

# **INNOVATING THE NEXT GENERATION OF DEMENTIA AND ALZHEIMER'S DISEASE CARE INTERVENTIONS:**

## **ADDRESSING THE NEEDS OF PERSONS LIVING WITH DEMENTIA, CAREGIVERS, AND CARE PROVIDERS**



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**The National Institutes of Health  
National Institute on Aging**

# **Innovating the Next Generation of Dementia and Alzheimer's Disease Care Interventions**

***Addressing the Needs of Persons Living with Dementia,  
Caregivers, and Care Providers***

July 31–August 1, 2017  
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## Table of Contents

|                                                                                                                                                                         |           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| <b>Executive Summary</b> .....                                                                                                                                          | <b>iv</b> |
| <b>Recommendations for Future Research Priorities</b> .....                                                                                                             | <b>v</b>  |
| A) Focus Intervention Research on Improving Care for Persons Living with Dementia .....                                                                                 | v         |
| B) Coordinate a Research Agenda to Address All Stages of Intervention Development and<br>Implementation .....                                                           | vi        |
| C) Address Heterogeneity and Disparities .....                                                                                                                          | vii       |
| D) Address Measurement Issues and Multiple Outcomes of Interest.....                                                                                                    | viii      |
| <b>Meeting Summary</b> .....                                                                                                                                            | <b>10</b> |
| <b>Background</b> .....                                                                                                                                                 | <b>11</b> |
| <b>Interventions Focused on Outcomes for Caregivers and Persons Living with Dementia: Informal<br/>Settings</b> .....                                                   | <b>12</b> |
| Glass Half Full: Caregiving Interventions, Gaps, and Promising Directions.....                                                                                          | 12        |
| Sleep-health in Caregivers: Need for Targeted Interventions to Improve Insomnia and Reverse<br>Insomnia-related Inflammation and Cellular Aging .....                   | 14        |
| <b>Interventions Focused on Outcomes for Persons Living with Dementia and Care Providers: Formal<br/>Settings</b> .....                                                 | <b>16</b> |
| Non-drug Interventions for Agitation and Aggression .....                                                                                                               | 16        |
| Mouth Care Without a Battle: An Important Focus and Promising Prototype of Dementia Care<br>Across Settings of Care .....                                               | 17        |
| <b>Intervention Models and Methods</b> .....                                                                                                                            | <b>19</b> |
| NIH Stage Model: Facilitating the Development of Implementable Interventions .....                                                                                      | 19        |
| Taking Stock, Optimizing Impact: Using the NIH Stage Model to Map the Science of Mindfulness-<br>based Interventions.....                                               | 21        |
| Experimental Designs for Optimizing Multi-Component Interventions .....                                                                                                 | 22        |
| Emotional Functioning in Caregivers and Dementia Patients: Using Laboratory Studies to Identify<br>Intervention Targets.....                                            | 23        |
| <b>Overcoming Systemic Barriers to Scaling Up Effective Evidence-based Interventions to Improve<br/>Outcomes: Focus on Caregivers, Care Workers, and Outcomes</b> ..... | <b>24</b> |
| Lessons Learned in Leading Adaption and Adoption: The Indiana Experience.....                                                                                           | 24        |
| Barriers to Scaling Up: Payment, Work Force, Adoption, and Adaptation .....                                                                                             | 25        |
| Systems of Care and Diffusion of Interventions That Address Living with Alzheimer's Disease .....                                                                       | 27        |
| <b>Recommendations for Future Research Priorities</b> .....                                                                                                             | <b>28</b> |
| A) Focus Intervention Research on Improving Care for Persons Living with Dementia .....                                                                                 | 29        |
| B) Coordinate a Research Agenda to Address All Stages of Intervention Development and<br>Implementation .....                                                           | 29        |
| C) Address Heterogeneity and Disparities.....                                                                                                                           | 31        |
| D) Address Measurement Issues and Multiple Outcomes of Interest.....                                                                                                    | 32        |
| <b>Appendix 1: Agenda</b> .....                                                                                                                                         | <b>33</b> |
| <b>Appendix 2: Participant List</b> .....                                                                                                                               | <b>35</b> |

## Executive Summary

More than 5 million Americans live with dementia,<sup>1</sup> and the number of people with Alzheimer's disease, the most common cause of dementia, is projected to reach 13.8 million by 2050.<sup>2</sup> On average, persons living with dementia spend \$321,780 on care over the course of the disease, with most of the financial responsibility falling on families.<sup>3</sup> Most persons living with dementia live at home and are cared for by a family member or friend—typically a spouse or adult child. More than 15 million unpaid family and friends care for persons living with dementia,<sup>4</sup> and this number will increase as the baby boomer generation ages. Persons living with dementia and their caregivers often face difficulties in coping with and managing the condition. Persons living with dementia generally need more support from their caregivers than those without dementia. In addition to arranging health care visits, participating in medical decision making, and coordinating support services, caregivers of persons living with dementia must keep the person safe and address the behavioral and psychological symptoms experienced by 80 to 90 percent of persons living with dementia. Moreover, persons living with dementia and their caregivers should have the opportunity to experience positive outcomes and quality of life.

Currently, no pharmacological treatments exist to prevent, cure, or significantly delay the onset or progression of Alzheimer's disease and related dementias (ADRD). However, rigorous research has shown that some nonpharmacological interventions can have positive effects for persons living with dementia and/or their family caregivers. Although these evidence-based interventions have been shown to be efficacious in research settings, they have not been widely translated to community settings across the United States. Caregivers of persons living with dementia experience challenges in performing nursing tasks and assisting with activities of daily living, such as eating, bathing, and meal preparation.

Recognizing the need for action, the Division of Behavioral and Social Research (BSR) at the National Institute on Aging (NIA), National Institutes of Health (NIH), convened a meeting on July 31 and August 1, 2017, to obtain expert opinion on the state of research for evidence-based care interventions that target persons living with dementia and/or their caregivers, and to articulate a future research agenda. Presenters and discussants were asked to classify the various formal and informal care interventions in terms of the populations, outcomes targeted, and the settings in which they have been studied (e.g., at home, assisted living, nursing homes, physician's offices, community settings), and to present examples of specific interventions. Another meeting objective was to identify the barriers to adoption of evidence-based interventions and strategies to overcome such barriers.

Invited experts presented a range of original research, including interventions in mouthcare, caregiver sleep health, dementia care mapping, emotional functioning, and mindfulness, and findings from systematic reviews to illuminate gaps, promising directions, and future needs for the next generation of Alzheimer's and dementia care interventions. They also described intervention development research models, innovative research designs, and methods for addressing scalability, diffusion, and translation.

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<sup>1</sup> Hebert, L.E., Weuve, J., Scherr, P.A., & Evans, D.A. (2013). Alzheimer's disease in the United States (2010-2050) estimated using the 2010 Census. *Neurology*, 80, 1778-1783.

<sup>2</sup> See [http://www.alz.org/documents\\_custom/2017-facts-and-figures.pdf](http://www.alz.org/documents_custom/2017-facts-and-figures.pdf) (p. 24).

<sup>3</sup> Jutkowitz, E., Kane, R.L., Gaugler, J.E., MacLehose, R.F., Dowd, B., & Kuntz, K. M. (2017). Societal and family lifetime cost of dementia: Implications for Policy. *Journal of the American Geriatrics Society*, 10.1111/jgs.15043.

<sup>4</sup> See [http://www.alz.org/documents\\_custom/2017-facts-and-figures.pdf](http://www.alz.org/documents_custom/2017-facts-and-figures.pdf) (p. 33).

These efforts are consistent with the goals set forth by the National Alzheimer's Project Act (NAPA) (Public Law 111-375), which requires the Secretary of the U.S. Department of Health and Human Services (HHS) to establish the National Alzheimer's Project to create, maintain, and coordinate an integrated National Plan to overcome Alzheimer's disease. Recommendations from this meeting are intended to inform NIA's future research agenda priorities as well as the proceedings of the National Research Summit on Care, Services, and Supports for Persons with Dementia and Their Caregivers scheduled for October 2017.

## Recommendations for Future Research Priorities

Several themes for future research priorities for NIH and other funding agencies emerged from the presentations and session-specific and general discussions. Meeting organizers encouraged invited experts to frame their thoughts and recommendations around the stages of intervention research described in the NIH Stage Model.<sup>5</sup> Each invited expert reflected on the most pressing research needs and, in particular, strategies for ensuring a coordinated, systematic research agenda that addresses all research stages to maximize the effectiveness and implementability of efficacious and effective interventions in real-world settings.

Four primary themes for a future research agenda emerged: (A) focus intervention research on improving care for persons living with dementia; (B) coordinate a research agenda to address all phases of intervention development and implementation; (C) address heterogeneity and disparities; and (D) address measurement issues and multiple outcomes of interest. Meeting participants discussed and recommended research priorities for each theme.

### A) Focus Intervention Research on Improving Care for Persons Living with Dementia

- 1) **Funders should support research that focuses specifically on developing and testing interventions targeted at improving the quality of life and other outcomes of relevance for persons living with dementia in home settings and residential long-term care settings, including assisted living and nursing homes.** Expansion of evidence-based caregiver interventions is important. However, there is a research and policy vacuum for interventions specifically aimed at improving life for persons with ADRD. Such interventions should be user-friendly and include methods to ensure real-world fidelity, such as validated training materials. Interventions should be tested to determine the most potent components and the principles underlying these components, be consonant with patient and caregiver preferences, and address cost-effectiveness.

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<sup>5</sup> Onken, L., Carroll, K., Shoham, V., Cuthbert, B., & Riddle, M. (2014). Reenvisioning clinical science: Unifying the discipline to improve the public health. *Clinical Psychological Science*, 2, 22-34. Overview available from <https://www.nia.nih.gov/research/dbsr/stage-model-behavioral-intervention-development>.

- 2) **Technology-based interventions may improve care delivery for persons living with dementia.** More research should focus on how assistive and other technologies may allow persons living with dementia to live independently in their homes for a longer time. Technology-based interventions could address health and wellness, social connectivity, independent living, and/or caregiver supports in different settings. Such interventions could be targeted at the caregiver, the person living with dementia, or both, and could include the use of mobile devices, online platforms, telehealth, wearables, and home sensors.

