum of relevant biomedical databases
- reviewing and appraising retrieved articles to identify the most relevant and best-quality review articles and primary studies to answer the questions
- tabulating the results of the included studies and presenting a brief summary statement of the findings for each health question researched.

Initially, the topics shown in Section 3.1 were used to develop focused research questions using series of topic grids for this review. These grids, as well as details of the search strategy followed (including a list of the databases searched, and the search terms used), are shown in Appendix 2.

3.3 'Winnowing' and assessing papers

Relevant articles were selected using a two-stage process (Figure 3.1). We first downloaded the results of the literature searches into individual Endnote databases. We then 'winnowed' the articles by considering the titles and abstracts, excluding any that were obviously irrelevant; for example, those that were speculative and contained no evidence from epidemiological studies, and those for which the topic under review was not the main focus of the study.

The next step was to obtain full copies of the remaining articles in each Endnote database. These were primarily articles describing epidemiological studies of the relevant risk factors, eye infections and eye tests, and other articles directly relevant to the topics outlined above. The most relevant of these papers were then selected for possible inclusion in the review.

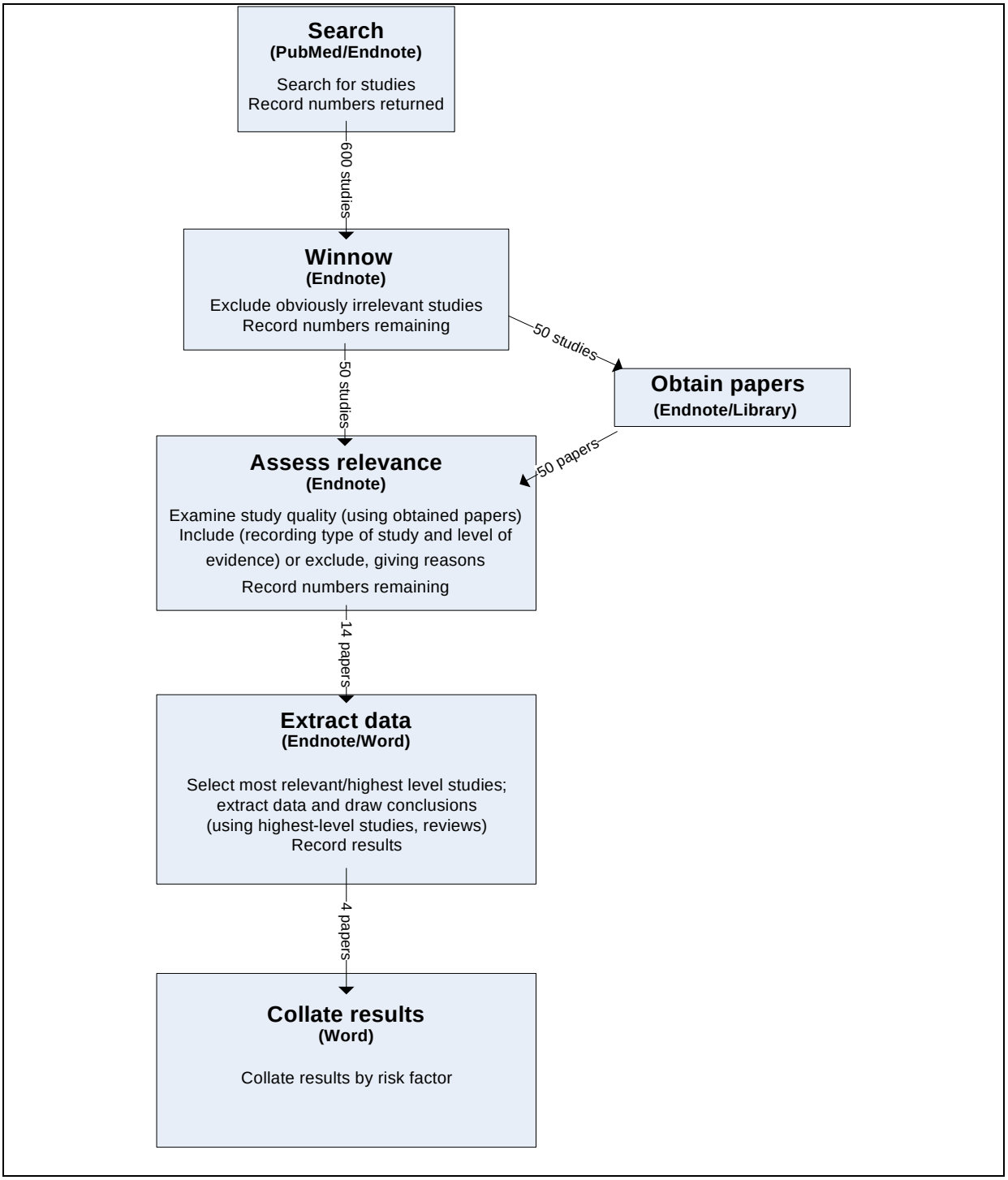
Given the broad scope of the review, it was not possible to follow best practice and have each database examined independently by two people who would then compare the results. However, each database was looked at twice (ie once to winnow out obviously irrelevant or inappropriate studies, and once to select the most appropriate of the remaining articles). In most cases, a different person examined the database at each of these stages, providing some independent review within the selection process.

We initially selected systematic reviews and primary research articles involving clinical trials (studies of the highest level). However, where high-level studies were lacking, or where the question under review covered a broad category (eg sport), we also selected studies of a lower level, such as case series and cross-sectional studies. Each article retrieved was assigned a unique identifying number.

