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Issues in Aging 2024

Monday April 29, 8:00 am - 3:45 pm

Navigating Challenges in Aging

6 CREDITS for Social Workers, Nurses, Physical Therapists, Occupational Therapists, Case Managers, OTAs, PTAs

COST (*Breakfast and lunch are included*):
\$65 Professionals
\$40 Students (No CEs issued)

LIVE EVENT, JOIN US IN PERSON:
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Right at Home

Senior Caregiver Resource
Network (SACRN)

Senior Helpers

Team Suzy

The Senior Alliance (AAA1C)

Waltonwood Senior Communities

AGENDA

8:00 am – Light Breakfast, Visit Vendors

8:30 am – ***Medication Management: One Too Many Prescriptions***

10:00 am – Break, Networking, Visit Vendors

10:30 am – ***Partnering with Families of Hospitalized Persons with Dementia: Lessons Learned***

Noon – Lunch

12:45 pm – ***CAPABLE: An Interdisciplinary Approach to Aging in Place***

2:15 pm – ***Structural Insights into the Neuropathology of Frontotemporal Dementia and ALS***

3:45 pm – Raffle Drawings, Closing



GARWOOD



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BARMADA

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**Medication Management:
One Too Many Prescriptions**

8:30 AM



Candice Garwood, PharmD, FCCP, BCPS, BCACP, Clinical Professor College of Pharmacy and Health Sciences, Wayne State University

Polypharmacy in geriatric patients refers to the concurrent use of multiple medications by these individuals. This is a common concern as it can lead to various issues such as increased risk of adverse drug reactions, drug interactions, and medication non-adherence. It is important for healthcare providers to regularly review the medication regimen of older adults to ensure the appropriate and safe use of medications.

Objectives:

- Discuss polypharmacy in geriatric patients.
- Develop strategies to reconcile medication therapies and minimize adverse drug events.
- Identify and list resources to optimize patient safety and medication use.

**Partnering with Families of Hospitalized Persons
with Dementia: Lessons Learned** 10:30 AM



Marie Boltz, PhD, GNP-BC, FGSA, FAAN, Eberly Endowed Professor, College of Nursing, Pennsylvania State University

Partnering with families of hospitalized persons with dementia is crucial for providing comprehensive and person-centered care. Through our experience, we have learned that open communication, education, and involving families in decision-making can greatly improve the well-being of the patient and enhance their overall hospital experience.

Objectives

- Discuss the critical role of family in the life of the person living with dementia.
- Describe challenges and rewards for family carers.
- Describe the state of the science related to interventions for family carers of persons living with dementia.
- Discuss the family carers' relationship with the health care system, including acute care.
- Discuss emerging issues in research, practice, and policy affecting the family living with dementia.

**CAPABLE: An Interdisciplinary Approach
to Aging in Place**

12:45 PM



GOODENOW FORD

Amanda Goodenow, MS, OTR/L, Strategic Partnership Coordinator, and **Tricia Ford**, BA, VP of Operations, CAPABLE National Center, CO

CAPABLE is an interdisciplinary program aimed at supporting older adults to comfortably stay in their homes. It combines expertise in occupational therapy, nursing, and home repair services to address the unique needs and challenges faced by older adults. By providing holistic support, CAPABLE promotes independence and enhances the overall quality of life for older adults aging in place.

Objectives:

- Describe the evidence that supports CAPABLE.
- Describe the program components and the team.
- Describe how CAPABLE addresses equity and promotes self-efficacy.

**Structural Insights into the Neuropathology
of Frontotemporal Dementia & ALS** 2:15 PM



Sami Barmada, MD, PhD – Welch Research Professor and Associate Professor of Neurology, University of Michigan; Director of Michigan Brain Bank

Studies have shown that in frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), there is a common pattern of cortical atrophy, particularly in the frontal and temporal lobes. Imaging techniques have detected abnormal protein aggregates in specific brain regions, further linking the structural changes to the neuropathology of these diseases. Understanding the structural aspects of FTD and ALS provides insights into their pathogenesis and has potential to guide the development of targeted therapies.

Objectives

- To describe the unique neuropathology of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), and the clues this provides to disease pathogenesis.
- To illustrate how this pathology can be recapitulated in a laboratory environment, and what this tells us about the origins of disease.
- Clarify mechanisms contributing to FTD/ALS, and new approaches to blocking neurodegeneration.





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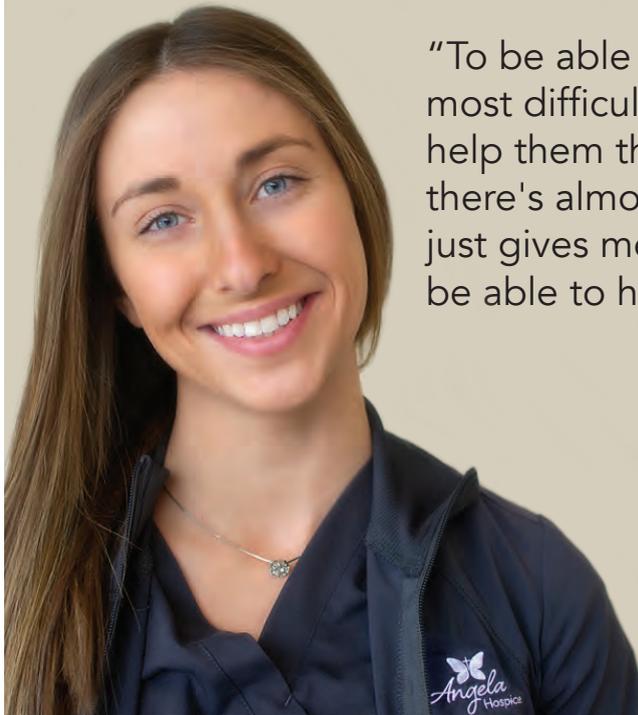
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– Talar, RN

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Area Agency on Aging 1-B



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POLYPHARMACY: ONE TOO MANY PRESCRIPTIONS

Candice Garwood, Pharm.D., FCCP, BCPS, BCACP

Clinical Professor, Wayne State University

Clinical Pharmacy Specialist, Harper University Hospital

Disclosures

- I have no actual or potential conflicts to disclose.

Audience Poll

What is your healthcare profession?

- a. Physical therapist
- b. Occupational therapist
- c. Nurse
- d. Social worker
- e. Pharmacist
- f. Case worker



Question

How often do you encounter polypharmacy with your patients?

- a. Many patients, daily
- b. Sometimes
- c. Not often
- d. I'm not really sure, what is polypharmacy?



Objectives



Discuss polypharmacy in older adults



Develop strategies to minimize adverse drug events in older adults



Identify and list resources to optimize patient safety and medication use in older adults

Multi-
morbidity

Polypharmacy

Multiple
Medications

Polypharmacy is Prevalent

Approximately 36% of people over age 65 take ≥ 5 prescription medications.

Nearly 50% of nursing home residents take ≥ 5 medications, and 24% use ≥ 10 medications.



Polypharmacy



Mortality



Falls



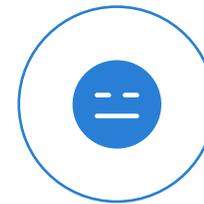
Adverse Drug
Events



Increase Length
of Stay



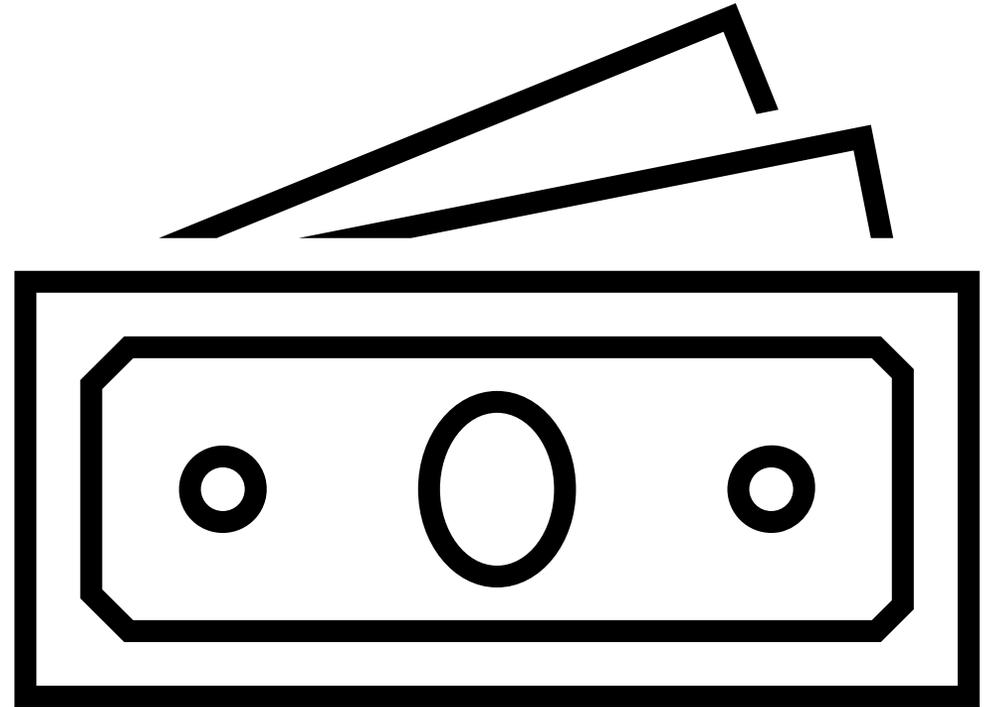
Hospital
Readmission



Medication
Non-adherence

Polypharmacy is Costly

- An estimated **\$8.7 billion** could be avoided by appropriate polypharmacy management.



