Sex as a Biological Variable (SABV) Primer Course Instructor Guide

Introduction

Welcome to the Sex as a Biological Variable (SABV) Primer course Instructor Guide!

This document serves as a resource for guided discussions of central tenets of the Sex as a Biological Variable (SABV) Primer online course. The instructor guide is not a replacement for the course but instead, when used with live instruction, will enhance learning and appreciation of key concepts underlying the SABV Policy and the application of SABV to the science, as presented in the online course. A bibliography of SABV Primer course materials is also provided in Appendix A.

Guide Structure and Use

For each module of the SABV Primer the instructor guide provides the following four sections:

1. learning objectives;
2. critical concepts and key definitions;
3. key literature; and
4. guided discussion topics.

The learning objectives are repeated from the online course at the beginning of each module. The critical concepts and key definitions are provided as a reference and for review without having to navigate through the online course material. Three to four papers are identified in the key literature sections of the guide, which could be reviewed before embarking on the guided discussions. Doing so may be helpful in exploring the content covered in the discussions. The guided discussion topics make up the core of the instructor guide. Three or four discussion topics are identified in each of the four modules. Within each topic, questions are provided which will help stimulate engagement and further interaction with material covered in the course.

Instructors: If you teach a course on SABV that makes use of the SABV Primer and this instructor guide, we would like to hear from you. Please send us your feedback in an email addressed to SABVPrimer@od.nih.gov.

Contents

Module 1: SABV and the Health of Women and Men

Module Learning Objectives

- Understand how consideration of sex and gender in biomedical research increases rigor of science and improves the health of women and men.
- Understand the NIH Sex as a Biological Variable (SABV) concept and Policy development.
- Recognize the meaning and importance of the NIH SABV Policy.
- Understand the role of SABV across the biomedical research continuum.

Critical Concepts and Key Definitions

- **Sex**: Sex is a biological classification that is encoded in every individual's DNA. It is defined by the genetic complement of sex chromosomes, with males having XY sex chromosomes and females having XX sex chromosomes. Sex is a biological attribute of every cell in your body. Therefore, sex can be determined for cells in culture based on their sex chromosome complement.
- **Gender**: Gender refers to the socially constructed roles, behaviors, expressions, and identities of girls, women, boys, men, and gender diverse people. It influences how people perceive themselves and each other, as well as how they act and interact. Gender is usually conceptualized as binary (girl/woman and boy/man), yet there is considerable diversity in how individuals and groups understand, experience, and express gender. Unlike sex, *gender is not defined at the cellular level*. Cells and biological tissue in and of themselves all have sex, but they do not have gender. However, the human from which the cells and tissue were sampled has both sex and gender. For example, a person who presents themselves as a woman may have their sex defined as male because at the cellular level this individual presents a male karyotype (i.e., with X and Y sex chromosomes). According to the definition of gender, mice and other non-human animals do not have gender.
- **Why is it important to distinguish between sex and gender?** Society all too often conflates the terms 'sex' and 'gender', but in biomedical science it is extremely important to be very clear about these definitions and the distinction between them. An individual is constructed from cells, and all those cells contain genetic material that encodes all the functions of the cell. The interaction of these cells with a substance (for instance a treatment intended to heal or alleviate pain) will, not considering the presence of other substances like hormones, be determined by the cell's genetics. Adding other substances like hormones or variation in an individual's social environment further complicates the interaction, which is why it is important to consider both sex *and* gender (where gender is appropriate) in biomedical research. There are several documented cases where

sex and gender were not considered in clinical trials which resulted in drugs that were prescribed to both women and men but were not equally as effective or safe for both.

- **Historical context of the NIH SABV Policy and the value of integrating the consideration of SABV across the biomedical research continuum**: The NIH SABV Policy emerged from the understanding that, not that long ago, women were insufficiently included in clinical research, and that the rigor and reproducibility of biomedical science also depends on the use of both male and female animal models as well as the consideration and reporting of potential sex effects in preclinical research. The specific factors that spurred development of the NIH SABV Policy have included: overreliance on male animals and cells; inattention to potential sex effects in research design and results; lack of transparency regarding the conduct and results of biomedical research; and inconsistent reporting of sex-specific findings in publications. These practices lead to an incomplete knowledge base and increase the likelihood of erroneous conclusions. They also do not maximize our return on investment (ROI) in science. In addition, such practices may lead to irreproducible results and toxicity surprises, and they may erode the public's trust in the investment of public funds. By accounting for SABV, we can enhance rigor, maximize ROI, and better support the generalizability of research findings.
- **Biological entities covered by the NIH SABV Policy**: As stated in the NIH SABV Policy (https://grants.nih.gov/grants/guide/notice-files/not-od-15-102.html) "NIH expects that sex as a biological variable will be factored into *research designs*, *analyses*, and *reporting* in vertebrate animal and human studies". This also covers products (cells or tissue) extracted from humans or vertebrate animals.
- **The 4 Cs of Studying Sex to Strengthen Science** offer informal guidance on application of the SABV Policy by scientific investigators. The 4 Cs are: 1. 'Consider' (i.e., design studies that take sex into account or explain why sex isn't incorporated); 2. 'Collect' (tabulate sex-based data); 3. 'Characterize' (analyze sex-based data); 4. 'Communicate' (report and publish sex-based data).

Key Literature

- Clayton, J. A., & Collins, F. S. (2014). Policy: NIH to balance sex in cell and animal studies. Nature, 509(7500), 282-283. doi:10.1038/509282a https://www.ncbi.nlm.nih.gov/pubmed/?term=24834516.

- Clayton, J. A. (2018). Applying the new SABV (sex as a biological variable) policy to research and clinical care. Physiol Behav, 187, 2-5. doi:10.1016/j.physbeh.2017.08.012. https://www.ncbi.nlm.nih.gov/pubmed/?term=28823546.

- Tannenbaum, C., Ellis, R. P., Eyssel, F., Zou, J., & Schiebinger, L. (2019). Sex and gender analysis improves science and engineering. Nature, 575(7781),137-146. doi: 10.1038/s41586-019-1657-6. https://www.ncbi.nlm.nih.gov/pubmed/?term=31695204.

Guided Discussion Topics

Topic 1 – Reflection on module material

Question: What do you feel is the impact of what you have learned in this module regarding:

1. Your project(s)?
2. Your scientific field?
3. The conduct of science outside your field?
4. The general public?

Discussion Prompts:

1. Your project(s):
    - Does your research project or projects utilize humans, vertebrate animals, or vertebrate animal or human products?
    - What biological entities does the NIH SABV Policy cover?
    - Given the biological entities involved in your research project(s) does the NIH SABV Policy apply to your work?
    - Are you already compliant with the NIH SABV Policy?
2. Your scientific field:
    - How well appreciated and integrated is SABV in your field?
    - Do you see variation in the degree of appreciation and integration of SABV as the science progresses from basic and preclinical research to clinical trials?
3. The conduct of science outside your field:
    - Do you believe that the NIH SABV Policy will have an impact on fields outside your own?
    - What do you think the impact of the NIH SABV Policy might be inside and outside your field?
    - Do you think expert reviewers might have different expectations for what counts as the appropriate factoring of sex into research designs, analyses, and reporting when it comes to different science disciplines (e.g., biophysics vs. endocrinology; biochemistry vs. behavior)?
4. The general public:
    - To what extent does the general public understand the difference between sex and gender?

- To what extent does the general public understand the importance of SABV to biomedical research and health care?

Topic 2 – Sex vs. gender

Question: Thinking on the importance of differentiating between what is meant by 'sex' and what by 'gender', is it right to consider gender as only being relevant to humans?

Discussion Prompts:

- Beyond the material given in the course, what are some examples of the influences of sex on health and disease?
- What are some examples of the influences of gender on health and disease?
- Can you think of a disease, condition, or aspect of health in which sex and gender influences interact with one another?
- Are there research paradigms or study designs in which such interactions could be tested?

Topic 3 – Rigor and reproducibility

Question: With rigor and reproducibility being highlighted in recent years as areas of concern in biomedical research, do you think that appropriately considering SABV will make a significant difference? In addition to the consideration of SABV, what else increases research rigor and reproducibility?

Discussion Prompts:

- Can the effect of the consideration of SABV on the return on investment (ROI) be quantified in any way? How might the effect of SABV on ROI be qualitatively examined?
- What do you think count as toxicity surprises? How might these relate to the lack of consideration of SABV at different stages of the biomedical research continuum?
- What does it mean to fully consider SABV and fully factor it into biomedical research?
- What are all the steps needed for SABV to have the greatest positive effect on scientific rigor and reproducibility?

Module 2: SABV and Experimental Design

Module Learning Objectives

- Explain what it means to consider and collect data on sex to strengthen science. ('Consider' and 'Collect' are the first two actions in the 4 Cs of Studying Sex to Strengthen Science.)
- Understand the NIH Policy on Sex as a Biological Variable (SABV) as it relates to the elements of experimental research design.
- Utilize the SABV Checklist to enhance study design.
- Recognize common misconceptions about SABV that might influence your thinking.
- Recognize how the NIH Policy on Sex as a Biological Variable applies across the Translational Science Spectrum.

Critical Concepts and Key Definitions

- **Principles of experimental design** include: choosing the appropriate study type and participants or experimental material that is suitable for the question to be addressed; applying proper randomization and blinding, when applicable; determining appropriate sample size(s); and selecting analysis approaches that will answer the research question(s).
- **Factorial design** is a type of experimental design consisting of two or more factors, each with discrete levels. For instance, the factor 'sex' typically takes on two values or levels in a preclinical experiment: 'female' and 'male'. Another factor might be 'drug treatment' (e.g., with levels: 'control' [vehicle only], 'low dose', and 'high dose'), and so forth. The factorial design uses analysis of variance (ANOVA). In a full factorial design, the experimental units (e.g., individuals of a laboratory mouse strain) take on all possible combinations of the levels across all factors in the study. Factorial designs are classified according to the number of factors and the number of levels of each factor (e.g., 2 x 2, 2 x 3, 3 x 3, etc.). When appropriate, the factorial design is an excellent approach for including females and males and considering SABV without needing too large an increase in sample size. A test of the treatment-by-sex interaction in the example above is equivalent to a test of whether the treatment response is sex-dependent. Miller et al. (2017), Beery (2018), and Buch et al. (2019) discuss the merits and limitations of factorial designs with respect to the consideration of SABV. Beltz et al. (2019) summarize a roadmap for this and other designs for considering SABV, depending on the extent and nature of sex difference(s), information available in the literature, and scientific question and research scenario.

