Theme 4: Participation of Persons with Dementia and their Caregivers in Research

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

March 24-25, 2020

Reporters, Data Sources, and Outcomes in Dementia Research

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March 24-25, 2020

Disclosures

- I have no conflicts of interest.

Disease-based vs. Patient-defined Outcomes

Disease-based Outcomes

- Disease-specific
- Medical outcomes
  - Survival, Biomarkers
  - Disease-specific symptoms
- Population health goals
- Universally applied
- For persons with a single chronic disease or longer life expectancy
- Can be person-centered; may not capture what is most important to the person

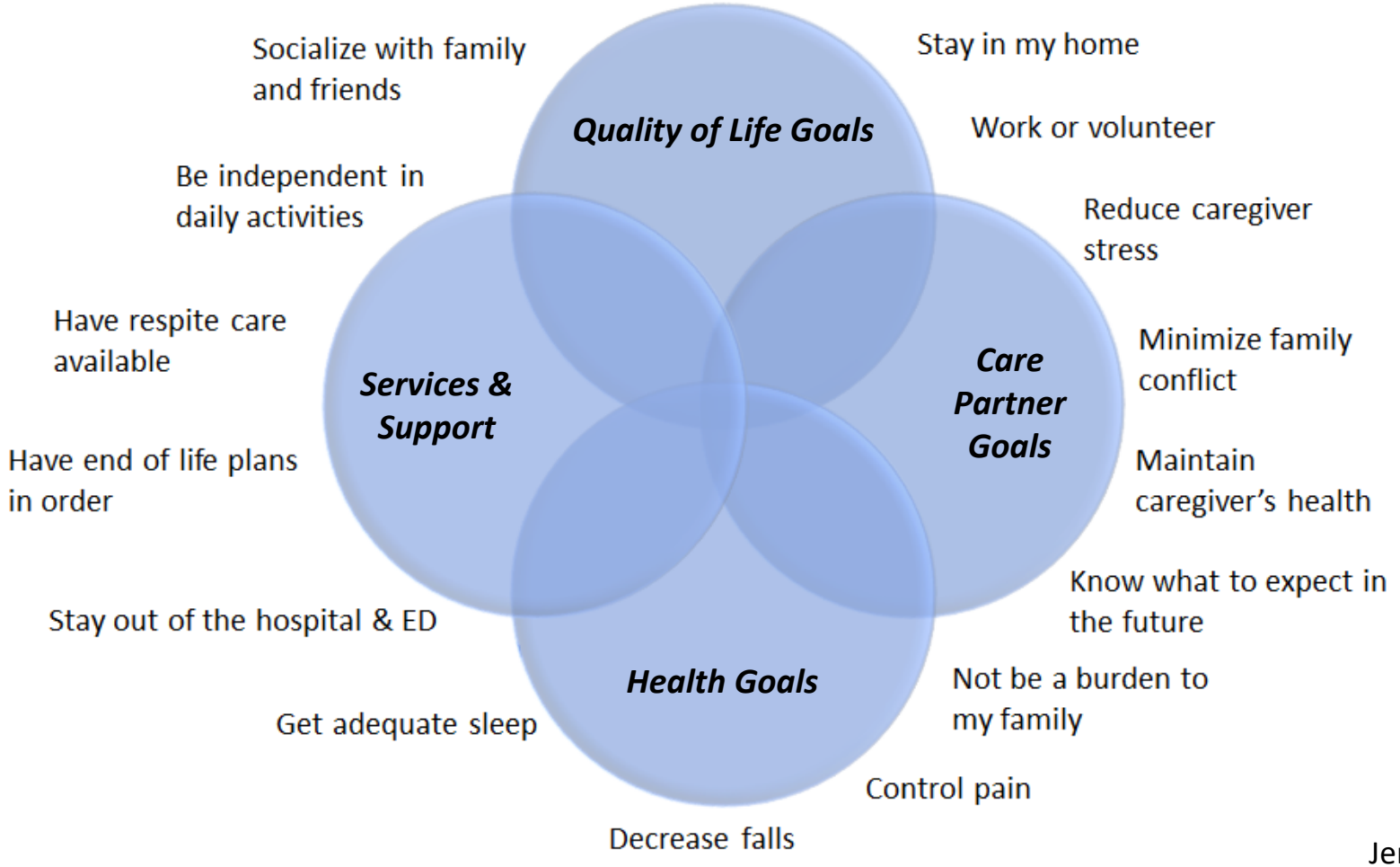
Person-defined Outcomes

- Span conditions
- Medical & non-medical outcomes
  - Functional independence
  - Social interaction
- Personal health goals
  - Individually determined
- For persons with multiple chronic conditions, limited life expectancy, or specific disabling diseases
- Always person-centered

Reuben DB, Tinetti ME. NEJM 2012;366(9):777-779.

What matters most?

Findings from Focus Groups with Persons with Dementia and their Care Partners



Jennings LA, et al. Quality of Life Research 2017; 26(3): 685-93.

Patient Reported Outcome Measures (PROMS)

- Efforts to include PROMS as research outcomes
- Examples in dementia research
  - Quality of Life-AD
  - Pain scales in dementia
  - Cornell Scale of Depression in Dementia
  - Neuropsychiatric Inventory Questionnaire
  - Functional status
  - Care partner strain, mood, self-efficacy, social support
- Pros: validated, self-administered; good for symptoms; can be followed longitudinally; easy to compare across studies and health systems