## **B) Coordinate a Research Agenda to Address All Stages of Intervention Development and Implementation**

- 1) **Basic mechanistic research is needed to determine the mechanisms underlying efficacious and effective interventions aimed at improving quality of life for persons with ADRD and their caregivers.** Questions regarding mechanisms of behavior change may be included most successfully in Stages 0, I, II, and III. Understanding the mechanisms of behavior change can promote implementation and translation of an intervention and can allow for more precise targeting of the most vulnerable and therefore improved intervention efficacy. In addition, such understanding makes it clear to people administering the intervention what they are doing, why they are doing it, and how they should be doing it. Factorial and adaptive research designs can be employed to understand better the potent components of an intervention and how best to sequence and tailor intervention components.
- 2) **Research is needed on translating existing care models, services, and technologies to improve the lives of persons with ADRD and their caregivers into real-world settings.** It is important to study the impediments to implementing such interventions in the real-world setting, which includes training caregivers (both formal and informal) and insuring that the interventions can be integrated into standard operating procedures of the existing care system be it the home, residential care setting, or even a senior center. Stage I research is needed to increase efficacy, more precisely match the intervention to the time-varying needs of persons with ADRD and their caregivers, determine the mechanisms or principles underlying the interventions, streamline interventions, modify interventions for the real world, develop training procedures and protocols for community interventionists, and develop measures to ensure fidelity. Stage II research tests interventions in research settings, and Stage III research tests efficacious interventions in real-world settings. Stage IV research is needed when interventions are ready to be tested in pragmatic clinical trials.
- 3) **Researchers should consider scalability and sustainability at the beginning of intervention development and throughout subsequent research.** Multiple studies may be required to determine what form(s) of the intervention can be optimally implemented. For example, to address all issues of scalability and sustainability, particularly for low-resource settings and populations, multiple Stage I and Stage III studies are often necessary to precede successful Stage IV pragmatic trials. Pragmatic trials allow researchers to collect the basic data needed to implement and translate an intervention in different settings and/or populations. Implementation science research is needed to emphasize studying the process of how practices, interventions, and policies are disseminated, adapted (as needed), adopted, integrated and sustained in everyday health-focused settings, and ultimately would inform successful translation.

- 4) **When appropriate, researchers should communicate with interdisciplinary colleagues and/or key stakeholders who can provide valuable input into the design of interventions.** Implementation science is characterized, in part, by partnerships with key stakeholder groups (e.g., end-users, providers, organizations, systems, and/or communities), and investigators should be encouraged early in the intervention design process to partner with these stakeholder groups. The research funders could facilitate these relationships, or signal the importance of such relationships in funding opportunity announcements. In addition, investigators should be encouraged to build interdisciplinary teams from the design stage forward to include not only academic social scientists but also their colleagues from schools of business, law, medicine, and others.
- 5) **Research should focus on using leverage points for diffusion of efficacious and effective interventions.** Interventions for persons with ADRD and their caregivers are not “owned” by any single component of the care system, and widespread adoption may require both a social care and a medical diffusion pathway. Such work should include considerations such as how to design evidence to inform actions available to government-funded programs, how to target health care systems, and how demographic shifts and labor market forces can advance diffusion of interventions that improve the lives of persons with ADRD. Incorporating the target for diffusion (e.g., a nursing home)—in addition to the target of the intervention (e.g., the person with ADRD)—into research will help build evidence for diffusion.

### C) Address Heterogeneity and Disparities

- 1) **Funders should support research on intervention development with diverse participant populations.** Diverse characteristics may include race and ethnicity, geographic location, home settings of the person with ADRD (living alone, with extended family, in an assisted living facility), socioeconomic status, educational background (for both the person with ADRD and caregivers), intellectual and developmental disability status, and family caregiver relationship (adult child versus spouse). It is also important to understand how and why interventions work for caregivers with a variety of characteristics, including those with and without mental illness and/or depression, multiple and/or chronic conditions, and demonstrated resilience. Given the diverse needs and recipients, different intervention components may work better for different participants.
- 2) **Caregiving research should prioritize studies that can determine not only whether an intervention has statistically significant positive outcomes for the entire sample, but also to characterize the persons living with dementia and/or family caregivers for whom the intervention does or does not work.** Given the heterogeneity of persons living with dementia, family caregivers, caregiving situations, and changes in the care needs of persons living with dementia over time, it is unlikely that any single evidence-based program will be effective for all families. However, little research has been conducted to identify what works for which persons living with dementia and caregivers under what circumstances in what settings. Understanding of the principles that guide an intervention's success for one group but not another would inform future research into the generalizability of the intervention to another population with similar characteristics. In addition, precision in matching the various interventions to the individual and time-varying needs of caregivers can increase efficacy and enable allocation of intervention resources to those most vulnerable. To acquire this nuanced understanding, researchers may need to conduct more than one study to determine which recipients did or did

not benefit. When evaluating the utility of an intervention for a population with specific characteristics, researchers should examine the mechanism(s) of behavior change of the intervention. In addition, they should design studies so that they can determine whether suboptimal results occurred because of inadequate exposure to or implementation of the intervention or because of sub-group differences.

- 3) **Research is needed to determine the implications of the different types of dementia on intervention outcomes.** Clinical scientists attribute importance to disease type (e.g., AD, frontal lobe, Lewy body dementia, vascular, young-onset Alzheimer's, and mixed dementia), but the unreliability of these diagnoses in real-world clinical practice is well known. It would be helpful to consider how important these diagnoses are for the outcomes experienced, particularly by the caregivers, and whether caregiver outcomes differ as a function of the type of dementia (independent of duration or symptom severity even though correlated). Many behavioral or caregiver intervention studies recruit from non-research-intensive clinical settings that might not differentiate diagnoses reliably. The field would benefit from greater understanding of the importance of heterogeneity of dementia type to the generalizability of the intervention.
- 4) **More research is needed—both to determine efficacy and effectiveness—to develop and/or test interventions that work for persons in the early stages of dementia and for their caregivers.** Much of the current caregiving research focuses on persons with later-stage dementia. Care research is needed that focuses on early detection and diagnosis of dementia for persons living in the community, the possible consequences of early diagnosis, and opportunities to intervene in the earlier stages of dementia.
- 5) **Funders should support research into developing interventions that aim to reduce multiple dimensions of disparities in access to high-quality dementia care and that attempts to understand how and why such interventions differentially impact persons with specific disparities.** Such disparities can be area-based (geography), person-based (race, ethnicity, gender, socioeconomic status), and/or insurance-based (Medicaid, Medicare, dual beneficiaries, private insurance).

#### **D) Address Measurement Issues and Multiple Outcomes of Interest**

- 1) **More research is needed to determine the best measurement strategies and outcomes of importance for persons living with dementia and their caregivers.** For example, it would be valuable to know what outcomes are important to key stakeholders, including the end-users, before interventions are developed. In addition to focusing on deficits, outcomes should include positive components, such as resilience, and health events and morbidities. The clinical health of caregivers has at times been minimized relative to the psychosocial issues of persons living with dementia. In addition, researchers should examine and test for bias in measurement tools and address how best to collect data in community settings.
- 2) **Research that builds longitudinal data systems is needed to support work on trajectories of dementia and dementia care and the progression of disease and caregiving needs.** Much intervention research is focused on one setting, episode, or point in time of a dementia trajectory. More work needs to be done to understand the changing needs of persons living with dementia, most appropriate interventions for each stage of dementia, and the types of caregiving supports needed at each stage. For example, a cohort of Medicare beneficiaries could

be created with important event data from which participants could be periodically recruited contingent upon the occurrence of critical events such as hospitalization, post-acute care use, and residential mobility. Such analysis could enhance understanding of experiences around crisis events within the longitudinal frame of dementia experience.

- 3) **Intervention development research for persons with ADRD and their caregivers should more often include a cost-effectiveness component.** Tests of cost-effectiveness, health care utilization, and savings assessments should be included in Stage IV work after the groundwork from earlier stages has been completed. Assessing cost-effectiveness, with an expansive definition of costs that includes all costs to whomever bears them, may be essential in promoting the widespread adoption of interventions. Knowing the actual cost of interventions can help to determine which interventions are likely to realize the greatest system-wide impact. Including health economists, actuaries, or cost-analysts in the research team starting in the design phase would increase the likelihood that these elements are considered.

## Meeting Summary

On July 31 and August 1, 2017, the Division of Behavioral and Social Research (BSR) at the National Institute on Aging (NIA), National Institutes of Health (NIH), sought expert opinion on the state of research for evidence-based care interventions that target caregivers and persons living with dementia and to guide a future research agenda. Presenters and discussants were asked to classify the types of care interventions in terms of the populations, targeted outcomes, and settings (e.g., at home, assisted living, nursing home, physician's office, community setting) and to provide examples of interventions. Another goal of the meeting was to identify the barriers that make adoption of evidence-based interventions difficult and strategies for overcoming such barriers. Recommendations from this meeting are intended to inform NIA's research agenda priorities as well as the proceedings of the National Research Summit on Care, Services, and Supports for Persons with Dementia and Their Caregivers scheduled for October 2017 at the NIH.

Workshop organizers Elena Fazio and Lisa Onken, and the NIA/BSR Director, John Haaga, welcomed participants and reiterated the goals of the meeting. Through research presentations and moderated discussions, NIA asked participants to consider a range of needs for both persons living with dementia and caregivers, explore changes that may be needed to interventions when used in a variety of settings, assess the research needs in different stages of disease, and be mindful of the role that technology might play in implementation and adoption of interventions.

Workshop organizers asked participants to consider priorities and research agendas through the lens of the NIH Stage Model. One concern is that current intervention research for persons with ADRD and their caregivers could be more strategically organized by a well-informed research agenda that addresses research gaps spanning basic behavioral research, intervention development, efficacy testing, real-world efficacy testing, effectiveness studies, and implementation and dissemination research. The NIA sought expert advice on how best to design a research agenda that would yield not only efficacious interventions, but also interventions that are effective in real-world settings for diverse persons living with dementia and their caregivers.

### **The National Research Summit on Care, Services, and Supports for Persons with Dementia and Their Caregivers**

The goal of the October 2017 Summit is to identify what is established and what still needs to be learned to accelerate the development, evaluation, translation, implementation, and scaling up of comprehensive care, services, and supports for persons with dementia, families, and other caregivers. The Summit is focused on research that is needed to improve quality of care and outcomes across care settings, including quality of life and the lived experience of persons living with dementia and their caregivers. This Summit will develop recommendations for research priorities to inform federal agencies, foundations, and private-sector organizations; identify evidence-based programs, strategies, and approaches that can be used now to improve care and services; and research milestones to track and guide acceleration and advancement of evidence-informed care and services.

According to a recent *The Lancet* special issue<sup>6</sup> that examined the state of the science, much more research is needed to help prepare for the dementia epidemic, and it will be future decades before preventive therapeutics become available. Current research is addressing questions that, when answered, will help persons living with dementia in the future. However, there is also a need to better determine how to manage dementia and to treat and care for persons living with dementia, and their caregivers, during the next 10 to 20 years.

## Background

More than 5 million Americans live with dementia,<sup>7</sup> and the number of people with Alzheimer's disease, the most common cause of dementia, is projected to reach 13.8 million persons by 2050.<sup>8</sup> On average, persons living with dementia spend \$321,780 on care over the course of the disease, with most of the financial responsibility falling on families.<sup>9</sup> Persons living with dementia and their caregivers often face great difficulties in coping with and managing the condition. Most individuals with dementia live at home and are cared for by a family member or friend—typically a spouse or adult child. More than 15 million unpaid family and friends care for persons living with dementia,<sup>10</sup> and as the baby boomer generation ages, this number will increase. Persons living with dementia generally need more support from their caregivers than those without dementia. In addition to arranging health care visits, participating in medical decision making, and coordinating support services, caregivers of persons with ADRD must keep the person safe and address the behavioral and psychological symptoms experienced by 80 to 90 percent of people with dementia. Caregivers of persons living with dementia also experience challenges in performing nursing tasks and helping with activities of daily living, such as eating, bathing, and meal preparation.

