

Advanced Dementia: Research Informing Practice

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Goals

- Learn about trajectory of advanced dementia research over past ~28 years
 - Evolution of a research field
 - Major milestones and findings
 - Research informing clinical decisions & practice
- Gain insight about current priorities and opportunities

Public Health Impact

- Over 5.2 million Americans have Alzheimer's disease and other dementias 16 million by 2030
- 6th leading cause of death in U.S.
- ~ 1 million with advanced disease
- Social and health care costs
 - \$226 billion in 2015
 - ~ \$288,000 last 5 years of life*
 - Out-of-pocket spending higher than other diseases

**Kelley A, Ann Intern Med 2015*

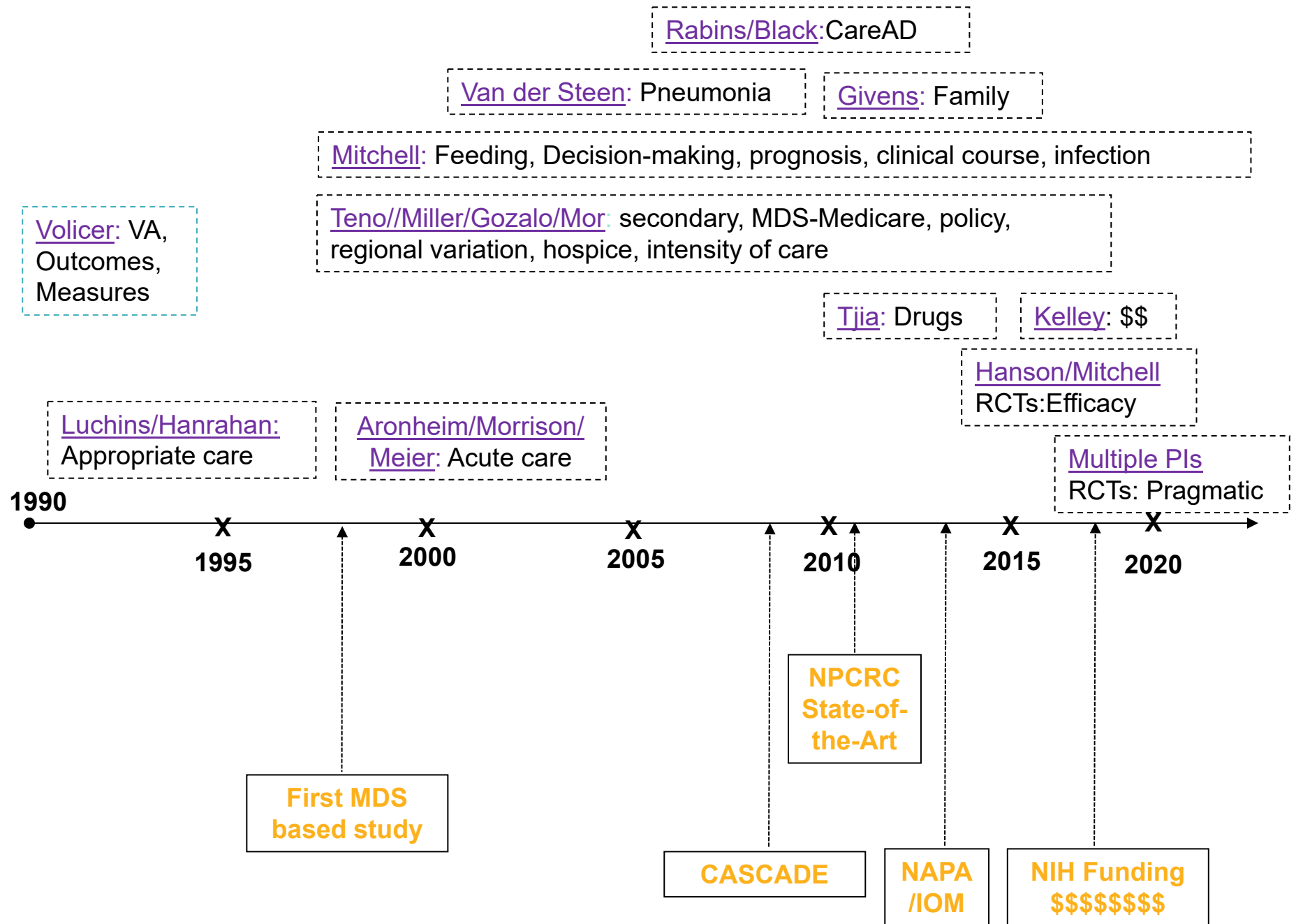
Advanced Dementia



Global Deterioration Scale Stage 7*

- Do not recognize family
- Loss of all verbal abilities
- Non-ambulatory
- Incontinent

* *Reisberg B, J Psychiatry 1982*



Retrospective: How and Why

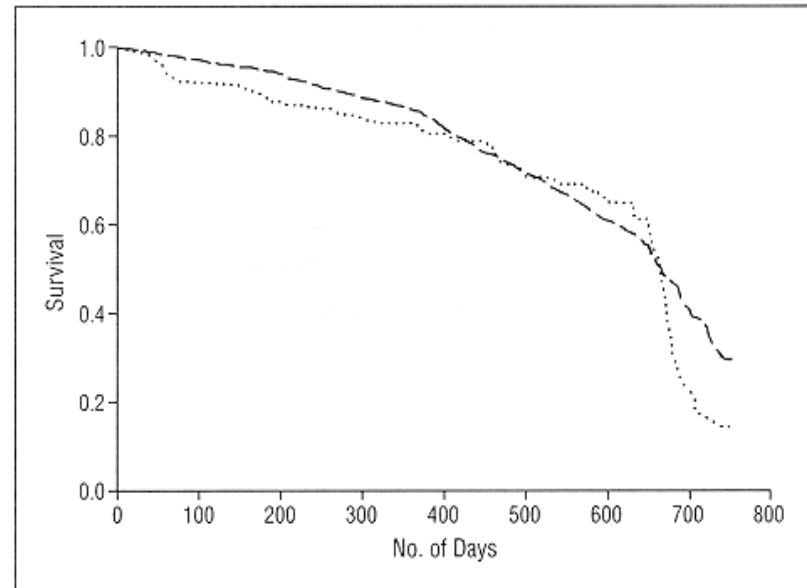
- Informed by clinical observation
- Facilitators
 - Large databases characterizing cohorts and outcomes
 - Minimum DataSet
 - Medicare