Polypharmacy Defined

World Health Organization

- “The concurrent use of multiple medications”

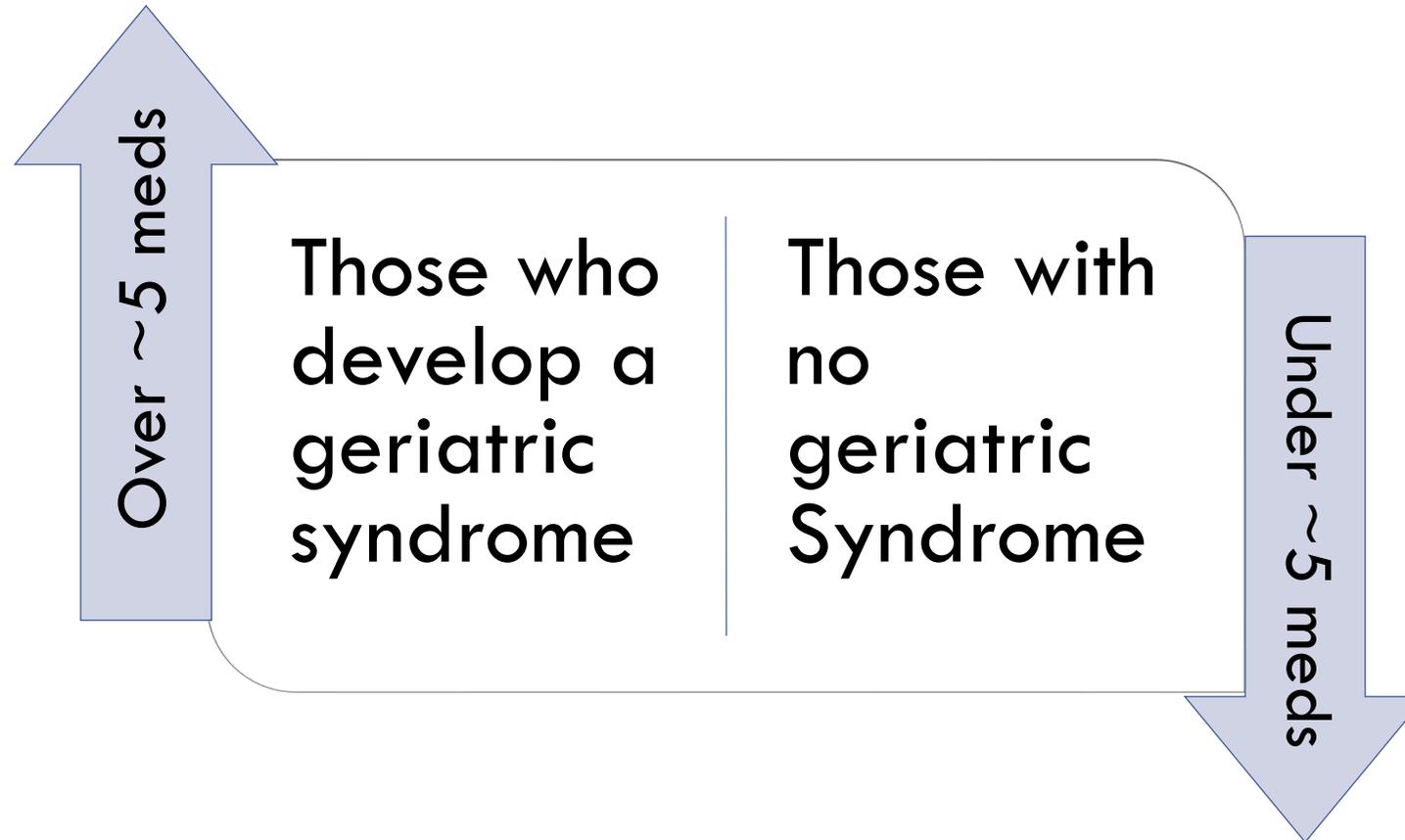
Multiple definitions exist

- Number; number + healthcare setting; descriptive

Most common definition

- ≥ 5 concurrent medications daily

Polypharmacy Defined as ≥ 5 Meds?

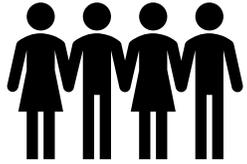


Hyper- polypharmacy

≥ 10 concurrent
medications



Doherty, et al. Adverse Drug Reactions and Associated Patient Characteristics in Older Community-Dwelling Adults



- Prospective cohort, Ireland
- N = 592, age ≥ 70 yrs
- Community dwelling
- ADR occurrence & severity

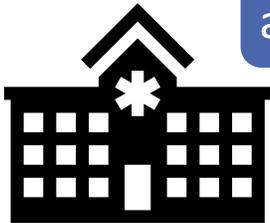
Design

- 1 in 4 people had ≥ 1 ADR
- ADR associated with polypharmacy

ADR Outcomes,
6-yr follow up

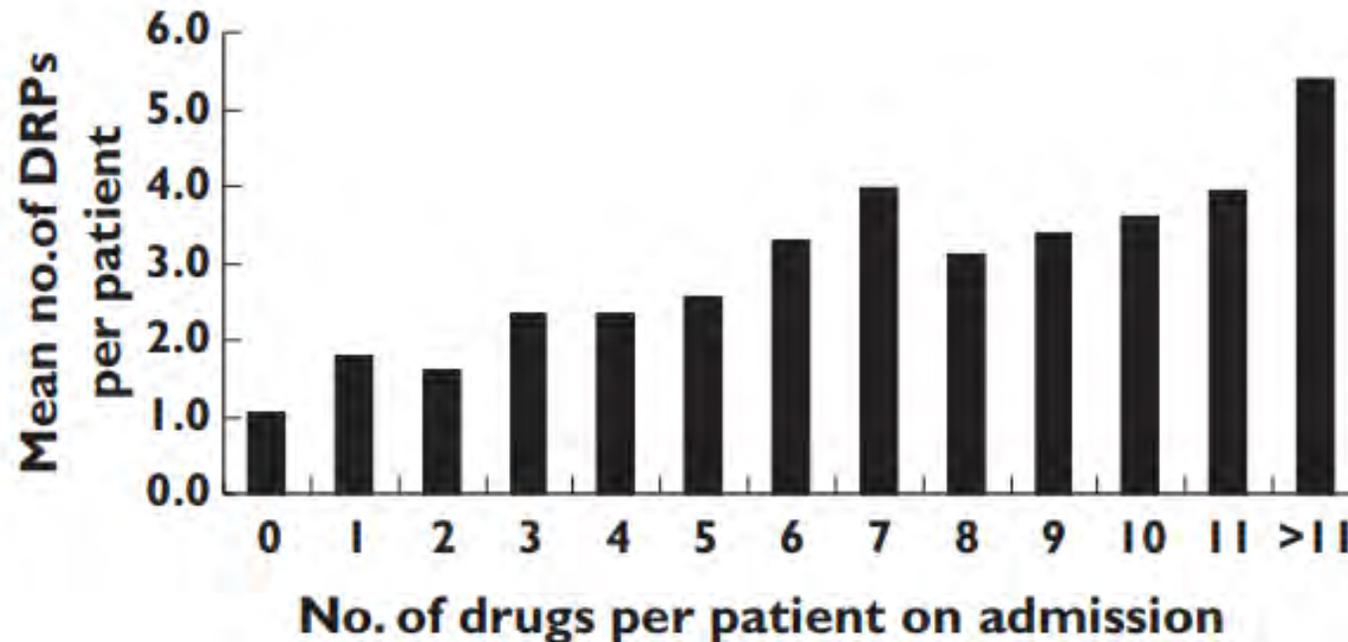
- 5-9 meds: $\sim 2x$ as likely to have ADR
- ≥ 10 meds: over $3x$ as likely ADR

Polypharmacy independently associate with ADR risk



Adverse Events Increase with No. of Meds

- A hospital-based study noted increased approximately linearly with an increase in number of drugs used.
- Each per-unit increase in medication use yielded an additional 8.6% risk for the number of adverse drug events.

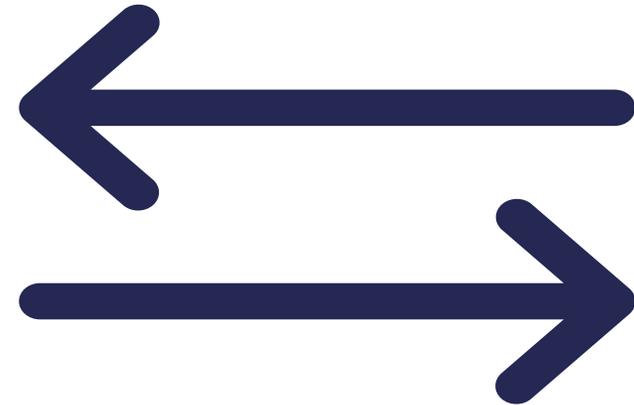


Polypharmacy: Redefined

Use of multiple drugs or more than are medically necessary

Terminology Shift

Appropriate Polypharmacy vs.
Inappropriate Polypharmacy



Inappropriate Polypharmacy

- Nearly 50% of older adults take one or more medications that are not medically necessary.
- Increases risk of adverse reactions.
 - Patients taking 5-9 medications have >50% chance of adverse reaction
 - Patients taking ≥ 20 medications have 100% chance of adverse reaction

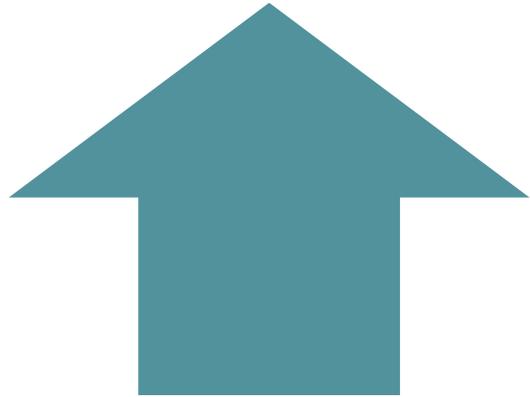


Appropriate Polypharmacy

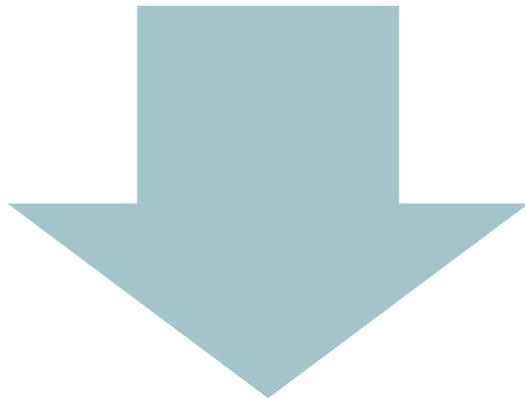
- At times, many drugs may be clinically appropriate