Currently, no pharmacological treatments exist to prevent, cure, or significantly delay the onset or progression of ADRD. Rigorous research has shown, however, that some nonpharmacological interventions can have positive effects for persons living with dementia and their caregivers. Although these evidence-based interventions have been shown to be efficacious in research settings, they have not been widely translated to community settings across the United States.

### National Alzheimer's Project Act

On January 4, 2011, the president signed into law the National Alzheimer's Project Act (NAPA) (Public Law 111-375), which requires the Secretary of the U.S. Department of Health and Human Services (HHS) to establish the National Alzheimer's Project to: (1) Create and maintain an integrated National Plan to overcome Alzheimer's disease; (2) Coordinate Alzheimer's disease research and services across all federal agencies; (3) Accelerate the development of treatments that would prevent, halt, or reverse the course of Alzheimer's disease; (4) Improve early diagnosis and coordination of care and treatment of Alzheimer's disease; (5) Decrease disparities in Alzheimer's disease for ethnic and racial minority populations that are at higher risk for Alzheimer's disease; and (6) Coordinate with international bodies to fight Alzheimer's disease globally.

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<sup>6</sup> See *The Lancet* special issue, Dementia Prevention, Intervention and Care, July 19, 2017, available at <http://www.thelancet.com/commissions/dementia2017>.

<sup>7</sup> Hebert, L.E., Weuve, J., Scherr, P.A., & Evans, D.A. (2013). Alzheimer's disease in the United States (2010-2050) estimated using the 2010 Census. *Neurology*, 80, 1778-1783.

<sup>8</sup> See [http://www.alz.org/documents\\_custom/2017-facts-and-figures.pdf](http://www.alz.org/documents_custom/2017-facts-and-figures.pdf) (p. 24).

<sup>9</sup> Jutkowitz, E., Kane, R.L., Gaugler, J.E., MacLehose, R.F., Dowd, B., & Kuntz, K.M. (2017). Societal and family lifetime cost of dementia: Implications for Policy. *Journal of the American Geriatrics Society*, 10.1111/jgs.15043.

<sup>10</sup> See [http://www.alz.org/documents\\_custom/2017-facts-and-figures.pdf](http://www.alz.org/documents_custom/2017-facts-and-figures.pdf) (p. 33).

## **Interventions Focused on Outcomes for Caregivers and Persons Living with Dementia: Informal Settings**

### **Glass Half Full: Caregiving Interventions, Gaps, and Promising Directions**

*Laura Gitlin, Johns Hopkins University*

#### ***State of the Science***

Caregiver intervention studies are continually improving in design, rigor, and inclusion of diverse populations. Through 7 meta-analyses and 17 systematic reviews including randomized controlled trials (RCTs) of 200 family caregiver support programs with more than 8,000 families, Gitlin and colleagues identified six broad types of interventions: professional support, psycho-education, behavior management/skills training, counseling/psychotherapy, self-care/relaxation training, and multi-component interventions. Outcome measures for caregivers included knowledge, burden, self-efficacy, psychological morbidity (anxiety/depression), and, for persons living with dementia, behavioral symptoms and time to institutionalization. However, a large gap remains between tested interventions and implementation in real settings. One promising new research direction is to embed studies of caregiving interventions in health systems for pragmatic trials (Stage IV).

Gitlin highlighted three studies from the meta-analyses and systematic reviews that show strong evidence for caregiver interventions tested in RCTs. The New York University Caregiver Counseling and Support study in 406 study patients reduced spousal caregiver upset and nursing home placement over time, but had no effect on behavioral frequency or severity. Resources for Enhancing Alzheimer's Caregiver Health (REACH) I and II, funded by NIA and the National Institute of Nursing Research, examined behavioral management, education, and support in 600 people. Results demonstrated improved caregiver well-being and perceived improvement in behaviors, but no effect on nursing home placement. Project Advancing Caregiver Training (ACT) focused on caregiver support and skill building through 10 sessions with occupational therapists and nurses. Results of the intervention at 16 weeks showed improvements in aspects of caregiver emotional well-being and caregiver skills as well as reductions in the frequency of behavioral symptoms of the person living with dementia, which was identified as most challenging to families.

This body of work has yielded several principles for successfully supporting caregivers, including assessing for unmet needs; tailoring the intervention to the stage of dementia and identified caregiver needs; providing repeated exposure to information and education that is easily accessible on the caregiver's own time and terms; and providing opportunities for hands-on learning. In addition, interventions that are multi-component, caregiver-centric, and long-term have been shown to be the most potent. Multi-component interventions address multiple caregiver needs (e.g., education, skills, counseling, environmental modification) and a broad range of needs for different stages, preferences, and values. Caregiver-centric programs address self-identified needs, which demonstrates respect for the caregiver role. Empowering caregivers to remain in control of how and when they receive information and providing opportunities to learn through doing are critical elements of caregiver supportive approaches that are effective. Lastly, it is most helpful when exposure to these interventions exists through treatment over time to delay nursing home placement. However, brief support and provision of education is also important to alleviate immediate challenges and situational distress.

### **Research Gaps**

Critical gaps in the research pose as a barrier to generalizing and replicating interventions. Information is lacking, for example, on which interventions work for different caregivers caring for persons at different stages of dementia (i.e., what intervention works for whom, under what circumstances, in what settings). There has been no RCT of a comprehensive dementia care approach that addresses the disease trajectory.

Caregiving needs differ in the early versus later stages of the disease process. There is great diversity in caregiver needs depending on the care setting, who is providing care and their resources, and the needs of the person living with dementia. In developing interventions, the opportunity exists to target the caregiver, the person living with dementia, the physical environment, or a combination of these, with some benefits being indirect (e.g., an intervention enhancing quality of life of the person with dementia may also reduce caregiver distress or vice versa). Other design considerations are how, when, and where an intervention will occur and be sustained.

The majority of caregiver intervention studies have been efficacy trials in research settings (Stage II) or settings that are not necessarily real world. With few exceptions, trials hire and train interventionists and do not employ community-based providers for delivery (Stage III). Furthermore, few address cost-effectiveness. The outcome evidence on health care utilization, health care savings, and physical disease burden is limited. The samples are often poorly characterized in terms of stage and type of dementia and disease state, and information is lacking regarding the impact of interventions for caregiver subgroups, including men, ethnic and racial minorities, and caregivers in rural areas, or those traveling long-distance to provide care. In addition, most existing studies are not linked to the needs identified in the epidemiologic record and are not representative of the general population of family members. Finally, the mechanisms of behavior change that explain why and how an intervention works are unclear, which makes scaling up, translation to different settings, and replication difficult.

### **Future Directions**

Collaborative care models linking social and clinical care that involve comprehensive assessment, referral, and linkages to other components are showing promise. Three examples were described: Partners in Dementia Care, which connects services from the Alzheimer's Association and Veterans Affairs; the Primary Care Collaborative Model, which has shown improvements for both ADRD patients and their caregivers; and the University of California, Los Angeles (UCLA) Alzheimer's and Dementia Care Program, which refers patients to services for unmet needs. Integrating proven interventions into existing care settings is also a highly promising approach. Gitlin highlighted the translation of REACH II in the Veterans Affairs system; a current effectiveness/implementation trial implementing the COPE intervention in Medicaid Waiver and community-based programs; and a similar hybrid trial augmenting adult day services (ADS) with systematic support of family caregivers (the ADS Plus program).

Gitlin recommended a robust future research agenda based on her extensive review of the existing literature and current body of caregiver intervention research. Investment in studies of intervention development and efficacy (both clinical and real-world) (Stages IA, IB, II, and III) need to be better balanced with studies of translation, implementation, and dissemination (Stage IV and V). Table 1 provides additional details on suggested future directions for dementia caregiver interventions.

**Table 1: Next Generation of Dementia Caregiver Interventions**

Source: Laura N. Gitlin, July 31, 2017

| Domain                                                                                                                  | Specifics                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Improve clinical relevance of trials</b>                                                                             | <ul style="list-style-type: none"> <li>Examine mechanisms or why interventions have positive effects</li> <li>Evaluate dose-response relationships</li> <li>Evaluate cost and willingness to pay</li> <li>Determine and report clinical significance</li> </ul>                                                                                                                                                                                                        |
| <b>Adequately describe interventions to enable reproducibility, replication, adaptation, widespread adoption</b>        | <ul style="list-style-type: none"> <li>Identify theory base guiding intervention</li> <li>Describe interventionist characteristics</li> <li>Detail number of sessions, duration and length of intervention</li> <li>Describe role of family caregiver in delivering intervention or supporting use of strategies for person with dementia</li> <li>Describe treatment fidelity plan and adherence rates</li> <li>Describe type of blinding applied to trial</li> </ul> |
| <b>Improve outcome measures</b>                                                                                         | <ul style="list-style-type: none"> <li>Derive consensus in the field as to set of outcome measures for cross-study comparisons</li> <li>Consider use of objective (performance-based), biological and subjective measures</li> </ul>                                                                                                                                                                                                                                   |
| <b>Enhance study designs</b>                                                                                            | <ul style="list-style-type: none"> <li>Locate design to stage model</li> <li>Mediation and moderation analyses</li> <li>Use pragmatic trial designs, hybrid designs and/or mixed methods to examine effectiveness and implementation processes simultaneously</li> <li>Standardize attention control groups used across studies to address attention, attrition</li> <li>Examine long-term treatments and treatment effects</li> </ul>                                 |
| <b>Map interventions to caregiver needs, dementia stage, persons needs, and race/ethnic/culturally diverse families</b> | <ul style="list-style-type: none"> <li>Address broader range of needs and for different stages, preferences, values</li> <li>Examine dyadic relationships and which types of interventions impact carer and person;</li> <li>Move beyond isolating primary caregiver and examine informal networks, family decision-making</li> </ul>                                                                                                                                  |

## Sleep-health in Caregivers: Need for Targeted Interventions to Improve Insomnia and Reverse Insomnia-related Inflammation and Cellular Aging

Michael Irwin, University of California, Los Angeles

### **Insomnia and Caregivers**

There are 5 million Alzheimer's caregivers in America, and a three-fold increase is projected over the next decade. Greater than 60 percent of ADRD caregivers report sleep disturbances. Despite this current landscape, of more than 120 clinical trials Irwin reviewed, none targeted clinical insomnia in caregivers. Given what is known about insomnia, the current research gaps, and the availability of effective treatments, addressing insomnia in caregivers is an important future research priority.