Feeding Problems

- Affect 90% of patients at end-stage
- Approaches:

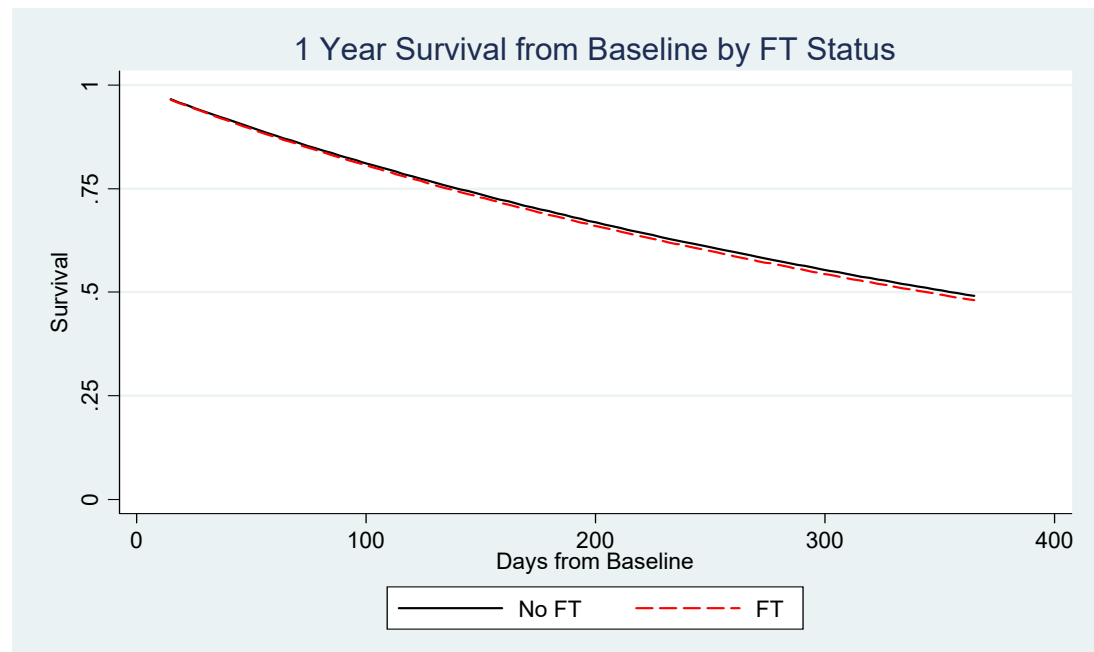


Arch Intern Med; 1997



A 24-month survival comparison of residents with severe cognitive impairment with (dotted line) and without (dashed line) feeding tubes.

