Working with ASPREE

Information for researchers interested in collaborating with ASPREE and ASPREE-XT regarding:

a) ASPREE/ASPREE-XT Data and Bio-specimens
b) New data generation, sub-study proposals
c) External data linkage
d) Publications

ASPirin in Reducing Events in the Elderly
ASPREE

Monash University, Berman Center for Outcomes & Clinical Research, National Institute on Aging

Table of Contents

INTRODUCTION

a. The ASPREE study was a double blind randomized clinical trial established to determine whether low dose aspirin prolongs healthy life amongst older Americans and Australians (*Contemp Clin Trials* 2013; 36:555-64).

b. The primary endpoint was a composite of death, dementia or persistent physical disability. Secondary endpoints included all-cause mortality, cardiovascular events, stroke, cancer, dementia, mild cognitive impairment, physical disability, depression and clinically significant bleeding (McNeil *et al.* J Gerontol 2017).

c. The study commenced recruitment in March, 2010. Enrolment was completed on December 31st 2014. Randomization of 19,114 participants was completed with 16,703 participants in Australia and 2,411 participants in the USA, with the latter focussing on minority group recruitment.

d. Study medication for ASPREE ceased on June 12 2017 and the trial failed to find benefit in the use of aspirin for primary prevention in these older individuals (McNeil et al NEJM 2018). Follow-up of participants in milestone visits continued until January 31 2018, and since this time the ASPREE-XT observational follow-up has continued to assess participants at annual visits.

e. Since the commencement of ASPREE, many sub-groups of participants have also volunteered for sub-studies; including bio-specimen collection at baseline (AUS participants) and in year three or four after entry (both AUS and US participants), medical imaging (brain MRI, knee MRI, retinal photography), hearing screening, sleep apnoea measures and additional data collection via questionnaires including medical, lifestyle and social data (AUS participants). Samples of cancer tissue from adjudicated ASPREE cancer cases are sought in both AUS and US.

f. The majority of sub-study data collection concluded in 2017. Two sub-studies had funding for extending follow up to year 5, ASPREE-AMD examining Macular Degeneration which concluded in 2021, and ASPREE-Central Hearing which concluded in 2019. A new sub-study, assessing gut microbiome composition has commenced in 2021 and will also involve a new collections of blood specimen and additional medical, lifestyle and social questionnaires in Australia and US.

g. The principal source of funding for the ASPREE trial is the US National Institute on Aging (NIA) (Appendix 13). Other agencies, including the US National Cancer Institute (NCI), Monash University, the Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO), the Victorian Government's Victorian Cancer Agency and the Australian Government's National Health and Medical Research Council (NHMRC) have made substantial financial contributions, primarily by funding sub-studies. Collaborators from all state and regional sites have provided substantial support to the study. The principal source of funding for the ASPREE-XT study is the US National Institute on Aging (NIA).

h. Both ASPREE and ASPREE-XT investigators and sponsors wish the data to be used as extensively as possible to improve health of the elderly. To achieve this goal the availability of the data is widely promoted amongst the research community.

This document outlines the ASPREE and ASPREE-XT policy in relation to a) access to data and bio-specimens from the ASPREE Clinical Trial and ASPREE-XT extension study, and from sub-studies including the ASPREE Healthy Ageing Biobank, for the purpose of producing publications

and abstracts, b) new sub-study proposals, c) new linkages with external data repositories. The procedures are based on, and are in keeping with, the Final NIH Statement on Sharing Research Data (2003) requirements for data-sharing.
http://www.grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm

This document recognises that 'the investigators who collect the data have a legitimate interest in benefiting from their investment of time and effort and should benefit from first and continuing use but not from prolonged exclusive use'.

COMPENDIUM OF TERMS

Access Management System (AMS): Accessible at https://ams.aspree.org/, this secure website is separate from the main ASPREE website and requires a username and password to track applications through the processes of expression of interest, approvals, detailed applications, project set up, conduct and conclusion. Access to this site is available to anyone who registers as a user and it is the portal through which an initial proposal EOI (Expression of Interest) can be created. Correspondence for assistance or with queries can be directed to aspree.ams@monash.edu.

Applicant: The person or persons applying for access to data, samples, analyses or is applying with a sub-study or data linkage proposal.

ASPREE Biospecimen Access Committee (or Biospecimen Access Committee): A committee consisting of representatives from the organizations responsible for funding and establishing the ASPREE Healthy Ageing Biobank and the ACES sub-study. This committee is responsible for reviewing requests for access to samples and then providing a recommendation about the access request to the ASPREE Governance Board and ISC if required. Investigators with specific content expertise may be seconded to the Biospecimen Access Committee, as needed.

ASPREE Cancer Endpoints Study (ACES): ACES focuses on cancer-related aspects of ASPREE, including the collection of additional cancer-related data and biospecimens. Through ACES, additional baseline samples were collected in Australia and a sample at year 3-4 in both countries. This sub-study of ASPREE was funded by the US Government's National Cancer Institute (NCI).

ASPREE Chief Investigators: The ASPREE Chief Investigators are those individuals who were named on the original NIH Grant which funded the ASPREE Trial and who continued as CIs in the study (Richard Grimm and John McNeil the Principal Investigators, and others listed alphabetically; Anne Murray [who succeeds Richard Grimm], Mark Nelson, Anne Newman, Christopher Reid, Raj Shah, Elsdon Storey, Andrew Tonkin, Jeff Williamson, Rory Wolfe and Robyn Woods).

ASPREE Clinical Trial (Principal Study): ASPirin in Reducing Events in the Elderly (ASPREE) was a double-blind, RCT of low dose (100mg) aspirin vs placebo in 19,000 healthy older people in

Australia (age 70+ yr) and the USA (age 65+ yr minority, others 70+ yr) to determine the treatment benefit *versus* risk over a 5-year period. The primary outcome was disability-free survival, using a composite primary endpoint of death, dementia and persistent physical disability.

ASPREE Healthy Ageing Biobank (or ASPREE Biobank): A biorepository of all samples collected in Australia from ASPREE participants in the first year of the ASPREE clinical trial (baseline) and third year. The Biobank is one of the sub-studies of ASPREE and was funded by the Australian Government's CSIRO (Commonwealth Scientific and Industrial Research Organisation).

ASPREE Governance Board: The ASPREE investigators who are responsible for the overall direction of the ongoing study, relating to study progress and financial management of the study in both countries.

ASPREE International Steering Committee (ISC): The committee responsible for the overall management and conduct of ASPREE and ASPREE-XT, overseeing protocol implementation and adherence, recruitment progress and approval of new sub-studies or manuscripts.

ASPREE Principal Investigators: Professor John McNeil and Professor Anne Murray (previously Professor Richard Grimm) are the Co-Principal Investigators of ASPREE in Australia and the USA, respectively.

ASPREE-XT Principal Investigators: Professor Andy Chan, Professor John McNeil, and Professor Anne Murray were the original Principal Investigators on the U19 funding award from NIA for the ASPREE-XT study and subsequently Professor Danny Liew has been added as a Principal Investigator.

ASPREE Publications, Presentations and Ancillary (PPA) Studies Committee: This committee was a sub-committee of the ISC. The PPA previously reviewed all publications and presentations that arose from the principal ASPREE study. This committee also reviewed proposals for new sub-studies in ASPREE, and any publications or presentations that may result from these sub-studies. The PPA Committee's role was finalised in 2019.

ASPREE Safe Haven: The ASPREE data facility containing the ASPREE data and sub-study data

ASPREE Sub-study: An additional research activity that addresses a scientific question relevant to the ASPREE Clinical Trial. A sub-study of ASPREE is a research project that may require access to data or records from the ASPREE Clinical Trial and/or may also involve collection of additional data, specimens, or records from participants enrolled in the principal study. Funding for sub-studies is not provided from the main ASPREE budget, but from outside sources, via grants and awards.

ASPREE Sub-study Committee: The investigators managing an ASPREE Sub-study. The principal investigator will also be involved in the review of any requests for data relating to that sub-study.

ASPREE Sub-study Investigator: An investigator named on the grant and/or protocol and/or an ethics submission for an ASPREE Sub-study.