Indication	Medication	Number
Diabetes	1-2 antihyperglycemic agents Ace inhibitor Statin	3-4
Hypertension	1-3 antihypertensive agents	1-3
Heart failure	ACE-I or ARNI Beta Blocker SGLT2 inhibitor Aldosterone antagonist +/- loop diuretic	4-5
STEMI with stents	Aspirin P2Y12 inhibitor Statin Beta Blocker ACE-I	5

Inappropriate Prescribing



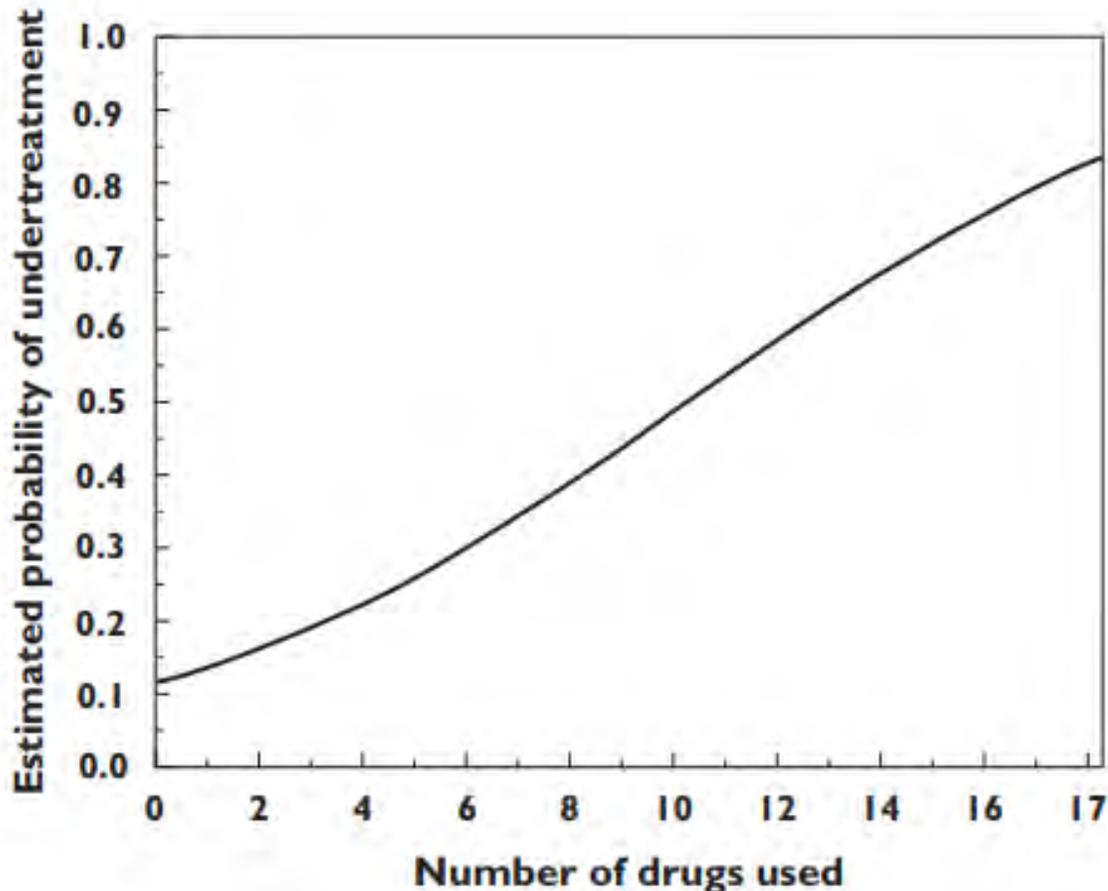
Overprescribing



Under-prescribing

Polypharmacy is also associated with under-prescribing in older people.

Probability of Under-prescribing Related to Number of Drugs Used



Of patients with polypharmacy, those who were undertreated:

≥ 5 drugs	≤ 4 drugs	Adj. OR (95% CI)
42.9%	13.5%	4.8 (2.0, 11.2)

Evaluating Polypharmacy

- Number of medications – a starting point
- Assess medications by indication, efficacy, potential for harm
- Combination = risk vs. benefits

More robust methods for evaluating influence of polypharmacy are needed



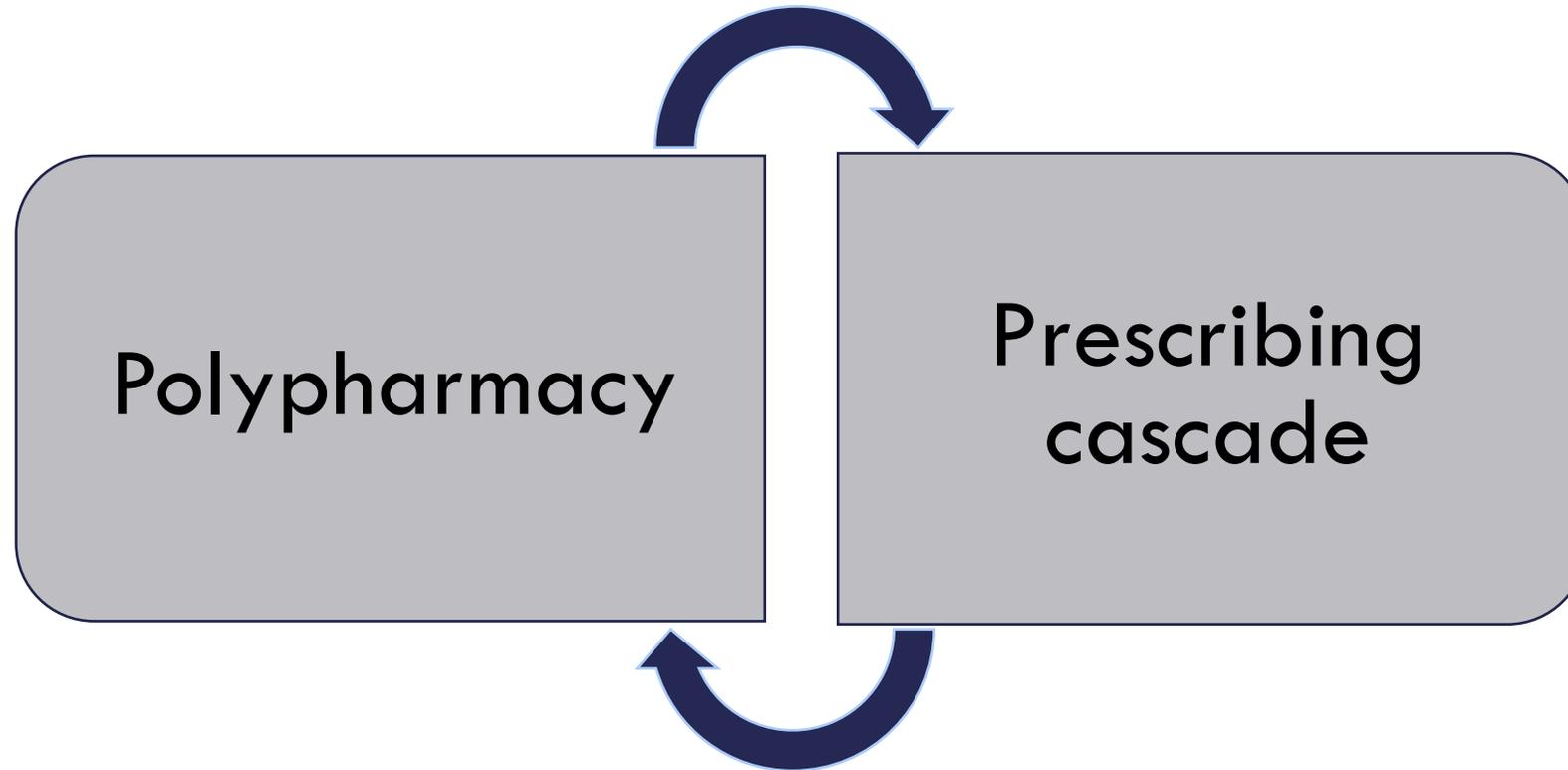
The following are potential impacts of polypharmacy EXCEPT:

- a. Reduced mortality
- b. Adverse drug events
- c. Increased healthcare costs
- d. Medication non-adherence



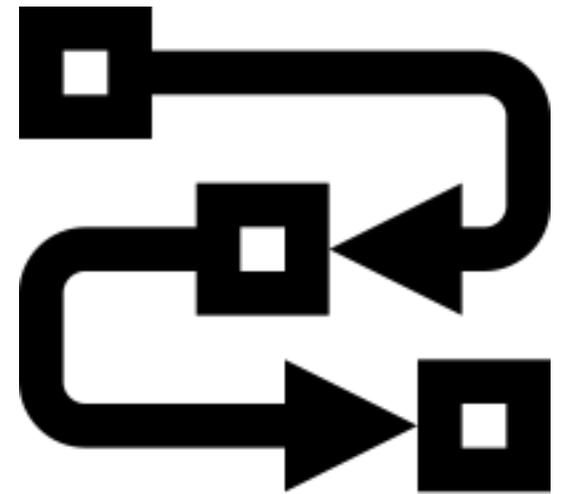
HOW DOES INAPPROPRIATE
POLYPHARMACY OCCUR?

How Does Inappropriate Polypharmacy Occur?

