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April 21, 2020

Arlene Bierman, MD, MS, Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Bierman:

The Society for Women's Health Research (SWHR) is pleased to comment on the draft report *Care Interventions of People with Dementia (PWD) and for their Caregivers*, prepared by the Effective Healthcare Program (EPC) of the Agency for Healthcare Research and Quality (AHRQ) at the request of the National Institute on Aging (NIA). Importantly, NIA asked AHRQ to conduct a rigorous systematic review to understand the evidence base for effective nondrug care and caregiving interventions that considers the complexities and multifaceted nature of dementia across diverse populations.

The draft report's executive summary states that "ultimately, we uncovered very little evidence to support interventions and programs for active, widespread dissemination because evidence was insufficient to draw conclusions about the effects of the vast majority of interventions studied."¹ SWHR is not surprised by this finding and strongly agrees that "in order for federal funders and stakeholders to expedite the transitional pipeline of idea development to implementation, as they aim to do, critical improvements are needed in dementia care research."²

SWHR is a 30-year-old national nonprofit dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. To help overcome evidence insufficiencies, we are writing to recommend:

- AHRQ's systematic review include the evidence base on sex and gender differences in dementia and caregiving burden.
- AHRQ's final report prioritize sex and gender differences in caregiving research to address knowledge gaps.
- AHRQ's expert committee seek representative input from relevant stakeholders to inform its assessment.



In 2016, SWHR launched an interdisciplinary network³ of eight top Alzheimer's disease (AD) researchers and clinicians to examine sex- and gender-based differences in AD. For the past four years, SWHR's AD network has surveyed the current state of AD research in women, examined research gaps, and published on their findings in peer-reviewed scientific journals⁴ as well as media outlets such as STAT⁵ and Scientific American.⁶ SWHR appreciates this opportunity to share evidence-based information and recommendations for the AHRQ EPC's consideration as it finalizes its systematic review and report.

SWHR Recommendation 1a: *Include evidence on sex and gender differences in dementia and caregiving*

Unfortunately, in reviewing relevant research, most AD and caregiving studies combine data for women and men. Even though much is known about caregiving burden and its consequences on both caregivers and care recipients, there is a paucity of information on the sex and gender differences that may be present between male and female caregivers.⁷

A 2018 paper published in the journal *BMJ Open* discusses the importance of studying sex and gender differences in family caregiving, the state of the science in this area, and how these differences impact the mental and physical health of caregivers.⁸ The paper outlines a protocol for a systematic review and synthesis of the literature that could inform AHRQ's work.

SWHR urges AHRQ to include existing evidence on sex and gender differences in dementia and caregiving, as well as in the separate drug intervention evidence review referenced on page 2: Diagnosis and Treatment of Clinical Alzheimer's-type Dementia (CATD).⁹

SWHR Recommendation 1b: *Prioritize sex and gender differences in caregiving research to address knowledge gaps*

In a 2018 paper published by SWHR's AD network in the peer-reviewed *Alzheimer's & Dementia* journal,¹⁰ SWHR highlighted the state of the science on sex and gender differences in AD and addressed the knowledge gaps in assessing sex and gender differences. The paper also identified 12 priority areas that merit future AD sex and gender research, one of which was the role of sex and gender differences in caregiving and caregiving burden. We ask the AHRQ EPC to consider the following in its preparation of its final report:

Nearly 70% of caregivers are women,¹¹ and rates are even higher for Hispanics and African Americans. The responsibilities of caring for someone with dementia frequently fall to women, with daughters comprising over one-third of dementia caregivers.¹²

Women assume multiple roles while caregiving: hands-on caregiver, case manager, companion, decision-maker, and advocate. Women who are caregivers report a twofold higher level of caregiver burden compared to those who are men. While men also provide assistance, women tend to spend more time providing care than men (21.9 vs. 17.4 hours per week). Further, women are likely to assist with more difficult caregiving tasks, such as toileting and bathing, while men are more likely to assist with finances or arrange for other care.¹³

Caregiving is associated with elevated levels of cortisol and impaired attention and executive function. Dementia caregivers are broadly at risk for a variety of health difficulties, including increased rates of chronic conditions, more frequent interactions with the health care system, decreased engagement in healthy preventative behaviors, and increased behavioral health concerns, such as smoking. Caregivers also demonstrate poorer immune responses to vaccines, slowed healing time, and reduced overall immunity to diseases.¹⁴

Further, it has been hypothesized that spousal caregivers may be at higher risk of cognitive impairment or dementia than noncaregiver spouses in response to several psychosocial (e.g., depression, social isolation, and sleep problems), behavioral (e.g., exercise and diet), and physiological (e.g., metabolic syndrome and inflammation) variables.¹⁵ These findings suggest that caregiving itself may have sex-dependent effects on disease risk and outcomes for caregivers. Developing and targeting sex-dependent interventions for these risks and disease outcomes early, prior to manifestation, could attenuate future disability or possibly prevent onset.

Caregiving has a broader economic impact as well. When faced with the need to forego employment to attend to a family member that requires full-time assistance, caregivers face hardships including loss of earnings and employee benefits, loss of social service benefits, and inability to contribute to a retirement fund or participate in a pension plan. Individuals facing financial restraints may be significantly less likely to attend to preventative health care behaviors or regular appointments, or may face challenging out-of-pocket costs for their own health care or for their family's care. This in turn creates increased financial burden to our national health care system. Given that women make up the majority of caregivers, they are disproportionately impacted by these concerns.

Thus, assessing sex and gender differences in dementia and caregiving represents an opportunity to improve early diagnosis, treatment plan, and the long-term care of individuals of any gender as well as their caregivers.

