Contents

Revision Date: 9/30/2016

1. Overview

The Washington State Twin Registry (WSTR) is a unique scientific resource for investigators throughout the world who wish to use twin participants in research. We welcome project proposals from investigators seeking to include WSTR pairs in new (primary data collection) studies, or to use existing archived survey data, geocoded environment data, biological samples, or clinical measures in ancillary or secondary data analyses. The contact to initiate this process is the Scientific Operations Manager of the WSTR. The investigator will be expected to engage in an ongoing dialogue about the project with the Director and Assistant Director, along with any other Registry affiliated faculty who may have specific project expertise. The Registry operates as a service center, thus there are specific charges associated with the use of Registry data, as explained in more detail in item 2.3 below.

The WSTR Director and Scientific Operations Manager are responsible for the overall management of the Registry and for fiscal oversight, protection of participants' rights to privacy and confidentiality, implementation and adherence to Registry policies and procedures (this document), and logistical and scientific oversight of studies involving Registry participants. The Assistant Director works in concert with the Director and Scientific Operations Manager.

1.1. Current Registry Staff

Director, Washington State University: Dr. Glen Duncan, PhD

Assistant Director, University of Washington: Dr. Elizabeth Blue, PhD

Scientific Operations Manager, Washington State University: Ally Avery, MS

1.2. Advisory Board

The WSTR has an advisory board consisting of faculty selected by the Director and Assistant Director, and a pair of twins from the Registry. The Director and Assistant Director will review applications, reporting their decisions to an advisory board on an annual basis. If the Director and Assistant Director cannot resolve a conflict, the matter will be brought to the advisory board within 2 weeks for resolution.

1.2.1. Current Advisory Board Members

Hans P. A. Van Dongen, PhD, Research Professor and Director of the Sleep and Performance Research Center, Washington State University

Naomi Chaytor, Associate Professor, Washington State University

Paul Whitney, Professor, Washington State University

Jack Goldberg, Research Professor of Epidemiology, University of Washington

Nicholas L. Smith, PhD, Professor, University of Washington

Eric Strachan, PhD, Assistant Professor, University of Washington

Eric Turkheimer, Professor, University of Virginia

Brent Lewis and Brian Lewis, WSTR members

2. Accessing the Registry

2.1. Process for primary data collection studies

After initial consultation with the Director, Assistant Director, and any other relevant faculty / staff, the next step is to complete a research application (see Appendix A). Once the completed research application is received and subsequently reviewed, which will be no later than 2 weeks after receipt, the Director or Assistant Director will contact the investigator to schedule a meeting or teleconference for further discussion about the project with the Scientific Operations Manager. This call will help to define the role that the Registry can play in the proposed study and set up a timeline for expected project implementation and completion. If the proposed use of the Registry is contingent on funding,

the investigator will continue dialogue with Registry staff throughout the development and review phases of the proposal. If the proposal is ultimately funded, the investigative team will work in concert with Registry faculty and staff to develop plans for project implementation. Preliminary data analysis may be conducted to determine if the Registry has sufficient resources (e.g., adequate twin participants or existing data in the form of survey measures, clinical measures, and/or biologic specimens) to support the project.

Factors that are considered in reviewing the application for new primary data collection studies include:

- Scientific merit of the proposed project.
- Appropriateness and utility of enrolling WSTR twins to accomplish the scientific aims.
- Level of subject burden imposed on WSTR twins.
- Privacy implications of the project to potential participants.
- Project's contribution to a balanced research portfolio for the WSTR.
- Availability of funding and the potential of the project to generate long-term, significant federal and non-federal support for further study.

The Scientific Operations Manager will work with the investigator to develop a budget for any resources required from or work that will be done by the Registry for the project. Depending on the nature of the project and available expertise and/or time (i.e., available effort in the form of FTE), it may be appropriate to include the Director or Assistant Director as a co-Principal Investigator or co-Investigator on the grant application. The Registry Director and Scientific Operations Manager must approve the portion of the budget pertaining to twin recruitment, the study protocols and procedures in which twins will participate, and any percentage of FTE allocated to Registry staff. The Director and/or Assistant Director of the WSTR will furnish a letter of support on behalf of the Registry to accompany the investigator's application to the funding agency if so desired. **As soon as an application has been submitted to a funding agency, one <u>complete</u> PDF copy of the application, including budget pages and budget justification, must be forwarded to the Scientific Operations Manager for filing.**

Prior to study implementation, the Principal Investigator of each approved research application must sign the WSTR usage agreement (see Appendix B).

Although funding is uncertain, planning for implementation of the study prior to a funding decision will ensure that if the study is ultimately funded, work can begin right away once the necessary Institutional Review Board (IRB) approvals are obtained from the investigator's institution and funds are released from the funding agency. Thus, based on the likelihood of successful funding, it may be advantageous for investigators to engage with Registry staff to plan the study and seek necessary approvals ahead of time.