Data Analysis Handbook: A document containing all the relevant information to handle and analyse data. This includes links to the ASPREE and ASPREE-XT study protocols, the data dictionary, data quality, sample data recording sheets, and a list of approved sub-studies. Applicants will be given login details to the AMS to view the Data Analysis Handbook, once their Expression of Interest is approved, or earlier at the discretion of the ASPREE-XT Principal Investigators or their nominee.

Detailed Application: A detailed online description of a proposed ASPREE sub-study or new data collection. The Detailed Application requires background, aims, hypotheses, methods, analysis plan, sample requests, and a brief description of proposed collaborators. All Detailed Applications are reviewed by the ASPREE Governance Board for new sub-studies.

Expression of Interest (EOI): An abbreviated, online description of a proposed ASPREE or ASPREE-XT project, ASPREE or ASPREE-XT sub-study. The Expression of Interest requires a brief rationale, project aims, methods and a list of Investigators. All EOIs are reviewed by the ASPREE-XT Principal Investigators and, as required, the Biospecimen Access Committee and ASPREE Governance Board.

DOCUMENTATION

Study Protocols and key study documents can be accessed in the following locations:

a. ASPREE Study Protocol: Australia

   https://aspree.org/aus/wp-content/uploads/sites/2/2014/04/ASPREE-Protocol-AUS-Version-9-Nov-2014-Monash-approved.pdf

b. ASPREE Study Protocol: USA

   https://aspree.org/usa/wp-content/uploads/sites/3/2014/04/ASPREE-Protocol-Version-9_-Nov2014_FINAL.pdf

c. ASPREE-XT Study Protocol: www.aspree.org

d. ASPREE Clinical Trial registration:

   https://clinicaltrials.gov/ct2/show/NCT01038583

e. ASPREE and ASPREE-XT Study Details

   www.aspree.org

f. ASPREE Study Expression of Interest Memorandum of Understanding

   https://ams.aspree.org/

g. ASPREE Data Dictionary: https://ams.aspree.org/

h. ASPREE Data Analysis Handbook: available to registered applicants

   https://ams.aspree.org/

i. ASPREE Data Use Policy
   https://ams.aspree.org/

APPLICATION AND APPROVAL PROCESS

Project Applications

The stages of ASPREE project applications and approvals are outlined in Figures 1-3 below. The following project types are considered:

1. Data access: analysis of existing ASPREE or ASPREE sub-study data
2. Biospecimen access
3. Sub-study: New data collection/ generation or linkage in which ASPREE receives new data

The steps of User creation, Project Creation and Expression of Interest submission outlined below are relevant to all applications. If the application is for a new data collection, then after an initial EOI outlining the concept of the collection is approved more detail is required in a Detailed Application (step 4).

An online process is used for the efficient and systematic appraisal of all new applications to utilize ASPREE data. Preliminary discussions are welcomed by the ASPREE clinical trial Principal Investigators or their nominees directly or via email to aspree.ams@monash.edu. Applications are submitted and tracked through the online application website https://ams.aspree.org/ .

The ASPREE Governance Board will determine whether:

a. the proposal represents a desirable and appropriate use of ASPREE or ASPREE-XT data;
b. the proposal is feasible in terms of resource requirement, ethical constraints and administrative burden;
c. the proposal duplicates any already-approved work of other investigators;
d. it would be appropriate to involve specific ASPREE or ASPREE-XT investigators in the proposal.

Step 1: AMS User Registration

All applicants must initially be registered users of the ASPREE Access Management Website.

To self-register, enter the website https://ams.aspree.org/ and complete the contact and research affiliation details. Registered users will be provided with a login and password to the ASPREE AMS website to complete their application(s) online.

Step 2: AMS Project Creation (see Appendix 1)

New projects are created in the ASPREE Access Management System (AMS) https://ams.aspree.org/ by the applicant (see example Appendix 1a).

Applicants should be alert to the initial selection of 'project type' when creating a new EOI as this will drive the application to different review processes. Applicants are advised to carefully select one of the three project types: (1. Data access: analysis of existing ASPREE or ASPREE sub-study data, 2. Biospecimen access, or 3. Sub-study: New data collection/ generation or linkage in which ASPREE receives new data). A matrix to guide selection is provided in Figure 4.

Projects can be discussed by forwarding correspondence to aspree.ams@monash.edu. The proposal outline may be forwarded to the relevant Principal Investigators (see a-c below) for preliminary discussion of suitability.

a. US PIs and investigators: Anne Murray and Andy Chan (or nominees)
b. Australian PIs and investigators: John McNeil and Danny Liew (or nominees)
c. Sub-study PIs (if proposal involves an existing sub-study)

Step 3: Expression of Interest Submission (see Appendix 1)

Expressions of interest are submitted by the applicant through the ASPREE AMS at https://ams.aspree.org. The online EOI requires a brief description of the project aims and methods, details on project funding, and a list of proposed co-investigators, nominating at least one relevant ASPREE investigator and a data analyst (see examples in the Appendix 1b-1c). A typical EOI request outlines a body of work that would form the basis of 1 or 2 manuscripts for peer-review publication.

Applicants who choose the option of 'Data access: analysis of existing ASPREE or ASPREE sub-study data' as the project type will also need to select how they would like to access data. The default option is to conduct analysis in the ASPREE Safe haven, however certain circumstances may require alternative arrangements. A matrix to guide selection is provided in Figure 5.

All applications are reviewed by the ASPREE-XT Principal Investigators. An EOI review is expected to take less than 2 weeks, although may be longer if biospecimen access is requested, and depending on the outcome of review and meeting cycles. Sub-study data availability varies among the numerous sub-studies and it is best to discuss the timing of data availability with the relevant sub-study PIs before submitting an application.

The status and progress of an application can be determined at any time after project creation by logging into the AMS website. A workflow of approval steps for each of the three different project types can be found in Figures 1-3.

Step 4: Detailed Applications (see Appendix 2)

Applications which propose a new ASPREE or ASPREE-XT data collection (project type "Sub-study: New data collection/ generation or linkage in which ASPREE receives new data") require more detail. A protocol, ethics approval, and ASPREE data support may be required. Funding may be required if a sub-study will involve substantial time input from ASPREE staff. A Detailed Application is submitted by the project applicant or nominee, online via the ASPREE AMS website after approval of the initial Sub-study Expression of Interest that outlined the brief concept of the data collection. The Detailed Application is reviewed by the ASPREE Governance Board's Sub-study review panel. Consultation with other committees may be required. Detailed Applications are also submitted to the International Steering Committee where additional considerations related to participant or study burden, suitability of the proposal to the ASPREE or ASPREE-XT participant population may be reviewed.

The **timeline** for the Detailed Application reviews may take 1-2 months depending on meeting cycles, the number of committees involved, and any revisions that need to be considered.

Detailed Application review principles:

(1) The purpose of the Detailed Application review is to:

- Consider further the issues referred to in the proposal;
- Ensure that the governance requirements are adhered to (*e.g.*, appropriate authorisations sought);
- Assess the scientific merit of the proposal and make suggestions about possible improvements;
- Ensure that the resources of the ASPREE study are used wisely and effectively, and has gained appropriate ethics support;
- Ensure there is no duplication of effort;
- Ensure that there is recognition of effort and involvement amongst the ASPREE investigators and other significant contributors. This may involve a request for specific ASPREE investigators to be a part of the application.
- Protect the pre-defined research interests and questions of the ASPREE Investigators (Appendix 4) to ensure they have a preserved opportunity to analyse

data and publish, based on these interests. This will be with due consideration of the data sharing policy or other requirements of the funding agencies (NIA, NCI and NHMRC).

(2) If access to bio-specimens or sub-study data is sought, the relevant committee must approve access. The terms of conditions for such access may contribute to a Collaboration Agreement, both of which are tailored to the specific project and require legal support outside the AMS.

(3) A Resource or Data Use Agreement and, if required, a Material Transfer Agreement may need to be completed if resources, data or samples need to be transferred.

(4) Evidence of ethics approval (and funding for the project) is submitted in the Detailed Application.

Applicants may track the progress of their project's Detailed Application, via the ASPREE AMS website.

Stages from Approval to Implementation

Stage 1: ASPREE Project Approval

Approval is notified to an applicant by correspondence.

The central collation point of all signed approval documentation is the ASPREE National Coordinating Centre (Monash University).