JAGS; 2012



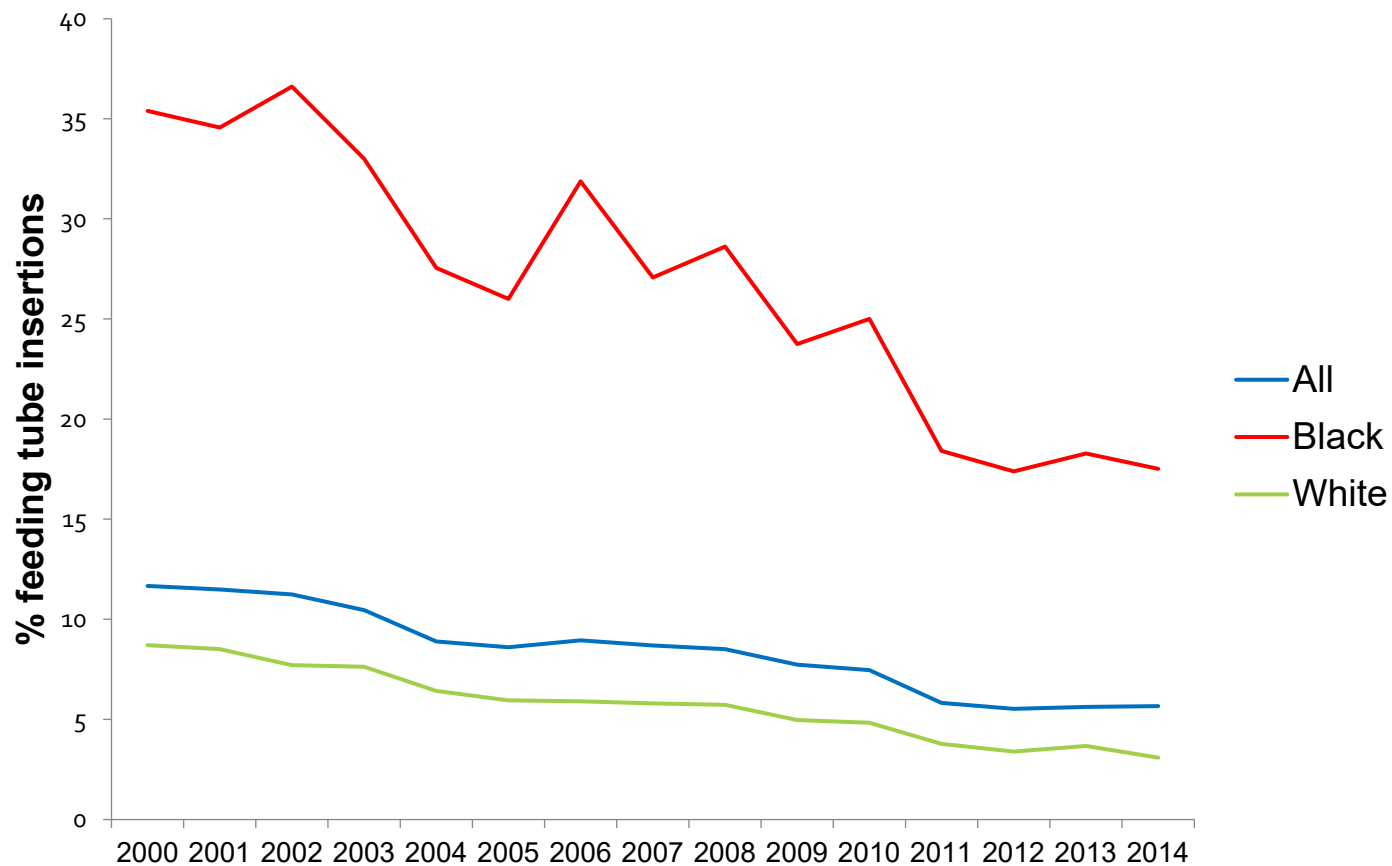
Retrospective: Tube-Feeding

- Cochrane Review
- No demonstrable benefits
 - Prevent Aspiration **NO**
 - Heal Malnutrition/Pressure Ulcers **NO**
 - Improve Survival **NO**
 - Promote Comfort **NO**
- Risks
 - Worsen pressure ulcers **YES**
 - Greater Agitation **YES**
 - Increase hospital transfer **YES**

Tube-Feeding

- Expert opinion and multiple position statements (AGS, AA, AAHPM, Choose Wisely)
 - tube-feeding has no demonstrable benefits and should not be offered

Tube-Feeding Trends



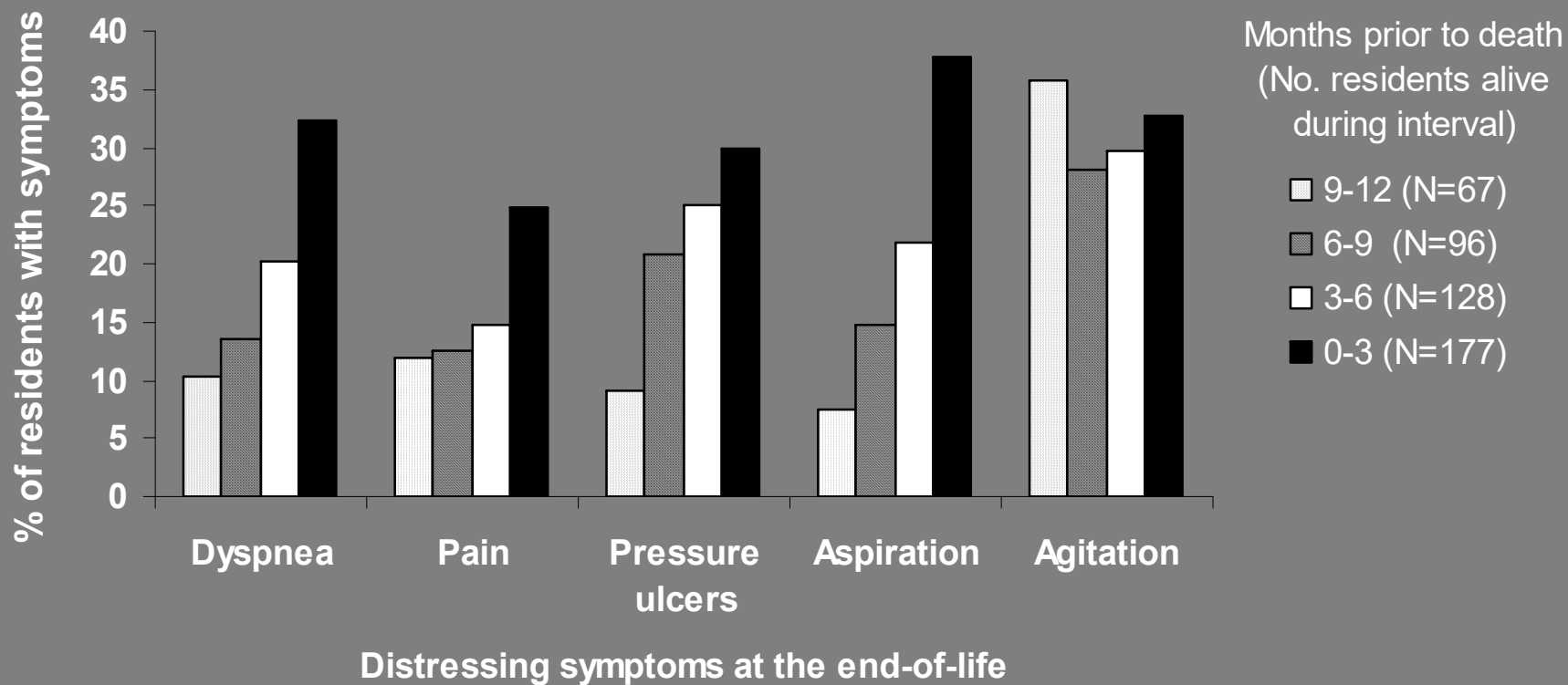
Prospective: CASCADE



The Clinical Course of Advanced Dementia

- Choices, Attitudes, Strategies and Care for Advanced Dementia at the End-of-Life
- 323 patients advanced dementia, follow 18 months
 - Mortality rate: 55%
 - Most common complications
 - ~ 90% eating problems
 - ~ 50% recurrent infections/fever
 - Others rare (stroke, fracture, MI)
 - Less aggressive care when families informed

Prospective: CASCADE



Prospective: CASCADE

- Under-reporting of dementia on death certificates

JAMA[®]

Online article and related content
current as of December 10, 2008.