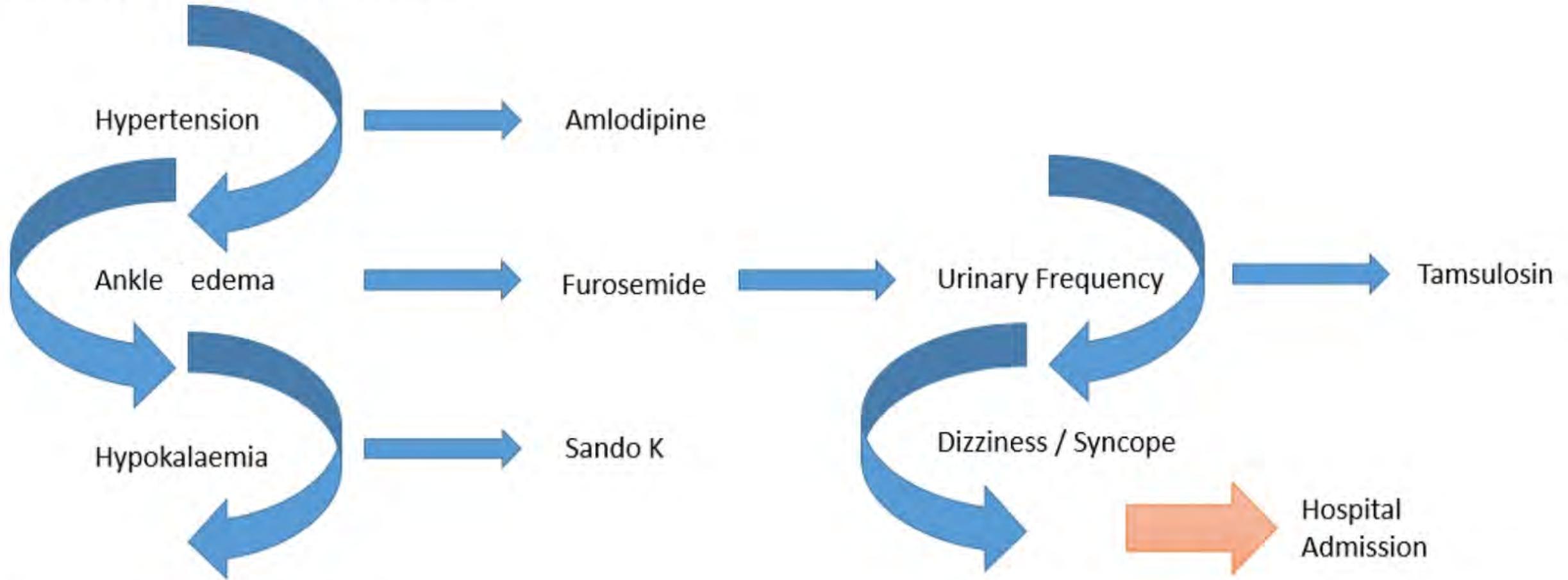


Prescribing Cascade

A new medicine is prescribed to “treat” and adverse reaction caused by another medicine.



From: Deprescribing, Polypharmacy and Prescribing Cascades in Older People with Type 2 Diabetes: A Focused Review



Diagrammatic example of a prescribing cascade.

Managing prescribing cascades



1) Identify a prescribing cascade



2) Deprescribe medications

Evaluation of the Prescribing Cascade

Defining Prescribing Cascade	Score
Existence of ADR, either expected or unknown	
Doubtful	0
Yes	1
Yes, but misunderstood	2
Action followed against the ADR	
Treatment discontinuation	0
Continued with dose reduction	1
Continued unchanged or with another drug of the same group	2
Existence of a second drug treatment for the ADR	
No	0
Yes	1
Overall result of this new treatment	
Patient improves	0
Patient worsens or unchanged	1
New ADR appears	2
New ADR requires a third drug treatment	3

Sum of ≥ 4
associated with
prescribing
cascade

ThinkCascades Tool

Drug A		Side effect		Drug B
Cardiovascular System (n=2)				
Calcium Channel Blocker	➡	Peripheral edema	➡	Diuretic
Diuretic	➡	Urinary incontinence	➡	Overactive bladder medication
Central Nervous System (n=4)				
Antipsychotic	➡	Extrapyramidal symptoms	➡	Antiparkinsonian agent
Benzodiazepine	➡	Cognitive impairment	➡	Cholinesterase Inhibitor or memantine
Benzodiazepine	➡	Paradoxical agitation or agitation secondary to withdrawal	➡	Antipsychotic
Selective Serotonin Reuptake Inhibitor (SSRI) / Serotonin-norepinephrine Reuptake Inhibitor (SNRI)	➡	Insomnia	➡	Sleep agent (e.g., Benzodiazepines, Benzodiazepine Receptor Agonists, Sedating antidepressant, Melatonin)
Musculoskeletal System (n=1)				
NSAID	➡	Hypertension	➡	Antihypertensive
Urogenital System (n=2)				
Urinary Anticholinergics	➡	Cognitive impairment	➡	Cholinesterase inhibitor or memantine
Alpha-1 Receptor Blocker	➡	Orthostatic hypotension, dizziness	➡	Vestibular sedative (e.g., betahistine, Antihistamines, Benzodiazepines)

Patient Case

A 71-year-old, woman with HTN, type 2 diabetes, depression, osteoarthritis and Meniere's disease presented to the ER following a fall.

- **4 months prior:** Her family physician prescribed clonidine 0.1 mg BID for her blood pressure.
- **3 weeks later:** Her psychiatrist prescribed sertraline 50 mg daily for worsening depression. Simultaneously the patient began using her meclizine 25 mg TID for increased dizziness attributed to Meniere's disease.
- **3 more weeks passed:** She was prescribed a hypnotic, zolpidem 5 mg at bedtime for insomnia.
- **1 month later:** She lost her balance in the bathroom, fell, hit her head against the bathtub, leading her to present to the emergency department.

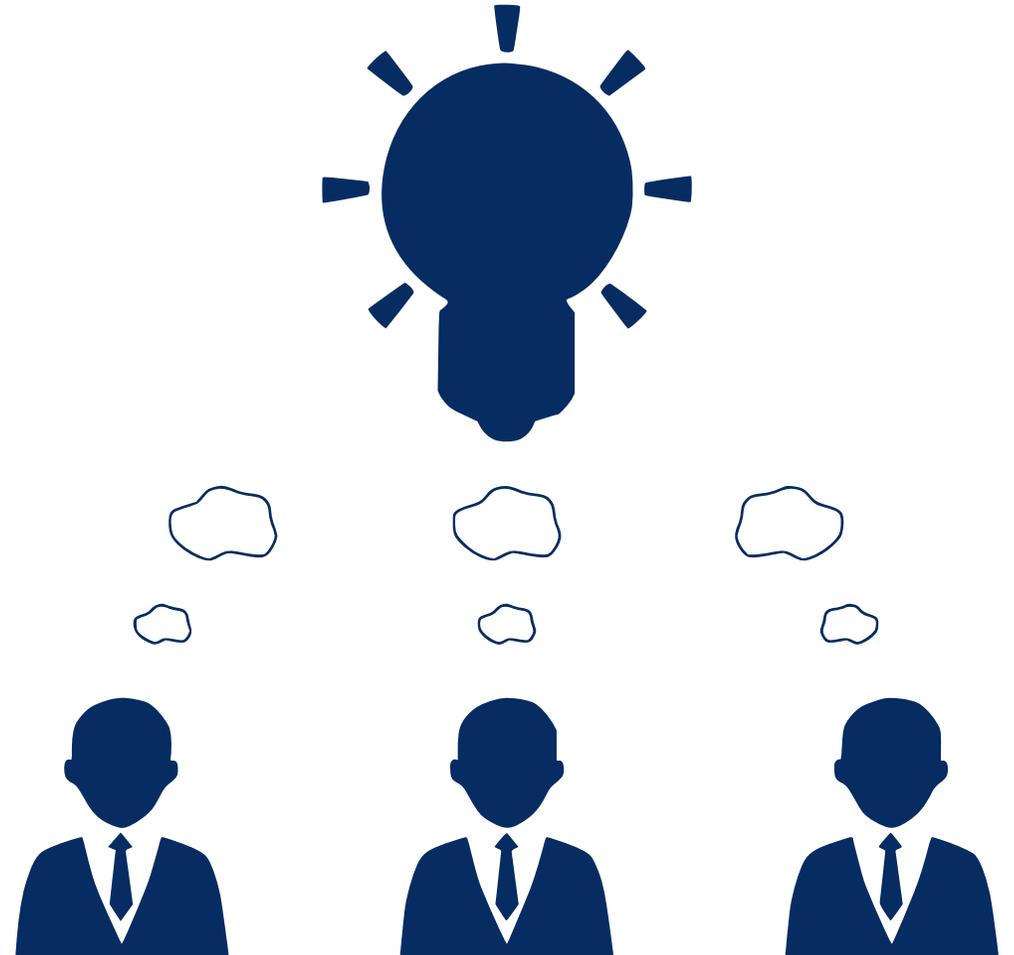
Medications

Drug	Indication
Metformin 1 000 mg BID	diabetes
Lisinopril 40 mg daily	Blood pressure
Hydrochlorothiazide 25 mg daily	Blood pressure
Clonidine 0.1 mg BID	Blood pressure
Sertraline 50 mg daily	Depression
Zolpidem 5 mg every night	Sleep
Meclizine 25 mg TID as needed	Dizziness related to Meniere's
Tramadol 50 mg BID	Arthritis pain
Aspirin 81 mg daily	Stroke prevention

Activity

Think-Share-Pair:

Using tools we have discussed,
identify a prescribing cascade



Avoiding Inappropriate Polypharmacy – Key Tips

- Avoid “A pill for every ill”
 - Consider non-pharmacologic approaches
- When prescribing, “start low and go slow”
- Optimize the dose of one drug before adding another
- Avoid starting two medications at the same time
- Thoroughly review medications regularly
 - Carry an updated medication list
- Eliminate duplicate medications, medications without therapeutic benefit, and those at high risk of harm



ASSESSMENT TOOLS & CRITERIA



Potentially Inappropriate Medications (PIMs)

- More than 50% of older adults in the US report taking a drug deemed potentially inappropriate

American Geriatrics Society 2023 updated AGS Beers Criteria[®] for potentially inappropriate medication use in older adults

- **What:** List of potentially inappropriate medications for use in older adults
- **Purpose:** to identify medication for which potential harm outweighs the expected benefit.
- **Admin Time:** Operator dependent - 5 mins for an expert, up to 20-30 mins
- **Target:** Practicing clinicians, pharmacists, regulators
- **Intent:** 1) improve patient safety; 2) Serve as a tool to evaluate drug use and quality of care.

Beer's is Composed of 5 Criteria

1. Potentially Inappropriate Medications (PIM) list
2. PIMs due to Drug – Disease/Syndrome Interaction
3. Medications to be used with caution
4. Potentially Clinically Important Drug–Drug Interactions
5. Medications that should be avoided or have dosage reduced with varying levels of kidney function

Beer's Criteria Utilized by:



Practicing Clinicians



Healthcare consumers



Researchers



Pharmacy benefits managers



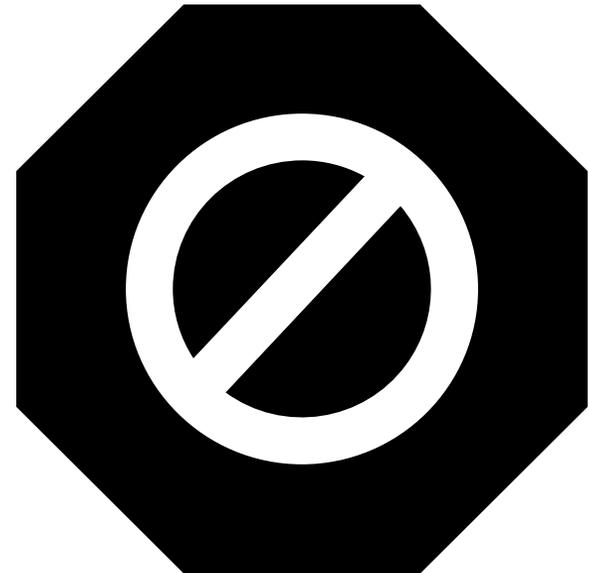
Regulators



Policy makers

What is Not Included in Beer's Criteria?