Stage 2: Project is implemented and conducted in a secure data environment

The project may proceed after all the approvals have been obtained and a project is activated. Access to data is provided in the ASPREE secure Safe Haven environment. Guidance to the Safe Haven is provided to approved applicants. Any new data or derived variables generated by sub-studies must be fed back to the ASPREE data centre.

Stage 3: Manuscript drafts, Presentations, Abstracts and Publications

Notification of progress, and/or conclusion of a project is the obligation of the applicant at six monthly reviews. Manuscripts, abstracts, reports or public presentations are welcomed as part of the review process. Authors are expected to adhere to the ICMJE guidelines. Please also refer to Appendix 6 and 7.

Figure 1. Approval Process for ASPREE or ASPREE-XT Data Analysis Projects in Safe Haven

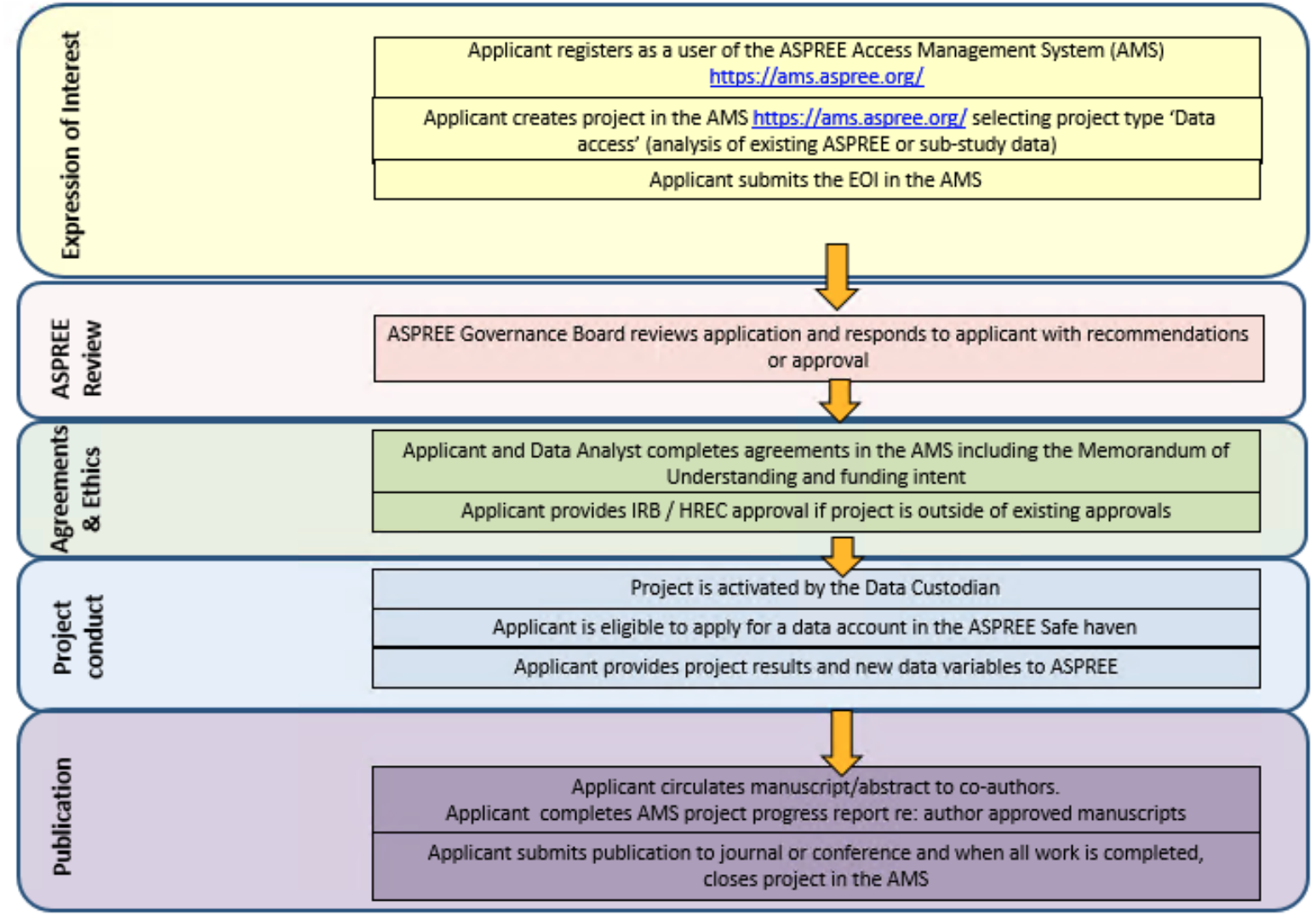


Figure 2. Approval Process for ASPREE or ASPREE-XT Biospecimen Access Projects

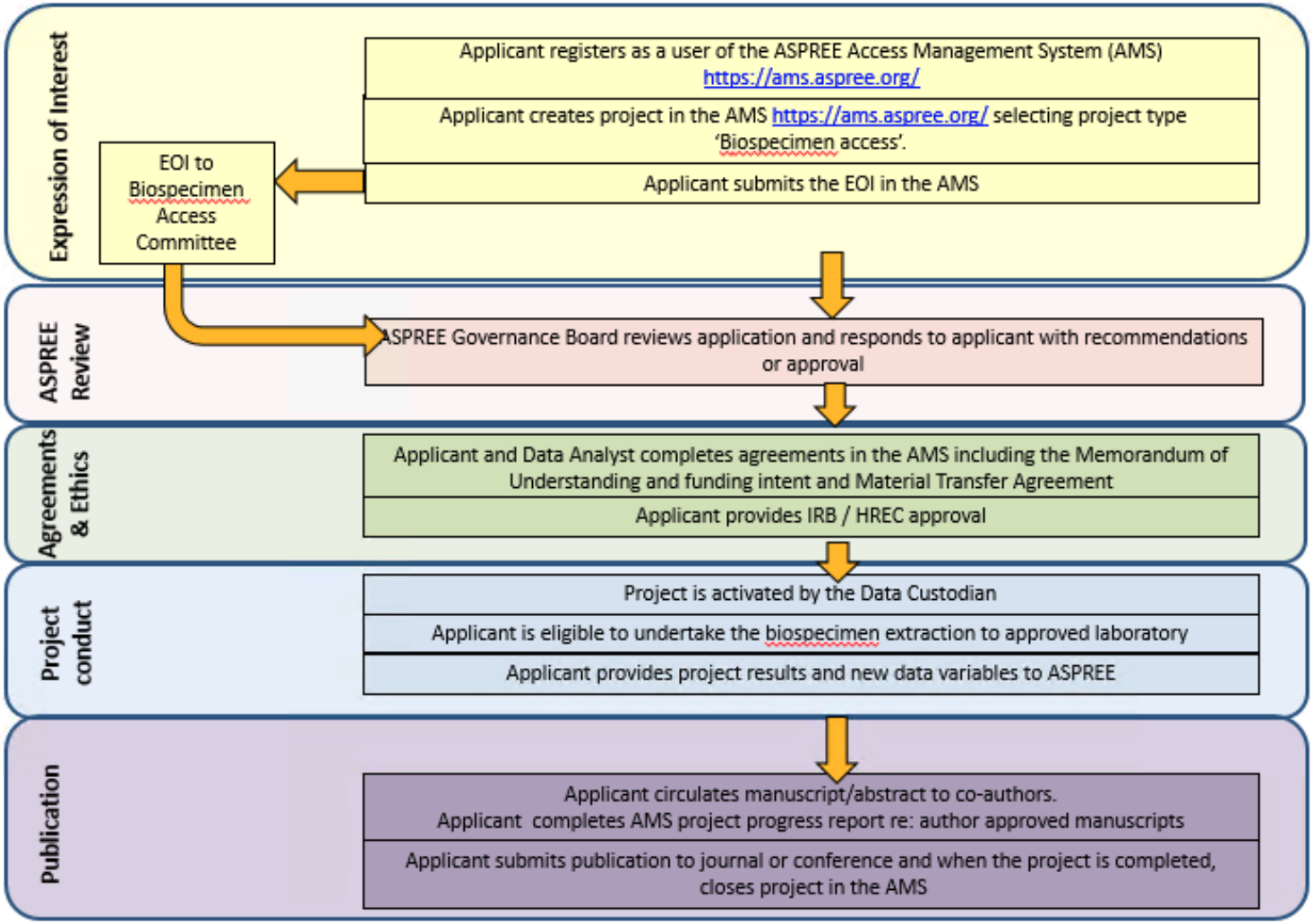


Figure 3. Approval Process for ASPREE or ASPREE-XT Sub-study Projects (new data collection/generation, or linkage in which ASPREE receives new data)