- **Misconceptions about SABV**: "Considering SABV (the first of the 4 Cs) always means that a study must be designed to detect sex differences." "Cost is a valid reason for excluding females from experimental design." "Use of both sexes reduces statistical power and slows progress in preclinical studies with rodents." "The estrous cycle renders female rodents intrinsically more variable than male rodents." All these statements are false. These and other misconceptions and biases around the topic of sex may influence and limit the way investigators form hypotheses, design experiments, carry out analyses, and interpret and report their results. As a result of such misconceptions, investigators may even omit consideration of SABV in their experimental design, which may prevent important discoveries from being made.
- **Tools to assist the consideration of SABV**: A tool to guide investigators through the incorporation of SABV into research is the SABV Checklist, created by ORWH. The checklist reminds investigators to do the eight things: 1. Consider the influence of sex when formulating research questions. 2. Review available literature for the influence of sex. 3. Account for the influence of sex in study design. 4. Incorporate both males and females. 5. Alternatively, articulate a strong justification for a single-sex study. 6. Collect and analyze data, and report those data disaggregated by sex. 7. Characterize the influence of sex in the interpretation of results. 8. Communicate appropriately generalized research findings. NIH has also developed a decision tree that describes how reviewers will evaluate the consideration of SABV in grant applications (available at https://grants.nih.gov/grants/peer/guidelines_general/sabv_decision_tree_for_reviewers.pdf).

Key Literature

- Miller, L. R., Marks, C., Becker, J. B., Hurn, P. D., Chen, W. J., Woodruff, T., . . . Clayton, J. A. (2017). Considering sex as a biological variable in preclinical research. Faseb j, 31(1), 29-34. doi:10.1096/fj.201600781R. https://www.ncbi.nlm.nih.gov/pubmed/?term=27682203.

- Beery, A. K. (2018). Inclusion of females does not increase variability in rodent research studies. Curr Opin Behav Sci, 23, 143-149. doi:10.1016/j.cobeha.2018.06.016. https://www.ncbi.nlm.nih.gov/pubmed/?term=30560152.

- Buch, T., Moos, K., Ferreira, F. M., Fröhlich, H., Gebhard, C., & Tresch, A. (2019). Benefits of a factorial design focusing on inclusion of female and male animals in one experiment. J Mol Med (Berl). 97(6), 871-877. doi: 10.1007/s00109-019-01774-0. https://www.ncbi.nlm.nih.gov/pubmed/?term=30980104.

Guided Discussion Topics

Topic 1 – Reflection on module material

Question: What do you feel is the impact of what you have learned in this module regarding:

1. Your project(s)?
2. Your scientific field?
3. The conduct of science outside your field?
4. The general public?

Discussion Prompts:

1. Your project(s):
    - How have you accounted for SABV in one or more of your recent research designs? Alternatively, how do you expect to account for SABV in the design of a future research project?
    - How have you accounted for SABV in the analysis of one or more of your recent studies? Alternatively, how do you expect to account for SABV in the analysis of a future research project?
2. Your scientific field:
    - Does SABV influence biological phenomena in your field? If so, what is the nature of the sex influences or sex differences?
    - How does the nature of the sex difference (e.g., sex-limited trait; qualitative vs. quantitative sex difference; latent sex difference; population-level sex difference [see Beltz et al., 2019]) affect one's approach to hypothesis formulation, study design, and data analysis?
    - How does published information from prior studies influence study design and analysis approaches in your field?
3. The conduct of science outside your field:
    - Can you think of a field other than your own in which investigators take a very different approach to addressing SABV in their research designs and analyses?
    - If you were a reviewer of a grant application proposing to take such an approach, would you acknowledge the approach as a weakness or strength? How would this impact your score of the proposal?
4. The general public:
    - To what extent do you think the general public is aware of the history in which sex and gender were once not widely factored into the design and analysis of federally-funded research?
    - To what extent do you think the general public appreciates how widespread sex influences on health and disease are? Does the public appreciate the nuances of different kinds of sex differences and how these affect experimental design and analysis?

Topic 2 – Applicability and scope of the NIH SABV Policy

Question: What are the biological entities to which the NIH SABV Policy applies?

Discussion Prompts:

- Discussants should first consider the definition of the NIH SABV Policy. They should then think about possible reasons that the Policy was limited to vertebrate animals and humans.
- How does the NIH SABV Policy apply to primary cell culture derived from humans or other vertebrate animals?
- Why is it that the Policy does not apply to immortalized cells and cell lines? What is it that precludes these categories of experimental material from the Policy?
- Should the NIH SABV Policy be extended to cover flies and worms (or other invertebrates)? What would be the implications of this?
- Are there vertebrate animal models that pose particular challenges or opportunities with respect to understanding SABV? (E.g., many reptile and fish species exhibit temperature-dependent sex determination.)
- Can NIH-funded research topics outside the scope of the SABV Policy offer useful inspiration and guidance for factoring SABV into research designs and analysis for topics where the SABV Policy does apply?

Topic 3 – Including both sexes, experimental design, analysis approach, and power

Question: The NIH SABV Policy (NOT-OD-15-102) states the following: "NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex." When including both sexes in a preclinical vertebrate animal study, when is it important to perform and report explicit tests of sex influences (including sex differences and sex-by-treatment interactions)? When and how should one qualify the results of those tests?

Discussion Prompts:

- As preclinical researchers comply with the NIH SABV Policy, do you think most of their studies will be sufficiently powered to examine statistical patterns in males and females separately, or to explicitly test for sex differences (or sex influences)?
- What should one do when the requisite power is lacking? How does this issue affect one's choice of the optimal experimental design and analysis approach?
- Depending on the line of research and research scenario, what are some experimental designs and analysis approaches that are well suited to studying

both sexes and finding the right balance among: rigor, reproducibility, efficiency, cost, and statistical power?
- When and how should randomization and blinding be applied to studies that include both males and females?
- When one designs a study to include females and males and one then tests for sex differences but does not find any, what should one conclude?
- A post-hoc sex-stratified approach to data exploration would test all response variables (or endpoints) for statistical associations in each sex stratum. It is tempting to attach a lot of biological significance to cases where a strong statistical pattern is found for a certain variable in one sex but not the other. How should you interpret this kind of finding, particularly when a large number of variables are tested post hoc? What is the danger of such results making it into the literature without proper qualifications and caveats?

Topic 4 – Assessment of design and analysis in an example publication

This topic relies on discussants being notified of the selected publication in advance of the discussion, such that discussants have ample time to read the selected paper. Without sufficient lead time, it will not be possible for the discussants to adequately assess the authors' consideration of sex in their experimental design and analyses.

Exercise: Select a research paper for which to critique how well the authors accounted for SABV in their research design and analyses.

Discussion Prompts:
- How well did the authors design their study to incorporate SABV?
- Were the authors' analyses appropriate for considering SABV? Why or why not?
- Can you make any specific recommendations for improvement?

Module 3: SABV and Analyses

Module Learning Objectives

- Explain the rationale to characterize and analyze sex-based data. ('Characterize' is the third action in the 4 Cs of Studying Sex to Strengthen Science.)
- Understand the limitations of analyses that ignore sex influences and differences.
- Utilize statistical and power analyses to detect sex differences.
- Apply statistical approaches to measure sex influences and differences.

Critical Concepts and Key Definitions

- **To fully consider SABV** (in studies of vertebrate animals or humans) you must collect data for both sexes and then **characterize** (i.e., analyze) the data by sex, unless there is strong justification for a single-sex study. If no statistically significant sex difference or sex influence is found, or if the study is underpowered to test for a sex difference or sex influence, the data should still be reported (e.g., tabulated) by sex, so that other researchers can apply the results to meta-analyses, power calculations, their interpretation of the science, and/or the planning of future studies. Limitations related to the interpretation of the reported results should be transparently acknowledged and/or discussed in reports and publications. For example, finding no sex differences in a study that was underpowered to detect such differences does not count as evidence of a lack of sex differences in the particular trait or disease under investigation. Absence of evidence is not evidence of absence.
- **Statistical power** is the probability of detecting an effect that genuinely exists. In other words, power is the probability of rejecting the null hypothesis (H_0) of no difference (or no effect) when a specific alternative hypothesis (H_1) is true. More formally, statistical power = 1- β, where β is the probability of making a type II error (i.e., a false-negative error). The higher the power, the higher the probability of correctly rejecting the null hypothesis when a true difference or effect exists.
- **Power analysis** is performed to determine the minimum sample size necessary to ensure that the probability of a type I error (i.e., a false-positive error) is less than or equal to some desired threshold (customarily $\alpha = 0.05$) and that the probability of a type II error is less than or equal to another desired threshold (often $\beta = 0.20$, corresponding to 80% power). In addition to depending on α and β, the calculations involved in power analyses depend on the statistical model to be used, and they require prior estimates of group mean(s) and standard deviation(s) [or standardized effect sizes], as well as knowledge about the sidedness of the test (one-sided vs. two-sided; i.e., one-tailed vs. two-tailed). A number of power analysis calculators are freely available online (e.g., Diester et al., 2019) or as functions in statistical programming languages. Moreover, Buch

et al. (2019) provide, as supplementary material to their paper [cited as key literature in Module 2], a power analysis calculator for 2 x 2 factorial designs for detecting the effects of two main factors (e.g., drug treatment and sex) and their interaction. The power analysis calculator of Buch et al. (2019) comes in the form of an Excel spreadsheet and depends on the installation of the 'Real Statistics' add-in for Excel. The authors' power analysis calculator computes the total number of samples needed as a function of expected mean values in each experimental group, expected variance within groups, desired significance level, desired power level, and whether corrections will be made for multiple testing (essential for confirmatory tests, as opposed to exploratory tests, in factorial designs).

- **Standardized effect size** (in the case of a comparison between two groups) is the difference between the means of the two groups divided by their pooled standard deviation. Festing (2018) outlined a reversed approach to choosing sample sizes. In this approach one first uses common sense, tradition, or experience to choose a provisional sample size, or one uses what is called the "resource equation" [i.e., the total number of experimental units minus the number of treatment groups should fall between 10 and 20]. Next, one uses power analysis to estimate the standardized effect size likely to be detected with the provisional sample size. With knowledge of the literature, or given one's scientific experience, one can decide if the detectable effect size should suffice for the proposed experiment (details in Festing, 2018).
- **Stratified randomization by sex**: In this approach, treatment levels or experimental conditions are randomly allocated to females and males separately, in order to balance the numbers of females and males across the different experimental groups or interventions. Designs with balanced numbers of males and females often (though not always) yield the greatest statistical power.
- **Characterizing and analyzing sex-based data** is a key step in considering SABV. You can only analyze data by sex if you have collected data that includes different sexes. Key points to bear in mind when characterizing and analyzing sex-based data are the following:
    - Data analysis can take many different forms, depending on the design of your study and your primary research questions.
    - Consideration of SABV in your data analysis first requires determining whether you are conducting research to identify a sex difference, to evaluate the possible influence of SABV on your outcome variable, or to control for sex as a potential confounding variable.
    - Characterizing sex-based data requires, at a minimum, reporting the results by sex.
    - A study that seeks to include direct comparison of treatment effects in females to treatment effects in males, or evaluation of effect modification by sex, would require power calculations to determine the minimum sample size necessary to detect a sex effect.

- Feasibility limits to sample size may make it impossible to draw conclusions regarding sex differences with confidence. However, preliminary analyses may indicate areas for further investigation.