- Drugs with risks not unique to elderly
- Not intended to be used for people in hospice or end of life
- Drugs considered to be low-usage



BEER'S CRITERIA HIGHLIGHTS

A more detailed pocket guide can be found at:
[AGS-2023-BEERS-POCKET-PRINTABLE.PDF](#)
[\(USC.EDU\)](#)

Note: The recommendations listed are a selection of recommendations from the 2023 criteria and are not an exhaustive list. These medications are commonly prescribed to older adults, or are medications whose harms are of greatest concern.

Potentially Inappropriate Medications

Drug	Recommendation
Antihistamines (First Generation) Ex: diphenhydramine/Benadryl	Avoid. Highly anticholinergic.
Cardiovascular Drugs	
Aspirin - primary CV disease prevention	Avoid initiating for primary prevention of cardiovascular disease. <u>Consider deprescribing.</u>
Warfarin for Afib or VTE	Avoid as initial therapy for Afib or VTE unless alternative options are contraindicated/substantial barriers to their use
Rivaroxaban for Afib or VTE	Avoid as treatment over other anticoagulants for Afib or VTE
Alpha-1 blockers Ex: doxazosin, prazosin, terazosin	Avoid as treatment for hypertension
Central alpha-2 blockers Ex: clonidine	Avoid as first line or routine treatment for hypertension
Nifedipine immediate-release	Avoid as treatment for hypertension

Potentially Inappropriate Medications

Drug	Recommendation
Cardiovascular drugs	
Amiodarone	Avoid as first-line unless patient has heart failure
Dronedarone	Avoid in patients with Afib and heart failure
Digoxin	Avoid for rate control in Afib or for heart failure
Central nervous system	
Antidepressants with strong anticholinergic effects Ex: Tricyclics and paroxetine	Avoid and instead use antidepressants with lower anticholinergic burden.
Antipsychotics (conventional or atypical)	Avoid except in FDA labelled indications such as schizophrenia, bipolar disorder, Parkinson's psychosis. Increase CVA risk; cognitive decline and mortality in dementia.
Benzodiazepines and non-benzo hypnotics (aka "Z-drugs")	Avoid due to cognitive effects and injury; avoid in combo with opioids.

Potentially Inappropriate Medications

Drug	Recommendation
Endocrine drugs	
Androgens	Avoid unless confirmed hypogonadism
Estrogens	Do not initiate systemic estrogens. <u>Consider deprescribing.</u> Vaginal cream or tablets acceptable for vaginal symptoms.
Insulin sliding scale	Avoid regimens that include only short acting insulin dosed according to current blood glucose readings without a concurrent basal insulin.
Sulfonylureas Ex: glyburide, glipizide, glimepiride	Avoid as first or second line therapy unless there is substantial barrier to use of safer agents.
Megestrol	Avoid. Has minimal effect on weight, increase thrombosis

Potentially Inappropriate Medications

Drug	Recommendation
Gastrointestinal drugs	
Proton pump inhibitors	Avoid as scheduled use for > 8 weeks unless high-risk (eg Barrett's esophagitis, pathologic hypersecretory states). Risk of pneumonia, GI malignancy, <i>C. difficile</i> , bone loss, fractures.
Metoclopramide	Avoid unless for gastroparesis with duration less than 12 weeks
GI antispasmodics	Avoid due to high anticholinergic effects
Mineral oil used daily	Avoid due to aspiration risk and safer alternatives
Pain medication	
NSAIDs Ex: ibuprofen, naproxen, etc.	Avoid chronic use unless other alternatives not effective. Avoid short term combination with antiplatelet, anticoagulants, steroids.
Indomethacin	Avoid due to increase GI bleed and potential kidney injury
Skeletal muscle relaxants	Avoid due to anticholinergic effects. This criterion does not apply to agents used for spasticity – baclofen and tizanidine.

What adverse outcomes support the 2023 Beers Criteria rationale to avoid the use of proton pump inhibitors in older adults?

- a. *Clostridioides difficile* infection
- b. GI malignancy
- c. Bone loss and fracture
- d. Pneumonia
- e. All of the above



STOPP/START criteria for potentially inappropriate prescribing in older people: version 3

Denis O'Mahony^{1,2} · Antonio Cherubini³ · Anna Renom Guiteras⁴ · Michael Denkinger⁵ · Jean-Baptiste Beuscart⁶ · Graziano Onder⁷ · Adalsteinn Gudmundsson⁸ · Alfonso J. Cruz-Jentoft⁹ · Wilma Knol¹⁰ · Gülistan Bahat¹¹ · Nathalie van der Velde¹² · Mirko Petrovic¹³ · Denis Curtin²

Purpose: Decision aid for supporting medication review. Reducing medication burden (STOPP) and adding in potentially beneficial therapy (START)

Admin time: Highly operator dependent - 5 mins for an expert, up to 20-30 mins

User Friendly: Moderate

Administered by: GP, Physician, Community Pharmacist

Criteria: total of 190 criteria (version 3)

- 133 STOPP criteria
- 57 START criteria

STOPP/START Criteria Version 3

The latest version of the START/STOPP tool can be found at:

https://static-content.springer.com/esm/art%3A10.1007%2Fs41999-023-00777-y/MediaObjects/41999_2023_777_MOESM1_ESM.pdf

STOPP: Screening Tool of Older Peoples potentially inappropriate Prescriptions - Example

Cardiovascular system	
Digoxin	Long-term use >125 µg/day in patients with renal dysfunction
Loop diuretic	For dependent ankle edema only (no signs of heart failure); compression hosiery usually more appropriate
Thiazide diuretic	With history of gout (may exacerbate gout)
Noncardioselective β-blocker	With COPD (risk for increased bronchospasm)
Diltiazem or verapamil	With NYHA class III or IV heart failure (may worsen heart failure)
Calcium channel blocker	With chronic constipation (may exacerbate constipation)
Warfarin	For first uncomplicated DVT >6 months For first uncomplicated pulmonary embolus >12 months (no proven benefit)
Central nervous system and psychotropic drugs	
TCA	With dementia (risk for worsening cognitive impairment)
SSRI	With hyponatremia
Gastrointestinal system	
PPI	For peptic ulcer disease at full therapeutic doses for >8 weeks
NSAID	With moderate to severe hypertension or heart failure

COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; NYHA, New York Heart Association; PPI, proton pump inhibitor; NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitor; STOPP, Screening Tool of Older Person's Prescriptions; TCA, tricyclic antidepressant.

Adapted from Gallagher P et al. *Int J Clin Pharmacol Ther.* 2008;46(2):72-83.³⁶

START: **S**creening **T**ool to **A**lert to **R**ight **T**reatment - Example

Medication	Recommendation
Warfarin	In chronic atrial fibrillation
Aspirin	In chronic atrial fibrillation when warfarin is contraindicated
Antihypertensive therapy	Systolic blood pressure consistently >160 mm Hg
Statin	History of coronary, cerebral, or peripheral vascular disease, when patient is functionally independent for activities of daily living and life expectancy >5 years
ACEI	With chronic heart failure Following acute myocardial infarction
β -Blocker	With chronic stable angina
Bisphosphonate	With maintenance corticosteroid therapy
Calcium and vitamin D	Osteoporosis (fragility fracture, acquired dorsal kyphosis)
Antiplatelet agent	In diabetes mellitus with major cardiovascular risk factors (hypertension, hypercholesterolemia, smoking history)

ACEI, angiotensin-converting enzyme inhibitor; START, Screening Tool to Alert Doctors to Right Treatment.

Adapted from Gallagher P et al. *Int J Clin Pharmacol Ther.* 2008;46(2):72-83.³⁶

Beer's and STOPP Criteria Predict Adverse Drug Events

- 174,275 insured people ≥ 65 yrs in US
- Retrospective cohort evaluated with use of Beer's Criteria and STOPP criteria to identify PIM exposure.
- ICD 9 codes evaluated for:
 - Adverse drug events
 - All-cause ED visits
 - All-cause hospitalizations

Beer's and STOPP were modestly prognostic for:

- Adverse Drug Events
- ED Visits
- Hospitalizations

STOPP slightly outperformed Beer's in predictability. Criteria can be used in complimentary fashion to enhance sensitivity.

Patient Case

A 67-year-old, woman presents to the primary care clinic with a racing heart and shortness of breath. She also has HTN, Type 2 diabetes and osteoarthritis. Her blood pressure is elevated at 145/78 mmHg, heart rate is 110 bpm. An EKG in office identifies atrial fibrillation. Her current medications include:

Drug	Indication
Metformin 500 mg BID	Diabetes
Glipizide 10 mg BID	Diabetes
Ibuprofen 400 mg BID	Arthritis pain
Aspirin 81 mg daily	CV risk prevention
Amlodipine 10 mg daily	Blood pressure

Based on the Beer's Criteria, are there any medications that should be discontinued/deprescribed?

Combining Info from the Beer's Criteria and the STOPP/START Criteria, what is the best anticoagulant therapy for this patient?

- a. Warfarin (Coumadin[®])
- b. Apixaban (Eliquis[®])
- c. Rivaroxaban (Xarelto[®])
- d. Aspirin



MEDICATION-RELATED FALL ASSESSMENT

Polypharmacy



Mortality



Falls



Adverse Drug
Events



Increase Length
of Stay



Hospital
Readmission



Medication
Non-adherence

Which medications increase the risk of falls?