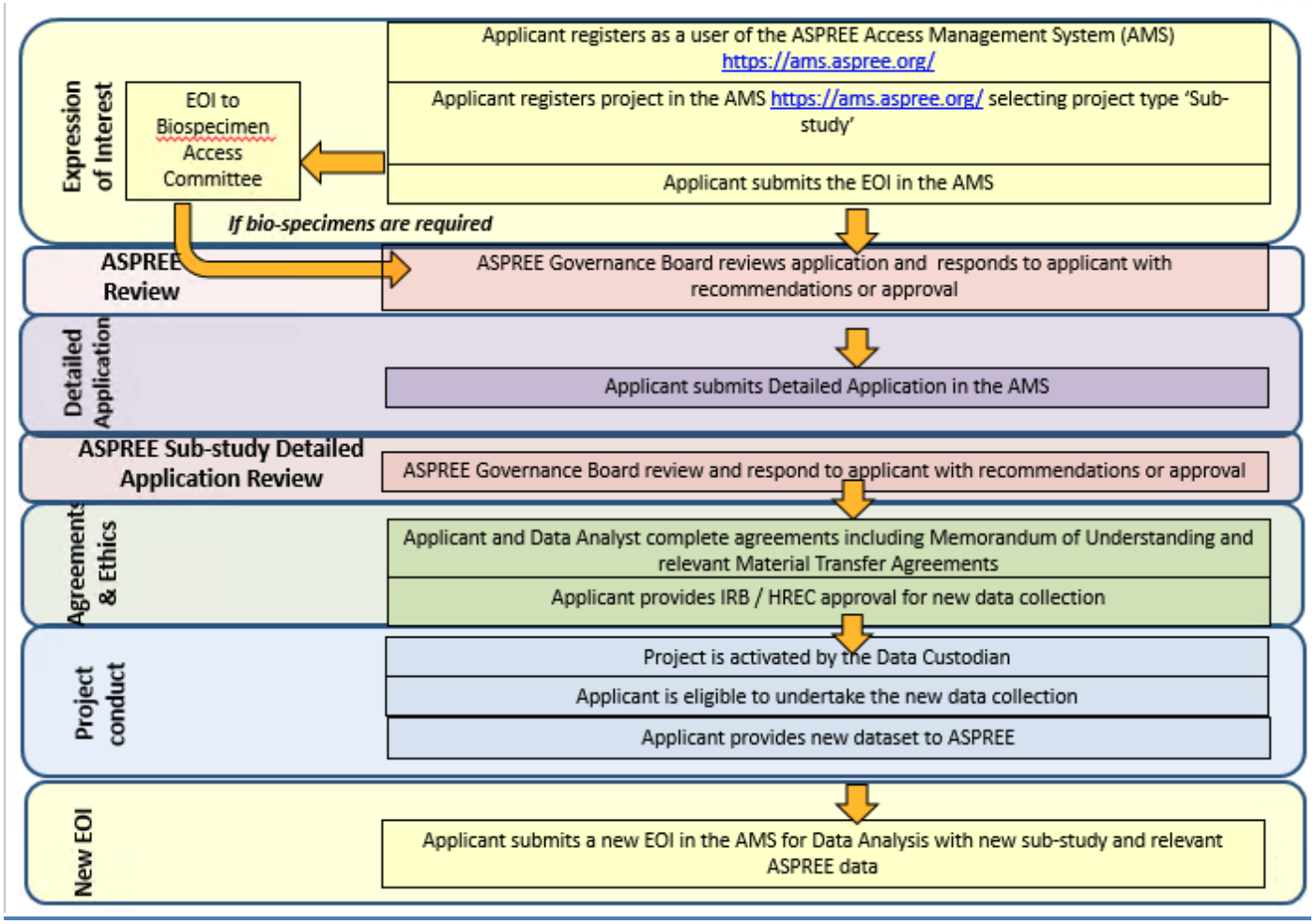
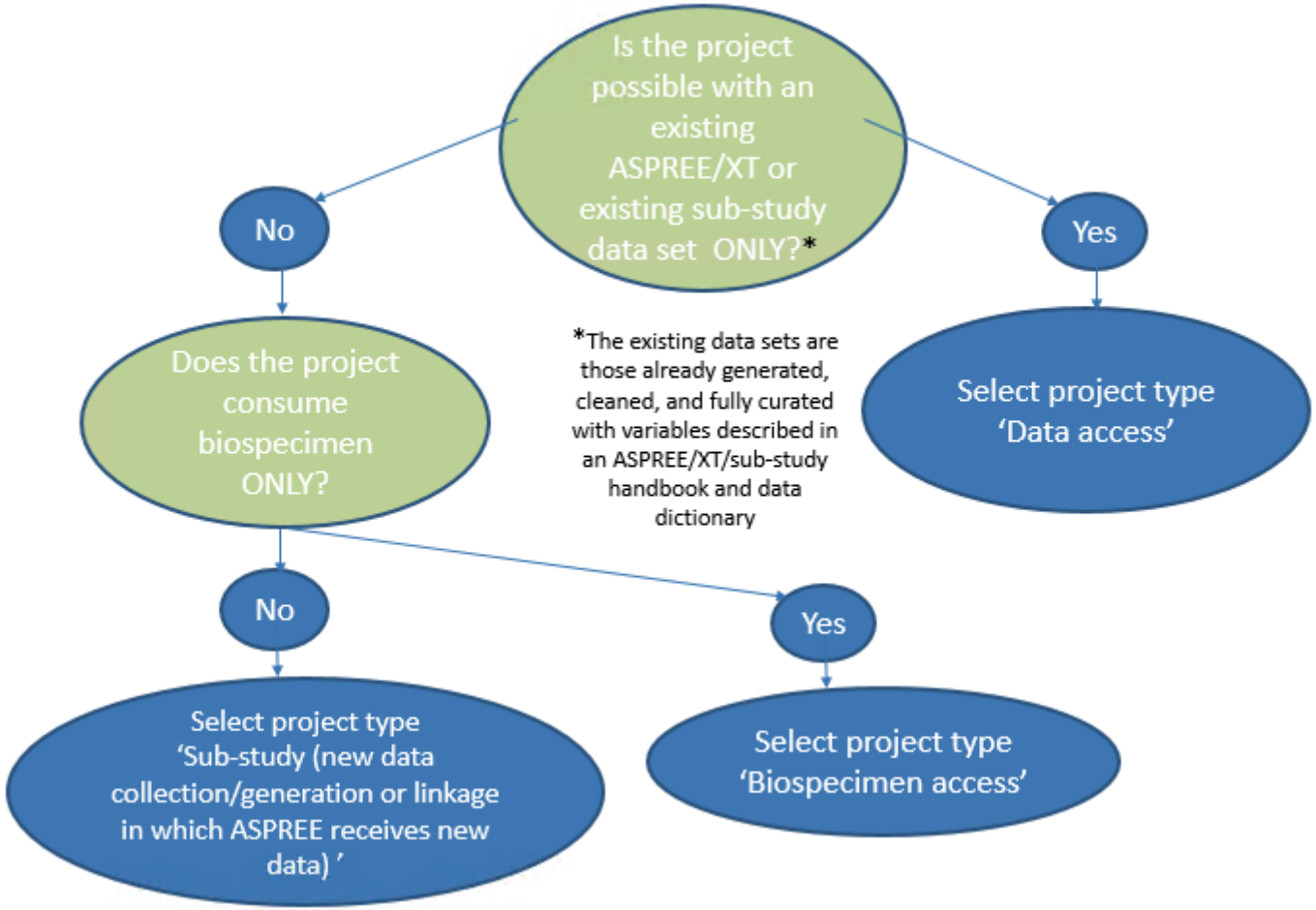


