Dunedin Multidisciplinary Health & Development Study

Concept Paper Form

Provisional Paper Title: Characterising the 45-year-old ocular surface and tear film: a New Zealand cohort study.
Proposing Author: Jennifer Craig, along with Michael Wang (PhD student) and Graham Wilson (PI vision).
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P.I. Sponsor: Jennifer Craig / Graham Wilson
Today's Date: 1 April 2019

Objective of the study:

Dry eye disease is a growing public health concern globally, and can have profound impacts on ocular comfort, vision, quality of life, and work productivity.[1-3] While dry eye is not evaluated by the Global Burden of disease, over 5 million Americans over the age of 50 have dry eye. The recently convened second international Tear Film and Ocular Surface Society Dry Eye Workshop (TFOS DEWS II) highlighted that there were significant gaps in the scientific literature with regard to the natural history of dry eye disease.[4-7] Furthermore, the TFOS DEWS II epidemiology subcommittee report identified a lack of population-based prevalence studies from the Southern Hemisphere published in the last 10 years.[4] The objectives of the proposed study is therefore to characterise the ocular surface and tear film parameters of a large 45-year-old New Zealand cohort, recruited through the Dunedin Multidisciplinary Health and Development Study, and to assess the prevalence of dry eye disease.

Data analysis methods:

Ocular surface and tear film parameters will be presented as mean ± SD for normally distributed continuous measures, median (IQR) for non-normally distributed continuous and ordinal measures, and proportions calculated for categorical data. The presence of dry eye disease will be determined according to established diagnostic cut-off values for dry eye symptomology measures and clinical markers of ocular surface homeostasis markers,[8] and the cohort prevalence calculated accordingly. Subgroup analysis will be conducted according to demographic characteristics including gender,

ethnicity, location, (and potentially markers of socioeconomic status). Comparisons of normally distributed continuous measures will be conducted using the unpaired t-test, non-normally distributed continuous and ordinal measures analysed using the Mann-Whitney U-test, and categorical data compared using the chi-squared and Fisher's exact tests.

Variables needed at which ages:

Dry eye variables at age 45 (only age available to date), including:[8]

Clinical variable	Measurement
Dry eye symptomology	Symptom Assessment in Dry Eye (SANDE) questionnaire
Tear film stability	Non-invasive tear film breakup time
Aqueous tear production	Tear meniscus height
Meibomian gland function	Tear film lipid layer grade
Meibomian gland morphology	Superior and inferior eyelid percentage meibomian gland dropout

Demographic variables at age 45, including:

- Age
- Gender
- Ethnicity
- Location
- Markers of socioeconomic status (income, education attainment, occupation)

Significance of the Study (for theory, research methods or clinical practice):

The TFOS DEWS II epidemiology subcommittee report recently identified that there were limited scientific literature investigating the natural history of dry eye disease,[4-7] and the proposed study will be the first of its magnitude to characterise the ocular surface and tear film parameters within a large age-controlled cohort. Developing a greater understanding towards the natural history of the progression and development of dry eye disease will have significant impacts on informing recommendations surrounding population-wide preventative efforts, as well as the clinical management for individual patients at higher risk of developing dry eye.[4,7,9] In addition, the TFOS DEWS II epidemiology subcommittee report also highlighted a lack of population-based prevalence studies from the Southern Hemisphere published in the last 10 years.[1] The New Zealand-based cohort study proposed would help to fill this identified gap within the scientific literature.

Most existing epidemiology studies evaluating the clinical markers of ocular surface homeostasis comprise of self-selected cohorts, due to the recruitment and advertising strategies employed.[4] Such methodological limitations introduce the potential for selection bias, which may consequently affect the interpretation and applicability of study findings.[4,8] The proposed study would be unique in evaluating the clinical ocular surface and tear film parameters in a large age-controlled cohort nested within a larger multidisciplinary health and development study, without an inherent focus on dry eye disease. This would reduce the potential for self-selection bias for participants with poorer levels of dry eye signs and symptomology.

Also, techniques for evaluating the ocular surface and investigating dry eye disease and its risk factors have improved in recent years, such that these are now available for clinical evaluation.[8,10] There has also been significant growth in the interest of the meibomian glands and their role in dry eye development within the scientific literature.[11-13] The proposed epidemiological study will be the first of its magnitude to report the morphology and function of the meibomian glands. It would also allow for the exploration of the relative contributions of the two main aetiological subtypes of dry eye disease (evaporative and aqueous deficiency),[14] at a population level.

Finally, this work will enable the development of a novel dry eye work-horse variable that will be utilized in future multi-disciplinary dry eye research, for instance, is dry eye a marker of biological ageing?

References:

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Data Security Agreement

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Please keep one copy for your records and return one to the PI Sponsor

Please initial your agreement: (customize as necessary)

JPC	I am current on Human Subjects Training [CITI www.citigrogram.org] or equivalent.
JPC	My project is covered by the Dunedin Study's ethics approval AND I will obtain ethical approval from my home institution (please specify).
JPC	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: • encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) • password-protected • configured to lock-out after 15 minutes of inactivity AND • has an antivirus client installed as well as being patched regularly.
JPC	I will not "sync" the data to a mobile device.
JPC	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact my PI Sponsor or Study Director, Richie Poulton (richie.poulton@otago.ac.nz).
JPC	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
JPC	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to your PI Sponsor or Richie Poulton for strategies for achieving compliance with data-sharing policies of journals.*
JPC	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.

Signature:  _____