Key Literature

- McGregor, A.J., Hasnain, M., Sandberg, K., Morrison, M. F., Berlin, M., & Trott, J. (2016). How to study the impact of sex and gender in medical research: a review of resources. Biol Sex Diff. 7(Suppl 1):46. doi: 10.1186/s13293-016-0099-1. https://www.ncbi.nlm.nih.gov/pubmed/?term=27785348.

- Festing, M. F. (2018). On determining sample size in experiments involving laboratory animals. Lab Anim, 52(4), 341-350. doi:10.1177/0023677217738268. https://www.ncbi.nlm.nih.gov/pubmed/?term=29310487.

- Beltz, A. M., Beery, A. K., & Becker, J. B. (2019). Analysis of sex differences in pre-clinical and clinical data sets. Neuropsychopharmacology. Epub ahead of print. doi: 10.1038/s41386-019-0524-3. https://www.ncbi.nlm.nih.gov/pubmed/?term=31527863.

- Diester, C. M., Banks, M. L., Neigh, G. N., & Negus, S.S. (2019). Experimental design and analysis for consideration of sex as a biological variable. Neuropsychopharmacology. Epub ahead of print. doi: 10.1038/s41386-019-0458-9. https://www.ncbi.nlm.nih.gov/pubmed/?term=31277076.

Guided Discussion Topics

Topic 1 – Reflection on module material

Question: What do you feel is the impact of what you have learned in this module regarding:

1. Your project(s)?
2. Your scientific field?
3. The conduct of science outside your field?
4. The general public?

Discussion Prompts:

1. Your project(s):
    - Have you characterized sex influences or sex differences in a recent or current research project? Why or why not?
    - Whether or not sex influences or sex differences were tested, how did you estimate or justify sample sizes for that recent or current research project?

2. Your scientific field:
    - What are some of the different experimental designs and statistical approaches with which investigators test for sex influences or sex differences or at least control for sex influences in their research studies?
    - Why do you think the SABV Policy does not mandate specific experimental designs or statistical approaches?
    - Do you think the Policy's generality and lack of methodological constraint was intentional?
    - Who ultimately decides if a research proposal appropriately adheres to the SABV Policy?
3. The conduct of science outside your field:
    - In what field do you see the most diversity and creativity of approaches to characterize and analyze sex influences or sex differences?
    - In what field do you see the least diversity and creativity of approaches to characterize and analyze sex influences or sex differences?
4. The general public:
    - To what extent have you encountered analyses of sex influences or sex differences mentioned in science news pieces or mainstream journalism?
    - Does the public appreciate the incremental nature of scientific progress and how past work shapes the way scientists design their experiments and analyze their data, whether or not sex influences or sex differences are characterized?

Topic 2 – Choosing and planning your statistical analyses

This topic relies on discussants being asked to come to the discussion having already read Festing (2018) plus one or more papers showing tabulated or plotted means and standard deviations for males and females (under two or more experimental conditions or treatments). Ideally, choose a paper (or papers) with data suggestive of sex differences for which tests of such differences were not pre-planned or sufficiently powered.

Exercise: Select a research paper showing tabulated or plotted means and standard deviations for males and females under two or more experimental conditions or treatments. Discuss next steps for subsequent research.

Discussion Prompts:

- What is an interesting and important research question suggested by the findings in the selected paper? (Remember that sex differences or sex influences do not need to be the focus of one's next line of research for one to consider SABV and adhere to the Policy. Sex differences are very often not the focus of NIH-funded research in vertebrate animals or humans, yet that research still needs to consider SABV as mandated by the Policy.)

- Would male and female animals or research subjects be used in the proposed research? If not, explain your justification for a single sex study.
- Would one the aims of your next study be to determine whether a sex influence or sex difference exists? Would one of the aims be to test the interaction of sex with an intervention?
- What is your desired statistical power and chance of a type I error? Will you use one-sided or two-sided tests, and what is your justification for that decision?
- What is the minimum clinically or biologically relevant difference you wish to detect?
- What would be your proposed sample sizes for the various experimental conditions across all experimental factors (including sex, if appropriate)? Use "the resource equation", Table 1, Figure 3, and the overall approach of Festing (2018), or results of an online power analysis calculator, to aid your discussion.
- How will you randomize individuals to the different experimental conditions?
- What kind of minimum effect sizes (or standardized effect sizes) should you be able to detect in your upcoming experiment? Are these target effect sizes reasonable given the findings already documented in the literature and your study goals?
- What kind of feasibility limitations to sample size might you encounter? How would this affect the way you consider SABV in your research plan?

Topic 3 – Questions frequently asked about SABV in regard to rigor and transparency

Question: Given what you have learned so far, what do you think the answers are to the following FAQs (frequently asked questions) on SABV?

Discussion Prompts:

- What does it mean to consider SABV?
- Does the sex of primary cells or tissue explants (i.e. cells or tissues removed directly from the animal or human) need to be accounted for under the SABV Policy?
- How should applicants incorporate consideration of SABV when they are using previously established datasets?
- How does one decide whether to include both males and females in their basic research?
- Will animal costs increase as a result of the SABV Policy?
- How should applicants address SABV when the research involves scarce animal resources?

See other FAQs related to SABV as well as NIH's responses to all these FAQs on the following website: https://grants.nih.gov/reproducibility/faqs.htm#4837.

Module 4: SABV and Reporting

Module Learning Objectives

- Recognize the rationale for communicating and reporting data by sex. ('Communicate' is the fourth action in the 4 Cs of Studying Sex to Strengthen Science.)
- Recognize how Sex as a Biological Variable (SABV) can be incorporated into the reporting of experimental methodology and results.
- Identify the basic elements of guidelines for reporting of sex and gender in research.
- Know the guidelines for publishing in scientific journals and ways that communicate sex-based findings.
- Know how to share information about sex and gender outside of the scientific community.

Critical Concepts and Key Definitions

- **NIH's recommended standards for reporting SABV** were based on workshops conducted with various stakeholders and experts, including academic researchers, reviewers, journal editors, and funding agency representatives, among others. The extent to which these standards can be applied to basic or bench-oriented research depends on type of experiment and whether the experiment is designed to detect sex differences. For example, authors who have used a single sex in a study or whose results apply to only one sex or gender should explicitly state this in their title/abstract. Minimally, authors should always attempt to report the sex of the cells, tissues, or animals used in their work, or disclose when the sex of biological materials is unknown. Research reports should also disclose: whether the study was powered to detect a sex difference, whether statistical analyses were designed prior to data collection, and whether SABV was factored into these *a priori* analyses. Whether or not one's analyses identify possible sex-based differences, the presentation of descriptive statistics by sex is important to inform sample size and power calculations and to enable sex-based meta-analyses in future studies.
- **Sex and Gender Equity in Research (SAGER) Guidelines**: Editors play an influential role in the conduct of science—for example, in the advancement of research rigor and transparency—because editors are among the main 'gatekeepers' of science. Recognizing their responsibility to promote SABV reporting, the European Association of Science Editors (EASE) established a Gender Policy Committee (GPC) in 2012. This committee was charged with developing a set of guidelines and best practices for the reporting of Sex and Gender Equity in Research (SAGER). The Chairperson of the GPC (Dr. Shirin

Heidari) convened a panel of 13 experts from nine countries. The panel developed the guidelines based on teleconferences, conference presentations, a two-day workshop, a literature search on sex and gender policies in scientific publishing, and a survey of more than 700 journal editors. The resulting SAGER guidelines are designed to guide authors in preparing scientific manuscripts, and they are also a useful resource for reviewers and editors during the manuscript review process. The SAGER guidelines are summarized in Table 1 of Heidari et al. (2016). That paper also contains: a glossary of sex- and gender-related terms; a checklist for authors; and a flowchart that guides editors as they screen manuscripts. Basic elements of the SAGER guidelines include: the correct use of 'sex' and 'gender' terminology; specification of sex in the title and abstract; indication of whether sex differences are expected based on scientific literature; and incorporation of SABV in methods, results, and discussion sections.

- **Other stakeholders that have issued guidelines on the incorporation of sex and gender into the reporting of biomedical research**: Institute of Medicine (IOM) of the National Academies; International Committee of Medical Journal Editors (ICMJE); Committee on Publication Ethics (COPE); SPIRIT Group (i.e., SPIRIT 2013 Statement); and the 'instructions for authors,' manuscript preparation guidelines, and publication policies of numerous scientific journals.
- **Sharing sex and gender information outside the scientific community**: While several authors and groups have offered tips for sharing sex and gender information outside the scientific community, specific guidance on speaking about sex and gender is lacking. Consideration of general guidance on media interactions together with the SAGER guidelines yields the following list of suggestions (by no means complete). Use the terms 'sex' and 'gender' appropriately. Be clear about the specific variables studied and do not generalize beyond the data. If you studied animals, be clear that the data may not generalize to people. Be clear if your study did not specifically test for sex differences. Refer to the prior literature or rationale that suggested there might be sex differences related to your research question. Note the justification for your inclusion/exclusion criteria.

Key Literature

- Heidari, S., Babor, T. F., De Castro, P., Tort, S., & Curno, M. (2016). Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev, 1, 2. doi:10.1186/s41073-016-0007-6. https://www.ncbi.nlm.nih.gov/pubmed/?term=29451543.

  Will, T. R., Proano, S. B., Thomas, A. M., Kunz, L. M., Thompson, K. C., Ginnari, L. A., . . . Meitzen, J. (2017). Problems and Progress regarding Sex Bias and Omission in Neuroscience Research. eNeuro, 4(6). doi:10.1523/eneuro.0278-17.2017. https://www.ncbi.nlm.nih.gov/pubmed/?term=29134192.

- Docherty, J. R., Stanford, S. C., Panattieri, R. A., Alexander, S. P. H., Cirino, G., et al. (2019). Sex: a change in our guidelines to authors to ensure that this is no longer an ignored experimental variable. Br J Pharmacol. 1-6. doi: 10.1111/bph.14761. https://www.ncbi.nlm.nih.gov/pubmed/?term=31441038.

Guided Discussion Topics

Topic 1 – Reflection on module material

Question: What do you feel is the impact of what you have learned in this module regarding:

1. Your project(s)?
2. Your scientific field?
3. The conduct of science outside your field?
4. The general public?

Discussion Prompts:

1. Your project(s):
    - If you have published research findings already, to what extent have you adhered to the SAGER guidelines or similar guidelines for incorporating SABV into the reporting of biomedical research (perhaps without even knowing about these guidelines)?
    - If you have not published yet, how do you think you will adhere to the SAGER or similar guidelines, given the nature of your work?
2. Your scientific field:
    - How well are sex and gender considerations incorporated into the overall 'reporting culture' of your field?
    - On balance, in what respects is your field doing a good job regarding the SAGER guidelines? In what respects are improvements needed most?
3. The conduct of science outside your field:
    - Do you know of fields that are doing better than your field in terms of the overall culture of reporting sex and gender in research? What are those fields? Can you see any of the benefits resulting from their better incorporation of sex and gender into results reporting?
    - Are there fields that are doing worse than yours in terms of the overall culture of reporting sex and gender in publications? Can you see any examples of the costs that those fields have incurred as a result of their worse reporting practices?
4. The general public:
    - How well do you think scientists share sex and gender information outside the scientific community? How can they further improve in this regard?