Figure 4. Selecting ASPREE Project Type when Creating a New Project



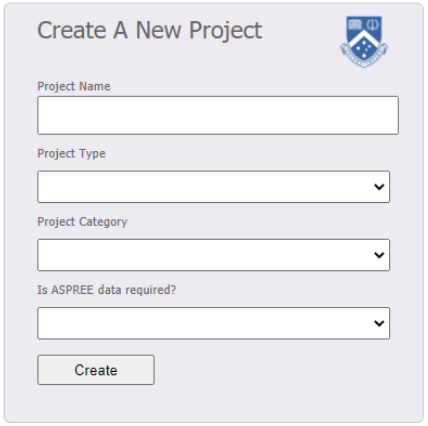
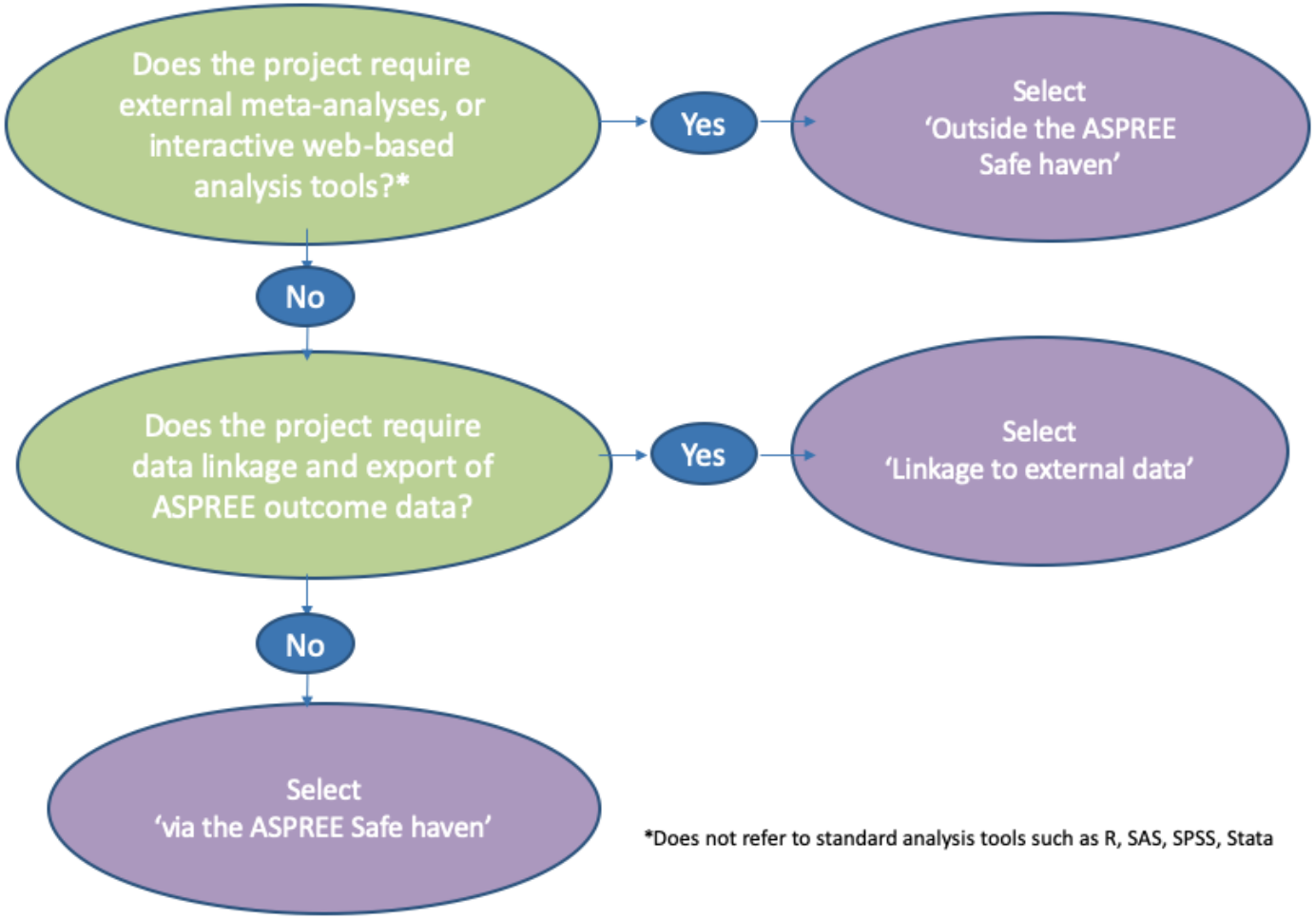


Figure 5. Selecting How You Would Like to Access Data



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McNeil JJ, Woods RL, Nelson MR, Murray AM, Reid CM, Kirpach B, Storey E, Shah RC, Wolfe RS, Tonkin AM, Newman AB, Williamson JD, Lockery JE, Margolis KL, Ernst ME, Abhayaratna WP, Stocks N, Fitzgerald SM, Trevaks RE, Orchard SG, Beilin LJ, Donnan GA, Gibbs P, Johnston CI, Grimm RH, ASPREE Investigator Group, Baseline characteristics of participants in the ASPREE(ASPirin in Reducing Events in the Elderly) study. J Gerontol A Biol Sci Med Sci. 2017 Oct 12;72(11):1586-1593. doi: 10.1093/gerona/glw342

McNeil JJ*, Woods RL*, Nelson MR, Reid CM, Kirpach B, Wolfe R, Storey E, Shah RC, Lockery JE, Tonkin AM, Newman AB, Williamson JD, Margolis KL, Ernst ME, Abhayaratna WP, Stocks N, Fitzgerald SM, Orchard SG, Trevaks RE, Beilin LJ, Donnan GA, Gibbs P, Johnston CI, Ryan J, Radziszewska B, Grimm R & Murray AM, on behalf of the ASPREE Investigator Group (* joint first authors). Effect of aspirin on disability-free survival in the healthy elderly. New England Journal of Medicine, 2018, 379:1499-1508. doi: 10.1056/nejmoa1800722

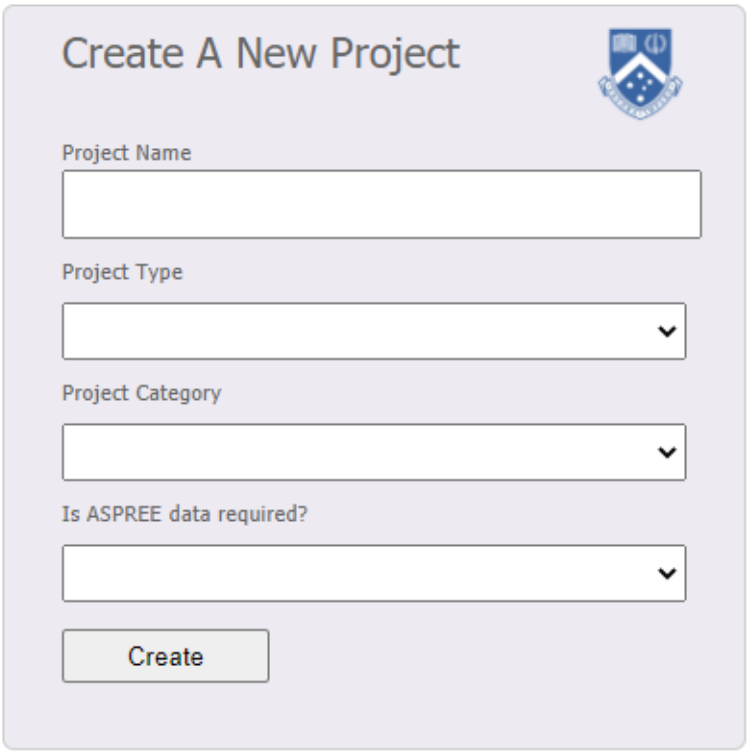
McNeil JJ*, Nelson MR*, Woods RL, Lockery JE, Wolfe R, Reid CM, Kirpach B, Shah RC, Ives DG, Storey E, Ryan J, Tonkin AM, Newman AB, Williamson JD, Margolis KL, Ernst ME, Abhayaratna WP, Stocks N, Fitzgerald SM, Orchard SG, Trevaks RE, Beilin LJ, Donnan GA, Gibbs P, Johnston CI, Radziszewska B, Grimm R & Murray AM, on behalf of the ASPREE Investigator Group (* joint first authors). Effect of aspirin on all-cause mortality in the healthy elderly. New England Journal of Medicine, 2018, 379:1499-1508. doi: 10.1056/NEJMoa1803955