Diuretics: 7% increased risk

Opioid painkillers: 10% increased risk

Anti-inflammatory drugs: 21% increased risk

Blood pressure medication: 24% increased risk

Sleeping pills (benzodiazepines): 47-57% increased risk

Antipsychotics: 59% increased risk

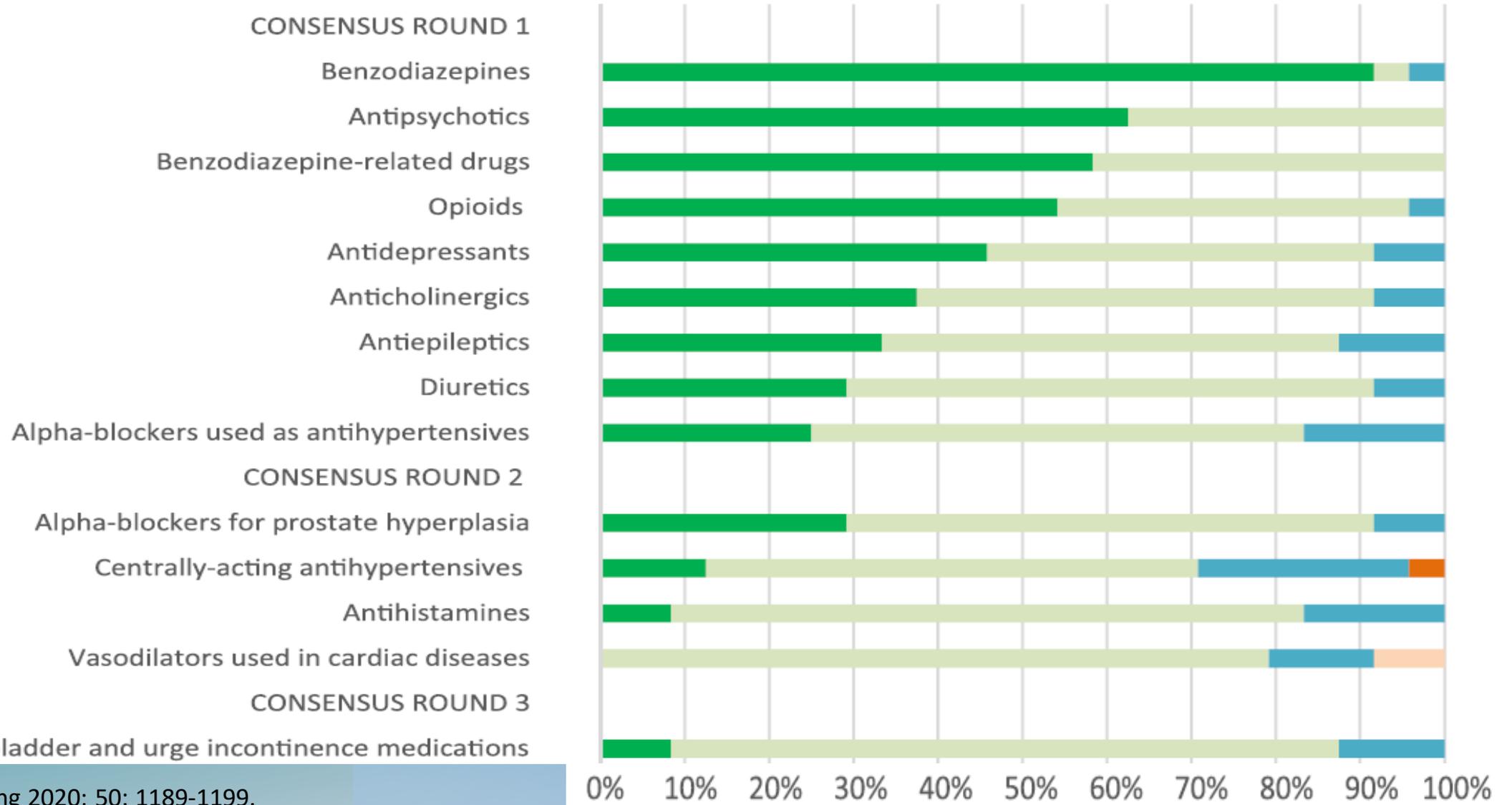
Antidepressants: 68% increased risk

STOPPFall

- The STOPPFall is formally part of the STOPP/START series and the results were incorporated into STOPP/START version 3.
- A screening tool to identify and facilitate the deprescribing of drug known to increase fall risk.
 - The STOPPFall has been combined with a practical deprescribing tool designed to assist in clinical decision-making.
- Decision tool found at:
 - kik.amc.nl/falls/decision-tree/

Medications Included in STOPPFall

by Level of Consensus Agreement



STOPPFall Deprescribing Tool

Choose a medication class to see the decision advice for withdrawing the medication among fallers

Benzodiazepines

Antidepressants

Antipsychotics

Opioids

Antiepileptics

Diuretics

Centrally-acting
antihypertensives

Vasodilators used in
cardiac diseases

Alpha-blocker antihypertensives

Alpha-blockers for benign
prostate hyperplasia

Sedative antihistamines

Medications for overactive bladder
and urge incontinence

Choose a medication class to see the decision advice for withdrawing the medication among fallers



Advice:

Stop the BZD in a stepwise manner: e.g., approximately 25% every two weeks, near the end 12.5%. After withdrawal or dose reduction monitor for change in symptoms e.g., dizziness, and sedation, fall incidents and anxiety, insomnia, and agitation.

Also, consider monitoring: delirium, seizures, confusion.

Organize follow-ups based on an individual basis e.g., based on occurrence of withdrawal symptoms.



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

STEADI—Older Adult Fall Prevention



- CDC's STEADI initiative - resources to integrate fall prevention into routine clinical practice.

STEADI-Rx

How STEADI-R_x works:

1. Screen patient for fall risk at the pharmacy.
2. Perform a medication review.
3. Share information with the patient and provider.
4. Provider responds to shared information.

STEADI-Rx: Community Pharmacy Algorithm for Fall Risk Screening, Assessment, and Care Coordination

START HERE

1

SCREEN for fall risk yearly for older adults (≥ 65 years) taking ≥ 4 chronic medications or ≥ 1 high-risk medication or any time patient presents with an acute fall.

Three key questions to ask patients [at risk if YES to any question]:

1. Feels unsteady when standing or walking?
2. Worries about falling?
3. Fell in the past year?
> If YES ask, "How many times?" "Were you injured?"

SCREENED **NOT AT RISK**

PREVENT future risk by recommending effective prevention strategies.

- Educate patient on fall prevention
- Refer to community exercise or fall prevention program
- Reassess yearly or any time patient presents with an acute fall

Document answers to three key questions and education provided to patient

Share answers to three key questions with the patient's primary care provider using the *Provider Consult Form*

SCREENED **AT RISK**

2

ASSESS patient's modifiable risk factors.

Document answers to three key questions and education provided to patient

Identify medications that increase fall risk

- Schedule medication review with patient
- Review medications utilizing the *Community Pharmacy Falls Risk Checklist* and a geriatric-specific medication decision-support tool (e.g., The UNC High Risk Medication Recommendations or the Beers Criteria)
- Identify any medication therapy problems (MTPs) associated with the use of high-risk medications

Inquire about postural hypotension

- Symptoms of lightheadedness or dizziness from lying to standing?
- Can assess for postural hypotension by measuring blood pressure from lying to standing

Reduce risk by recommending effective prevention strategies

- Educate patient on fall prevention
- Refer to community exercise or fall prevention program

3

COORDINATE CARE with primary care or prescribing provider to reduce identified risk factors using effective interventions.

Share answers to three key questions and education provided to patient with the patient's provider using the *Provider Consult Form*

Share identified MTPs and recommendations with the patient's provider using the *Provider Consult Form*

- Medication information should include medication name, strength, dose, and frequency

Refer to provider for an evaluation of gait, strength, & balance using the *Provider Consult Form*

RESPONSE RECEIVED FROM PROVIDER

RESPONSE NOT RECEIVED FROM PROVIDER WITHIN 7 DAYS

Call provider's office to verify they received the *Provider Consult Form*

Resend *Provider Consult Form* if provider did not receive it

FOLLOW UP with patient in 30-90 days.

Patient:	
Date of Birth:	Date:

Fall Risk Factor(s) Identified

FALL HISTORY	PRESENT?		NOTES
Any falls in the past year?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Worries about falling?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Feels unsteady when standing or walking?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
POSTURAL HYPOTENSION			
Patient-reported symptoms of lightheadedness or dizziness from lying to standing?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	

MEDICATION CLASSES WITH FALL RISK	MEDICATION(S) Include medication name, dosage prescribed, and administration directions.
Anticonvulsants	
Antidepressants	
Antihypertensives	
Antipsychotics	
Antispasmodics	
Benzodiazepines	
Opioids	
Sedative hypnotics	
Tricyclic antidepressants	
Other (e.g., OTC agents)	

Medication Fall Risk Checklist

Patient Case

Mr. Parker is an 85-year-old African American man. He is generally well but complains of back pain, recent gout attacks, and insomnia related to pain. He takes the city bus to the pharmacy to pick up his medications. He experience a fall when getting off the bus yesterday.

Blood pressure: 150/70, HR 80; denies symptoms of dizziness

Medications (upon medication review)

Drug	Indication
Lisinopril 40 mg daily	Blood pressure
Indomethacin 50 mg three times daily	Gout
Tylenol #3 with codeine three times daily as needed	Foot pain
Gabapentin 300mg three times daily	Back pain
Tylenol PM 1 tablet at night	Sleep

Audience Activity

Use the Medication Fall Checklist to evaluate and identify medications placing Mr. Parker at risk for adverse drug events, especially for falls.





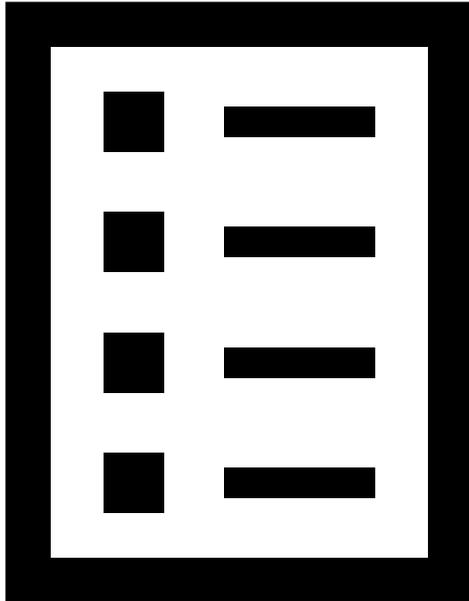
INTERVENTIONS: POLYPHARMACY AND PRESCRIBING CASCADES

Deprescribing

A systematic process of identifying and discontinuing medications based on an assessment that the risks of a given medication may outweigh the benefits.