- Can you think of a case (or cases) in which scientists and/or the media excelled in disseminating information about sex and gender to the public? What made this case (or these cases) so compelling?
- What are potential pitfalls and strategies for avoiding them when it comes to speaking to journalists about scientific results in general, as well as results related to sex and gender in particular?

Topic 2 – Considering SABV in the reporting of biomedical research and approaches to reporting data by sex

Question: What are all the different parts of a scientific publication or research report in which sex and gender should be considered and potentially incorporated?

Discussion Prompts:

- Name one of the standard parts of a peer-reviewed research paper and discuss when and how sex and gender should be incorporated into that part of the scientific report.
- What are all the different ways that sex-disaggregated results can be reported and shown in a scientific paper? When having this discussion, do not limit yourself to the sections of text in a standard research paper. Also think about what can go into supplementary information, how data tables can be structured, and how data can be portrayed in different kinds of figures (including scatter plots).
- Why is it important to provide results by sex even when one finds no significant differences between sexes or no sex-by-treatment interactions, or when studies were underpowered to test for sex differences in the first place?
- Is there any room for misinterpretation by the readership if one reports sex-disaggregated results when there is no evidence of sex differences, or the evidence of sex differences comes from post hoc analyses? How can potential misinterpretation be avoided through the acknowledgement of caveats, the discussion of limitations associated with post-hoc testing, or other appropriate disclosures? In what part(s) of a research paper should these acknowledgments and disclosures be made?

Topic 3 – Assessment of SABV reporting in one or more publications

This topic relies on discussants being notified of the selected publication(s) in advance of the discussion, such that discussants have ample time to read the selected papers. Without sufficient lead time, it will not be possible for the discussants to adequately assess the degree of SABV reporting. A more complete evaluation of one or more articles is preferable to the cursory assessment of just the titles and abstracts of a larger number of articles.

Exercise: Select one or more research papers for which to critique how well the authors incorporated SABV into their reporting. If two or more papers are selected, try choosing: (1) papers from different disciplines or journals; (2) papers from lines of research in which sex differences are more expected or less anticipated based on prior research findings; or (3) papers that vary in how well SABV was integrated into the reporting of scientific research.

Discussion Prompts:

- How well did the authors incorporate SABV and integrate sex and gender into their title, abstract, introduction, methods, results, and discussion? How would you grade the paper in terms of the authors' reporting of sex, or in terms of their overall rigor and transparency?
- Did the authors incorporate SABV into their tables, figures, and/or supplementary information (if present)?
- Can you make any specific recommendations for improvement?

Topic 4 – Translating the consideration of SABV into improved health care for women and men

Question: What effect is the consideration of SABV in biomedical research having on the treatment of diseases and conditions and the health outcomes experienced by women and men?

Note: An entire discussion could be devoted to this one topic, after all four modules have been completed.

Discussion Prompts:

- What are the main factors that doctors must consider in the precision medicine approach, as opposed to a one-size-fits-all approach to medicine? How important is SABV among those factors generally?
- In what ways is clinical care limited when researchers do not consider SABV?
- How can consideration of SABV in research improve health care? Can you think of specific disease examples in which empirically based, sex-specific treatments may be beneficial for patient care?
- To what extent do the most salient factors influencing health and disease, including sex and gender, vary in importance among medical disciplines?
- Discuss a medical discipline or disease category for which sex and gender are already recognized as being critically important to disease manifestation, presentation, diagnosis, treatment, symptom management, and/or patient outcomes, including effects on quality of life. Are healthcare practices and treatments already optimized according to sex and gender in that area of medicine?

- Discuss a medical discipline or disease category for which sex and gender are not regarded as being that important to disease manifestation, presentation, diagnosis, treatment, symptom management, and/or patient outcomes. Does evidence from the latest research suggest that sex and gender considerations will have a more important role in that area of medicine in the years to come?
- Given our current understanding of how health care would be improved by being more sex- and gender-aware, how can we facilitate growth of that awareness and its translation into improved medical practice? In answering this question, think about the different roles that all the relevant stakeholders could play, such as medical educators, medical boards, professional societies, healthcare providers, the research enterprise, medical journals, etc. What role could patients play in creating a stronger demand for improved health care that is optimized according to one's sex and gender?
- In what ways do you feel most excited about incorporating sex and gender considerations into your work as a physician or researcher? What effects might this have on your patients and discoveries in the future?

Appendix A: Course References and Resources

This appendix is not intended to provide a comprehensive bibliography of all SABV-relevant literature and resources. There are many other excellent publications and available resources relevant to SABV and the application of the NIH SABV Policy, which could also be consulted.

Books and Book Chapters

Reference	Topic(s)
Ellis, P. D. (2010). The essential guide to effect sizes : statistical power, meta-analysis, and the interpretation of research results. Cambridge: Cambridge University Press.	Utilize Statistical and Power Analyses to Detect Sex Differences;
Festing, M. F. W. (2018). The Principles of Experimental Design and the Determination of Sample Size When Using Animal Models of Traumatic Brain Injury. In A. K. Srivastava & C. S. Cox (Eds.), Pre-Clinical and Clinical Methods in Brain Trauma Research (pp. 201-225). New York, NY: Springer New York.	SABV in Experimental Design;
Institute of Medicine (U.S.) Board on Population Health and Public Health Practice. (2012). Sex-specific reporting of scientific research: a workshop summary. Washington, DC. National Academies Press. IMPLICATIONS FOR JOURNALS OF SEX-SPECIFIC REPORTING POLICIES OF JOURNALS.	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
Kirk, R. E. (2012). Experimental Design. In Handbook of Psychology, Second Edition (eds I. Weiner, J. A. Schinka and W. F. Velicer). doi:10.1002/9781118133880.hop202001	SABV in Experimental Design;
NIH Revitalization Act of 1993 Public Law 103-43(B): Clinical Research Equity Regarding Women and Minorities	SABV Policy: Concepts and Significance;
Weiss, A. J., Bailey, M. K., O'Malley, L., Barrett, M. L., Elixhauser, A., & Steiner, C. A. (2006). Patient Characteristics of Opioid-Related Inpatient Stays and Emergency Department Visits Nationally and by State, 2014: Statistical Brief #224. In Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD).	SABV Policy Across the Translational Science Spectrum – Clinical Research;

Wizeman, T. M., & Pardue, M.-L. (eds). (2001). Exploring the biological contributions to human health: does sex matter? National Academy Press, Washington, DC.

Recognizing How SABV Can Be Incorporated into the Reporting of Results - Basic/Bench-Oriented Research;

Journal Articles

Reference	Link URL	Topic(s)
Anderson, G. D. (2005). Sex and racial differences in pharmacological response: where is the evidence? Pharmacogenetics, pharmacokinetics, and pharmacodynamics. J Womens Health (Larchmt), 14(1), 19-29. doi:10.1089/jwh.2005.14.19	https://www.ncbi.nlm.nih.gov/pubmed/?term=15692274	Understand the Limitations of Pooled Data to Detect Sex Differences;
Anker, J. J., & Carroll, M. E. (2011). Females are more vulnerable to drug abuse than males: evidence from preclinical studies and the role of ovarian hormones. Curr Top Behav Neurosci, 8, 73-96. doi:10.1007/7854_2010_93	https://www.ncbi.nlm.nih.gov/pubmed/?term=21769724	Example: Addiction;
Arnold, A. P. (2014). Conceptual frameworks and mouse models for studying sex differences in physiology and disease: why compensation changes the game. Exp Neurol, 259, 2-9. doi:10.1016/j.expneurol.2014.01.021	https://www.ncbi.nlm.nih.gov/pubmed/?term=24509348	Apply Statistical Approaches to Measure Sex Influences and Differences;
Becker, D. M., Segal, J., Vaidya, D., Yanek, L. R., Herrera-Galeano, J. E., Bray, P. F., . . . Faraday, N. (2006). Sex differences in platelet reactivity and response to low-dose aspirin therapy. Jama, 295(12), 1420-1427. doi:10.1001/jama.295.12.1420	https://www.ncbi.nlm.nih.gov/pubmed/?term=16551714	Example: Cardiovascular Health;
Becker, J. B., & Koob, G. F. (2016). Sex Differences in Animal Models: Focus on Addiction. Pharmacol Rev, 68(2), 242-263. doi:10.1124/pr.115.011163	https://www.ncbi.nlm.nih.gov/pubmed/?term=26772794	Apply Statistical Approaches to Measure Sex Influences and Differences;
Becker, J. B., Arnold, A. P., Berkley, K. J., Blaustein, J. D., Eckel, L. A., Hampson, E., . . . Young, E. (2005). Strategies and methods for research on sex differences in brain and behavior. Endocrinology, 146(4), 1650-1673. doi:10.1210/en.2004-1142	https://www.ncbi.nlm.nih.gov/pubmed/?term=27870394	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Becker, J. B., McClellan, M. L., & Reed, B. G. (2017). Sex differences, gender and addiction. J Neurosci Res, 95(1-2), 136-147. doi:10.1002/jnr.23963	https://www.ncbi.nlm.nih.gov/pubmed/?term=15618360	Apply Statistical Approaches to Measure Sex Influences and Differences;

Beery, A. K. (2018). Inclusion of females does not increase variability in rodent research studies. Curr Opin Behav Sci, 23, 143-149. doi:10.1016/j.cobeha.2018.06.016	https://www.ncbi.nlm.nih.gov/pubmed/?term=30560152	Common Misconceptions about SABV; SABV Policy Across the Translational Science Spectrum – Pre-clinical Research; Utilize Statistical and Power Analyses to Detect Sex Differences; Apply Statistical Approaches to Measure Sex Influences and Differences;
Beery, A. K., & Zucker, I. (2011). Sex bias in neuroscience and biomedical research. Neurosci Biobehav Rev, 35(3), 565-572. doi:10.1016/j.neubiorev.2010.07.002	https://www.ncbi.nlm.nih.gov/pubmed/?term=20620164	Recognizing How SABV Can Be Incorporated into the Reporting of Results - Basic/Bench-Oriented Research;
Blaustein, J. D. (2012). Animals have a sex, and so should titles and methods sections of articles in Endocrinology. Endocrinology, 153(6), 2539-2540. doi:10.1210/en.2012-1365	https://www.ncbi.nlm.nih.gov/pubmed/?term=22610963	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Brouwers, L., van der Meiden-van Roest, A. J., Savelkoul, C., Vogelvang, T. E., Lely, A. T., Franx, A., & van Rijn, B. B. (2018). Recurrence of pre-eclampsia and the risk of future hypertension and cardiovascular disease: a systematic review and meta-analysis. Bjog, 125(13), 1642-1654. doi:10.1111/1471-0528.15394	https://www.ncbi.nlm.nih.gov/pubmed/?term=29978553	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Chan, A. W., Tetzlaff, J. M., Altman, D. G., Laupacis, A., Gotzsche, P. C., Krleza-Jeric, K., . . . Moher, D. (2013). SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med, 158(3), 200-207. doi:10.7326/0003-4819-158-3-201302050-00583	https://www.ncbi.nlm.nih.gov/pubmed/?term=23295957	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards; Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Clayton, J. A. (2016). Studying both sexes: a guiding principle for biomedicine. Faseb j, 30(2), 519-524. doi:10.1096/fj.15-279554	https://www.ncbi.nlm.nih.gov/pubmed/?term=29480590	Communicating and Reporting Data by Sex;
Clayton, J. A. (2018). Applying the new SABV (sex as a biological variable) policy to research and clinical care. Physiol Behav, 187, 2-5. doi:10.1016/j.physbeh.2017.08.012	https://www.ncbi.nlm.nih.gov/pubmed/?term=28823546	SABV Policy: Concepts and Significance; Understand the Limitations of Pooled Data to Detect Sex Differences;