McNeil JJ, Wolfe R, Woods RL, Tonkin AM, Donnan GA, Nelson MR, Reid CM, Lockery JE, Kirpach B, Storey E, Shah RC, Williamson JD, Margolis KL, Ernst ME, Abhayaratna WP, Stocks N, Fitzgerald SM, Orchard SG, Trevaks RE, Beilin LJ, Johnston CI, Ryan J, Radziszewska B, Jelinek M, Malik M, Eaton C, Brauer D, Cloud G, Wood E, Mahady SE, Satterfield S, Grimm R & Murray AM, on behalf of the ASPREE Investigator Group. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. New England Journal of Medicine, 2018, 379:1499-1508. doi: 10.1056/nejmoa1805819

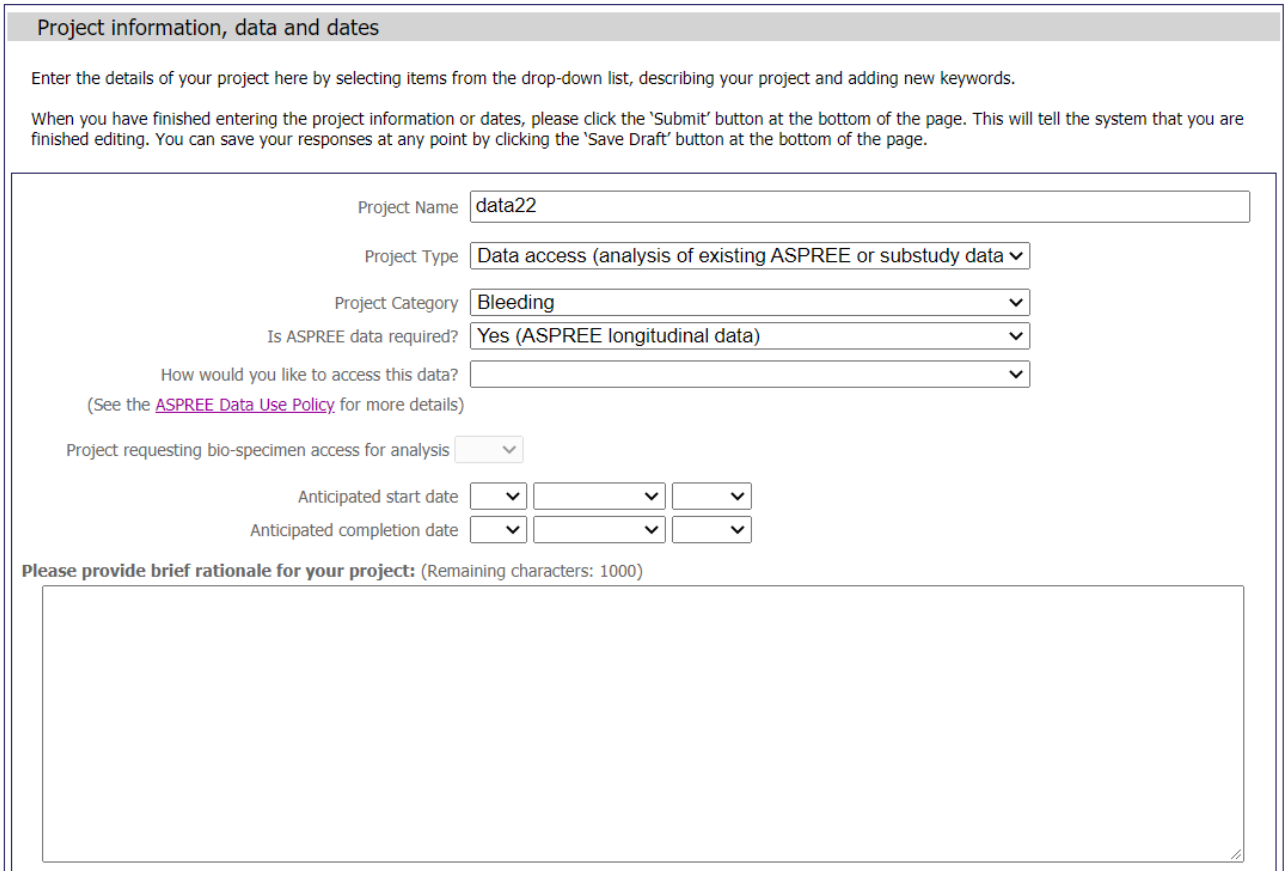
APPENDICES

Appendix 1: Expressions of Interest

Appendix 1a: Example Creating A New Project in the AMS



Appendix 1b: Example EOI for Data access: analysis of existing ASPREE or ASPREE-XT sub-study data



Project information, data and dates

Enter the details of your project here by selecting items from the drop-down list, describing your project and adding new keywords.

When you have finished entering the project information or dates, please click the 'Submit' button at the bottom of the page. This will tell the system that you are finished editing. You can save your responses at any point by clicking the 'Save Draft' button at the bottom of the page.

Project Name: data22

Project Type: Data access (analysis of existing ASPREE or substudy data

Project Category: Bleeding

Is ASPREE data required?: Yes (ASPREE longitudinal data)

How would you like to access this data?:

(See the ASPREE Data Use Policy for more details)

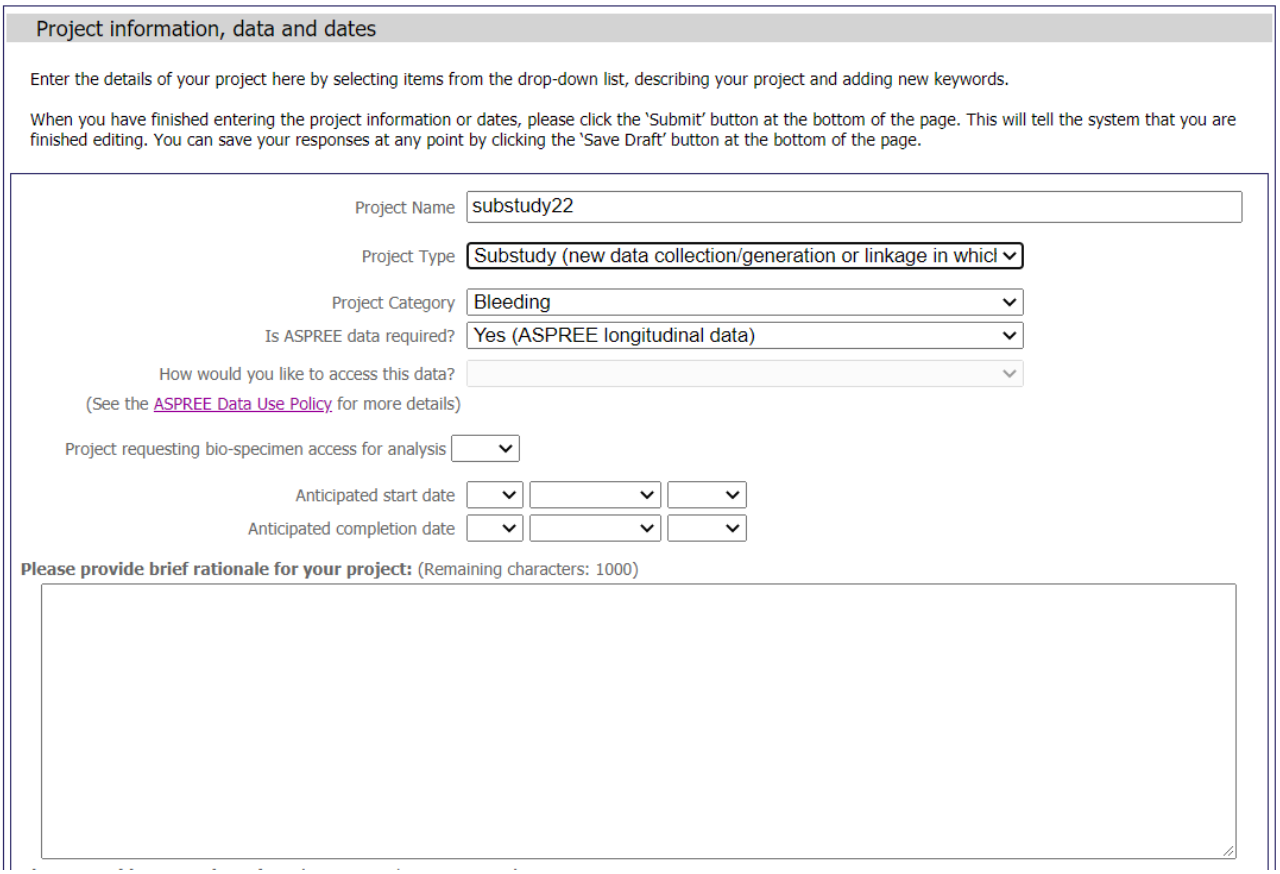
Project requesting bio-specimen access for analysis