Gaugler JE, et al. Alzheimer's & Dementia 2019;5:388-397.
https://www.neurodegenerationresearch.eu/wp-content/uploads/2015/10/JPND-Report-Fountain.pdf

Challenges with PROMS in Dementia Research

- May be too generic
- May not be relevant or high priority to a PLWD
- Progressive worsening of cognition—repeated measures, consent
- Proxy reporting: What can a care partner report for a PLWD?
  - Ex: Pain vs. ADL impairment; Mood vs. Sleep pattern; QoL vs. Mobility
- Multiple care partners or change in care partner
  - Role and relationship of care partner
- Care partner outcomes vs. PLWD outcomes
- Combining data from multiple reporters
  - How to handle reporter discordance?

Kiyak HA, et al. *The Gerontologist.* 1994;34(3):324-330; Frank L, et al. *Alzheimer's Research & Therapy.* 2011;3(6):35; Hirschman KB, et al. J G*eriatr Psychiatry Neurol.* 2004;17(2):55-60; Karlawish JH, et al. *Neurology.* 2005;64(9):1514-1519.

Personalized or Individual-Specific Outcomes:
Goal Attainment Scaling as an Example

- Way to make a personalized health goal S.M.A.R.T.
  - Specific, Measurable, Attainable, Relevant, Time-bound
- Framework for care planning (action plan)
- Measures goal achievement
  - Goal is individualized, measurement is standardized

Goal	Much less than expected (-2)	Less than expected (-1)	Expected goal attainment (0)	More than expected (+1)	Much more than expected (+2)	Action Plan
Increase social engagement	Not participating in any activities; stops watching movies	Watches movies at home; does not get out (current state)	1 activity outside home once per week; more in-home activities	Activities outside home >1d/wk; more in-home activities	Activities outside home most days; more in-home activities	Hire part-time caregiver

Jennings LA, et al. JAGS 2018;66(11):2120-27.