Clayton, J. A., & Arnegard, M. E. (2018). Taking cardiology clinical trials to the next level: A call to action. Clin Cardiol, 41(2), 179-184. doi:10.1002/clc.22907	https://www.ncbi.nlm.nih.gov/pubmed/?term=27802482	Definitions of Sex and Gender; Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research - Reporting Demographic Data; Applying Guidelines for Publishing in Scientific Journals - Sex and Gender Equity in Research (SAGER) Gui
Clayton, J. A., & Collins, F. S. (2014). Policy: NIH to balance sex in cell and animal studies. Nature, 509(7500), 282-283. doi:10.1038/509282a	https://www.ncbi.nlm.nih.gov/pubmed/?term=24834516	The Impact of SABV on Research; Risk/Potential Impact of NOT Including SABV; Consider and Collect Data on Sex for Strengthening Science; A Checklist to Enhance SABV in Study Design; Common Misconceptions about SABV; SABV Policy Across the Translational Sc
Clayton, J. A., & Tannenbaum, C. (2016). Reporting Sex, Gender, or Both in Clinical Research? Jama, 316(18), 1863-1864. doi:10.1001/jama.2016.16405	https://www.ncbi.nlm.nih.gov/pubmed/?term=24834516	SABV Policy: Concepts and Significance; Common Misconceptions about SABV; SABV Policy Across the Translational Science Spectrum – Basic Research;
Collins, F. S., & Tabak, L. A. (2014). Policy: NIH plans to enhance reproducibility. Nature, 505(7485), 612-613. doi:10.1038/505612a	https://www.ncbi.nlm.nih.gov/pubmed/?term=24482835	Risk/Potential Impact of NOT Including SABV;
Collins, L. M., Dziak, J. J., & Li, R. (2009). Design of experiments with multiple independent variables: a resource management perspective on complete and reduced factorial designs. Psychol Methods, 14(3), 202-224. doi:10.1037/a0015826	https://www.ncbi.nlm.nih.gov/pubmed/?term=19719358	Utilize Statistical and Power Analyses to Detect Sex Differences;
Cornelison T.L. & Clayton J.A. Considering sex as a biological variable in biomedical research. Gender and the Genome, 2017;1(2), 89- 93.	https://doi.org/10.1089/gg.2017.0006	Example: Cardiovascular Health; Apply Statistical Approaches to Measure Sex Influences and Differences; Identifying the Basic Elements of Guidelines for

		Reporting of Sex and Gender in Research – Negative Results;
Cox, K. H., Bonthuis, P. J., & Rissman, E. F. (2014). Mouse model systems to study sex chromosome genes and behavior: relevance to humans. Front Neuroendocrinol, 35(4), 405-419. doi:10.1016/j.yfrne.2013.12.004	https://www.ncbi.nlm.nih.gov/pubmed/?term=24388960	Apply Statistical Approaches to Measure Sex Influences and Differences;
Curtis, M. J., Bond, R. A., Spina, D., Ahluwalia, A., Alexander, S. P., Giembycz, M. A., . . . McGrath, J. C. (2015). Experimental design and analysis and their reporting: new guidance for publication in BJP. Br J Pharmacol, 172(14), 3461-3471. doi:10.1111/bph.12856	https://www.ncbi.nlm.nih.gov/pubmed/?term=26114403	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Dance, A. (2018). On the record. Nature, 562(7725), 153-155. doi:10.1038/d41586-018-06871-7	https://www.ncbi.nlm.nih.gov/pubmed/?term=30275559	Sharing Sex and Gender Information Outside the Scientific Community;
Davis, M., & Sanders, B. (2019). Preeclampsia and future stroke risk in women: What NPs need to know. Nurse Pract, 44(4), 50-54. doi:10.1097/01.NPR.0000554088.97825.ad	https://www.ncbi.nlm.nih.gov/pubmed/?term=30889110	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Day, S., Mason, R., Lagosky, S., & Rochon, P. A. (2016). Integrating and evaluating sex and gender in health research. Health Res Policy Syst, 14(1), 75. doi:10.1186/s12961-016-0147-7	https://www.ncbi.nlm.nih.gov/pubmed/?term=27724961	SABV Policy: Concepts and Significance;
Du, L., Bayir, H., Lai, Y., Zhang, X., Kochanek, P. M., Watkins, S. C., . . . Clark, R. S. (2004). Innate gender-based proclivity in response to cytotoxicity and programmed cell death pathway. J Biol Chem, 279(37), 38563-38570. doi:10.1074/jbc.M405461200	https://www.ncbi.nlm.nih.gov/pubmed/?term=15234982	SABV Policy Across the Translational Science Spectrum – Basic Research;
Evans, S. M., & Foltin, R. W. (2006). Exogenous progesterone attenuates the subjective effects of smoked cocaine in women, but not in men. Neuropsychopharmacology, 31(3), 659-674. doi:10.1038/sj.npp.1300887	https://www.ncbi.nlm.nih.gov/pubmed/?term=16160708	Example: Addiction;
Festing, M. F. (2018). On determining sample size in experiments involving laboratory animals. Lab Anim, 52(4), 341-350. doi:10.1177/0023677217738268	https://www.ncbi.nlm.nih.gov/pubmed/?term=29310487	Utilize Statistical and Power Analyses to Detect Sex Differences; Apply Statistical Approaches to

		Measure Sex Influences and Differences;
Fisher, E. M., Beer-Romero, P., Brown, L. G., Ridley, A., McNeil, J. A., Lawrence, J. B., . . . Page, D. C. (1990). Homologous ribosomal protein genes on the human X and Y chromosomes: escape from X inactivation and possible implications for Turner syndrome. Cell, 63(6), 1205-1218. doi:10.1016/0092-8674(90)90416-c	https://www.ncbi.nlm.nih.gov/pubmed/?term=2124517	SABV Policy Across the Translational Science Spectrum – Basic Research;
Fox, H. C., Morgan, P. T., & Sinha, R. (2014). Sex differences in guanfacine effects on drug craving and stress arousal in cocaine-dependent individuals. Neuropsychopharmacology, 39(6), 1527-1537. doi:10.1038/npp.2014.1	https://www.ncbi.nlm.nih.gov/pubmed/?term=24395021	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Franconi, F., Brunelleschi, S., Steardo, L., & Cuomo, V. (2007). Gender differences in drug responses. Pharmacol Res, 55(2), 81-95. doi:10.1016/j.phrs.2006.11.001	https://www.ncbi.nlm.nih.gov/pubmed/?term=17129734	Example: Cardiovascular Health;
Frezza, M., di Padova, C., Pozzato, G., Terpin, M., Baraona, E., & Lieber, C. S. (1990). High blood alcohol levels in women. The role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. N Engl J Med, 322(2), 95-99. doi:10.1056/nejm199001113220205	https://www.ncbi.nlm.nih.gov/pubmed/?term=2248624	Example: Addiction;
Gorham, L. S., Jernigan, T., Hudziak, J., & Barch, D. M. (2019). Involvement in Sports, Hippocampal Volume, and Depressive Symptoms in Children. Biol Psychiatry Cogn Neurosci Neuroimaging, 4(5), 484-492. doi:10.1016/j.bpsc.2019.01.011	https://www.ncbi.nlm.nih.gov/pubmed/?term=30905689	Consider and Collect Data on Sex for Strengthening Science; Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research - Reporting Demographic Data;
Greenblatt, D. J., Harmatz, J. S., von Moltke, L. L., Wright, C. E., Durol, A. L., Harrel-Joseph, L. M., & Shader, R. I. (2000). Comparative kinetics and response to the benzodiazepine agonists triazolam and zolpidem: evaluation of sex-dependent differences. J Pharmacol Exp Ther, 293(2), 435-443.	https://www.ncbi.nlm.nih.gov/pubmed/?term=10773013	Understand the Limitations of Pooled Data to Detect Sex Differences;
Gum, P. A., Kottke-Marchant, K., Poggio, E. D., Gurm, H., Welsh, P. A., Brooks, L., . . . Topol, E. J. (2001). Profile and prevalence of	https://www.ncbi.nlm.nih.gov/pubmed/?term=11472699	Example: Cardiovascular Health;

aspirin resistance in patients with cardiovascular disease. Am J Cardiol, 88(3), 230-235. doi:10.1016/s0002-9149(01)01631-9		
Haight, S. C., Ko, J. Y., Tong, V. T., Bohm, M. K., & Callaghan, W. M. (2018). Opioid Use Disorder Documented at Delivery Hospitalization - United States, 1999-2014. MMWR Morb Mortal Wkly Rep, 67(31), 845-849. doi:10.15585/mmwr.mm6731a1	https://www.ncbi.nlm.nih.gov/pubmed/?term=30091969	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Hankivsky, O., Springer, K. W., & Hunting, G. (2018). Beyond sex and gender difference in funding and reporting of health research. Res Integr Peer Rev, 3, 6. doi:10.1186/s41073-018-0050-6	https://www.ncbi.nlm.nih.gov/pubmed/?term=30167330	Applying Guidelines for Publishing in Scientific Journals - Publishing in Scientific Journals;
Hartung, D. M., & Touchette, D. (2009). Overview of clinical research design. Am J Health Syst Pharm, 66(4), 398-408. doi:10.2146/ajhp080300	https://www.ncbi.nlm.nih.gov/pubmed/?term=19202050	SABV in Experimental Design;
Harvey, R. E., Coffman, K. E., & Miller, V. M. (2015). Women-specific factors to consider in risk, diagnosis and treatment of cardiovascular disease. Womens Health (Lond), 11(2), 239-257. doi:10.2217/whe.14.64	https://www.ncbi.nlm.nih.gov/pubmed/?term=25776297	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Heidari, S., Babor, T. F., De Castro, P., Tort, S., & Curno, M. (2016). Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev, 1, 2. doi:10.1186/s41073-016-0007-6	https://www.ncbi.nlm.nih.gov/pubmed/?term=29451543	Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research - Reporting Demographic Data; Applying Guidelines for Publishing in Scientific Journals - Publishing in Scientific Journals; Applying Guidelines for Publishing in Sci
Hewitt, J. A., Brown, L. L., Murphy, S. J., Grieder, F., & Silberberg, S. D. (2017). Accelerating Biomedical Discoveries through Rigor and Transparency. Ilar j, 58(1), 115-128. doi:10.1093/ilar/ilx011	https://www.ncbi.nlm.nih.gov/pubmed/?term=28575443	The Impact of SABV on Research;
Hilderbrand, E. R., & Lasek, A. W. (2018). Studying Sex Differences in Animal Models of Addiction: An Emphasis on Alcohol-Related Behaviors. ACS Chem Neurosci, 9(8), 1907-1916. doi:10.1021/acschemneuro.7b00449	https://www.ncbi.nlm.nih.gov/pubmed/?term=29227676	Apply Statistical Approaches to Measure Sex Influences and Differences;