Anticipated start date

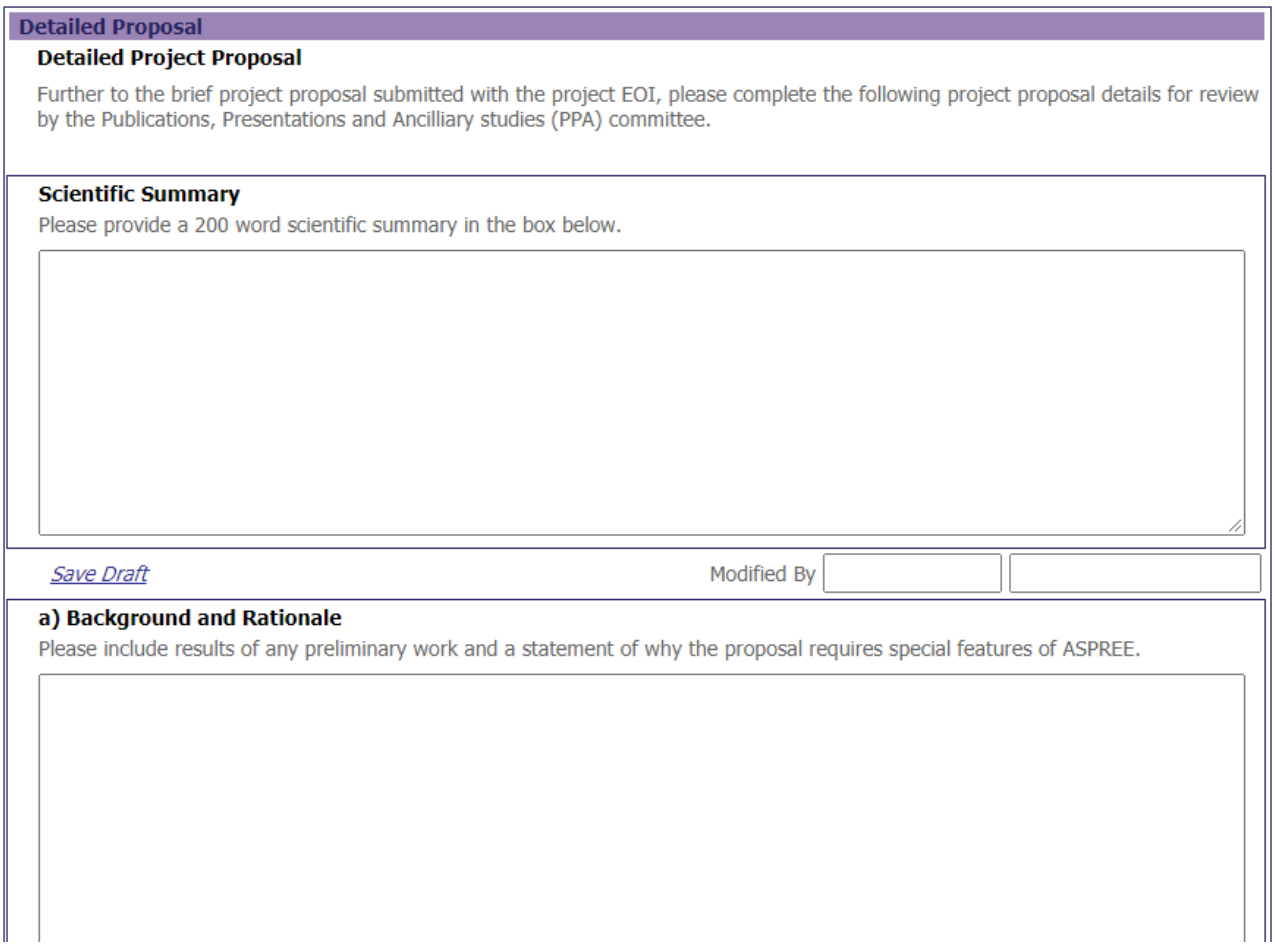
Anticipated completion date

Please provide brief rationale for your project: (Remaining characters: 1000)

Appendix 1c: Example EOI for Sub-study: New data collection/generation or linkage in which ASPREE receives new data



Appendix : Example of Detailed Application



Detailed Proposal

Detailed Project Proposal

Further to the brief project proposal submitted with the project EOI, please complete the following project proposal details for review by the Publications, Presentations and Ancilliary studies (PPA) committee.

Scientific Summary

Please provide a 200 word scientific summary in the box below.

Save Draft

Modified By

a) Background and Rationale

Please include results of any preliminary work and a statement of why the proposal requires special features of ASPREE.

Appendix 3: Existing Pre-defined Analyses

Existing pre-defined analyses are those which the ASPREE and ASPREE-XT investigators have existing rights to conduct themselves. These include:

a. The rationale, design and other details of the principal study and funded sub-studies as described in the protocols or methods papers (refer to Appendix 9);

b. The impact of aspirin therapy on disability-free survival (primary research question);

c. The impact of aspirin on pre-defined ASPREE and ASPREE-XT secondary end-points including mortality, dementia, physical disability, cognition, cancer, bleeding, cardiovascular disease and stroke, depression;

d. The impact of aspirin on conditions that are the focus of sub-studies (*e.g.* macular degeneration, brain and knee MRI changes, retinal vascular imaging, depression, hearing, infections, fractures and falls, cerebral micro-bleeds, anaemia);

e. Genetic and other biomarker predictors of heart disease, stroke, cognitive decline, cancer, renal disease, frailty, deafness, AMD, and depression. (Note: Biomarker predictors of dementia, colon cancer and obesity have been pre-specified as areas of potential interest by the Australian CSIRO which was the principal funding organisation for the Biobank);

f. The impact of changes in inflammatory markers on chronic disease incidence.

Appendix 4: ASPREE Investigator involvement in manuscripts and research proposals

a. ASPREE Executive Committee members should have the opportunity to request authorship in all ASPREE pre-defined manuscripts. The Executive members are John McNeil, Anne Murray, Robyn Woods, Brenda Kirpach, Christopher Reid and Mark Nelson.

b. ASPREE principal investigators (listed on the original NIA grant) should be authors of all of the principal study manuscripts and on primary publications related to pre-defined secondary endpoints.

c. ASPREE International Steering Committee members may be co-authors on the principal study manuscript and on publications related to pre-defined secondary endpoints in their areas of expertise.

d. ASPREE principal investigators should be offered the opportunity to be co-authors on the primary outcome manuscript for each of the sub-studies.

e. Sub-study members and members of advisory groups should be offered the opportunity to be co-authors on publications resulting from their sub-study (but not necessarily on other ASPREE manuscripts).

f. Members of Endpoint Adjudication Committees should be offered the opportunity to be co-authors on manuscripts arising from the areas of their adjudication.

g. ASPREE Study Staff should be co-authors in areas where they have made a significant intellectual contribution.

h. All publications will be ‘on behalf of the ASPREE investigators’ or ‘and the ASPREE investigators’ who will be listed individually on the principal study publication(s), on the ASPREE website and in any supplementary material allowed by the journal.

i. If conflicts arise, their resolution will be the responsibilities of the PIs, taking into account the views of other ASPREE Governance Board members.

Appendix 5: Student involvement in ASPREE

a. ASPREE encourages requests for use of data and publications from students and all requests will be reviewed by the processes described.

b. ASPREE data may not be used by students if the data relate to major ASPREE papers planned or in progress or if the Governance Board deems the data to be necessary for future papers authored by the ASPREE investigators and identified as core business as per Appendix 3.