Reporting Dementia on the Death Certificates of Nursing Home Residents Dying With End-Stage Dementia

Melissa Wachterman; Dan K. Kiely; Susan L. Mitchell

JAMA. 2008;300(22):2608-2610 (doi:10.1001/jama.2008.768)

<http://jama.ama-assn.org/cgi/content/full/300/22/2608-b>

ORIGINAL INVESTIGATION

ONLINE FIRST | HEALTH CARE REFORM

Medicare Expenditures Among Nursing Home Residents With Advanced Dementia

Keith S. Goldfeld, MPA, MS; David G. Stevenson, PhD; Mary Beth Hamel, MD, MPH; Susan L. Mitchell, MD, MPH

- Large % of Medicare costs for acute care

Scales for the Evaluation of End-of-Life Care in Advanced Dementia *Sensitivity to Change*

Dan K. Kiely, MPH, MA,* Michele L. Shaffer, PhD,† and Susan L. Mitchell, MD, MPH*‡

- Measurement validation

ORIGINAL INVESTIGATION

Survival and Comfort After Treatment of Pneumonia in Advanced Dementia

Jane L. Givens, MD, MSCE; Richard N. Jones, ScD; Michele L. Shaffer, PhD; Dan K. Kiely, MPH; Susan L. Mitchell, MD, MPH

- Pneumonia: Antibiotics may prolong life but add to discomfort

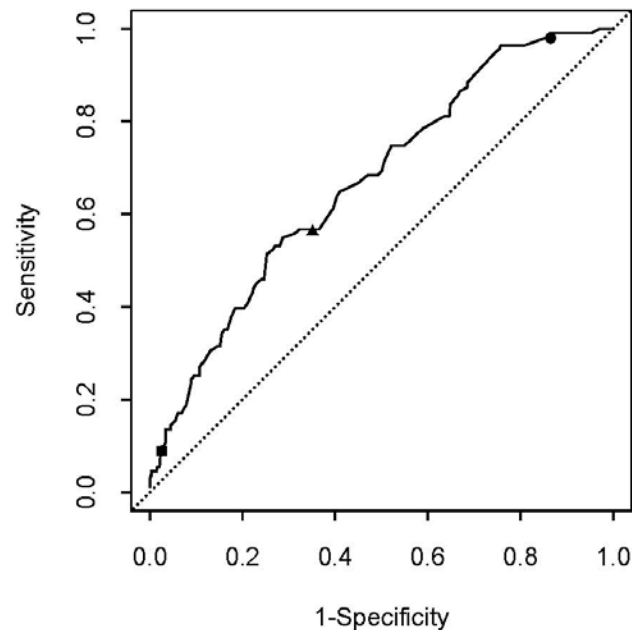
ORIGINAL INVESTIGATION

Patterns of Antimicrobial Use Among Nursing Home Residents With Advanced Dementia

Erika D'Agata, MD, MPH; Susan L. Mitchell, MD, MPH

- Over-use of antibiotics

Advanced DEmentia Prognostic Tool



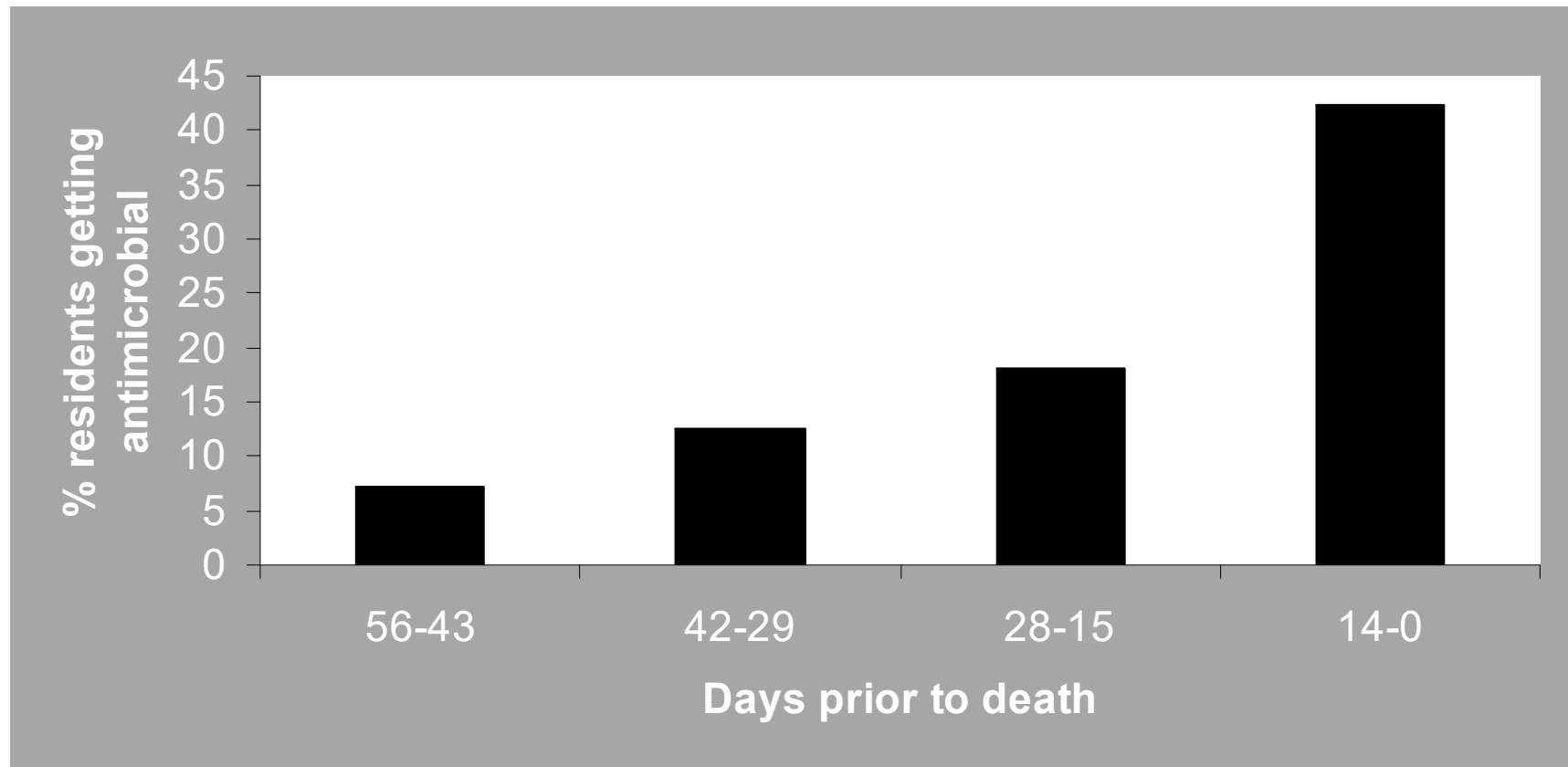
Goal: Develop and prospectively validate a 6- month mortality risk score in advanced dementia