Deprescribing is **NOT** denying medication that will provide benefit.





Deprescribing Goals

- Decreasing pill burden
- Increase quality of life
- Reduction in falls
- Improve cognition

Evidence Supporting Deprescribing



Reduced costs



Reduced number of medications

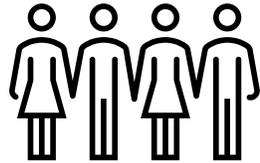
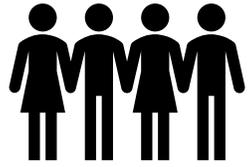


Reduced mortality (data more scant)



Deprescribing is feasible
in clinical practice.

Potter, et al. Deprescribing in Frail Older People: A Randomized Controlled Trial



- Residential facility living
- N = 95 randomized to:

Intervention: planned
deprescribing of non-
beneficial meds n=47

vs.

Usual Care n=48

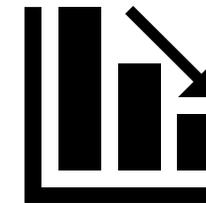
Design

12-month
follow up

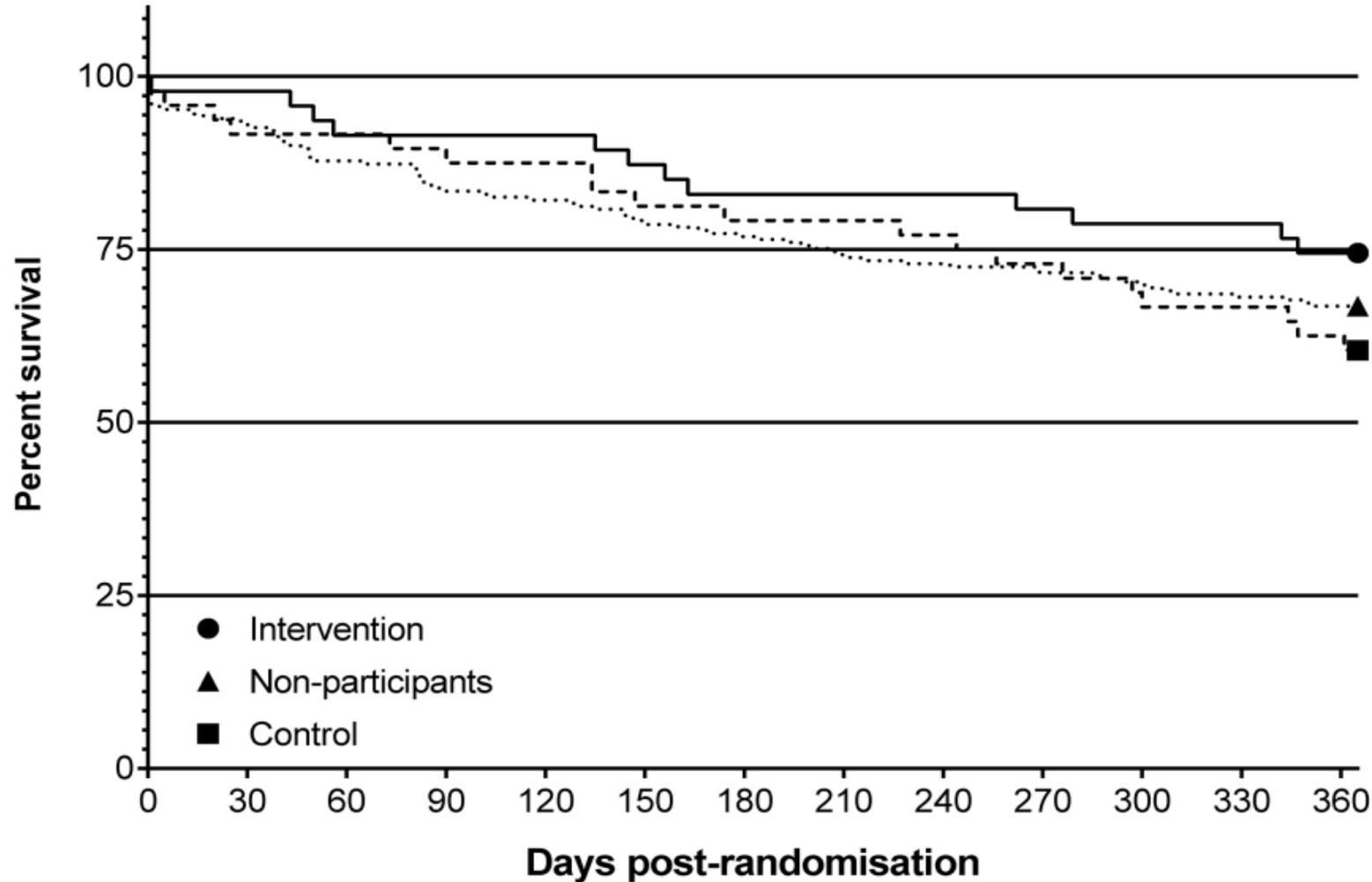
- **Primary outcome:**
Change in #
medications
- **Secondary outcome:**
Survival

- Mean Δ in # meds:
-1.9 \pm 1.4 intervention
v. +0.1 \pm 3.5 control

Difference 2.0 \pm 0.9
95% CI 0.8-3.8; p=0.04



Deprescribing Outcomes: Survival Plot 12 Months Post-Randomization

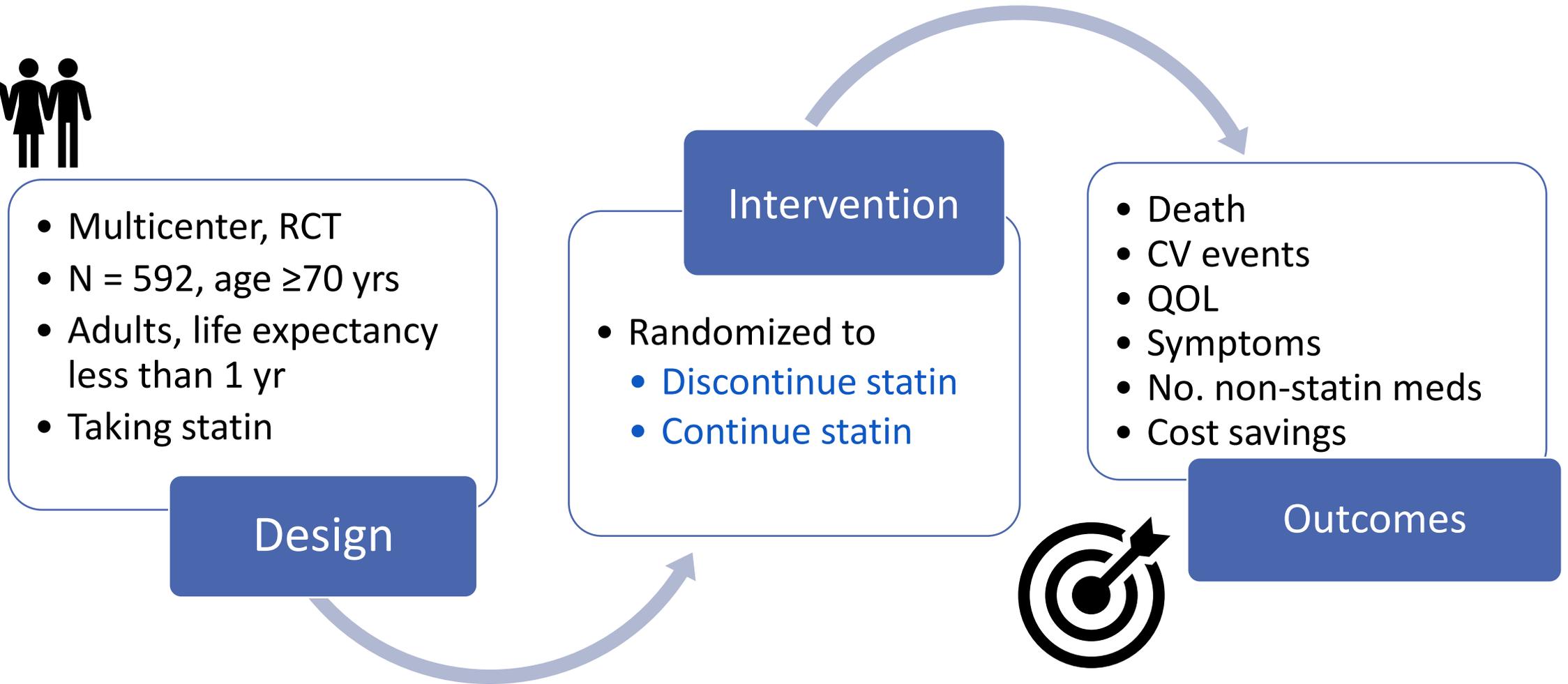
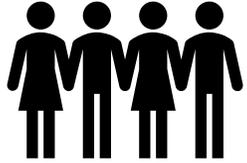