SWHR Recommendation 2: Seek representative input from stakeholders who have direct experience and expertise with dementia, people with dementia, and their caregivers

We understand that a second phase of this project will involve an assessment of the AHRQ-EPC findings on this topic by an expert committee filled by the National Academies of Sciences, Engineering and Medicine (NASEM). The draft report states that because the project is following a unique model, there is no separate, independent technical expert panel.

To develop a report that conveys the current state of knowledge and describes relevant research gaps in the field, the NASEM expert committee should ensure representation from core stakeholders, including:

- Researchers and health care professionals with caregiving expertise especially those with knowledge of sex- and gender-based disparities.
- Mental health professionals who specialize in working with caregivers.
- Caregivers themselves, particularly those who assist people with dementia in their daily lives.



- Health care professionals (e.g., physicians, nurses, therapists) who specialize in clinical care for individuals living with dementia.
- Individuals with dementia diagnoses, as well as those individuals who have a diagnosed genetic predisposition to dementia.

Since nearly 70% of caregivers identify as women,¹⁶ we would strongly urge proportional sex and gender representation across stakeholder groups.

We applaud the NASEM committee for convening a public workshop on April 15, 2020, during the public comment period, to provide an overview of the AHRQ systematic review purpose, scope, methods, findings and implications. SWHR was pleased to join the virtual event. We agree with comments raised by several participants that obtaining input from individuals with dementia is needed and important, despite the possible challenges presented.

Thank you for the opportunity to comment, and we look forward to serving as a resource on this topic and seeing the final report. If you have any questions, please feel free to contact our Director of Science Policy and head of the SWHR Interdisciplinary Network on Alzheimer's disease, Melissa Laitner, PhD, MPH, at melissa@swhr.org or 202-496-5002 or Sarah Wells Kocsis, our Vice President of Public Policy and SWHR AHRQ lead, at swellskocsis@swhr.org or 202-496-5003.

Sincerely,

A handwritten signature in black ink that reads "Amy M. Miller".

Amy M. Miller, PhD
President and Chief Executive Officer
Society for Women's Health Research

Cc:

Mary Butler, PhD, MBA, Co-Director
Minnesota Evidence-based Practice Center, University of Minnesota School of Public Health

Timothy J. Wilt, MD, MPH, Co-Director
Minnesota Evidence-based Practice Center, Minneapolis VA Center for Chronic Diseases
Outcomes Research

¹ Agency for Healthcare Research and Quality Effective Healthcare Program. Care Interventions for people with dementia and for their caregivers. Retrieved from: <https://effectivehealthcare.ahrq.gov/products/care-interventions-pwd/draft-report>

² Ibid.

³ Society for Women's Health Research. Retrieved from: <https://swhr.org/society-for-womens-health-research-launches-new-interdisciplinary-network-to-focus-on-sex-differences-in-alzheimers-disease/>

⁴ As-Sanie, S., Black, R., Giudice, L., Valbrun, T., Gupta, J., Jones, B., Laufer, M., Milspaw, A., Missmer, S., Norman, A., Taylor, R., Wallace, K., Williams, Z., Yong, P., Nebel, R. 2019. Assessing Research Gaps and Unmet Needs in Endometriosis *American Journal of Obstetrics and Gynecology* 221(2), 86-94.
<https://dx.doi.org/10.1016/j.ajog.2019.02.033>

⁵ Miller, A. & Nebel, R. 2018. Studying sex differences will improve health for women and men. *Stat*. Retrieved from: <https://www.statnews.com/2018/06/13/studying-sex-differences-women-men/>

⁶ Nebel, R. 2018. Alzheimer's hits men and women differently, and we need to understand why. *Scientific American*. 2018 Retrieved from: <https://www.scientificamerican.com/article/alzheimers-hits-men-and-women-differently-and-we-need-to-understand-why/>

⁷ Xiong C, et al. Sex and gender differences in caregiving burden experienced by family caregivers of persons with dementia: a systematic review protocol. *BMJ Open*. 2018; 8:e022779. doi:10.1136/bmjopen-2018-022779.

⁸ Family Caregiving Alliance. Family Caregiving and Transitional Care: A Critical Review. 2012. Retrieved from: <https://www.caregiver.org/family-caregiving-and-transitional-care-critical-review-2012>

⁹ Agency for Healthcare Research and Quality Effective Healthcare Program. Diagnosis and Treatment of Clinical Alzheimer's-type Dementia (CATD) research protocol. Retrieved from:
<https://effectivehealthcare.ahrq.gov/products/alzheimers-type-dementia/protocol>

¹⁰ Nebel, RA., et al. Understanding the impact of sex and gender in Alzheimer's disease: A call to action. *Alzheimer's & Dementia*. 2018 1-13.

¹¹ Family Caregiver Alliance. Who Are Family Caregivers? Retrieved from:
<https://www.apa.org/pi/about/publications/caregivers/faq/statistics>.

¹² Alzheimer's Association. 2018 Alzheimer's disease Facts and Figures. *Alzheimer's Dement* 2018;14(3):367-429.

¹³ Family Caregiving Alliance. Family Caregiving and Transitional Care: A Critical Review. 2012. Retrieved from: <https://www.caregiver.org/family-caregiving-and-transitional-care-critical-review-2012>.

¹⁴ Brodaty, H. and Donkin, M. Family caregivers of people with dementia. *Dialogues of Clinical Neuroscience*, 2009 Jun; 11(2), 217-28.

¹⁵ Ibid.

¹⁶ Family Caregiver Alliance. Who Are Family Caregivers? Retrieved from:
<https://www.apa.org/pi/about/publications/caregivers/faq/statistics>.