Findings: ADEPT tool ability to predict 6 month survival is modest: AUROC = 0.68) (vs. hospice eligibility = 0.55)

Implications:

Access to palliative care should be based on preference not prognosis

Antimicrobial Exposure



**D'Agata EMD, Mitchell SL Arch Int Med 2007*

Prospective: SPREAD

Original Investigation

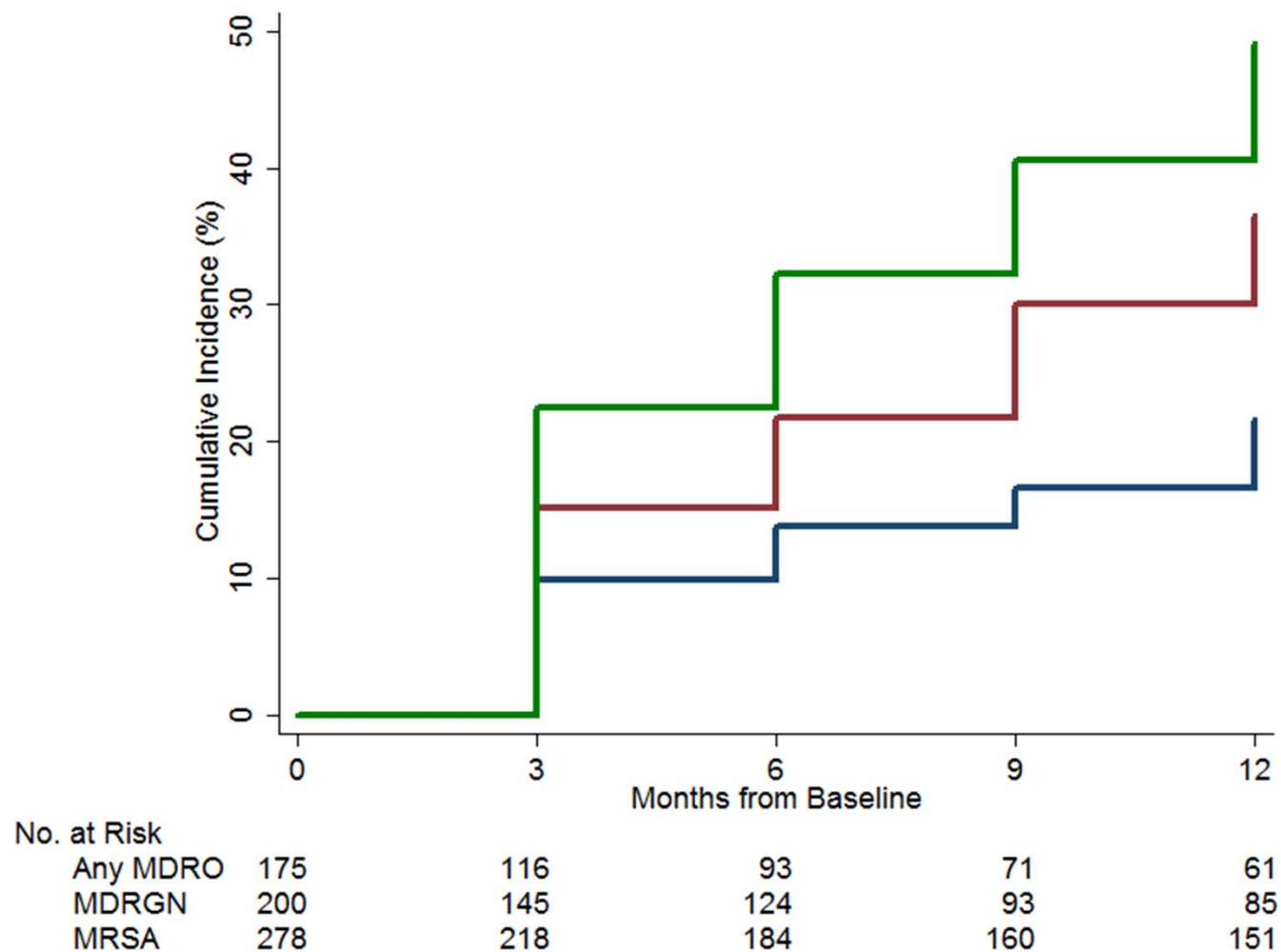
Infection Management and Multidrug-Resistant Organisms in Nursing Home Residents With Advanced Dementia

- Study of Pathogen Resistance and Exposure to Antimicrobials in Dementia
- 362 NH residents with advanced dementia
- 12 months follow-up
- Outcomes
 - Antimicrobial use
 - Multi-drug resistant organisms (MDRO)

Prospective: SPREAD

| | Source of suspected infectious episodes | | | | |
|---|---|---------------------|---------------------|--------------------|--------------------|
| | All | LRI | UTI | Skin | Fever only |
| Episodes, No. | 486 | 144 | 193 | 68 | 81 |
| Treated with antimicrobials, No. (%) | 354 (73) | 103 (72) | 145 (75) | 65 (96) | 41 (51) |
| Minimal criteria met , No. (%) | 157 (44) | 35 (34) | 28 (19) | 62 (95) | 32 (78) |