2.2. Process for ancillary and secondary data analysis studies

Similar to 2.1 above, after initial consultation with the Director, Assistant Director, and any other relevant faculty/staff, the next step is to complete a research application (see Appendix A). Once the completed research application is received and subsequently reviewed and approved, which will be no later than 2 weeks after receipt, the Director or Assistant Director will contact the investigator to schedule a meeting or teleconference for further discussion about the project with the Scientific Operations Manager. This call will help to define the role that the Registry can play in the proposed study and set up a timeline for expected project implementation and completion. Once again, the Principal Investigator must sign a WSTR usage agreement (see Appendix B) prior to study implementation. Personal identifying information of WSTR members is not shared directly with investigators for sample-only (i.e., ancillary studies) or data analysis-only (i.e., secondary data analysis) research. If the data analysis is of benefit to the Registry, and if no IRB modifications are required, the dataset can be created in a relatively short amount of time. The Scientific Operations Manager will work with the investigator to determine which variables are needed. Finished datasets are transmitted using a secure online file sharing system. Ancillary and secondary data analysis studies go through the same review process as primary data collection studies, however, are generally much quicker. If the proposed ancillary or secondary data analysis project is contingent on grant funding, the same engagement process as described in item 2.1 above applies.

2.3. Administrative access fees

The WSTR is administratively housed at Washington State University. In addition to the significant costs associated with Registry recruitment and maintenance, requests from investigators and institutions require Registry resources and staff time. For this reason, the WSTR charges fees to all investigators who use the Registry. These access fees cover the administrative costs incurred in support of the project, as well as recurring costs of Registry operations. Without these fees, the resources that enable investigators to access the Registry would not be available.

Fees are charged to a WSU service center budget; rates are reviewed and approved annually by WSU General Accounting. A complete listing of current WSTR fees is presented in Appendix C.

Access fees are subject to change. When a research project is funded, fees will be charged as services are provided. This approach ensures the accuracy of cost accounting practices. Payments will be deposited in the WSTR service center account, which is managed by the Registry for the sole purpose of Registry operations.

Investigators are responsible for all study-specific costs. These costs include, but are not limited to, the support of study-specific research personnel for recruitment, data collection, and data analysis, as well as study-specific recruitment costs such as supplies and equipment.

2.4. Budgets for WSU investigators

Investigators who are affiliated with WSU will be required to submit a sub-budget that will be managed by IREACH, the administrative unit of the WSTR, for costs such as FTE, data access, study materials, and F&A.

2.5. Budgets for non-WSU Investigators

Investigators who are not affiliated with WSU have two options for study specific costs. If the investigator would prefer to have the WSTR manage the budget, they will be required to issue a subcontract to the WSTR for costs such as FTE, data access fees, study materials, and F&A. Alternatively, the investigator can be billed by the WSTR for all study-specific costs. No revenue will be generated from this method, and all study-specific costs will be billed to the investigator “at cost.” A listing of study-specific costs is presented in Appendix C.

3. Safeguarding Data

Because the Registry’s existence relies on the continued participation of member twins, we are vigilant in our protection of participants’ rights to privacy and the confidentiality of their data.

All WSTR personnel have signed confidentiality agreements to ensure that they are compliant with Washington State privacy laws. **All** study personnel that will be associated with an approved WSTR study must sign a confidentiality agreement (Appendix D) and be compliant with Washington State privacy laws. **Access to WSTR data is restricted to individuals who have a signed access agreement with the WSTR**. All investigators and their staff who work with Registry twins and with data derived from the twins are expected to observe the highest professional standards of confidentiality. If new staff members are added to the study at any point in the research, the investigator must contact the scientific operations manager as soon as possible to ensure that a signed access agreement is on file. Access agreements will be updated every two years to ensure that all study staff are aware of current Registry procedures.

All Registry data are considered privileged and confidential and cannot be shared or released without prior written approval from the WSTR Director. In some cases, the WSTR may request that the investigator obtain a Certificate of Confidentiality from the U.S. Department of Health and Human Services to provide additional protection for participant data.

Access to WSTR data or resources is granted only for the duration of the approved project. Any WSTR data made available for, or collected through, any research project is for use solely by that project. Use of data is limited to the scope of the study as it was reviewed and approved during the application process. If the scope or nature of the study changes for any reason, then the investigator

must bring this information to the attention of the scientific operations manager. Depending on the nature and extent of the changes, an amended application and review process may be required. **Furthermore, study data cannot be shared or transmitted to other investigators without prior written approval from the Director of the WSTR.** At the conclusion of the approved project period, the PI must sign a project end form (see Appendix E) stating that all data and/or resources have been destroyed at the end of the usage period.