Appendix 6: Writing Groups and Authorship Policy

a. Writing groups will be appointed by the ASPREE Governance Board in accordance with the following principles:

   i. The ISC listed Chief Investigators will form the nucleus of the writing groups for publications relating to the analysis of the principal study hypotheses, baseline data and methodology and the defined secondary endpoints.

   ii. Authorship on publications relating to defined secondary endpoints will be comprised of the ASPREE Executive Committee and ISC listed Chief Investigators plus members of Endpoint adjudication Committees with relevant specialty interests.

   iii. Sub-study investigators together with volunteering ASPREE Investigators will form the nucleus of the writing groups for funded sub-study manuscripts.

   iv. In other cases, the lead author may propose a writing group (which must include ASPREE investigators) and this will be put forward for endorsement by the ASPREE Governance Board.

b. Chairs of writing groups will be responsible for:

   i. Preparation of manuscript outline and assignment of tasks

   ii. Meeting agreed timelines and reporting progress to the ASPREE Governance Board

   iii. Coordinating analyses

   iv. Selection of Journal(s)

   v. Determination of authorship order

   vi. Correspondence with Journal

c. For manuscripts and abstracts in which the work reported reflects the collaborative effort of most sites and principal investigators, the author line should be followed with the phrase 'for the ASPREE Investigator group', or 'and the ASPREE Investigators' and all co-investigators will be listed as co-authors (in format defined by selected journal). It is the intent of ASPREE that all individuals who have worked in the design and conduct of the study to claim authorship credit for such papers.

d. Manuscripts will be required to include a standard funding acknowledgement statement that is consistent across manuscripts for the Principal ASPREE Clinical Trial and any relevant sub-study funding.

e. Manuscripts must adhere strictly to international guidelines for authorship.

f. In keeping with the authorship code, consideration of all authorship and authorship positions will involve consideration of an individual's contribution to the whole project ranging from conception of the project, management of the study, preparation of operational material and procedures to analysis and presentation of results. Individuals contributing as paid staff of the project should be included as authors wherever they have made a substantial intellectual contribution.

g. If a Writing Group member does not accomplish the tasks assigned to him/her and has not contributed, he/she can be removed from the Writing Group. The Lead Author must send a letter to the ASPREE Governance Committee.

h. Disagreement regarding the order of authors will be resolved by the ASPREE Governance Board as necessary.

Appendix 7: Required Acknowledgements and PubMed requirements

a) The ASPREE and ASPREE-XT studies are supported by grants (U01AG029824 and U19AG062682) from the National Institute on Aging and the National Cancer Institute at the National Institutes of Health in the United States, by grants (334047 and 1127060) from the National Health and Medical Research Council of Australia, and by Monash University and the Victorian Cancer Agency.

b) With biospecimen measures, the Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO) and the US National Cancer Institute

c) Australian General practitioners listed on website (aspree.org)

d) US Study sites

e) Bayer Pharma AG for drug supply

f) Study staff

g) The NIH Public Access Policy implements Division F Section 217 of PL 111-8 (Omnibus Appropriations Act, 2009). The law states:

   The Director of the National Institutes of Health ('NIH') shall require in the current fiscal year and thereafter that all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication: Provided, that the NIH shall implement the public access policy in a manner consistent with copyright law. http://publicaccess.nih.gov/policy.htm

Appendix 8: Forms of Agreement (located on the AMS when finalised)

a. Memorandum of Understanding Agreement (for projects)

b. Data Use Agreement or Data Transfer Agreement (for data transfer)

c. Material Transfer Agreement (e.g. for sample transfer)

Once the respective Institutions have approved the Agreements, signatures will be obtained from the relevant approvers and a copy held at the ASPREE national coordinating centre

Appendix 9: Listing of funded Sub-studies

Sub-study Name	Project Summary	Participants & Location	Funding Source	Principal Investigators	Co-investigators
Biobank	A repository of blood, urine and saliva samples that will be available to researchers to investigate biomarkers associated with ageing disease and aspirin use.	AUS ~12,250 baseline and 11,600 3 yr blood/urine; ~AUS 1,800saliva; US ~1,500 3-4 yr blood/urine/saliva	CSIRO, Monash, NHMRC, VCA NIH-NCI	JJ McNeil,	RL Woods, C Reid, M Nelson, W Abhayaratna, T Lockett, A Tonkin
ASPREE Cancer Endpoint Study (ACES)	An additional bank of tumour biospecimens (collected during diagnostic or treatment procedures) from ASPREE participants who develop cancer during the course of the trial.	AUS ~2500; US ~200	NIH-NCI (1R01AG029824-01A2)	A Murray, RL Woods	B Kirpach, JJ McNeil, S Schmechel, A Haydon, J Millar, S Orchard, M Dumas, C Maclean
ENVIS-ion	Uses MRI, retinal photography and additional cognitive tests to determine if aspirin slows age-related changes to the brain and its micro-vessels, retinal blood vessels and decline in brain function.	AUS 600	NHMRC (ID471460)	W Abhayaratna, E Storey	A Tonkin, C Reid, T Wong, RL Woods, J McNeil, A Janke, R Essex, A Kam
ALSOP	A questionnaire-based study of health, lifestyle, social and economic factors that have the potential to influence health and well-being as people age.	AUS ~14,800	Monash	JJ McNeil	S Ward, C Britt, RL Woods, A Owen, L Beilin
SNORE-ASA	Explores if aspirin can slow any effects of sleep apnoea on brain function using a home sleep study device and additional cognitive tests. For some participants MRI and retinal photography will also study the health of brain micro-vessels.	AUS 1500	NHMRC (ID1028368)	E Storey, S Ward	G Hamilton, M Naughton, RL Woods, F O'Donoghue, A Janke, R Wolfe, R Kawasaki, C Reid
ASPREE - AMD	Explores if aspirin can prevent the onset or slow the progression of age-related macular degeneration (AMD), the most common cause of vision loss in older people.	AUS ~5500	NHMRC (ID1051625)	JJ McNeil	R Guymer, L Robman, RL Woods, J Falk, M Ernst, M Abramoff
ASPREE Knee	Investigates if aspirin can slow or prevent cartilage loss and subsequently, osteoarthritis using MRI of the knee.	AUS 165	Monash	A Wluka	F Ciccuttini, G Egan, RL Woods, C Ding, JJ McNeil, N Ferris, J Lockery
ASPREE Hearing	A study to determine if aspirin reduces age-related hearing	AUS ~1260	Monash	JJ McNeil, E Storey	RL Woods, H Dillon, G Rance, F Lin, C

	loss, and whether this may be due to inflammation or changes in blood flow (measured by retinal photography).				Britt, J Lowthian, S Ward, M Nelson
Antisepsis	A study to determine whether aspirin influences episodes of major sepsis requiring hospitalisation or resulting in death.	AUS ~16,500	NHMRC (ID1041986)	D Eisen	E McBryde, K Leder, D Pilcher, R Wolfe, RL Woods, J Lockery, JJ McNeil
Fractures and Falls	Explores if aspirin reduces the incidence of fractures and falls in healthy older people.	AUS ~16,500	NHMRC (ID1067242)	A Barker	JJ McNeil, S Ward, K Sanders, J Pasco, R Cumming, RL Woods, J Lockery
ASPREE-NEURO	A study to determine through MRI of the brain whether aspirin influences intracerebral microhaemorrhages and whether these predict the risk of later stroke or decline in cognition.	AUS ~560	NHMRC (ID1086188)	JJ McNeil	E Storey, S Ward, G Egan, N Ferris, R Wolfe, A Brodtman, RL Woods, P Raniga, P Yates
ASPREE-D	To determine whether low dose aspirin reduces the risk of depression in individuals aged 65 years and older	AUS & US all participants	NHMRC (ID1081901)	M Berk	JJ McNeil, MR Nelson, R Shah, RL Woods, M Mohebbi, J Lockery, E Storey, R Wolfe, SM Fitzgerald, A Murray
ASPREE-SHOW		AUS participants ~5000	NHMRC	S. Davis	S Davis, R Bell. D Handelsman, JJ McNeil, MR Nelson, RL Woods, C Reid J Lockery T Gilbert P.Robinson E Parker,
ASPREE-Genomics		AUS and US participants ~14000	Monash	JJ McNeil	P. Lacaze R Woods M Nelson C Reid A Murray
ASPREE-Gut Microbiome		AUS and US participants	Monash	A Chan	R Woods, S Orchard, Alice Owen