Hoeppner, B. B., Paskausky, A. L., Jackson, K. M., & Barnett, N. P. (2013). Sex differences in college student adherence to NIAAA drinking guidelines. Alcohol Clin Exp Res, 37(10), 1779-1786. doi:10.1111/acer.12159	https://www.ncbi.nlm.nih.gov/pubmed/?term=23682991	Example: Addiction;
Joel, D., & McCarthy, M. M. (2017). Incorporating Sex As a Biological Variable in Neuropsychiatric Research: Where Are We Now and Where Should We Be? Neuropsychopharmacology, 42(2), 379-385. doi:10.1038/npp.2016.79	https://www.ncbi.nlm.nih.gov/pubmed/?term=27240659	The Impact of SABV on Research;
Justice, A. J., & De Wit, H. (2000). Acute effects of d-amphetamine during the early and late follicular phases of the menstrual cycle in women. Pharmacol Biochem Behav, 66(3), 509-515. doi:10.1016/s0091-3057(00)00218-5	https://www.ncbi.nlm.nih.gov/pubmed/?term=10899363	Example: Addiction;
Karp, N. A., & Reavey, N. (2018). Sex bias in preclinical research and an exploration of how to change the status quo. Br J Pharmacol. doi:10.1111/bph.14539	https://www.ncbi.nlm.nih.gov/pubmed/?term=30418665	Understand the Limitations of Pooled Data to Detect Sex Differences;
Kibbe, M. R. (2018). Reporting of Sex as a Variable in Research Published in Surgical Journals. JAMA Surg, 153(11), 983. doi:10.1001/jamasurg.2018.2450	https://www.ncbi.nlm.nih.gov/pubmed/?term=30073308	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Kilkenny, C., Browne, W. J., Cuthill, I. C., Emerson, M., & Altman, D. G. (2010). Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. PLoS Biol, 8(6), e1000412. doi:10.1371/journal.pbio.1000412	https://www.ncbi.nlm.nih.gov/pubmed/?term=20613859	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
Kong, B. Y., Haugh, I. M., Schlosser, B. J., Getsios, S., & Paller, A. S. (2016). Mind the Gap: Sex Bias in Basic Skin Research. J Invest Dermatol, 136(1), 12-14. doi:10.1038/jid.2015.298	https://www.ncbi.nlm.nih.gov/pubmed/?term=26763418	Risk/Potential Impact of NOT Including SABV;
Landis, S. C., Amara, S. G., Asadullah, K., Austin, C. P., Blumenstein, R., Bradley, E. W., . . . Silberberg, S. D. (2012). A call for transparent reporting to optimize the predictive value of preclinical research. Nature, 490(7419), 187-191. doi:10.1038/nature11556	https://www.ncbi.nlm.nih.gov/pubmed/?term=23060188	Communicating and Reporting Data by Sex; Recognizing How SABV Can Be Incorporated into the Reporting of Results; Recognizing How SABV Can Be Incorporated into the Reporting of Results - Randomization and Blinding;

Lee, S. K. (2018). Sex as an important biological variable in biomedical research. BMB Rep, 51(4), 167-173. doi:10.5483/bmbrep.2018.51.4.034	https://www.ncbi.nlm.nih.gov/pubmed/?term=29429452	SABV Policy: Concepts and Significance; Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research – Negative Results; Applying Guidelines for Publishing in Scientific Journals - Sex and Gender Equity in Research (SAGER) Guid
Loyd, D. R., & Murphy, A. Z. (2006). Sex differences in the anatomical and functional organization of the periaqueductal gray-rostral ventromedial medullary pathway in the rat: a potential circuit mediating the sexually dimorphic actions of morphine. J Comp Neurol, 496(5), 723-738. doi:10.1002/cne.20962	https://www.ncbi.nlm.nih.gov/pubmed/?term=17540508	Risk/Potential Impact of NOT Including SABV;
Loyd, D. R., Morgan, M. M., & Murphy, A. Z. (2007). Morphine preferentially activates the periaqueductal gray-rostral ventromedial medullary pathway in the male rat: a potential mechanism for sex differences in antinociception. Neuroscience, 147(2), 456-468. doi:10.1016/j.neuroscience.2007.03.053	https://www.ncbi.nlm.nih.gov/pubmed/?term=18364026	Risk/Potential Impact of NOT Including SABV;
Loyd, D. R., Morgan, M. M., & Murphy, A. Z. (2008). Sexually dimorphic activation of the periaqueductal gray-rostral ventromedial medullary circuit during the development of tolerance to morphine in the rat. Eur J Neurosci, 27(6), 1517-1524. doi:10.1111/j.1460-9568.2008.06100.x	https://www.ncbi.nlm.nih.gov/pubmed/?term=19109484	Risk/Potential Impact of NOT Including SABV;
Loyd, D. R., Wang, X., & Murphy, A. Z. (2008). Sex differences in micro-opioid receptor expression in the rat midbrain periaqueductal gray are essential for eliciting sex differences in morphine analgesia. J Neurosci, 28(52), 14007-14017. doi:10.1523/jneurosci.4123-08.2008	https://www.ncbi.nlm.nih.gov/pubmed/?term=16615128	Risk/Potential Impact of NOT Including SABV;
Lynch, W. J. (2018). Modeling the development of drug addiction in male and female animals. Pharmacol Biochem Behav, 164, 50-61. doi:10.1016/j.pbb.2017.06.006	https://www.ncbi.nlm.nih.gov/pubmed/?term=28624586	Apply Statistical Approaches to Measure Sex Influences and Differences;

Majid, A., Bae, O. N., Redgrave, J., Teare, D., Ali, A., & Zemke, D. (2015). The Potential of Adaptive Design in Animal Studies. Int J Mol Sci, 16(10), 24048-24058. doi:10.3390/ijms161024048	https://www.ncbi.nlm.nih.gov/pubmed/?term=26473839	SABV in Experimental Design;
Mapplebeck, J. C. S., Dalgarno, R., Tu, Y., Moriarty, O., Beggs, S., Kwok, C. H. T., . . . Salter, M. W. (2018). Microglial P2X4R-evoked pain hypersensitivity is sexually dimorphic in rats. Pain, 159(9), 1752-1763. doi:10.1097/j.pain.0000000000001265	https://www.ncbi.nlm.nih.gov/pubmed/?term=29927790	Risk/Potential Impact of NOT Including SABV;
Masca, N. G., Hensor, E. M., Cornelius, V. R., Buffa, F. M., Marriott, H. M., Eales, J. M., . . . Teare, M. D. (2015). RIPOSTE: a framework for improving the design and analysis of laboratory-based research. Elife, 4. doi:10.7554/eLife.05519	https://www.ncbi.nlm.nih.gov/pubmed/?term=25951517	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards; Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
McCarthy, M. M. (2015). Incorporating Sex as a Variable in Preclinical Neuropsychiatric Research. Schizophr Bull, 41(5), 1016-1020. doi:10.1093/schbul/sbv077	https://www.ncbi.nlm.nih.gov/pubmed/?term=29097784	The Impact of SABV on Research; Risk/Potential Impact of NOT Including SABV; SABV in Experimental Design;
McCarthy, M. M., Arnold, A. P., Ball, G. F., Blaustein, J. D., & De Vries, G. J. (2012). Sex differences in the brain: the not so inconvenient truth. J Neurosci, 32(7), 2241-2247. doi:10.1523/jneurosci.5372-11.2012	https://www.ncbi.nlm.nih.gov/pubmed/?term=26067001	Apply Statistical Approaches to Measure Sex Influences and Differences; Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
McCarthy, M. M., Woolley, C. S., & Arnold, A. P. (2017). Incorporating sex as a biological variable in neuroscience: what do we gain? Nat Rev Neurosci, 18(12), 707-708. doi:10.1038/nrn.2017.137	https://www.ncbi.nlm.nih.gov/pubmed/?term=22396398	Apply Statistical Approaches to Measure Sex Influences and Differences;
McEwen, B. S., & Alves, S. E. (1999). Estrogen actions in the central nervous system. Endocr Rev, 20(3), 279-307. doi:10.1210/edrv.20.3.0365	https://www.ncbi.nlm.nih.gov/pubmed/?term=10368772	Apply Statistical Approaches to Measure Sex Influences and Differences;
Miller, L. R., Marks, C., Becker, J. B., Hurn, P. D., Chen, W. J., Woodruff, T., . . . Clayton, J. A. (2017). Considering sex as a biological variable in preclinical research. Faseb j, 31(1), 29-34. doi:10.1096/fj.201600781R	https://www.ncbi.nlm.nih.gov/pubmed/?term=27682203	Definitions of Sex and Gender; SABV Policy: Concepts and Significance; The Impact of SABV on Research; Consider and Collect