4. Procedures for new data collection

For studies that require grant funding, upon funding, the investigator of an approved project must submit copies of the notice of grant award and any other documentation pertaining to the project before implementation.

If the study will be conducted on behalf of the investigator by WSTR staff, the Scientific Operations Manager will meet with the investigator and the study coordinator to write the human subjects application, organize study materials, and develop a plan for recruitment of subjects. If the study will be conducted outside of the WSTR, the investigator will be required to provide the Registry with all required IRB-approved documents before study implementation (see below).

4.1. Proof of Human Subject Protection Review

No research project shall be initiated without proof from the investigator that the project has received approval from the IRB at the investigator's home institution. A copy of the approval memorandum from the appropriate IRB must be submitted to the Scientific Operations Manager of the WSTR. All subsequent annual status reports must also be submitted to the Scientific Operations Manager. If any modifications are made to the research procedures or recruitment processes, updated documents must be submitted as soon as they are approved.

For studies requiring a Certificate of Confidentiality, a copy must be provided to the WSTR before study activities can begin.

4.2. Submission of Data Collection Instruments and Protocols

The investigator must provide a copy of all data collection instruments to the scientific operations manager, including supporting materials, scientific publications describing the instruments, interview scripts, and tissue collection protocols. The Registry will keep copies of all final IRB-approved materials. In addition, the Registry may ask to review data collection instruments before data collection begins. When a new project requires variables from the WSTR database, these variables must be requested and paid for before data collection begins.

4.3. Online or mailed surveys

If a proposed study will collect new data by using questionnaires that are either mailed or emailed to Registry participants, Registry staff will send the survey to eligible twin pairs on behalf of the investigator after appropriate human subjects approvals have been obtained. To ensure consistency and data integrity, the Registry will develop the questionnaire, collect and store the data, and send the investigators a dataset with unique, study-specific identifiers once data collection has been completed.

4.4. In-person collection

Registry personnel (defined as Scientific Operations Manager or personnel who are directly and solely under the supervision of the Scientific Operations Manager) will contact Registry members on behalf of the investigators. "Supervision" in this case refers to oversight of all Registry-related activities and not necessarily supervision for payroll or other human resources purposes. For clinical protocols that require direct interaction of Registry twins with investigators and/or their coordinator, Registry staff will make the initial contact on behalf of the investigators with the twins of interest, and if necessary, screen them for the study. Once eligible pairs have been identified by Registry staff, contact information will be released to the investigator and/or their study coordinator for subsequent scheduling of clinical examinations or study procedures.

In cases of potential unethical practices by an investigator, the WSTR will contact the appropriate authorities (e.g., IRB officials) to request an inquiry that could result in halting that investigator's study. If unethical practices are verified, the WSTR will deny the investigator further access to the Registry. Complaints of unethical practices by WSTR personnel will also be reported to the IRB and appropriate action will be taken.

4.4.1. WSTR Member Participation

The WSTR normally has several studies in the field at any given time. These vary in size, scope, and duration. The Registry will make every effort to minimize the burden and effort of participation in studies by registered twins. We recognize that study procedures may sometimes overlap across multiple investigators, which could increase participant burden. However, if concurrent studies pose a minimal perceived burden of participation, at the discretion of the WSTR staff, such studies may be allowed to coordinate their recruitment and data collection efforts by contacting twins simultaneously for multiple studies.

4.4.2. Notification of Updated Contact Information

The WSTR has sole responsibility for maintaining contact with all Registry members. If the study coordinator requires updated contact information (addresses or telephone numbers), the Scientific Operations Manager will provide this information if and when it becomes available. **If investigators become aware of new contact information for Registry members during the course of a study, this information must be reported to the Scientific Operations Manager.**

4.4.3. Notification of Twin Request to Withdraw

Investigators must notify the Scientific Operations Manager within three working days if a Registry twin expresses a desire to withdraw from a specific study and/or the WSTR. If a Registry twin contacts the Scientific Operations Manager before the study team, the Scientific Operations Manager will share this information with the study coordinator. The Registry twin and their co-twin must be removed from the recruitment list and have their contact information destroyed or anonymized.

4.4.4. Notification of Deviation from Protocol or Unanticipated Risks to Subjects

Investigators are required to make an immediate report to the Scientific Operations Manager if any deviation from the approved research protocol occurs during the conduct of the study, whether unintentional or motivated by unforeseen circumstances. Similarly, any discovery of adverse events or unanticipated risks to twins must be reported immediately.