Prospective: SPREAD



Intervention Studies: How and Why

•Research Field at a Crossroads

LOGO
ONLINE
ONLY→

Annals of Internal Medicine

MEDICINE AND PUBLIC ISSUES

Advanced Dementia: State of the Art and Priorities for the Next Decade

Susan L. Mitchell, MD, MPH; Betty S. Black, PhD; Mary Ersek, RN, PhD; Laura C. Hanson, MD, MPH;
Susan C. Miller, PhD; Greg A. Sachs, MD; Joan M. Teno, MD, MS; and R. Sean Morrison, MD

Dementia is a leading cause of death in the United States. This article outlines the current understanding of advanced dementia and identifies research priorities for the next decade. Research over the past 25 years has largely focused on describing the experience of patients with advanced dementia. This work has delineated abundant opportunities for improvement, including greater recognition of advanced dementia as a terminal illness, better treatment of distressing symptoms, increase access to hospice and palliative care services, and less use of costly and aggressive treatments that may be of limited clinical benefit. Addressing those opportunities must be the overarching objective for the field in the coming

decade. Priority areas include design and testing interventions that promote high-quality, goal-directed care; health policy research to identify strategies that incentivize cost-effective and evidence-based care; implementation studies of promising interventions and policies; and further development of disease-specific outcome measures. There is great need and opportunity to improve outcomes, contain expenditures, reduce disparities, and better coordinate care for the millions of persons in the United States who have advanced dementia.

Ann Intern Med. 2012;156:* * * FILL THIS IN * * *.
For author affiliations, see end of text.

www.annals.org

Intervention Studies since 2015

| | PI (s) | Funding | Design | Setting |
|-----------------------------|-----------------------|------------------|-----------------------|------------------|
| COMPLETED | | | | |
| Feeding DA | Hanson | NIH R01 | Cluster RCT | 24 NHs |
| Goals of Care DA | Hanson | NPCRC, NIH R01 | Cluster RCT | 22 NHs |
| EVINCE | Mitchell/Volandes | NIH R01 | Cluster RCT | 62 NHs |
| Hospital Consult | Hanson | NPCRC, NIH R21 | Pilot, RCT | Hospital |
| IN-PROGRESS | | | | |
| PROVEN | Mitchell/Volandes/Mor | NIH UH2/UH3 | Pragmatic RCT | 240 NHs |
| TRAIN-AD | Mitchell | NIH R21, NIH R01 | Cluster RCT | 24 NHs |
| Music and Memory | Mor | NIH R21/R33 | Pragmatic RCT | NHs |
| ACP Specialist | Unroe/Hickman | NIH R21/R33 | Pragmatic RCT | NHs |
| Community Hospice | Brody | NIH R66/R33 | Pragmatic RCT | NHs |
| IN-PEACE | Sachs | NIH R01 | Traditional RCT | Community |
| <i>IMPACT Collaboratory</i> | <i>Mitchell/Mor</i> | <i>U54</i> | <i>Infrastructure</i> | <i>Brown/HSL</i> |

Intervention Studies: Advanced Dementia

- Complex interventions
 - Multicomponent
 - Rigorous but adoptable/sustainable
- Cluster Designs
 - Statistical considerations
 - Regulatory and ethical regulations
 - Explanatory \longleftrightarrow Pragmatic
- Settings are challenging
- Outcomes
 - What is the primary outcome and how do you measure it?

Clinical Trials: Completed

Improving Decision-Making for Feeding Options in Advanced Dementia: A Randomized, Controlled Trial

Laura C. Hanson, MD, MPH,^{†‡} Timothy S. Carey, MD, MPH,^{‡§} Anthony J. Caprio, MD,^{*†} Tae Joon Lee, MD, CMD,^{||} Mary Ersek, PhD, RN,[#] Joanne Garrett, PhD,^{**} Anne Jackman, MSW,[‡] Robin Gilliam, MSW,[‡] Kathryn Wessell,[‡] and Susan L. Mitchell, MD, MPH^{††}*

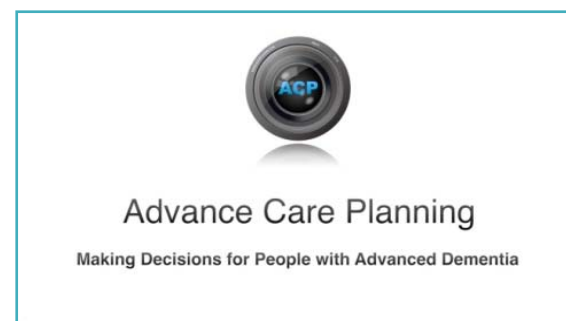
JAMA Internal Medicine | [Original Investigation](#)

Effect of the Goals of Care Intervention for Advanced Dementia A Randomized Clinical Trial

Laura C. Hanson, MD, MPH; Sheryl Zimmerman, PhD; Mi-Kyung Song, PhD, RN; Feng-Chang Lin, PhD; Cherie Rosemond, PhD; Timothy S. Carey, MD, MPH; Susan L. Mitchell, MD, MPH

Clinical Trials: EVINCE

- Title: EVINCE (Educational Video to Improve Nursing home Care in End-stage dementia)
- PIs: Mitchell/Volandes; NIH R01
- Design: Cluster RCT in 62 NHs
- Population: Proxies of Advanced Dementia Residents
- Intervention: ACP Goals of Care Video
- Outcomes:
 - 1^o Decision not to hospitalize
 - 2^o
 - Goal of Care
 - Other Directives



EVINCE Trial

| 6-Month Outcome | Intervention N=211 | Control N=189 | Adjusted Odds ratio (95% CI) |
|-----------------------------|-----------------------|------------------|---------------------------------|
| Comfort Care | 73% | 77% | 0.96 (0.58-1.58) |
| Do-not-hospitalize order | 63% | 63% | 1.08 (0.69-1.69) |