Personalized or Individual-Specific Outcomes

Advantages	Challenges
Specific, measurable health goals	Time constraints
Goals are personalized, meaningful to PLWD and care partners	Scaling takes training and practice
Accommodates diverse preferences	Culture of disease-based care
Goals can be revised as disease progresses	Some goals may be unrealistic
Facilitates care planning	Goals of and for others (e.g., family, clinician)

Reuben DB, Jennings LA. J Am Geriatr Soc. 2019;67(7):1342-1344

Novel Approaches to Outcome Measurement in Dementia Research

- Using technology
  - Wearable devices to track mobility, gait or falls
  - Video to observe behavioral symptoms or sleep
  - Smart phone or tablet apps
- Data Analysis: Triangulation of data sources
  - PROMs, individualized outcomes, technology, clinical data (e.g., cognitive testing, biomarkers), processes of care (quality), health care utilization/cost
  - Weighting strategies

Some Opportunities for Future Research

- Further develop of methods to address self-report with declining cognition
- Further develop individual-specific outcomes
  - Does the care we deliver help PLWD achieve what is most important to them?
  - How to shift culture from disease-based to person-defined outcomes?
- Identify measures that are most responsive to change and that translate to clinical significance
- Establish homogeneity of instruments across studies (core outcome sets)
- Identify outcomes relevant for payment coverage decisions
- Further development of methodologies to combine data sources and address multiple reporters

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Nomenclature

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

March 24-25, 2020

Disclosures

- **Roche, Inc.**
- **Merck, Inc.**
- **Genentech, Inc.**
- **Biogen, Inc.**
- **GE Healthcare**
- **Eisai, Inc.**

Cross-cutting theme Relevant to Nomenclature

- Ethics
- Health disparities
- Perspectives of persons living with dementia and/or caregivers
- Etiologies

Nomenclature
Words Matter

- **Nomenclature issues very important**
- **Cut across all spheres of investigation**
  - **Science/Research**
  - **Clinical Care**
  - **PLWD and Care Partners, Public Stakeholders**
    - **Government agencies**
    - **Advocacy groups**
    - **Research participants**
    - **Under-represented groups**

Confusion in the field on terminology

- **Alzheimer's Disease**
- **Frontotemporal Degeneration**
- **Dementia with Lewy Bodies**
- **Vascular cognitive impairment-dementia**

Alzheimer's Disease

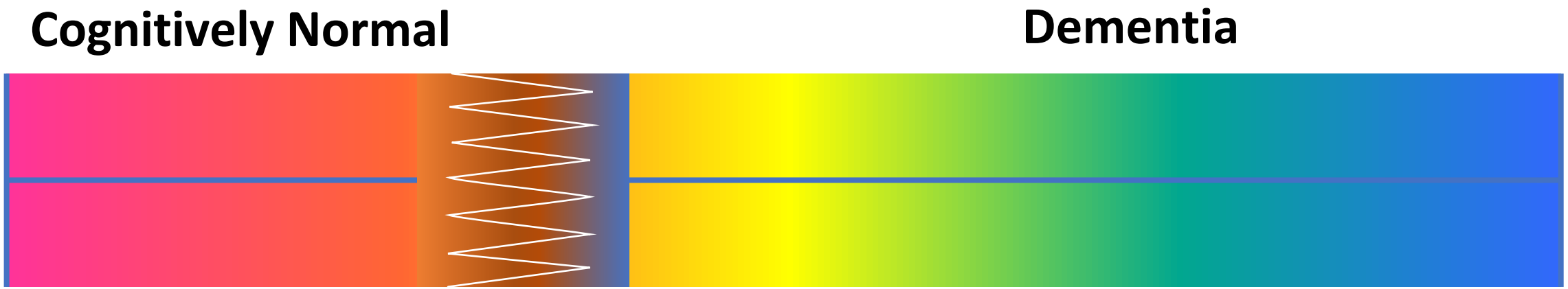
- **Syndrome**
- **Etiology**

Previous and Current Language Encounters

- **Previous psychiatric terms**
  - **IQ 0-25 “idiot”**
  - **IQ 26-50 “imbecile”**
  - **IQ 51-70 “moron”**
- **Alzheimer’s disease: Pre-senile dementia**

- **Current terms under consideration**
  - **Pre-clinical Alzheimer’s disease: positive amyloid status, cognitively unimpaired**