		Data on Sex for Strengthening Science; SABV in Experimental Design; A Checklist to Enhance SABV in Study Design; Common Misconcepti
Miller, V. M. (2012). In pursuit of scientific excellence: sex matters. Am J Physiol Regul Integr Comp Physiol, 302(9), R1023-1024. doi:10.1152/ajpregu.00105.2012	https://www.ncbi.nlm.nih.gov/pubmed/?term=22422666	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Mogil, J. S. (2016). Perspective: Equality need not be painful. Nature, 535(7611), S7. doi:10.1038/535S7a	https://www.ncbi.nlm.nih.gov/pubmed/?term=27410531	Risk/Potential Impact of NOT Including SABV;
Murray, J. E., Barrett, S. T., Brock, R. L., & Bevins, R. A. (2017). Caring about Power Analyses. ACS Chem Neurosci, 8(11), 2352-2354. doi:10.1021/acschemneuro.7b00341	https://www.ncbi.nlm.nih.gov/pubmed/?term=28933527	Utilize Statistical and Power Analyses to Detect Sex Differences;
Nebel, R. A., Aggarwal, N. T., Barnes, L. L., Gallagher, A., Goldstein, J. M., Kantarci, K., . . . Mielke, M. M. (2018). Understanding the impact of sex and gender in Alzheimer's disease: A call to action. Alzheimers Dement, 14(9), 1171-1183. doi:10.1016/j.jalz.2018.04.008	https://www.ncbi.nlm.nih.gov/pubmed/?term=29907423	SABV Policy Across the Translational Science Spectrum – Basic Research;
Noordzij, M., Dekker, F. W., Zoccali, C., & Jager, K. J. (2009). Study designs in clinical research. Nephron Clin Pract, 113(3), c218-221. doi:10.1159/000235610	https://www.ncbi.nlm.nih.gov/pubmed/?term=19690439	SABV in Experimental Design;
Pallmann, P., Bedding, A. W., Choodari-Oskooei, B., Dimairo, M., Flight, L., Hampson, L. V., . . . Jaki, T. (2018). Adaptive designs in clinical trials: why use them, and how to run and report them. BMC Med, 16(1), 29. doi:10.1186/s12916-018-1017-7	https://www.ncbi.nlm.nih.gov/pubmed/?term=29490655	SABV in Experimental Design;
Plasilova, M. L., Hayse, B., Killelea, B. K., Horowitz, N. R., Chagpar, A. B., & Lannin, D. R. (2016). Features of triple-negative breast cancer: Analysis of 38,813 cases from the national cancer database. Medicine (Baltimore), 95(35), e4614. doi:10.1097/md.0000000000004614	https://www.ncbi.nlm.nih.gov/pubmed/?term=27583878	Example: Breast Cancer;

Potenza, M. N., Hong, K. I., Lacadie, C. M., Fulbright, R. K., Tuit, K. L., & Sinha, R. (2012). Neural correlates of stress-induced and cue-induced drug craving: influences of sex and cocaine dependence. Am J Psychiatry, 169(4), 406-414. doi:10.1176/appi.ajp.2011.11020289	https://www.ncbi.nlm.nih.gov/pubmed/?term=22294257	Example: Addiction;
Potluri, T., Engle, K., Fink, A. L., Vom Steeg, L. G., & Klein, S. L. (2017). Sex Reporting in Preclinical Microbiological and Immunological Research. MBio, 8(6). doi:10.1128/mBio.01868-17	https://www.ncbi.nlm.nih.gov/pubmed/?term=29138308	Risk/Potential Impact of NOT Including SABV;
Prager, E. M. (2017). Addressing sex as a biological variable. J Neurosci Res, 95(1-2), 11. doi:10.1002/jnr.23979	https://www.ncbi.nlm.nih.gov/pubmed/?term=30506706	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
Prager, E. M., Chambers, K. E., Plotkin, J. L., McArthur, D. L., Bandrowski, A. E., Bansal, N., . . . Graf, C. (2019). Improving transparency and scientific rigor in academic publishing. J Neurosci Res, 97(4), 377-390. doi:10.1002/jnr.24340	https://www.ncbi.nlm.nih.gov/pubmed/?term=27870455	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Prendergast, B. J., Onishi, K. G., & Zucker, I. (2014). Female mice liberated for inclusion in neuroscience and biomedical research. Neurosci Biobehav Rev, 40, 1-5. doi:10.1016/j.neubiorev.2014.01.001	https://www.ncbi.nlm.nih.gov/pubmed/?term=24456941	Common Misconceptions about SABV; Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research – Negative Results;
Ranadive, S. M., Harvey, R. E., Lahr, B. D., Miller, V. M., Joyner, M. J., & Barnes, J. N. (2017). Sympathetic responsiveness is not increased in women with a history of hypertensive pregnancy. Am J Physiol Regul Integr Comp Physiol, 312(1), R49-r54. doi:10.1152/ajpregu.00379.2016	https://www.ncbi.nlm.nih.gov/pubmed/?term=27927625	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Rich-Edwards, J. W., Kaiser, U. B., Chen, G. L., Manson, J. E., & Goldstein, J. M. (2018). Sex and Gender Differences Research Design for Basic, Clinical, and Population Studies: Essentials for Investigators. Endocr Rev, 39(4), 424-439. doi:10.1210/er.2017-00246	https://www.ncbi.nlm.nih.gov/pubmed/?term=29668873	Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research - Considerations for Post Hoc Analyses;
Ridker, P. M., Cook, N. R., Lee, I. M., Gordon, D., Gaziano, J. M., Manson, J. E., . . . Buring, J. E. (2005). A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease	https://www.ncbi.nlm.nih.gov/pubmed/?term=15753114	Example: Cardiovascular Health;

in women. N Engl J Med, 352(13), 1293-1304. doi:10.1056/NEJMoa050613		
Ritz, S. A., Antle, D. M., Cote, J., Deroy, K., Fraleigh, N., Messing, K., . . . Mergler, D. (2014). First steps for integrating sex and gender considerations into basic experimental biomedical research. Faseb j, 28(1), 4-13. doi:10.1096/fj.13-233395	https://www.ncbi.nlm.nih.gov/pubmed/?term=24056086	Utilize Statistical and Power Analyses to Detect Sex Differences; Recognizing How SABV Can Be Incorporated into the Reporting of Results - Basic/Bench-Oriented Research;
Rohrig, B., du Prel, J. B., & Blettner, M. (2009). Study design in medical research: part 2 of a series on the evaluation of scientific publications. Dtsch Arztebl Int, 106(11), 184-189. doi:10.3238/arztebl.2009.0184	https://www.ncbi.nlm.nih.gov/pubmed/?term=19568374	Utilize Statistical and Power Analyses to Detect Sex Differences;
Scantlebury, D. C., Kattah, A. G., Weissgerber, T. L., Agarwal, S., Mielke, M. M., Weaver, A. L., . . . Garovic, V. D. (2018). Impact of a History of Hypertension in Pregnancy on Later Diagnosis of Atrial Fibrillation. J Am Heart Assoc, 7(10). doi:10.1161/jaha.117.007584	https://www.ncbi.nlm.nih.gov/pubmed/?term=29755033	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med, 152(11), 726-732. doi:10.7326/0003-4819-152-11-201006010-00232	https://www.ncbi.nlm.nih.gov/pubmed/?term=20335313	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
Shah, K., McCormack, C. E., & Bradbury, N. A. (2014). Do you know the sex of your cells? Am J Physiol Cell Physiol, 306(1), C3-18. doi:10.1152/ajpcell.00281.2013	https://www.ncbi.nlm.nih.gov/pubmed/?term=24196532	SABV Policy Across the Translational Science Spectrum – Basic Research;
Shaw, R., Festing, M. F., Peers, I., & Furlong, L. (2002). Use of factorial designs to optimize animal experiments and reduce animal use. Ilar j, 43(4), 223-232. doi:10.1093/ilar.43.4.223	https://www.ncbi.nlm.nih.gov/pubmed/?term=12391398	Utilize Statistical and Power Analyses to Detect Sex Differences;
Sorge, R. E., Mapplebeck, J. C., Rosen, S., Beggs, S., Taves, S., Alexander, J. K., . . . Mogil, J. S. (2015). Different immune cells mediate mechanical pain hypersensitivity in male and female mice. Nat Neurosci, 18(8), 1081-1083. doi:10.1038/nn.4053	https://www.ncbi.nlm.nih.gov/pubmed/?term=26120961	The Impact of SABV on Research; Risk/Potential Impact of NOT Including SABV; SABV Policy Across the Translational Science Spectrum – Pre-clinical Research;

Thiese, M. S. (2014). Observational and interventional study design types; an overview. Biochem Med (Zagreb), 24(2), 199-210. doi:10.11613/bm.2014.022	https://www.ncbi.nlm.nih.gov/pubmed/?term=24969913	SABV in Experimental Design;
Trushina E, Wilkins J, Trushin S. P1-143: Sex-specific metabolic and epigenetic changes in primary fibroblasts from patients with AD. Alzheimers Dement. 2017;13(7)Supplement, P297–P298.)	https://doi.org/10.1016/j.jalz.2017.06.210	SABV Policy Across the Translational Science Spectrum – Basic Research;
Trushina, E., Dutta, T., Persson, X. M., Mielke, M. M., & Petersen, R. C. (2013). Identification of altered metabolic pathways in plasma and CSF in mild cognitive impairment and Alzheimer's disease using metabolomics. PLoS One, 8(5), e63644. doi:10.1371/journal.pone.0063644	https://www.ncbi.nlm.nih.gov/pubmed/?term=23700429	SABV Policy Across the Translational Science Spectrum – Basic Research;
VanHouten, J. P., Rudd, R. A., Ballesteros, M. F., & Mack, K. A. (2019). Drug Overdose Deaths Among Women Aged 30-64 Years - United States, 1999-2017. MMWR Morb Mortal Wkly Rep, 68(1), 1-5. doi:10.15585/mmwr.mm6801a1	https://www.ncbi.nlm.nih.gov/pubmed/?term=30629574	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Verster, J. C., & Roth, T. (2012). Gender differences in highway driving performance after administration of sleep medication: a review of the literature. Traffic Inj Prev, 13(3), 286-292. doi:10.1080/15389588.2011.652751	https://www.ncbi.nlm.nih.gov/pubmed/?term=22607251	Example: Pharmacology;
Voskuhl, R. R., & Palaszynski, K. (2001). Sex hormones in experimental autoimmune encephalomyelitis: implications for multiple sclerosis. Neuroscientist, 7(3), 258-270. doi:10.1177/107385840100700310	https://www.ncbi.nlm.nih.gov/pubmed/?term=11499404	SABV Policy Across the Translational Science Spectrum – Translational Studies;
Weissgerber, T. L., Turner, S. T., Bailey, K. R., Mosley, T. H., Jr., Kardia, S. L., Wiste, H. J., . . . Garovic, V. D. (2013). Hypertension in pregnancy is a risk factor for peripheral arterial disease decades after pregnancy. Atherosclerosis, 229(1), 212-216. doi:10.1016/j.atherosclerosis.2013.04.012	https://www.ncbi.nlm.nih.gov/pubmed/?term=23659871	SABV Policy Across the Translational Science Spectrum – Clinical Research;
White, W. M., Mielke, M. M., Araoz, P. A., Lahr, B. D., Bailey, K. R., Jayachandran, M., . . . Garovic, V. D. (2016). A history of preeclampsia is associated with a risk for coronary artery calcification 3 decades later. Am J Obstet Gynecol, 214(4), 519.e511-519.e518. doi:10.1016/j.ajog.2016.02.003	https://www.ncbi.nlm.nih.gov/pubmed/?term=26874301	SABV Policy Across the Translational Science Spectrum – Clinical Research;