- Intervention
 - Not integrated into clinical care
 - Fundamentally difference that PROVEN
- Population
 - 60% wanted comfort care at beginning
 - Too late in disease course
 - Only those that consented
- Outcome
 - Did not capture not most important effect of enhanced ACP

Mitchell SL, JAMA IM 2018

EVINCE Results: Concordance of Preferences with Directives

| Documented ACP When Comfort Care was Preferred | | | |
|--|------------------------------------|-------------------------------|--|
| Directive | Intervention (n=334) No. (%) | Control (n=284) No. (%) | Adjusted Odds Ratio (95% Confidence Interval) |
| No Hospitalization | 250 (74.9) | 198 (69.7) | 1.50 (0.64-3.54) |
| No Tube-Feeding | 273 (81.7) | 170 (59.9) | 3.39 (1.62-7.11) |
| No Hospitalization and No Tube- Feeding | 241 (72.2) | 150 (52.8) | 2.68 (1.23-5.85) |

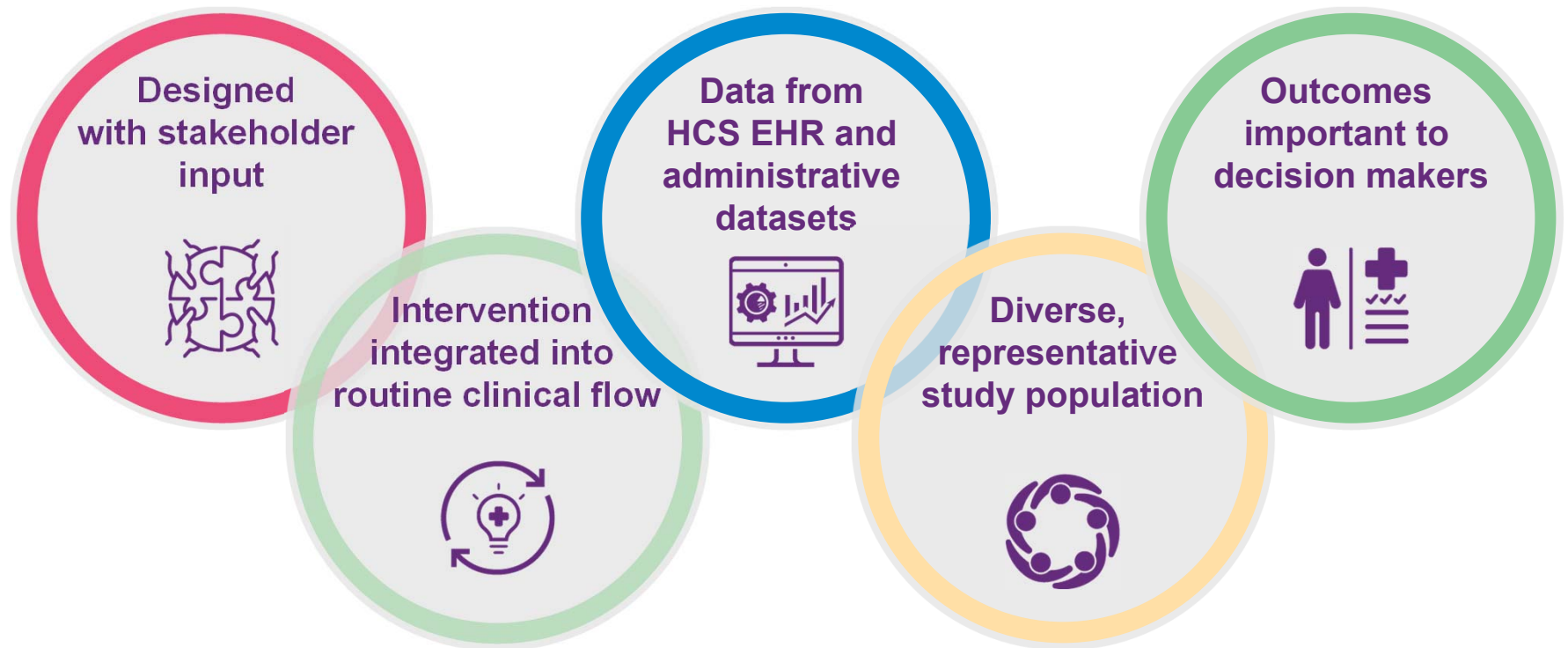
Clinical Trials: In Progress

- Title: TRAIN-AD: Trial to Reduce Antimicrobial use In Nursing home residents with Alzheimer's disease and other Dementias
- PI: Mitchell; NIH R01 (NIH R21 completed)
- Design: Cluster RCT in 24 NHs
- Intervention:
 - Program to improve infection management
 - Merges infectious disease and palliative care best practices
 - Provider training/proxy counseling
 - Multicomponent, standardized but flexible, delivered at NH level:
- Population: All patients with advanced dementia, consent waived
- Outcomes:
 - 1⁰: Total antimicrobial use
 - 2⁰ : Inappropriate antimicrobial use
 - ACP for infection management
 - Burdensome Interventions for infection work-up

Efficacy Trials

- Shortcoming of traditional RCTs
 - Stand-alone settings
 - Non-diverse populations
 - Underpowered
 - Expensive
 - Not applicable to “real-world”
- Disconnect between research and clinical care

ePCTs Bridge Research and Clinical Care



PRagmatic trial Of Video Education in Nursing Homes (PROVEN)

Setting: 360 NHs owned by 2 NH chains (Chain 1, N=297/Chain 2, N= 63)

Design:

- Parallel Cluster RCT
- Nursing homes are unaware they are in a trial

Intervention:

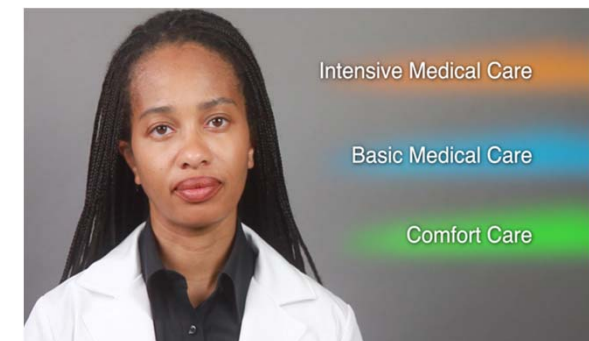
- Suite of ACP Videos
- Offered and shown by nursing home staff