Old Conception of Alzheimer's Disease



NINCDS-ADRDA Criteria 1984

views &reviews

Article abstract—Clinical criteria for the diagnosis of Alzheimer's disease include insidious onset and progressive impairment of memory and other cognitive functions. There are no motor, sensory, or coordination deficits early in the disease. The diagnosis cannot be determined by laboratory tests. These tests are important primarily in identifying other possible causes of dementia that must be excluded before the diagnosis of Alzheimer's disease may be made with confidence. Neuropsychological tests provide confirmatory evidence of the diagnosis of dementia and help to assess the course and response to therapy. The criteria proposed are intended to serve as a guide for the diagnosis of probable, possible, and definite Alzheimer's disease; these criteria will be revised as more definitive information becomes available.

Clinical diagnosis of Alzheimer's disease:

Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease

Guy McKhann, MD; David Drachman, MD; Marshall Folstein, MD; Robert Katzman, MD; Donald Price, MD; and Emanuel M. Stadlan, MD

Alzheimer's disease is a brain disorder characterized by a progressive dementia that occurs in middle or late life. The pathologic characteristics are degeneration of specific nerve cells, presence of neuritic plaques, and neurofibrillary tangles. Alterations in transmitter-specific markers include forebrain cholinergic systems, and, in some cases, noradrenergic and somatostatinergic systems that innervate the telencephalon.

A Work Group on the Diagnosis of Alzheimer's Disease was established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA). The group intended to establish and to describe clinical criteria for the diagnosis of Alzheimer's disease of particular importance for research protocols and to describe approaches that would be useful for assessing the natural history of the disease. The need to refine clinical diagnostic criteria has been emphasized because 20% or more of cases with the clinical diagnosis of Alzheimer's disease are found at autopsy to have other conditions and not Alzheimer's disease. Moreover, therapeutic trials can be meaningfully compared only if uniform criteria are used for diagnosis and response to treatment.

The need for this report was suggested by the National Advisory Council of the NINCDS. The report has been reviewed by workshop participants, representatives of the National Advisory Neurological and Communicative Disorders and Stroke Council, representatives of the ADRDA, and designated reviewers representing professional societies concerned with the diagnosis of Alzheimer's disease. (For list of professional societies and designated reviewers, see page 943.)

The report was developed by subgroups that addressed medical history, clinical examination, neuropsychological testing, and laboratory assessments; the report was then discussed in plenary session. Based on a consensus of the participants, criteria were developed to serve as a clinical basis for diagnosis. These criteria should be useful also for comparative studies of patients in different kinds of investigations, including case control studies, therapeutic trials, evaluation of new diagnostic laboratory tests, and clinicopathologic correlations.

The criteria are not yet fully operational because of insufficient knowledge about the disease. The criteria are compatible with definitions in the current Diagnostic and Statistical Manual of Mental Disorders (DSM III) and in the International Classification of Diseases. These criteria must be regarded as tentative and subject to change. Additional longitudinal studies, confirmed by autopsy, are necessary to establish the validity of these criteria in com-

*For Work Group Participants and Affiliations, see page 943.

Accepted for publication March 20, 1984.

Address correspondence and reprint requests to Dr. Stadlan, 7550 Wisconsin Avenue, Federal Building, Room 700, Bethesda, MD 20205.

Alzheimer's Disease as a Clinical – Pathological Entity

Alzheimer's Disease

1984

NINCDS-ADRDA Criteria

Clinical-Pathological definition

↓

2011

NIA-AA Criteria

Clinical syndrome with biomarkers for amyloid and neurodegeneration

↓

2018

NIA-AA Framework

Alzheimer's disease as a biological entity
defined by positive biomarkers for amyloid and tau

Clinical Spectra Independent

Alzheimer's Disease

- **Syndrome - not part of definition**

- **Etiology – defines the disease (plaques and tangles)**

Very confusing for most

Nomenclature
Implications for Research

- **Science/Research: Must be precise**
- **Clinicians: Must translate science to patients and vice versa**
- **Public stakeholders: Stigma, willingness to participate in research**
  - **Sensitivity in under-represented groups**

Plans for Future

Co-chair, Angela Taylor, LBDA

- **Convene groups to address these issues**
  - **Research/Science**
  - **Clinical practice**
  - **Public stakeholders**

- **Present issues and recommendations at future summits**

Putting the “Me” in Dementia Research

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March 24-25, 2020

Disclosures

- I have nothing to disclose.