Insomnia and sleep disturbance is both a risk factor and an outcome of caregiver burden. Caregiver burden and distress can lead to insomnia. In turn, insomnia contributes to caregiver burden, symptoms of distress, difficulty maintaining a healthy lifestyle (e.g., diet, exercise), lack of adherence to medical regimens, increased risk of depressive symptoms and depression, and increased risk of morbidity and mortality possibly by accelerating biological mechanisms of aging (e.g., inflammation, molecular aging). Insomnia and sleep disturbance are often neglected in the assessment of caregivers. Importantly, insomnia is a modifiable risk factor, which can be effectively treated.

### **Insomnia and Inflammation**

Individuals with insomnia experience waking repeatedly throughout the night, difficulty falling or staying asleep, non-restorative sleep, and daytime impairments such as fatigue and depressed mood. Insomnia can increase morbidity and mortality risk and is a contributing factor to the development of many chronic conditions including diabetes, cardiovascular disease, rheumatoid arthritis, cancer, and depression.

Inflammation is one mechanism that is thought to drive increased mortality and morbidity risk in insomnia. In a systematic review of sleep disturbance, sleep duration, and inflammation, Irwin and colleagues found evidence of activation of morning cellular and genomic levels of inflammation, epigenetic accelerated aging, and shorter telomere length in association with sleep disturbance. Inflammation is easily measured and thus allows researchers to use a biomedical marker to track biologic responses to sleep interventions; treatment of insomnia has been found to reduce systemic, cellular, and genomic markers of inflammation. Lack of sleep can also drive biologic aging because inflammation accelerates molecular aging and, in turn, cellular aging leads to increases in inflammation. Given that markers of molecular aging correlate with morbidity and mortality, intervention studies should include markers of molecular aging, such as telomere length to understand how treatment of insomnia might impact age-related chronic disease risk. Patients with insomnia have shorter telomeres, and older adults are particularly sensitive to this effect (i.e., the rate of shortening is increased).

### ***Treatments for Insomnia***

Insomnia treatments include pharmacotherapy approaches, cognitive-behavioral therapy (CBT), and mind-body interventions such as yoga, meditation, mindfulness, or tai-chi. All three types have been found to be efficacious treatments for insomnia, although pharmacotherapy might not be safe for family caregivers who themselves might be elderly. CBT is the treatment of choice of the American Academy of Sleep Medicine, but it requires intensive training by a trained therapist, which might not be feasible for caregivers. Mind-body interventions are safe, efficacious if adhered to, and could be more feasible for caregivers than intensive CBT.

Irwin and colleagues developed and tested a promising mindful awareness practice for insomnia (MAP-I), which is based on Mindfulness Based Stress Reduction. MAP-I is a validated and curriculum-based mind-body intervention that trains participants in the systematic practice of attending to moment-by-moment experiences, thoughts, and emotions from a nonjudgmental perspective. The treatment targets insomnia by incorporating practice prior to bed, use of practice in the bed during night-time awakenings, and a daily body scan. More than 50,000 Americans have received MAP-I in community settings. One study that measured biologic markers showed improvements in depression and fatigue as well as lowered C-reactive protein measures indicating diminished inflammation.

### ***Future Directions***

Targeting insomnia in caregivers is significant and innovative, because prior caregiver intervention trials have primarily focused on skills-based training and support. Insomnia is prevalent in ADRD caregivers, and treatment of sleep problems may reduce caregiver burden. Because sleep disturbance impacts risk of depressive symptoms and chronic medical morbidity, targeting sleep disturbance may prevent or forestall onset of depression and progression of age-related declines in health span in ADRD caregivers. Mind-body interventions including meditation, Tai Chi, and yoga have robust effects in the treatment of insomnia, with additional benefits in reversing systemic inflammation, cellular inflammation, and inflammatory gene expression, and in slowing the biological clock of molecular aging.

The next generation of caregiver interventions, such as treatment of insomnia, have the potential to target behavioral symptoms while evaluating biological mechanisms. Innovative RCTs can bridge, for example, the continuum from behavioral factors (i.e., sleep) to molecular stress, and identify interventional strategies that can target behaviors as well as alter the course of the biological mechanisms of aging, to optimize health over the lifespan.

## Interventions Focused on Outcomes for Persons Living with Dementia and Care Providers: Formal Settings

### Non-drug Interventions for Agitation and Aggression

*Vincent Mor and Eric Jutkowitz, Brown University*

Fundamental assumptions underpin much of the work on behavioral interventions. For example, interventions can always make a meaningful difference, that they should be used regardless of situation, and that they will eventually be implementable in real-world settings. We need to think carefully about these assumptions. There is a need to better understand not only what interventions work, but also how they work and in which settings and populations.

#### ***Systematic Review and Meta-analysis of Non-drug Interventions***

The Agency for Healthcare Research and Quality (AHRQ) funded a systematic review of non-pharmacologic interventions addressing agitation and aggression. Lessons from the systematic review broadly highlight challenges of developing, evaluating, and implementing dementia interventions. To conduct the review, investigators searched multiple electronic databases for RCTs that evaluated the efficacy, effectiveness, or comparative effectiveness of non-drug approaches for preventing or responding to agitation or aggression in persons with dementia. Comparison arms included standard care, placebo, other behavioral approaches, and pharmacologic interventions. The primary outcomes were frequency, duration, and severity of agitation, aggression, general behavioral symptoms, and admission to a long-term care facility. Secondary outcomes included staff and caregiver distress and burden and perceived quality of life for the person with dementia. Studies were grouped by setting (facility vs community), delivery mechanism (e.g., through a formal care provider, through an informal caregiver, or directly to the person with dementia), and by intervention type (e.g., music therapy or dementia care mapping). The presentation for the current workshop focused specifically on interventions delivered in long-term care facilities.

The review determined that studies showed either insufficient or low strength evidence (as defined by AHRQ) for no difference between intervention and control groups on the primary (i.e., agitation and aggression) and secondary outcomes. Most of the studies included in the review were single trials that were not replicated.

#### ***Case Study: Dementia Care Mapping—Issues with Measurement and Implementation***

Dementia Care Mapping (DCM) was used as a case study to highlight challenges of implementing dementia interventions in long-term care facilities. DCM represents one potential approach for addressing agitation and aggression among persons with AD/DRD in a long-term care facility. DCM involves using specially trained staff or experts to systematically observe a person with dementia. Feedback is then provided to care staff who use the information to develop person-centered care plans. The approach requires expert training and is labor intensive.

Three studies highlight the challenges associated with implementing DCM.<sup>11</sup> In an early phase trial by Chenoweth and colleagues, researchers and DCM-trained facility staff carried out observation sessions.

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<sup>11</sup> Chenoweth, L. et al. (2009). Caring for aged dementia care resident study (CADRES) of person-centered care, dementia-care mapping, and usual care in dementia: A cluster-randomized trial. *The Lancet Neurology*, 8, 317-325.

Following the observation sessions, the researchers and facility staff developed and then implemented care plans. At follow up, those in the intervention group had significantly less agitation and aggression compared to those in usual care as measured by the Cohen Mansfield Agitation Inventory. In a follow-up study, Rokstad and colleagues evaluated DCM. Staff trained in DCM joined researchers to conduct observation sessions. Following observation, staff developed and implemented care plans without researcher input. The authors reported no significant difference between intervention and control groups on the primary measure of agitation and aggression. On a secondary measure of agitation and aggression (NPI agitation subscale), the authors reported a statistically significant reduction in agitation and aggression, favoring DCM over usual care. However, it was unclear whether the statistical benefit translated to a clinically meaningful effect. Finally, Van de Ven and colleagues evaluated another version of DCM, in which staff were trained to conduct observations and develop care plans. At follow-up, there was no statistical difference on the primary measure of agitation or aggression for those in the intervention group compared to the usual care group. The DCM literature shows that effectiveness declined as the level of control shifted from researchers to staff.

Overall, there are many challenges to testing and implementing dementia care interventions. In general, trials are small and vary in terms of study design, interventions tested, and outcome measures. In addition, as a comparison group, usual care has not been well characterized. Sustained use of an intervention can be costly, and the fidelity and consistency of an intervention's adoption can be difficult to ensure. Regarding measurement, more than 45 different instruments have been used to evaluate behavioral symptoms. Although distinct behaviors, agitation and aggression are often evaluated using a combined measure. Some trials evaluated general behavior versus more specific behaviors (e.g., agitation and aggression).

### **Future Directions**

First, researchers should agree on the measures to use and then use them consistently. Second, future research should be pursued in a more systematic manner (i.e., variations in treatment should be tested sequentially and under defined conditions as part of a larger research plan). Third, environmental interventions (e.g., requiring more sunlight in a nursing home) have the potential to impact many residents and are less likely to suffer from challenges associated with treatment fidelity. Finally, future research should examine subgroups and different populations, as these considerations were not evident in the systematic review studies.

## **Mouth Care Without a Battle: An Important Focus and Promising Prototype of Dementia Care Across Settings of Care**

*Sheryl Zimmerman, University of North Carolina, Chapel Hill*

Care interventions for persons living with dementia and their caregivers often focus on psychosocial components of care and outcomes, and less so on care that may decrease morbidities and improve health outcomes. Given the multiple morbidities of older adults with ADRD, this oversight is consequential. For this population, health-related interventions must consider both the health care needs of persons living with dementia and how to provide that care in a dementia-sensitive manner.

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Rokstad, A. M. et al. (2013). The effect of person-centred dementia care to prevent agitation and other neuropsychiatric symptoms and enhance quality of life in nursing home patients: A 10-month randomized controlled trial. *Dementia and Geriatric Cognitive Disorders*, 36, 340-353.

Van de Ven, G. et al. (2013). Effects of dementia-care mapping on residents and staff of care homes: A pragmatic cluster-randomised controlled trial. *PLoS ONE*, 8, e67325.

Mouth care, when provided in a dementia-sensitive manner, can promote health outcomes, and serves as a prototype of dementia-related health care that can be used across settings of care.

### ***Daily Mouth Care in Formal Care Settings***

An estimated two-thirds of residents in nursing homes have bacterial pathogens in their dental plaque, in large part resulting from poor oral hygiene. When these bacteria are inhaled, they may lead to aspiration pneumonia. In nursing homes, routine daily mouth care is deficient because nursing aides are not trained to deal with resistant residents, have competing priorities and distaste for and fear of the task, and no accountability. Pilot studies have shown that routine dental care can reduce pneumonias by up to 50 percent (e.g., weekly visits from a dental hygienist reduced pneumonia by 42 percent, and systematic mouth care after meals reduced pneumonia by 56 percent).

### ***Mouth Care Without a Battle***

When University of North Carolina (UNC) investigators began plans to develop a program to improve mouth care in nursing homes, they considered feasibility of use and ultimate widespread adoption. As they developed their program, they named it “Mouth Care Without a Battle,” building on the national recognition of the earlier intervention work in which they were involved, called “Bathing Without a Battle.” The bathing program proved so successful that it has been distributed to all nursing homes in the United States, is recognized as an indicator of culture change by the Commonwealth Fund, and is recognized by the Centers for Medicare and Medicaid Services (CMS) as a clinical practice guideline. Such widespread adoption is not typical of clinical interventions. Consequently, Zimmerman and colleagues used the name *Mouth Care Without a Battle* to capitalize on its recognizability and reputation and to promote adoption.