We reviewed the papers for a topic as a whole and selected those that were of highest quality and most relevant. Where there was a systematic review that was completed at an earlier date than the end date for this search (eg completed in 2004, when the search

terminated in December 2006), we also considered any relevant papers published after the completion date. Every effort was made to include all relevant issues; however, given the breadth of the topics, we may have missed some relevant papers.

At each stage of the process, we kept electronic records of the search and analysis. Thus, for each combination of risk factor and condition, we produced an Endnote database showing the full search results, the papers winnowed out at the first pass and the final papers selected, with notes on type of study, level of evidence and reasons for including or excluding the studies. We also produced an Excel spreadsheet indicating the name of the person undertaking each stage, the date at which it was completed and the number of papers remaining at each stage. These electronic records have been provided to the NHMRC in electronic form (on a CD-ROM); hard copies of all included papers were also supplied to the NHMRC. A summary of the results of each search, from search terms to final number of papers used to determine the finding, is given in Appendix 3.



Note: The numbers given in the figure represent a single, typical search

Figure 3.1 Summary of process for selecting and assessing papers

3.4 Extracting and summarising data

For each research question for which studies were identified, we entered results from the relevant articles into a summary table based on the NHMRC minimum requirements for clinical practice guidelines development. These results tables are provided in Appendix 4.

Each results table includes:

- the identifying number and authors of the paper
- the type of study (systematic review, prospective or retrospective cohort, case–control, case series, etc)
- information on the population under study, the risk factor, the comparator and the number of subjects
- the level of evidence (see below) and any quality information
- the main findings of the study.

Levels of evidence were based on the NHMRC additional levels of evidence (NHMRC 2005). Relevant levels for aetiology and intervention studies are shown in Table 3.1.

Table 3.1 NHMRC levels of evidence for aetiology and intervention questions

Level	Intervention	Aetiology
I	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A prospective cohort study
III-1	A pseudo-randomised controlled trial (ie alternative allocation or some other method)	All or none[a]
III-2	A comparative study with concurrent controls: • nonrandomised, experimental trial • cohort study • case–control study • interrupted time series with a control group	A retrospective cohort study
III-3	A comparative study without concurrent controls: • historical control study • two or more single-arm studies[b] • interrupted time series without a parallel control group	A case–control study
IV	Case series with either post-test or pre-test and post-test outcomes	A cross-sectional study

a All or none of a series of people (case series) with the risk factor(s) experience the outcome.
b Comparing single-arm studies (ie case series from two studies).
Source: *Additional Levels of Evidence and Grades of Recommendations for Developers of Guidelines: Pilot Program 2005–07* (NHMRC 2005)

Where appropriate, further information was also included on the quality of the studies. However, owing to the very large scope of this review, it was only possible to do a critical appraisal for systematic reviews. For these studies (systematic reviews), data on the study design and quality were extracted using a form based on the NHMRC minimum requirements for clinical practice guidelines development and the Scottish Intercollegiate Guidelines Network (SIGN) critical appraisal form for systematic reviews. The completed extraction forms are included in Appendix 5, organised by each paper's identifying number. The quality of each systematic review (identified as 'good', 'adequate' or 'poor') was included in the results summary table. Data on design and quality were extracted separately from the results because a single systematic review often included results relevant to several different questions.

Some prospective cohort studies (level II evidence for aetiology questions) and cross-sectional studies (level IV) were based on large population studies that have been conducted over many years using standardised methodology (eg Blue Mountains Eye Study, Beaver Dam Study). Many papers have been published from these studies, which

have thus been subject to frequent peer review. These studies are designated in the table as 'LPS' (large population study).

Below each results table is a summary statement that combines the overall results for the particular question. Also, to assist in the development of key findings based on this review, each summary statement is assigned to a particular group, as shown below in Table 3.2. The table lists the groups used, explains the meaning of each group and provides notes on how the findings were assigned to a specific group, based on number, type and quality of studies that supported the overall finding.

The assignment of each summary to a particular group is intended only to assist in sorting the large number of research questions according to the overall findings of the review. They should not be confused with levels of evidence and grades of recommendations.

Table 3.2 Categories of summary statements

Group	Meaning	Notes
1	Clear association/causality	Studies of at least adequate quality that show a statistically significant causality or association between the risk factor and outcome.
2	Possible association/causality (more research needed)	Some studies, but of poor quality or too underpowered to show a statistically significant causality or association.
3	Lack of association/causality	Studies of at least adequate quality that show no statistically significant association between the risk factor and outcome.
4	Possible lack of association/causality (more research needed	Some studies, but of poor quality or too underpowered to confirm no statistically significant association.
5	Conflicting results	Some studies, but results inconsistent so that it is not possible to draw a firm conclusion.
6	Possible protection	Some studies indicating that the factor under study may protect against the particular condition, but of poor quality or too underpowered to confirm statistically significant protection.
7	No studies	No relevant studies were found in the time period (1996–2006) covered by this review. This could mean that no relevant articles were published in the time period covered by the review; however, in some situations, it could mean that studies carried out before 1996 have clearly shown an association or lack of association, and no further studies were published during the period covered by the review.

3.5 Collating and checking results

To collate the results, the summary statements from the results tables in Appendix 3 were entered into the tables shown in Chapter 4 (Tables 4.1–4.5). These tables list, for each of the topics for which clinical questions were formulated and for which relevant studies were identified:

- the statement summarising the findings for that particular question (taken from the appropriate results table in Appendix 4)
- the group to which the findings were assigned (as explained above in Section 3.4)
- the number of the relevant results table in Appendix 4.

To ensure that all major relevant studies were identified and the findings were valid, two relevant experts (Dr Ian Morgan and Dr Kathryn Rose — see Appendix 1) were asked to check the final results tables and summary information. The experts provided advice only; Biotext takes full responsibility for the findings of this report.