Defining Terms

Patient Participation **VS.** **Engagement (US)/Involvement (UK)**

- Role is primarily as a subject of the research, not as a contributor
- “Research is done TO/ON patients”
- Traditional within ADRD Clinical Trials
- Study outcomes may or may not be *relevant or meaningful* to patients or caregivers

- Role is shaping and contributing to various aspects of the study process
- Research is done WITH patients
- Not a new concept in other fields
  - Cancer
  - Diabetes
  - Mental Health

Spectrum of Engagement in Research

Learn	CONSULT	INVOLVE	COLLABORATE	LEAD
Open atmosphere to share knowledge	Priority-setting Focus Groups	Working Groups, Health Panels.	Co-Investigators, Research, Advisory, Committees.	Principal Investigators

HOW?

Patients & Caregivers: Steps in Research Engagement

Steps in Designing a Research Study	N	Percent
1: Deciding what question to ask	9	47%
2: Determining who the study subjects should be	11	58%
3: Figuring out where to identify or recruit the study	6	32%
subjects 4: Deciding what type of information should be	16	84%
collected	11	58%
5: Deciding what types of comparisons should be made	14	74%

6: Identifying types of outcomes that should be reported

Note: Of the 20 persons in the focus groups, 12 were either PLWD or caregivers who were not affiliated with community groups (not “activated” or “advocates”).

(Adapted from Majid, et. al. ISPE Task Force Paper)

Care Management Concepts added through Engagement

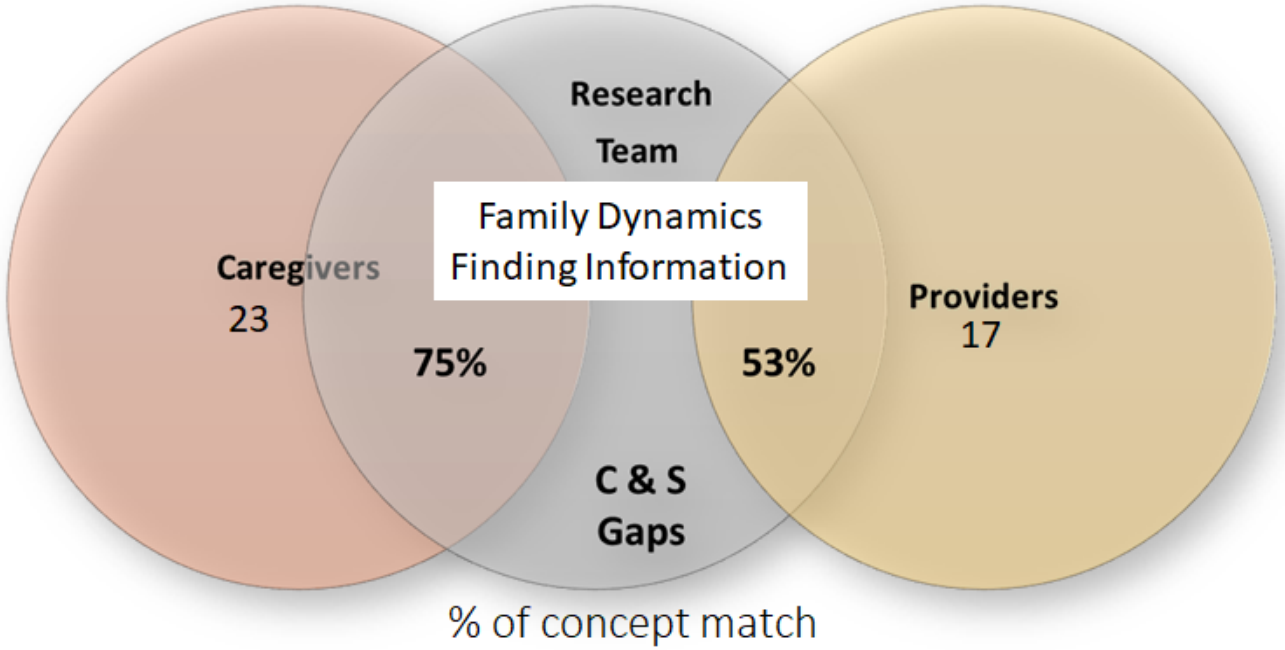
- Atypical behavior observations and management
- Advocating for PLWD
- Navigation of health care and services
- Formal diagnosis and reaction
- Finding and exchanging information
- Building a support network & balance
- Managing future expectations