Population:

- All patients in NH
- Consent waived
- Target population for analyses:
 - ✓ long-stay with advanced illness identified by MDS

Outcomes:

- All ascertained from existing data (Medicare Claims)
- 1^o : Hospital transfer in target population/person-day alive



PROVEN

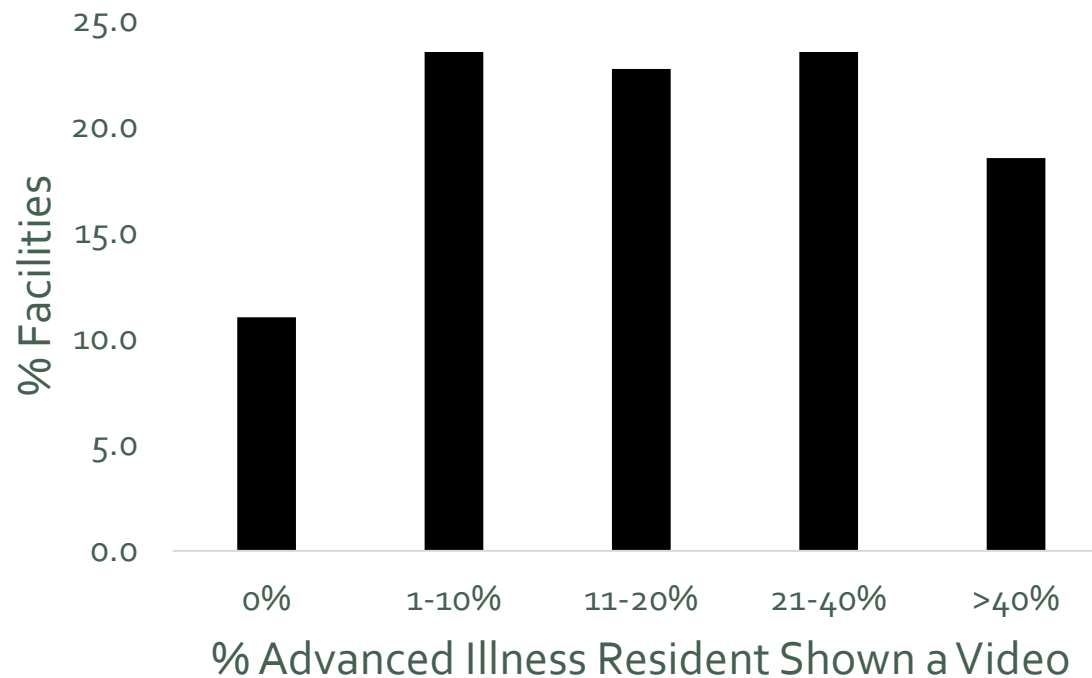
| | Intervention N=4171 | Control N=8308 | Marginal Rate Difference (SE) (95% CI) |
|--|----------------------------|---------------------------|--|
| Primary Outcome | Rate (SE) (95% CI) | | |
| Hospital transfers/1000 person-days alive | 3.7 (0.2) (3.4-4.0) | 3.9 (0.3) (3.6-4.1) | -0.2 (0.3) (-0.5,0.2) |
| Secondary Outcomes | Percent (SE) (95% CI) | | Marginal Risk Difference (SE) (95% CI) |
| ≥ 1 hospital transfer | 40.9 (1.2) (38.4-43.2) | 41.6 (0.9) (39.7,43.3) | -0.7 (1.5) (-3.7, 2.3) |
| ≥ 1 burdensome treatment | 9.6 (0.8) (8.0,11.3) | 10.7 (0.7) (9.4,12.1) | -1.1 (1.1) (-3.2,1.1) |
| Enrolled in hospice* | 24.9 (1.2) (22.6, 27.2) | 25.5 (0.9) (23.3,27.2) | -0.6 (1.5) (-3.4, 2.4) |

*Excluded residents enrolled in hospice at baseline

Mitchell SL, JAMA IM 2020

Fidelity

- 55.6% advanced illness residents (or proxies) offered a video
- 21.6% advanced illness residents (or proxies) shown a video
- Variability across facilities



National Infrastructure for Pragmatic Trials...for AD/ADRD



Funding Opportunity Title

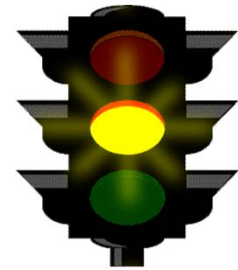
NIA AD/ADRD Health Care Systems Research Collaboratory (U54
Clinical Trial Required)



Next Steps: Advance Dementia Research

- Clinical Trials

- Learn from experience
- Continuum from explanatory to pragmatic
- Challenge for complex interventions
- Think carefully about stage/design
- Traditional efficacy study may not be right first step
- Sustainable, real world but avoid implementation error



- Disparities

- Explain and reduce

- Impact of new health care structures & policies

- Pipe-line of New Investigators

Thanks to...

- Funders: NIH, NPCRC, AA
- Mentees:
- Co-investigators:
 - Joan Teno MD, MSc
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 - Angelo Volandes MD, MPH
 - Mary Beth Hamel, MD, MPH
 - David Grabowski PhD
 - Jane Givens, MD, MSCE
 - Erika D'Agata, MD, MPH
 - Michele Shaffer PhD
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 - Ellen McCarthy, PhD, MPH
- Project Directors:
 - Ruth Carroll RN
 - Elaine Bergman MS
 - Phoebe Lehman
 - Erin Luers
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- Field Staff
- Analysts:
 - Dan K. Kiely
 - Daniel Habtemariam
 - Tim Tsai
- Patients and Families
- Nursing Homes