Mouth Care Without a Battle is a nursing home-based mouth care intervention conducted by trained nursing assistants. All nursing assistants are trained in mouth care, and a dedicated oral health aide is identified as the champion for mouth care. The program is based on the known relationship between bacteria and pneumonia (Stage “0”, basic research) and was pilot tested in three nursing homes, with two trained oral care–certified nursing assistants per home, and 97 residents (Stage “1” research). The intervention is designed to (1) remove plaque; (2) treat gingivitis; (3) prevent tooth decay; (4) clean dentures and gums; (5) meet behavioral challenges; and (6) assess and monitor care. The results from this study showed that with the use of mouth care techniques, greater than 90 percent of residents had clean teeth surfaces (both upper and lower, inner and outer), and 88 to 91 percent had clean interdental spaces (an improvement from 0 percent). Improvement in plaque and gingivitis measures were significant and sustained at 6 months. In addition, trained staff felt significantly more comfortable in their ability to provide mouth care, even to residents who resisted care.

From this Stage I pilot study, the researchers designed a Stage III system-level, cluster RCT. In this study, 14 nursing homes were randomized, half each to intervention or control, which was usual care. Intervention site staff were provided standardized training and ongoing support. The study was monitored for fidelity across sites, and outcomes included change in oral hygiene, pneumonia incidence, hospitalization, and costs. Results are preliminary, but indicate less gingivitis and plaque. They appear promising in terms of less incidence of pneumonia at 1 year, but there may be a reduction in fidelity and benefit by 2 years.

### ***Future Directions***

The pilot and subsequent Stage III study of Mouth Care Without a Battle serve as an important health care (oral health) and quality-of-life focus for persons living with dementia, as well as a promising prototype for structuring intervention development studies in accordance with the NIH Stage Model.

Some conclusions that can be drawn include (1) linkages between basic and applied clinical science are important; (2) understanding the mechanisms of change facilitates implementation; (3) this model is applicable for all stages of dementia and other impairments; (4) person-centered culture change can be successful; (4) standardization of the intervention facilitates dissemination; and (5) this model is feasible in community settings and applicable across settings of care. It also is important that stakeholders widely concur with the importance of the intervention (as has become the case with oral hygiene), if widespread adoption is to occur. One component of the model—a dedicated oral care aide to provide care to residents who require more time and attention—may require evidence of cost savings to be widely adopted.

## Intervention Models and Methods

### NIH Stage Model: Facilitating the Development of Implementable Interventions

*Lisa Onken, National Institute on Aging*

A behavioral intervention development model that paralleled drug development was first created in the 1990s: create the intervention, test for efficacy, and test for effectiveness. Many efficacious interventions were developed with this model, yet very few were shown to be effective in large real-world effectiveness trials. Behavioral interventions studied in efficacy trials are typically implemented with a high degree of fidelity, because measures to ensure fidelity of delivery are an inherent part of traditional efficacy trials. Behavioral interventions could be efficacious but not effective in the real world for a variety of reasons that affect fidelity of implementation, including the level of complexity, how difficult the intervention is to learn, and how much training and supervision are required.

Often interventions are changed, modified, or adapted—intentionally or unintentionally—when applied to real-world settings. Changing components of an intervention is particularly problematic for behavioral interventions when the mechanism of action is unknown, because the changed intervention may no longer have the same mechanism of action, and may no longer work. A greater understanding of mechanisms of action in behavioral interventions should reduce the risk associated with real-world flexible adaptation or modification of interventions and should increase the potency of interventions by preserving and emphasizing the active ingredients in implementation.

Examining mechanisms of behavior change involves asking basic science questions within the context of behavioral intervention development. The updated NIH Stage Model was created to address previous behavioral intervention development failures and to provide a conceptual framework that capitalizes on basic science while striving for optimally scalable interventions.<sup>12</sup> The Stage Model, which is consistent with an experimental therapeutics approach, emphasizes theory, the role of basic science, and the importance of understanding underlying mechanisms. Implementability, as well as potency, are the ultimate goals of this model. The stage model is translational, iterative and recursive, nonlinear, and non-prescriptive.

The main differences between this model and previous iterations are the greater emphasis on basic science and mechanisms, the broadening of Stage I to address fidelity and implementation issues, and the inclusion of Stage III, which is a hybrid efficacy-effectiveness stage.

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<sup>12</sup> Onken, L., Carroll, K., Shoham, V., Cuthbert, B., & Riddle, M. (2014). Reenvisioning clinical science: Unifying the discipline to improve the public health. *Clinical Psychological Science*, 2, 22-34.

**1. Stage 0: Basic Research**

- a. Basic science that occurs prior to intervention development but is relevant to development
- b. Research on mechanisms of behavior change involves asking basic science questions about behavior change within the context of all Stages of behavioral intervention development

**2. Stage I: Intervention Generation and/or Refinement**

- a. Stage I studies can be conducted in research or community settings
- b. All activities related to the creation and preliminary testing of a new behavioral intervention
- c. Can include the generation of new behavioral interventions as well as the modification, adaptation, or refinement of existing interventions (Stage IA)
- d. Culminates in feasibility and pilot testing (Stage IB)

**3. Stage II: Efficacy in Research Settings**

- a. Efficacy research consists of experimental testing of promising behavioral interventions in research settings with research-based providers

**4. Stage III: Efficacy in Community Settings**

- a. Efficacy in the real world consists of experimental testing of promising behavioral interventions in community settings with community-based providers or caregivers
- b. A high level of control is maintained to establish internal validity
- c. This is sometimes referred to as a hybrid efficacy-effectiveness stage.

**5. Stage IV: Effectiveness**

- a. Effectiveness research examines empirically supported behavioral interventions in community settings with community-based providers or caregivers
- b. Maximizes external validity

**6. Stage V: Implementation and Dissemination**

- a. Implementation and dissemination research examines strategies of implementation and adoption of empirically supported interventions in community settings

Many efficacious interventions fail to show real-world effectiveness and few are implemented. The NIH Stage Model emphasizes determining the principles of interventions, determining the best ways to teach people the principles, components, and techniques of interventions, and developing ways to ensure that people can faithfully administer interventions. Addressing these factors should facilitate the success of real-world studies, increasing the chance that the best behavioral interventions become accessible to the people who need them. Basic research on the mechanisms of behavior change does not need to occur prior to intervention development; rather, it can occur within any stage.

One challenge in behavioral intervention development is that in Stage II the interventionists are hired and/or trained by the research team, whereas in Stage III or IV the interventionists are staff in community settings and therefore may receive suboptimal training. Likewise, it can be difficult to ensure fidelity in community settings. Stage II, where fidelity may be the highest, may be a critical stage to determine mechanisms of behavior change and therefore better understand the principles underlying the intervention. Once delineated, these principles can inform real-world providers on how to administer the intervention with fidelity even when administered flexibly—thereby increasing the ultimate implementability of an intervention, as well as the chances of successful Stage III, IV, and V research on the intervention.

In summary, the model is intended to (1) emphasize both the scientific and practical value of determining the mechanism(s) of behavior change of interventions; (2) help articulate the mechanism(s) of behavior change to those who deliver interventions; (3) help to create a cumulative, progressive field; (4) address barriers in real-world implementation and translation; and (5) produce potent behavioral interventions that are accessible to the people who need them.

## **Taking Stock, Optimizing Impact: Using the NIH Stage Model to Map the Science of Mindfulness-based Interventions**

*Sona Dimidjian, University of Colorado, Boulder*

Mapping mindfulness research to the NIH Stage Model can be instructive for considering how it applies to intervention research for persons with ADRD and their caregivers. Although the mindfulness population examined in Dimidjian's research differs from the ADRD population, it provides useful information about how to use the Stage Model to optimize a field of research, and the lessons learned can be applied to research on dementia care.

In recent years there has been exponential growth in the number of mindfulness studies. Dimidjian and colleagues reviewed the state of the science. In establishing a measure of success, they determined that the intervention work is not complete until it reaches the highest level of potency and is implementable in the maximum number of people in the populations for which it was developed.

The team reviewed 308 publications on mindfulness studies using CBT and stress reduction to treat depression and categorized them by the NIH Stage Model. Recommendations for each Stage emerged from the analysis:

- Stage 0: Attend to the basics: Intervention targets and populations
- Stage I: Do not conflate promise with efficacy
- Stage II: Get specific about the specific effects
- Stage III: Consider skipping to but not over Stage III
- Stage IV: Efficacy is necessary but not sufficient for effectiveness
- Stage V: Beware of developing orphan innovations, falling off the implementation cliff, or getting caught in implementation limbo

In Stage 0 it is critical that researchers attend to the basics; they should know the intervention targets and the population under investigation. Only 25 percent of the depression studies included a description of the nature of the intervention, the target, and the population. With no conceptual or theoretical framework, it is impossible to advance to other stages. In addition, the intervention should have boundary conditions. For example, the specific underlying assumption for the use of mindfulness in depression is that preventing or inhibiting the activation of incongruent thoughts can improve mood. In one study, the degree of reactivity to challenges prospectively predicted depression relapse risk over time. The question then becomes how to help people who carry these vulnerability factors to interrupt thought patterns to minimize depression.

In Stage I it is often forgotten that there is a hierarchy of evidence and a need to move in the direction of more rigorous designs. Moreover, there should be a strong link back to Stage 0 and recognition that the application can outpace the data available.

In the depression studies, there was no clear map from Stage I to V, which can lead to developing research outside a larger pipeline strategy. For example, a depression study revealed that mindfulness therapy was as effective as medication, but the researchers could not explain why. It is important to understand what study outcomes matter for whom.

Although it is possible to skip Stage II, researchers should not skip Stage III, which allows for research that documents the control and comparison. Some Stage III studies can potentially be embedded in observational settings. Evidence from depression studies demonstrates that although efficacy may be necessary, it is not sufficient for effectiveness, which has implications for Stage IV. For Stage V, even when an intervention has been tested in each of the stages, researchers should avoid developing orphan innovations.

### ***Future Directions***

Mapping mindfulness-based interventions onto the NIH Stage Model can yield recommendations that may guide programmatic research to optimize impact. New areas of inquiry would benefit from similar mapping strategy to contextualize research questions and identify gaps and linkages.

## **Experimental Designs for Optimizing Multi-Component Interventions**

*Inbal Nahum-Shani, University of Michigan*

Various experimental approaches exist for determining the best combination of components in multi-component interventions. Components include the content of the intervention (e.g., topics in prevention program), intervention modality (e.g., phone calls/emails), and/or features to promote compliance or adherence (e.g., reminder emails). Nahum-Shani used examples from weight loss interventions to stimulate discussion on how these methods could best be used in research on interventions for persons living with dementia and their caregivers.

### ***Factorial Designs***

Factorial designs can answer questions about the efficacy of Individual components in an intervention package. For example: Which components are effective? Which level is more appropriate? Which components work well together?