Themes of Care Management from other Caregiver Studies

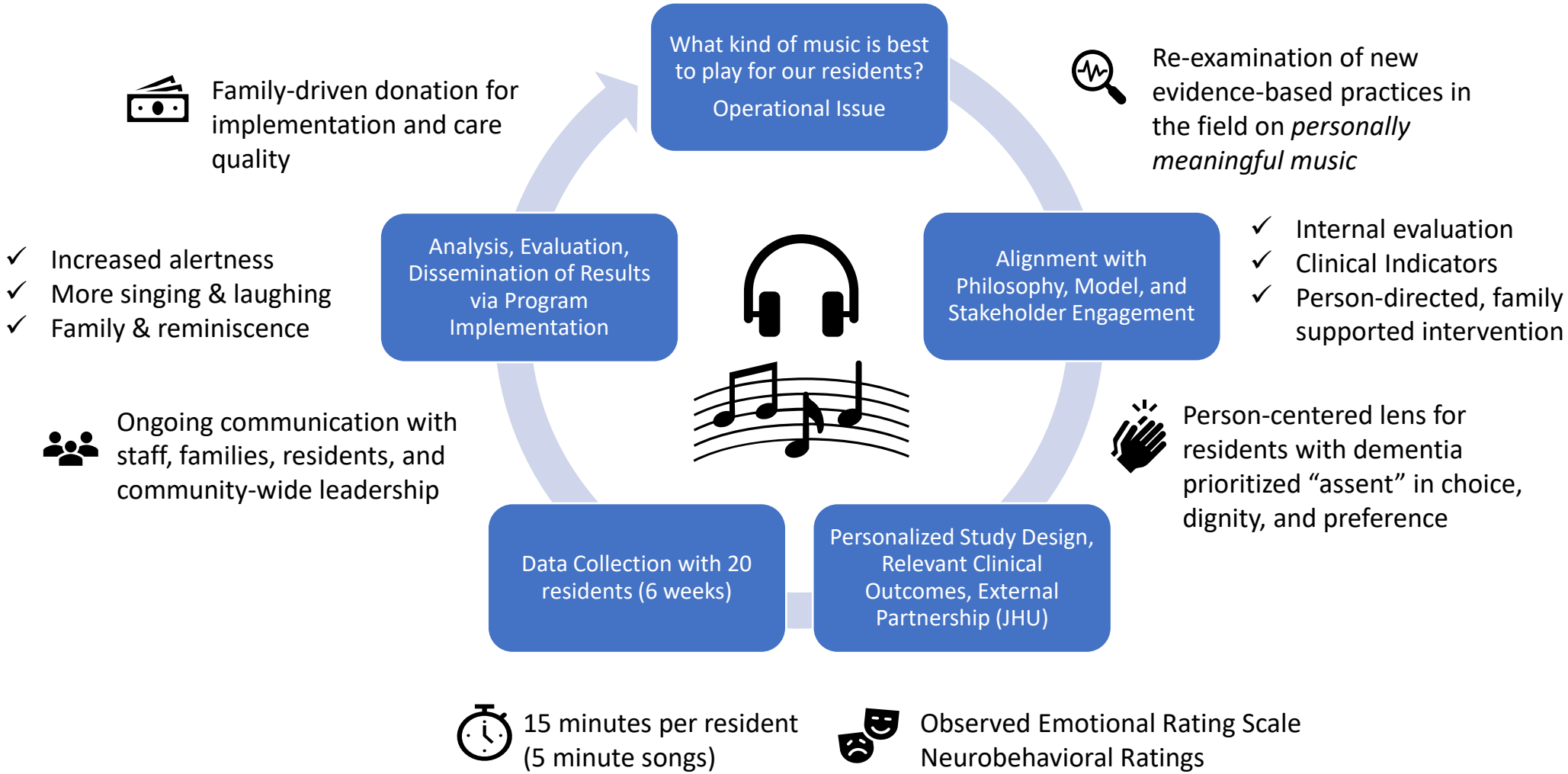
- **Assessing treatment options & goals**
- **Managing your own/PLWD's emotions.**
- **Family & societal dynamics**
- **Advice for others**