Will, T. R., Proano, S. B., Thomas, A. M., Kunz, L. M., Thompson, K. C., Ginnari, L. A., . . . Meitzen, J. (2017). Problems and Progress regarding Sex Bias and Omission in Neuroscience Research. eNeuro, 4(6). doi:10.1523/eneuro.0278-17.2017	https://www.ncbi.nlm.nih.gov/pubmed/?term=29134192	Risk/Potential Impact of NOT Including SABV;
Women's health. Report of the Public Health Service Task Force on Women's Health Issues. (1985). Public Health Rep, 100(1), 73-106.	https://www.ncbi.nlm.nih.gov/pubmed/?term=3918328	SABV Policy: Concepts and Significance;
Woods, C. M., Applebaum, B., Green, Y., Kallgren, D. L., & Kappeler, E. (2015). Women's health: 30 years of progress in the U.S. Department of Health and Human Services. Public Health Rep, 130(2), 123-127. doi:10.1177/003335491513000204	https://www.ncbi.nlm.nih.gov/pubmed/?term=25729100	SABV Policy: Concepts and Significance;
Ying, W., Catov, J. M., & Ouyang, P. (2018). Hypertensive Disorders of Pregnancy and Future Maternal Cardiovascular Risk. J Am Heart Assoc, 7(17), e009382. doi:10.1161/jaha.118.009382	https://www.ncbi.nlm.nih.gov/pubmed/?term=30371154	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Yoon, D. Y., Mansukhani, N. A., Stubbs, V. C., Helenowski, I. B., Woodruff, T. K., & Kibbe, M. R. (2014). Sex bias exists in basic science and translational surgical research. Surgery, 156(3), 508-516. doi:10.1016/j.surg.2014.07.001	https://www.ncbi.nlm.nih.gov/pubmed/?term=25175501	Risk/Potential Impact of NOT Including SABV;
Zakiniaeiz, Y., Cosgrove, K. P., Potenza, M. N., & Mazure, C. M. (2016). Balance of the Sexes: Addressing Sex Differences in Preclinical Research. Yale J Biol Med, 89(2), 255-259.	https://www.ncbi.nlm.nih.gov/pubmed/?term=27354851	Understand the Limitations of Pooled Data to Detect Sex Differences;

Online and Other Resources

Reference	URL	Topic(s)
1990 GAO Report: Problems in Implementing Policy on Women in Study Populations	https://www.gao.gov/assets/110/103418.pdf	SABV Policy: Concepts and Significance;
3Rs—Reduction (Interactive Course on Experimental Design)	http://www.3rs-reduction.co.uk/	SABV in Experimental Design; Apply Statistical Approaches to Measure Sex Influences and Differences;
ABCD conference report 2018, AllofUs presentation by Joni Rutter.		Risk/Potential Impact of NOT Including SABV;
Alcohol material from https://orwh.od.nih.gov/sex-gender/sexgender-influences-health-and-disease/how-sexgender-influence-health-disease-z	https://orwh.od.nih.gov/sex-gender/sexgender-influences-health-and-disease/how-sexgender-influence-health-disease-z	Example: Addiction;
Amendment: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (NOT-OD-18-014)	https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html	SABV and Experimental Design - Additional Resources from NIH;
American Association for the Advancement of Science, Center for Public Engagement with Science & Technology. (2019). Communicating to engage.	https://www.aaas.org/resources/communication-toolkit	Sharing Sex and Gender Information Outside the Scientific Community;
Center for Behavioral Health Statistics and Quality. Results from the 2017 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2018.	https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHDetailedTabs2017/NSDUHDetailedTabs2017.pdf	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Centers for Disease Control and Prevention. Analysis of the National Vital Statistics System Multiple Cause of Death data, Wide-ranging On Line Data for Epidemiologic Research (WONDER). 2017.		SABV Policy Across the Translational Science Spectrum – Clinical Research;

Centers for Disease Control and Prevention. Fact Sheets - Excessive Alcohol Use and Risks to Women's Health. March 7, 2016. https://www.cdc.gov/alcohol/fact-sheets/womens-health.htm	https://www.cdc.gov/alcohol/fact-sheets/womens-health.htm	Example: Addiction;
Clayton J.A., & White J.M. (2017). Considering sex as a biological variable (SABV). Association for Women in Science Magazine. 03(49): 34-35, 48.	https://magazine.awis.org/publication/?i=451674&p=36&%7B%22page%22%3A%2236%22%2C%22issue_id%22%3A451674	A Checklist to Enhance SABV in Study Design; SABV and Experimental Design - Additional Resources from NIH; Identifying the Basic Elements of Guidelines for Reporting of Sex and Gender in Research - Interpretation and Generalization of Results;
Committee on Publication Ethics (COPE). (2019). COPE endorses EASE SAGER guidelines.	https://publicationethics.org/news/cope-endorses-ease-sager-guidelines	Applying Guidelines for Publishing in Scientific Journals - Journals are Making an Effort to Set Standards;
Consideration of Sex as a Biological Variable in NIH-funded Research (NOT-OD-15-102)	https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html	SABV and Experimental Design - Additional Resources from NIH; Communicating and Reporting Data by Sex;
Consideration of Sex as a Biological Variable in NIH-funded Research (NOT-OD-15-102) Guidance	https://orwh.od.nih.gov/sites/orwh/files/docs/NOT-OD-15-102_Guidance.pdf	SABV Policy: Concepts and Significance; Explain the Rationale for Characterizing and Analyzing Sex-Based Data; Apply Statistical Approaches to Measure Sex Influences and Differences; Communicating and Reporting Data by Sex; Identifying the Basic Elements
Design Institute for Six Sigma. Concepts of Experimental Design: A SAS White Paper, 2005.	http://support.sas.com/resources/papers/sixsigma1.pdf	SABV in Experimental Design;

Enhancing Reproducibility through Rigor and Transparency (NOT-OD-15-103)	https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-103.html	SABV Policy: Concepts and Significance; SABV and Experimental Design - Additional Resources from NIH; Communicating and Reporting Data by Sex;
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Gendered Innovations in Science, Health & Medicine, Engineering, and Environment. (2019). Sex and gender analysis policies of peer-reviewed journals.	https://genderedinnovations.stanford.edu/sex-and-gender-analysis-policies-peer-reviewed-journals.html	Applying Guidelines for Publishing in Scientific Journals - Specific Guidance Provided by Journals;
Genetic Components of Sex and Gender from the World Health Organization	https://www.who.int/genomics/gender/en/index1.html	A Checklist to Enhance SABV in Study Design;
Genetics Home Reference: Turner Syndrome	https://ghr.nlm.nih.gov/condition/turner-syndrome	Definitions of Sex and Gender;
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Nadel MV. Washington, DC: General Accounting Office; 1990. National Institutes of Health: Problems in Implementing Policy on Women in Study Populations. https://www.gao.gov/products/T-HRD-90-50	https://www.gao.gov/products/T-HRD-90-50	SABV Policy: Concepts and Significance;
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NIH Grants Policy Website	https://grants.nih.gov/policy/index.htm	SABV Policy: Concepts and Significance; Communicating and Reporting Data by Sex;
NIH NEWS In HEALTH--NIH. Sex and Gender. NIH News in Health. May 2016.	https://newsinhealth.nih.gov/2016/05/sex-gender	Definitions of Sex and Gender; Influence of Sex and Gender on Health;
NIH Website	https://grants.nih.gov/grants/oer.htm	SABV Policy: Concepts and Significance; Communicating and Reporting Data by Sex;
NIH Website: Administrative Supplements for Research on Sex/Gender Differences	https://orwh.od.nih.gov/research/funded-research/administrative-supplements	SABV Policy: Concepts and Significance;
NIH Website: Enhancing Reproducibility Through Rigor and Transparency	https://grants.nih.gov/policy/reproducibility/index.htm	The Impact of SABV on Research; SABV and Experimental Design - Additional Resources from NIH;

NIH Website: Legislative Mandate	https://orwh.od.nih.gov/career/mentored/legislative-mandate	SABV Policy: Concepts and Significance;
NIH Website: Rigor and Reproducibility	https://www.nih.gov/research-training/rigor-reproducibility	The Impact of SABV on Research;
Office of Women's Health, U.S. Department of Health and Human Services. Final Report: Opioid Use, Misuse, and Overdose in Women. July 19, 2017. Washington, DC.	https://www.womenshealth.gov/files/documents/final-report-opioid-508.pdf	SABV Policy Across the Translational Science Spectrum – Clinical Research;
Pragmatic & Group-Randomized Trials in Public Health and Medicine— Part 4: Power and Sample Size	https://prevention.nih.gov/education-training/pragmatic-and-group-randomized-trials-public-health-and-medicine/part-4-power-and-sample-size	Utilize Statistical and Power Analyses to Detect Sex Differences;
Principles and Guidelines for Reporting Preclinical Research (NIH)	https://www.nih.gov/research-training/rigor-reproducibility/principles-guidelines-reporting-preclinical-research	SABV Policy: Concepts and Significance; Recognizing How SABV Can Be Incorporated into the Reporting of Results; Recognizing How SABV Can Be Incorporated into the Reporting of Results - Data Handling and Analysis;
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Rigor and Reproducibility in NIH Applications: Resource Chart	https://grants.nih.gov/grants/RigorandReproducibilityChart508.pdf	The Impact of SABV on Research;
Rigor and reproducibility in NIH Applications: Resource chart.	https://grants.nih.gov/reproducibility/documents/grant-guideline.pdf	SABV Policy: Concepts and Significance; SABV and Experimental Design - Additional Resources from NIH; Communicating and Reporting Data by Sex;
Schiebinger, L., Klinge, I., Paik, H. Y., Sánchez de Madariaga, I., Schraudner, M., and Stefanick, M. (Eds.) (2011-2018). Gendered	https://genderedinnovations.stanford.edu	SABV Policy: Concepts and Significance;

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Science Media Centre. (2019). Top Tips for Media Work: A Guide for Scientists.	https://www.sciencemediacentre.org/wp-content/uploads/2013/08/SMC-Top-Tips-2015.pdf	Sharing Sex and Gender Information Outside the Scientific Community;
Specific guidance for researchers on addressing SABV in the design of cell and tissue experiments	http://genderedinnovations.stanford.edu/methods/tissues_cells	SABV Policy Across the Translational Science Spectrum – Basic Research;
The Social Issues Research Centre and Amsterdam School of Communications Research. (2019). Guidelines for scientists on communicating with the media.	http://www.sirc.org/messenger/	Sharing Sex and Gender Information Outside the Scientific Community;
The Translational Science Spectrum	https://ncats.nih.gov/translation/spectrum	SABV Policy Across the Translational Science Spectrum;
Triple-Negative Breast Cancer at BreastCancer.org	https://www.breastcancer.org/symptoms/diagnosis/trip_neg	Example: Breast Cancer;
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Union of Concerned Scientists. (2019). A scientist's guide to talking with the media desk reference. Based on the book by Richard Hayes and Daniel Grossman.	https://www.ucsusa.org/sites/default/files/legacy/assets/documents/global_warming/UCS_Desk_Reference_Scientists_Guide.pdf	Sharing Sex and Gender Information Outside the Scientific Community;
Women have higher rates of opioid-related hospitalizations in most states. (AHRQ Fast Stats)	https://www.ahrq.gov/sites/default/files/wysiwyg/data/infographics/opioid-men-women-2014.pdf	SABV Policy Across the Translational Science Spectrum – Clinical Research;