A factorial design is a randomized trial containing more than a single factor, whereby the levels of each factor are crossed to form a design with multiple experimental conditions. For example, to investigate whether text messages and meal replacement should be included in a weight loss intervention, a factorial design with two factors (2x2) can be conducted, whereby the two levels of the text messages factor (on/off) and the two levels of the meal replacement factor (on/off) are crossed to form a design with four experimental conditions: (1) both text messages and meal replacement are offered; (2) only text messages are offered; (3) only meal replacement is offered; and (4) neither text messages or meal replacement are offered. Factorial designs can enable examination of the efficacy of individual components as well as a combination of components. They can also be used to investigate whether baseline variables moderate the effect of specific components, and whether the effects of different components are mediated by different processes or mechanisms of change. Importantly, randomization to multiple experimental conditions does not mean lower power because the research questions motivating the design *do not* concern the comparison of individual cells (conditions) in the design.

### ***SMART Designs***

An adaptive intervention is an intervention design that uses dynamic (ongoing) information about the individual's progress during treatment to decide which component to offer, when, and how. Adaptive

interventions can be operationalized via decision rules. For example, at week 2 of a weight loss intervention, if the person is nonresponsive, coaching phone calls should be provided; whereas if the person is responsive, the initial treatment should continue. Adaptive intervention can be used to address heterogeneity in response to treatment (e.g., modify the treatment for individuals who show early signs of inadequate progress to prevent ultimate nonresponse) and to offer treatments in a cost-effective manner (e.g., offer more costly treatment components only to those who need it most, such as early nonresponders). An adaptive intervention *does not* include randomizations.

The Sequential, Multiple Assignment, Randomized Trials (SMART) is an experimental design that can be used to empirically inform the construction of adaptive interventions. SMART can aid in answering questions about the optimal sequencing and individualization of intervention components. For example: Which component should be offered first? Which component should be offered subsequently? How should components be tailored over time? SMART designs are randomized trials that consist of multiple stages of randomization; each stage corresponds to a scientific question concerning the selection and individualization of intervention components in an adaptive intervention.

### ***Future Directions***

Factorial designs and SMART designs can aid in the construction of empirically based multi-component interventions. Factorial designs can be used to address questions concerning the efficacy of individual intervention components; SMART can be used to answer questions about the sequencing and adaptation of intervention components over time. Factorial designs and SMART designs are only two of many experimental tools that can be used to inform the development of interventions with multiple components. Which design to use in a study should be determined by the scientific questions motivating the study.

## **Emotional Functioning in Caregivers and Dementia Patients: Using Laboratory Studies to Identify Intervention Targets**

*Robert Levenson, University of California, Berkeley*

An emerging theme in ADRD research is that behavioral symptoms can be much more toxic than cognitive and functional loss for caregivers to manage. Caregiving is known to take a toll on caregivers. Rates of depression, anxiety, and use of psychotropic medication are significantly higher among caregivers of persons with ADRD than for the healthy population. In addition, caregivers' physical health is affected by caregiving duties. Very few studies characterize different challenges for caregivers for persons with different types of dementias.

### ***Behavioral and Psychological Symptoms of Dementia***

Behavioral and psychological symptoms of dementia include aggression, agitation, sleep disturbance, wandering, hallucinations, and delusions. All of these impact caregiver burden and health. Although it is known that these symptoms are highly toxic for caregivers, there is lack of agreement on which symptoms to measure and how best to measure them. Many of these symptoms involve emotions. Three aspects of emotion that are manifested in dementia include reactivity (blunting, apathy), regulation (agitation), and recognition (lack of empathy).

Levenson and colleagues have studied these emotions in 175 persons with ADRD—caregiver dyads in a laboratory setting to assess emotional qualities in the patient, the caregiver, and their relationship that are linked to adverse caregiver outcomes. A number of these emotional behaviors have been identified, with three examples being visual avoidance, pronouns (use of I and you versus we), and linkage. Greater

decline in caregivers was associated with (a) less visual avoidance (looking away from unpleasant things) in the person with ADRD, (b) less use of “we” pronouns by caregivers and the person with ADRD and greater use of pronouns that refer to the person with ADRD, and (c) lower levels of linkage or synchrony of their activity levels during waking hours in the home.

### ***Depression and Mental Illness in Caregivers***

Previous studies have demonstrated greater risk of mortality for caregivers of persons with ADRD who are experiencing high levels of stress and strain. In a new study of 176 individuals diagnosed with a range of neurodegenerative diseases, Levenson and colleagues found that lower levels of caregiver mental health predicted shorter survival times for patients (controlling for diagnosis, sex, age, disease severity, and mental health of the care receiver). Persons with ADRD being cared for by caregivers whose mental health scores were 1 standard deviation below the sample mean died about 14 months sooner than those with caregivers scoring 1 standard deviation above the mean.

### ***Future Directions***

Levenson described several implications of his work for caregiver intervention development. Bio-behavioral pathways connecting problematic behaviors in persons with ADRD and their relationships with caregivers are excellent targets for interventions. However, longitudinal research is necessary to properly analyze mediators/mechanisms and to determine directions of causal influence. Some of the major emotional pathways emerging in theory and empirical research include caregiver anger, fear/worry, embarrassment, loneliness, and suppression/stonewalling. Interventions for caregivers that target these pathways may improve and prolong the lives of both persons with ADRD and caregivers.

## **Overcoming Systemic Barriers to Scaling Up Effective Evidence-based Interventions to Improve Outcomes: Focus on Caregivers, Care Workers, and Outcomes**

### **Lessons Learned in Leading Adaption and Adoption: The Indiana Experience**

*Christopher Callahan, Indiana University*

There are several challenges to implementation and scalability of interventions into real-world settings. Callahan discussed the modern research infrastructure needed to support successful Stage V research. Research investments often focus on basic research. Callahan posited instead that the required investment for the basic research infrastructure is far less than what is needed for Stage V research. As a parallel, investments in the pharmaceutical industry demonstrate this understanding as evidenced by the amount of money spent to market products to consumers.

### ***Scalability***

Research on scalability is hampered by patient-clinician dyad heterogeneity, unclear boundaries between the medical system and social system, uncertainty in balancing personal autonomy with safety, uncertainty about what works, and disagreement over who should fund implementation science.

Scalability is the issue that should be of most concern when developing a new intervention. An intervention for ADRD that costs \$10,000 per person may not be implementable or scalable. What efficacious and effective intervention can be designed that costs \$100 per person? An intervention with a small effect size that can be made available widely can have a huge population effect and thus be more impactful than an expensive intervention with a large effect size that reaches very few individuals.

Another issue related to scalability is access to trained clinicians who can implement the intervention. Workforce distribution can impact scalability if those required to implement the intervention are not available in certain geographic areas. For example, many areas in the country lack access to a neurologist. Therefore, an intervention delivered by a neurologist would not lend itself to a scalable model.

A review of 20 years of behavioral intervention work at Indiana University provide insights on diffusion and the role of Stage V research. Stage II to Stage IV research required development of new local treatment protocols and outcome measures, a mobile electronic medical record, local economic benchmarks to sell the intervention, workforce training, and a new clinical program.

### ***Diffusion of Innovations***

Callahan presented a useful framework for Stage V research based on diffusion of innovations. In his book on this topic, Everett Rogers identified five stages of diffusion: (1) knowledge (awareness), (2) persuasion, (3) decision, (4) implementation, and (5) confirmation. Each of these stages relies on two-way communication channels. Some innovations diffuse more easily than others because of relative advantage, compatibility, ease or difficulty of implementation, trial-ability, adaptability, and/or observed effectiveness.

Diffusion of innovations requires a perceived need and an active social network. Social networks for ADRD caregivers are not widely known or utilized. Interventions typically involve communication that is directive rather than two-way to enable exploration of caregiver needs. To facilitate adoption, the caregiver user must see a relative advantage to the intervention and it must be compatible, adoptable, and feasible.

### ***Future Directions***

Implementation science should be considered in all of the research stages. The evidence base is only one step in a multi-step process. Scalability must be built into the model design. A much stronger and faster network of learning laboratories is needed to bridge the adoption gaps. Criteria for stopping the research and making the most of limited research resources needs to be determined. Research and development efforts must be coupled with political and community activism.

## **Barriers to Scaling Up: Payment, Work Force, Adoption, and Adaptation**

*Lee Jennings, University of Oklahoma*

### ***UCLA's Alzheimer's and Dementia Care Program***

Jennings presented research on the UCLA Alzheimer's and Dementia Care Program to demonstrate the challenges of dissemination. The clinical program goals are to maximize patient function, independence, and dignity; minimize caregiver strain; and reduce unnecessary costs. The longitudinal study began in 2011 and has enrolled more than 2,100 patients. The program requires collaboration between a nurse practitioner dementia care manager and primary care provider. Key components of the program are an in-person needs assessment of the patient-caregiver dyad, 24/7 access to medical providers, an individualized dementia care and follow-up plan, and referrals to community-based services. Protocols have been developed for each of these elements.

The program uses five nurse practitioners who each care for up to 250 patients and bills Medicare for allowable services. All other services are provided free of charge to the patient and require coordination

with community-based organizations and primary care providers. Other financial support comes from in-kind support from the university, grants, and philanthropy.

Importantly, community providers are involved from the start of the study design and linkage with community partners is a service provided by the program. Because of the low interest and use of these community services by caregivers, a voucher system was put in place to encourage more widespread use. Despite the availability of these vouchers only 50 percent of participants accessed services, even when they were free.

### ***Outcomes and Results***

Results indicate 92 percent adherence to quality indicators in the UCLA program, demonstrating that it offers a model for providing dementia care in the community, compared to 32 percent adherence among community physician providers and 60 percent in models that add a nurse practitioner to work with community physician providers. After 1 year of the UCLA program, caregivers reported feeling more confident in knowing how to get help and in having access to health care professionals. Patients were found to have improvements in depressive symptoms and stabilization of behavior.

NORC at the University of Chicago conducted an external evaluation of costs and utilization using Medicare claims data for 2,166 dementia patients and 1,083 controls over 3 years. Patients were monitored for hospitalization and other health care visits. Although there were no changes in acute care utilization, there was a cost savings for those enrolled in the UCLA program of \$525 per patient as well as a significant 33 percent reduction in admissions to long-term care nursing homes. Future research by UCLA investigators will focus on understanding where and how the program can realize cost savings. UCLA plans to continue expanding both the number of patients and services and to conduct further research on how best to disseminate the program.

The UCLA Alzheimer's and Dementia Care Program is a proof-of-concept intervention that has succeeded in filling a gap in care, bringing a program to scale at UCLA, improving outcomes for patients and caregivers, and reducing costs and institutionalizations. However, there are barriers to wider dissemination.