Added after Engaging PLWD & Caregivers

Engaged Caregivers & Providers Prioritize & Define Care Management



Design Adaptation: A Resident-Driven Meaningful Music Study



Challenges & Opportunities of Engagement

Challenges

- Ways to incorporate care partners
- Identifying appropriate study methods and defining relevant outcomes
- Bias and representation in both sample and “engaged” group
- Benefits and risk of technology in recruitment, data collection, and participant connection across groups

Opportunities

- ID methods to increase engagement
- “Activated patient communities” later in dementia progression (residential setting)
- Optimal study design improvements prior to and during protocol development
- Creation of relevant, meaningful outcomes benefiting the dyadic nature of ADRD progression

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Theme 4: Research Opportunity 1

- Develop and test methods to address fluctuating and/or declining cognition, including loss of insight, to enhance appropriate use of self-report by PLWD.

Theme 4: Research Opportunity 2

- Develop and test methods to combine multiple sources of information, including clinical data, patient- and informant/caregiver-reported data, and technology-derived data, to optimize outcomes measurement; address multiple reporter concordance, discordance, and weighting strategies.

Theme 4: Research Opportunity 3

- Develop and test personalized or individual-specific outcomes as endpoints in intervention trials.

Theme 4: Research Opportunity 4

- Develop and test methods to capture well-being and health-related quality of life of PLWD and those that care for them (both paid and unpaid caregivers), across all stages of disease and symptomatology.

Theme 4: Research Opportunity 5

- Discover how language about aging and cognitive disorders affects the conduct of dementia studies.

Theme 4: Research Opportunity 6

- Understand how nomenclature influences recruitment into research and identify best practices for disclosure of research results.

Theme 4: Research Opportunity 7

- Determine how nomenclature for AD/ADRD and caregiving contributes to stigma, both self and public, and develop and test strategies that can mitigate stigma about dementia and dementia caregiving.

Theme 4: Research Opportunity 8

- Identify methods and implementation strategies to improve representation of underserved and under-included people in dementia care and services research, including for research to treat or prevent dementia.

Theme 4: Research Opportunity 9

- Identify methods to improve the validity, value and efficiency of studies given increased sharing of information among participants and potential participants as part of activated communities.

Theme 4: Research Opportunity 10

- Identify methods to increase stakeholder engagement in dementia studies across the full range of potential stakeholders, including involvement in research question generation and prioritization, review of funding applications, and dissemination of study results.

Inclusion

Theme 4: Research Opportunity 11

- Evaluate stakeholder engagement in dementia studies with attention to methods applicable across research settings.