5. Annual Status Reporting

Investigators must submit an annual status report that summarizes project activities over the past project year. If the project in question is funded by a grant, the investigators can simply send the same report to the WSTR that they send to their funding agency (e.g., an NIH eSNAP report), because in most cases the same information will be required. Because projects have different start dates and may be linked to reporting periods established by funding agencies, WSTR staff will establish a unique due date for the annual report for each project. This report should include, but is not limited to, the following information:

- Progress in relation to original project time line.
- Number of twins participating in the study.
- All copies of renewed IRB applications (status reports) and/or modifications, including all changes in the team of investigators and study personnel.
- Data management and data cleaning procedures.
- List of professional presentations, peer-reviewed publications, and manuscripts in preparation for peer review that arise from the project.

- Problems or difficulties, including any variations from the researcher agreement or from the WSTR protocol outlined in these guidelines, along with solutions to problems.

It is the responsibility of the Principal Investigator or Project Lead to submit this annual report to the WSTR on the due date established at the initiation of the study.

6. Post-data collection procedures

6.1. Personal Identifiers

At the end of data collection or grant funding for the project, whichever occurs earlier, names and identifying information of all WSTR members must be obliterated and files must be destroyed. These measures are required so that the WSTR can maintain its promise to its members that all possible steps are taken to protect the confidentiality of their identities and their data.

6.2. Completed Datasets

At the termination of data collection, a complete electronic copy of all study data must be transmitted back to the WSTR. These data files must contain sufficient documentation to enable their incorporation into the Registry database for future use. Data elements include, but are not limited to, primary variables, computed variables, data dictionaries, and scoring algorithms.

6.3. Biological Samples

All unused biological samples must be destroyed at the end of data collection. Under no circumstances will investigators be allowed to retain any amount of biological specimens (e.g., aliquot of blood) for any future analyses.

6.4. Additional Data

It is common for projects to need data from the WSTR to augment study-specific data; we provide these data to investigators for the purposes outlined in the specific aims of their approved projects. Investigators must obtain approval from the WSTR to use Registry data for analyses that differ from those specified in the original study protocol. A cost is associated with providing additional WSTR variables, as outlined in the cost center rate schedule in Appendix C.

6.5. Exclusivity Period

Investigators have exclusive use of data and biological samples collected as part of an individual approved project for **three years** after the conclusion of the first project period. At the end of the three-year period, data collected from such projects will be merged into the general WSTR database for WSTR staff and approved collaborators to use. After the three-year period, investigators retain the right to analyze the data collected as part of their research to the extent that their analyses are encompassed by the aims of the original study protocol. All obligations to the WSTR for data integrity, reporting, and manuscript review continue to apply to investigators after the three-year period ends.

7. Publications

7.1. WSTR Authorship Policy

The WSTR has established an authorship policy to 1) facilitate collaborations among Registry faculty, 2) facilitate collaborations between Registry faculty and outside researchers, and 3) prevent authorship disputes to the extent possible. The Registry has adopted the authorship guidelines established by the International Committee of Medical Journal Editors, which stipulate the following conditions:

- Making substantial contributions to the conception and design of the study, or the acquisition of study data, or the analysis and interpretation of study data.

- Drafting the manuscript critically or revising it for important intellectual content.
- Providing final approval of the version of the manuscript to be published.

All authors should meet all three conditions. In addition, all authors should be able to take public responsibility for their contribution to the work. Given these stipulations, WSTR staff or other investigators affiliated with the Registry will sometimes meet the requirements for authorship of publications based on data collected from Registry twins, and should therefore be involved as co-authors. Examples of contributions that may qualify for authorship include refining the design of the study, identifying a specific research question, providing substantial input on the analytic plan, and writing sections of the manuscript. In other circumstances, the contribution of the WSTR may not qualify for authorship. Examples of contributions that do not qualify for authorship include providing samples or data without further involvement in refining a research question, offering technical advice, and providing general supervision of the research group. Contributions that do not qualify for authorship must nevertheless be acknowledged in the resulting publication.

We strongly recommend the establishment of a written authorship agreement in the initial stages of any manuscript collaboration, with frequent communication among all authors while the manuscript is in development.

7.2. WSTR Publications Policy

Regardless of WSTR authorship status, ALL manuscripts based on data or samples provided by the Registry must be submitted to the WSTR Director before submission for publication. Manuscripts must be submitted along with all primary and computed variables that appear in the analysis. The WSTR Director will review each manuscript and grant or deny approval within two weeks of receiving it. On a yearly basis, investigators who use WSTR data or samples must also provide copies of abstracts presented at conferences and reprints of articles published. The WSTR may also ask investigators to furnish brief summaries of the status of their projects, suitable for publication in the Registry newsletter or on the Registry website.

7.3. Acknowledgment

All manuscripts, presentations, and other publications must acknowledge the use and support of the WSTR, including the grant or project number of any mechanism that provided financial support. We recommend the following language for the acknowledgement statement: “This project was conducted, in part, with support from the Washington State Twin Registry. We wish to thank the twins for taking part in the Registry.”