### ***Barriers to Dissemination***

Barriers to dissemination include payment, workforce issues, adaptation to other health care systems, settings, and populations, and the lengthy research process necessary to generate outcome data that is useful to the business case for intervention adoption. Current Medicare coverage allows for reimbursement of in-person nurse practitioner visits at 85 percent of what physicians receive, and there is no reimbursement for clinical work that does not involve in-person visits, except for Medicare chronic care management codes. There is no coverage for community-based services. The total fee-for-service reimbursement for a dementia patient for 1 year outside of a hospital setting is estimated to be \$906 at maximum. By comparison, the UCLA program costs approximately \$1,400 per person. Because Medicare does not reimburse for community services, adopting the program in communities will require partnering with community-based organizations and businesses and providing a way to compensate them for the services they provide.

Workforce challenges exist as well. In some areas of the country, not enough nurse practitioners are available to implement the program, demonstrating the importance of testing the program using other types of health care providers. For widespread adoption, the program also needs to be explored with non-professional workforce participants, in various settings, and in places with different levels of access

to services. Training family caregivers is a necessary part of the intervention and is done better in the community. Developing partnerships with community-based organizations takes time and effort, and services are largely uncovered.

Several questions remain about adaptation of the program to other health care systems, settings, and populations. For example, will this model work in other health care systems, with different patient populations, and with a different assortment of available local community resources? Related to evaluating the potent components of a multi-component intervention, it is unclear which, if any, components of the intervention can be changed without compromising the outcomes. More research is needed to determine the mechanisms of action and the immutable pillars of intervention.

The goal of a typical RCT is to determine causes and effects of treatment using rigid protocols and clear eligibility criteria. Such a process does not necessarily yield clinically relevant outcomes. A pragmatic trial is designed to address issues of dissemination and scalability within the trial. A pragmatic trial can test real-world treatments using flexible protocols and local customization, recruit a more representative population, and is designed to yield results that inform clinical decision making. Without more pragmatic trials, it takes a long time to show the types of outcomes necessary from RCTs to convince others to adopt and disseminate.

### ***Future Directions***

More research is needed on the adaptability of the intervention to determine how best to scale and disseminate it to different systems, settings, and populations. Additional funding for wider adoption will require champions to create a business case for such a program. Developing relationships and partnerships with community-based organizations that can help express the need is one potential solution. Research funders should invest more in pragmatic trials that include an implementation and dissemination evaluation component.

## **Systems of Care and Diffusion of Interventions That Address Living with Alzheimer's Disease**

*Julie P. W. Bynum, Dartmouth College*

Bynum focused on the current dementia care system and ownership of interventions/programs in that system, the levers of influence available to stimulate diffusion, connecting persons living with dementia and existing programs, and the contextual trends that should be considered in future intervention designs.

The economic costs of dementia accrue to multiple systems: medical, psychological, and behavioral costs to the health system; supervision, housing, and functional supports costs to social systems; spousal support and unpaid family care costs to informal care systems; and mortality, morbidity, and reduced paid work hours for informal caregivers result in productivity losses. Many persons with ADRD do not have resources or coverage for the social and informal care costs. Community services are excluded in the current health system-centric model. Research funding sources for the different systems also vary and are not always coordinated (e.g., CMS for health insurance, the Centers for Disease Control and Prevention for public health, the Administration for Community Living for social supports, and NIH and AHRQ for health research).

The comprehensive costs of ADRD have not been communicated effectively, and more work is needed in this area. Using data from the Dartmouth Atlas, two different cohorts—Medicare beneficiaries with

multiple chronic conditions and Medicare beneficiaries with ADRD—were compared to all beneficiaries during 2012. This analysis showed that ADRD patients were hospitalized five times as many days as the average beneficiary for a total of 22.5 days in 2012. However, there was tremendous variability across health markets. The ADRD cohort also had five more inpatient days compared to the cohort with chronic conditions. Despite the greater number of hospitalizations, ADRD patients had fewer contacts with the health system compared to those with chronic conditions.

### ***Levers for Diffusion***

The availability of levers is limited at the federal level, including regulations, block grants to states and agencies for specific programs or populations, and financial incentives through Medicaid and/or Medicare. However, health care systems have access to persons living with dementia and their caregivers and might serve as better leverage points for diffusion of interventions. The Dartmouth Atlas data on hospitalization rates of patients with ADRD, for example, are important for hospitals because hospitals generate more revenue with inpatient beds for surgeries, and thus this information could be a potential lever.

Stakeholders are also key levers. Findings from qualitative engagement with 11 stakeholders found that ADRD caregiving is not a priority for commercial plans or employers. Employers primarily obtain information in this area from consultants. The research community could be doing more to engage these stakeholders.

However, even if the health systems were on board there are challenges in what is required to diffuse intervention for persons with ADRD and their caregivers. One of the greatest challenges is that 62 percent of ADRD patients are undiagnosed, and diagnosis is uneven across states. Often clinical recognition of ADRD occurs late in the disease process. By the time of diagnosis, only 24 percent of persons with ADRD are at home. Another challenge is that, in many communities, the role of providers with expertise in dementia is limited.

### ***Future Directions***

The fundamental challenge is that interventions for persons with ADRD and their caregivers are not “owned” by any single component of the systems of care, and instead require both a social care and medical diffusion pathway. The research community needs to build pathways to access ADRD patients. Future research should focus on using leverage points for diffusion of efficacious and effective interventions and incorporating relevant considerations into research design—including how to design evidence to inform actions available to government-funded programs, how to target health care systems, and how to use demographic shifts and labor market forces to advance diffusion. Incorporating the target for diffusion (e.g., a nursing home)—in addition to the target of the intervention (e.g., the person with ADRD)—into research will help build evidence for diffusion. Contextual factors such as demographic trends, racial and ethnic disparities, and population health accountability for new payment models also need to be considered.

## **Recommendations for Future Research Priorities**

Several themes for future research priorities for NIH and other funding agencies emerged from the presentations and session-specific and general discussions. Meeting organizers encouraged invited experts to frame their thoughts and recommendations around the stages of intervention research

described in the NIH Stage Model.<sup>13</sup> Each invited expert reflected on the most pressing research needs and, in particular, strategies for ensuring a coordinated, systematic research agenda that addresses all research stages to maximize the effectiveness and implementability of efficacious and effective interventions in real-world settings.

Four primary themes for a future research agenda emerged: (A) focus intervention research on improving care for persons living with dementia; (B) coordinate a research agenda to address all phases of intervention development and implementation; (C) address heterogeneity and disparities; and (D) address measurement issues and multiple outcomes of interest. Meeting participants discussed and recommended research priorities for each theme.

### **A) Focus Intervention Research on Improving Care for Persons Living with Dementia**

- 1) **Funders should support research that focuses specifically on developing and testing interventions targeted at improving the quality of life and other outcomes of relevance for persons living with dementia in home settings and residential long-term care settings, including assisted living and nursing homes.** Expansion of evidence-based caregiver interventions is important. However, there is a research and policy vacuum for interventions specifically aimed at improving life for persons with ADRD. Such interventions should be user-friendly and include methods to ensure real-world fidelity, such as validated training materials. Interventions should be tested to determine the most potent components and the principles underlying these components, be consonant with patient and caregiver preferences, and address cost-effectiveness.
- 2) **Technology-based interventions may improve care delivery for persons living with dementia.** More research should focus on how assistive and other technologies may allow persons living with dementia to live independently in their homes for a longer time. Technology-based interventions could address health and wellness, social connectivity, independent living, and/or caregiver supports in different settings. Such interventions could be targeted at the caregiver, the person living with dementia, or both, and could include the use of mobile devices, online platforms, telehealth, wearables, and home sensors.

### **B) Coordinate a Research Agenda to Address All Stages of Intervention Development and Implementation**

- 1) **Basic mechanistic research is needed to determine the mechanisms underlying efficacious and effective interventions aimed at improving quality of life for persons with ADRD and their caregivers.** Questions regarding mechanisms of behavior change may be included most successfully in Stages 0, I, II, and III. Understanding the mechanisms of behavior change can promote implementation and translation of an intervention and can allow for more precise targeting of the most vulnerable and therefore improved intervention efficacy. In addition, such understanding makes it clear to people administering the intervention what they are doing, why they are doing it, and how they should be doing it. Factorial and adaptive research designs can

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<sup>13</sup> Onken, L., Carroll, K., Shoham, V., Cuthbert, B., & Riddle, M. (2014). Reenvisioning clinical science: Unifying the discipline to improve the public health. *Clinical Psychological Science*, 2, 22-34. Overview available from <https://www.nia.nih.gov/research/dbsr/stage-model-behavioral-intervention-development>.

be employed to understand better the potent components of an intervention and how best to sequence and tailor intervention components.

- 2) **Research is needed on translating existing care models, services, and technologies to improve the lives of persons with ADRD and their caregivers into real-world settings.** It is important to study the impediments to implementing such interventions in the real-world setting, which includes training caregivers (both formal and informal) and insuring that the interventions can be integrated into standard operating procedures of the existing care system be it the home, residential care setting, or even a senior center. Stage I research is needed to increase efficacy, more precisely match the intervention to the time-varying needs of persons with ADRD and their caregivers, determine the mechanisms or principles underlying the interventions, streamline interventions, modify interventions for the real world, develop training procedures and protocols for community interventionists, and develop measures to ensure fidelity. Stage II research tests interventions in research settings, and Stage III research tests efficacious interventions in real-world settings. Stage IV research is needed when interventions are ready to be tested in pragmatic clinical trials.
- 3) **Researchers should consider scalability and sustainability at the beginning of intervention development and throughout subsequent research.** Multiple studies may be required to determine what form(s) of the intervention can be optimally implemented. For example, to address all issues of scalability and sustainability, particularly for low-resource settings and populations, multiple Stage I and Stage III studies are often necessary to precede successful Stage IV pragmatic trials. Pragmatic trials allow researchers to collect the basic data needed to implement and translate an intervention in different settings and/or populations. Implementation science research is needed to emphasize studying the process of how practices, interventions, and policies are disseminated, adapted (as needed), adopted, integrated and sustained in everyday health-focused settings, and ultimately would inform successful translation.
- 4) **When appropriate, researchers should communicate with interdisciplinary colleagues and/or key stakeholders who can provide valuable input into the design of interventions.** Implementation science is characterized, in part, by partnerships with key stakeholder groups (e.g., end-users, providers, organizations, systems, and/or communities), and investigators should be encouraged early in the intervention design process to partner with these stakeholder groups. The research funders could facilitate these relationships, or signal the importance of such relationships in funding opportunity announcements. In addition, investigators should be encouraged to build interdisciplinary teams from the design stage forward to include not only academic social scientists but also their colleagues from schools of business, law, medicine, and others.
- 5) **Research should focus on using leverage points for diffusion of efficacious and effective interventions.** Interventions for persons with ADRD and their caregivers are not “owned” by any single component of the care system, and widespread adoption may require both a social care and a medical diffusion pathway. Such work should include considerations such as how to design evidence to inform actions available to government-funded programs, how to target health care systems, and how demographic shifts and labor market forces can advance diffusion of interventions that improve the lives of persons with ADRD. Incorporating the target for

diffusion (e.g., a nursing home)—in addition to the target of the intervention (e.g., the person with ADRD)—into research will help build evidence for diffusion.

### C) Address Heterogeneity and Disparities

- 1) **Funders should support research on intervention development with diverse participant populations.** Diverse characteristics may include race and ethnicity, geographic location, home settings of the person with ADRD (living alone, with extended family, in an assisted living facility), socioeconomic status, educational background (for both the person with ADRD and caregivers), intellectual and developmental disability status, and family caregiver relationship (adult child versus spouse). It is also important to understand how and why interventions work for caregivers with a variety of characteristics, including those with and without mental illness and/or depression, multiple and/or chronic conditions, and demonstrated resilience. Given the diverse needs and recipients, different intervention components may work better for different participants.
- 2) **Caregiving research should prioritize studies that can determine not only whether an intervention has statistically significant positive outcomes for the entire sample, but also to characterize the persons living with dementia and/or family caregivers for whom the intervention does or does not work.** Given the heterogeneity of persons living with dementia, family caregivers, caregiving situations, and changes in the care needs of persons living with dementia over time, it is unlikely that any single evidence-based program will be effective for all families. However, little research has been conducted to identify what works for which persons living with dementia and caregivers under what circumstances in what settings. Understanding of the principles that guide an intervention's success for one group but not another would inform future research into the generalizability of the intervention to another population with similar characteristics. In addition, precision in matching the various interventions to the individual and time-varying needs of caregivers can increase efficacy and enable allocation of intervention resources to those most vulnerable. To acquire this nuanced understanding, researchers may need to conduct more than one study to determine which recipients did or did not benefit. When evaluating the utility of an intervention for a population with specific characteristics, researchers should examine the mechanism(s) of behavior change of the intervention. In addition, they should design studies so that they can determine whether suboptimal results occurred because of inadequate exposure to or implementation of the intervention or because of sub-group differences.
- 3) **Research is needed to determine the implications of the different types of dementia on intervention outcomes.** Clinical scientists attribute importance to disease type (e.g., AD, frontal lobe, Lewy body dementia, vascular, young-onset Alzheimer's, and mixed dementia), but the unreliability of these diagnoses in real-world clinical practice is well known. It would be helpful to consider how important these diagnoses are for the outcomes experienced, particularly by the caregivers, and whether caregiver outcomes differ as a function of the type of dementia (independent of duration or symptom severity even though correlated). Many behavioral or caregiver intervention studies recruit from non-research-intensive clinical settings that might not differentiate diagnoses reliably. The field would benefit from greater understanding of the importance of heterogeneity of dementia type to the generalizability of the intervention.

- 4) **More research is needed—both to determine efficacy and effectiveness—to develop and/or test interventions that work for persons in the early stages of dementia and for their caregivers.** Much of the current caregiving research focuses on persons with later-stage dementia. Care research is needed that focuses on early detection and diagnosis of dementia for persons living in the community, the possible consequences of early diagnosis, and opportunities to intervene in the earlier stages of dementia.
- 5) **Funders should support research into developing interventions that aim to reduce multiple dimensions of disparities in access to high-quality dementia care and that attempts to understand how and why such interventions differentially impact persons with specific disparities.** Such disparities can be area-based (geography), person-based (race, ethnicity, gender, socioeconomic status), and/or insurance-based (Medicaid, Medicare, dual beneficiaries, private insurance).

#### **D) Address Measurement Issues and Multiple Outcomes of Interest**

- 1) **More research is needed to determine the best measurement strategies and outcomes of importance for persons living with dementia and their caregivers.** For example, it would be valuable to know what outcomes are important to key stakeholders, including the end-users, before interventions are developed. In addition to focusing on deficits, outcomes should include positive components, such as resilience, and health events and morbidities. The clinical health of caregivers has at times been minimized relative to the psychosocial issues of persons living with dementia. In addition, researchers should examine and test for bias in measurement tools and address how best to collect data in community settings.
- 2) **Research that builds longitudinal data systems is needed to support work on trajectories of dementia and dementia care and the progression of disease and caregiving needs.** Much intervention research is focused on one setting, episode, or point in time of a dementia trajectory. More work needs to be done to understand the changing needs of persons living with dementia, most appropriate interventions for each stage of dementia, and the types of caregiving supports needed at each stage. For example, a cohort of Medicare beneficiaries could be created with important event data from which participants could be periodically recruited contingent upon the occurrence of critical events such as hospitalization, post-acute care use, and residential mobility. Such analysis could enhance understanding of experiences around crisis events within the longitudinal frame of dementia experience.
- 3) **Intervention development research for persons with ADRD and their caregivers should more often include a cost-effectiveness component.** Tests of cost-effectiveness, health care utilization, and savings assessments should be included in Stage IV work after the groundwork from earlier stages has been completed. Assessing cost-effectiveness, with an expansive definition of costs that includes all costs to whomever bears them, may be essential in promoting the widespread adoption of interventions. Knowing the actual cost of interventions can help to determine which interventions are likely to realize the greatest system-wide impact. Including health economists, actuaries, or cost-analysts in the research team starting in the design phase would increase the likelihood that these elements are considered.

## Appendix 1: Agenda

*Revised July 27, 2017*

### Monday, July 31, 2017

8:30 a.m. Check-in

9:00 Welcome, Introductions, and Purpose  
Elena Fazio  
Lisa Onken  
John Haaga

#### **Session 1a: Interventions Focused on Outcomes for Caregivers and Persons Living with Dementia: Informal Settings**

9:15 Glass Half Full: Caregiving Interventions, Gaps, and Promising Directions Laura Gitlin

9:55 Sleep-health in Caregivers: Need for Targeted Interventions to Improve Insomnia and Reverse Insomnia-related Inflammation and Cellular Aging Michael Irwin

10:35 **BREAK**

#### **Session 1b: Interventions Focused on Outcomes for Persons Living with Dementia and Care Providers: Formal Settings**

10:50 Non-drug Interventions for Agitation and Aggression Vincent Mor  
Eric Jutkowitz

11:30 Mouth Care without a Battle: An Important Focus and Promising Prototype of Dementia Care Across Settings of Care Sheryl Zimmerman

12:10 Session 1 General Discussion Vincent Mor

12:30 **LUNCH**

#### **Session 2: Intervention Models and Methods**

2:00 NIH Stage Model: Facilitating the Development of Implementable Interventions Lisa Onken

2:40 Taking Stock, Optimizing Impact: Using the NIH Stage Model to Map the Science of Mindfulness-based Interventions Sona Dimidjian

3:20 **BREAK**

Innovating the Next Generation of Dementia and Alzheimer's Disease Care Interventions  
July 31–August 1, 2017

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|      |                                                                                                                      |                                      |
|------|----------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| 3:35 | Experimental Designs for Optimizing Multi-component Interventions                                                    | Inbal Nahum-Shani                    |
| 4:15 | Emotional Functioning in Caregivers and Dementia Patients: Using Laboratory Studies to Identify Intervention Targets | Robert Levenson                      |
| 4:55 | Session 2 General Discussion                                                                                         | <i>Moderator:</i><br>Robert Levenson |
| 5:05 | Day 1 General Discussion                                                                                             | <i>Moderator:</i><br>Elena Fazio     |
| 5:30 | <b>ADJOURN</b>                                                                                                       |                                      |

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**Tuesday, August 1, 2017**

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**Session 3: Overcoming Systemic Barriers to Scaling Up Effective Evidence-based Interventions to Improve Outcomes: Focus on Caregivers, Care Workers, and Outcomes**

|           |                                                                                             |                                              |
|-----------|---------------------------------------------------------------------------------------------|----------------------------------------------|
| 9:00 a.m. | Lessons Learned in Leading Adaption and Adoption: The Indiana Experience                    | Christopher Callahan                         |
| 9:40      | Barriers to Scaling Up: Payment, Work Force, Adoption, and Adaptation                       | Lee Jennings                                 |
| 10:20     | <b>BREAK</b>                                                                                |                                              |
| 10:35     | Systems of Care and Diffusion of Interventions that Address Living with Alzheimer's Disease | Julie P. W. Bynum                            |
| 11:15     | Session 3 General Discussion                                                                | <i>Moderator:</i><br>Jennifer Wolff          |
| 11:35     | Overall Workshop Discussion and Recommendations                                             | <i>Moderators:</i><br>Elena Fazio/Lisa Onken |
| 1:00 p.m. | <b>ADJOURN</b>                                                                              |                                              |

## Appendix 2: Participant List

### Invited Speakers

**Julie P.W. Bynum**, Dartmouth College  
**Christopher Callahan**, Indiana University  
**Sona Dimidjian**, University of Colorado, Boulder (*via WebEx*)  
**Laura Gitlin**, Johns Hopkins University  
**Michael Irwin**, University of California, Los Angeles  
**Lee Jennings**, University of Oklahoma  
**Eric Jutkowitz**, Brown University  
**Robert Levenson**, University of California, Berkeley  
**Vincent Mor**, Brown University  
**Inbal Nahum-Shani**, University of Michigan  
**Jennifer Wolff**, Johns Hopkins University  
**Sheryl Zimmerman**, University of North Carolina, Chapel Hill

### National Institutes of Health

**Partha Bhattacharyya**, Program Director, Division of Behavioral and Social Research (BSR), National Institute on Aging (NIA)  
**Desmond Bibio**, Research Program Analyst, BSR, NIA  
**Prisca Fall**, Research Program Analyst, BSR, NIA  
**Elena M. Fazio**, Health Scientist Administrator, BSR, NIA  
**Melissa Gerald**, Program Director, BSR, NIA  
**John G. Haaga**, Director, BSR, NIA  
**Amelia Karraker**, Health Scientist Administrator, BSR, NIA  
**Jonathan W. King**, Program Director, BSR, NIA  
**Laura Major**, Research Program Analyst, BSR, NIA  
**Kristina A. McLinden**, Program Director, Division of Neuroscience (DN), NIA  
**Lisbeth Nielsen**, Chief, Individual Behavioral Processes Branch, BSR, NIA  
**Lisa Onken**, Program Director, Behavior Change and Intervention, BSR, NIA  
**Dana Plude**, Deputy Director, BSR, NIA  
**Roxanne Semple**, Extramural Support Assistant, BSR, NIA  
**Charryse Shell**, Program Specialist, BSR, NIA  
**Cristan Smith**, Research Program Analyst, DN, NIA  
**Lois Tully**, Program Director, National Institute of Nursing Research  
**Courtney Wallin**, Office of the Director, National Institute on Aging

### Other Participants

**Hae-Ra Han**, Johns Hopkins University  
**Chandra Keller-Allen**, Project Manager, Rose Li and Associates, Inc.  
**Ian Kremer**, Executive Director, Leaders Engaged on Alzheimer's Disease  
**Sarah Landry**, Science Writer, Rose Li and Associates, Inc.  
**Katherine Marx**, Johns Hopkins University  
**Katie Maslow**, The Gerontological Society of America  
**Quincy Samus**, Johns Hopkins University