$p = 0.16$, HR 0.60,
95%CI 0.30 to 1.22

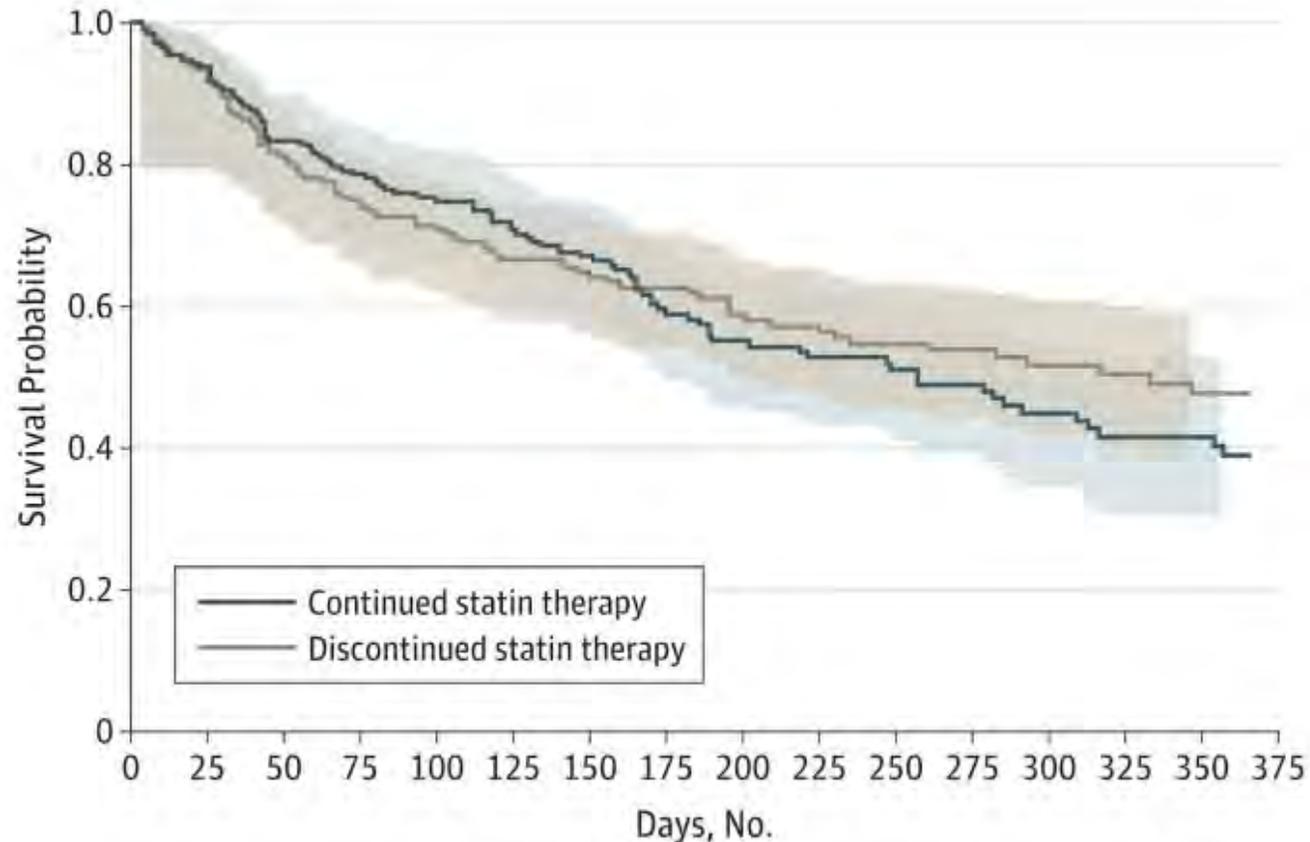
Deprescribing reduced the number of medicines taken with no significant adverse effects on survival [or other clinical outcomes].

TARGETED DEPRESCRIBING INTERVENTIONS

Kutner, et al. Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness



Benefit of Discontinuing Statin Therapy in Advanced Age and Illness



No. at risk	0	25	50	75	100	125	150	175	200	225	250	275	300	325	350	375
Continued statin therapy	192	149	105	64	47	32	21									
Discontinued statin therapy	189	135	93	68	52	36	26									

- No difference between survival between statin discontinuation vs continuation groups. 23.8% vs 20.3% (90% CI -3.5% - 10.5%, p=0.36)
- QOL was greater for statin discontinuation. (McGill QOL score 7.11 vs 6.85, p=0.04)

Aspirin for Primary Prevention of Cardiovascular Disease

- Reduces risk of CVD

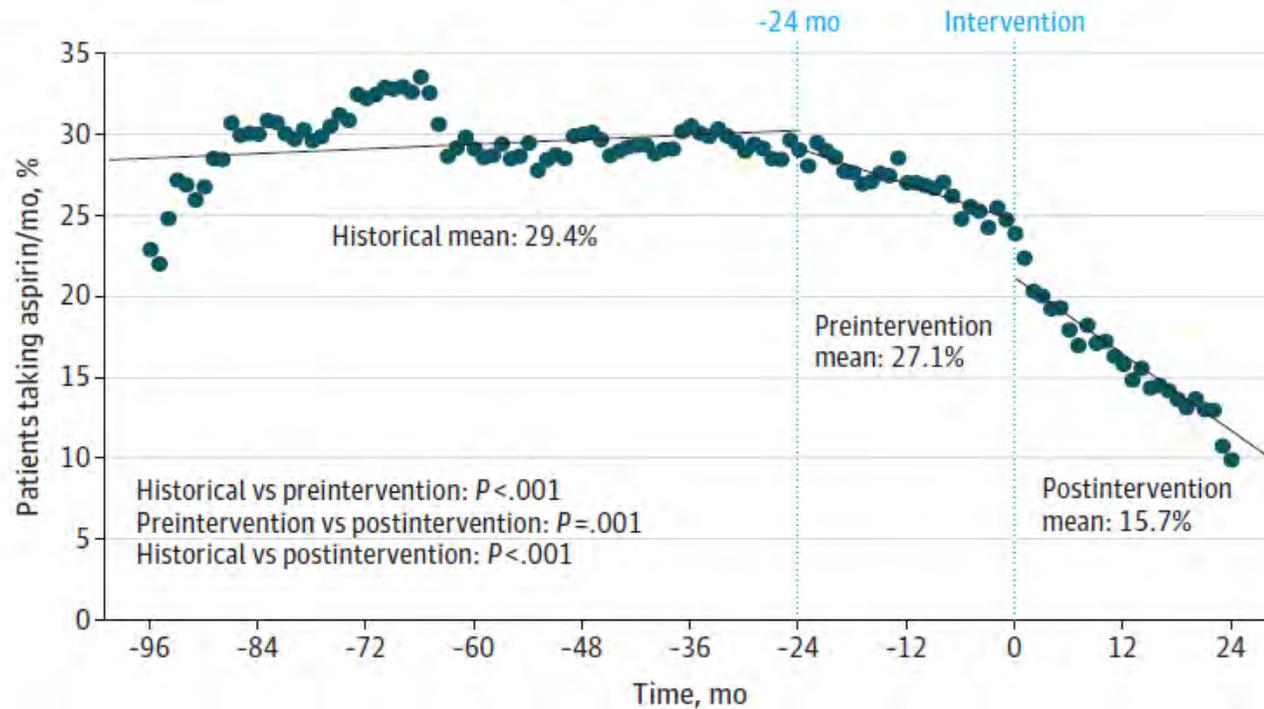
Benefits

Harms

- Increases risk of GI bleed
- Increases risk of hemorrhagic stroke

Aspirin Deprescribing Can Reduce Bleeding

Figure 1. Percentage of Warfarin-Treated Patients Taking Aspirin Without an Apparent Indication by Month



Aspirin deprescribing was associated with reduction in major bleeding, any bleeding & ED visits for bleeding

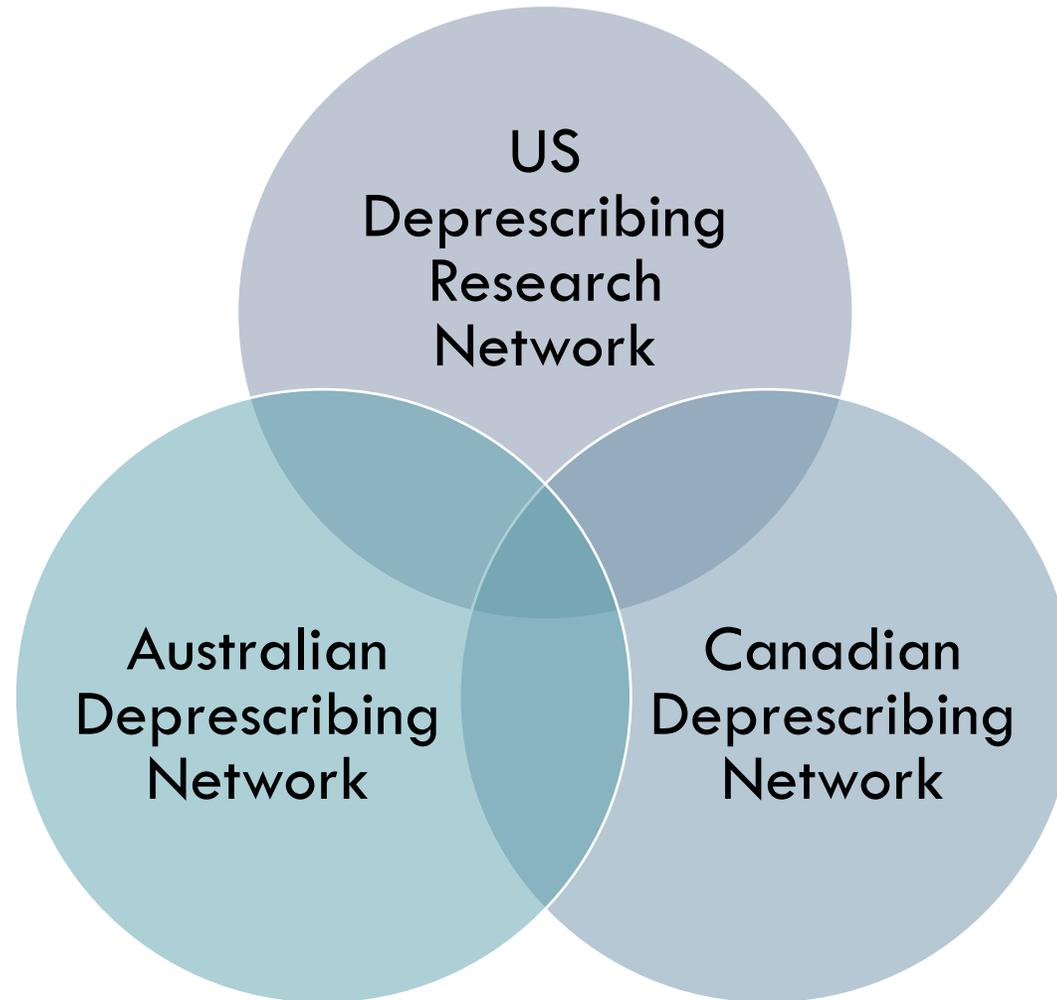
Challenges of Deprescribing

- Communication gaps & misunderstandings
 - Patient reluctance/fear of stopping
 - Coordination among clinicians
 - Dosage tapering
 - Withdrawal symptoms
 - Conveying stop orders to pharmacies
-And more!

Assistance in deprescribing:

- <https://deprescribing.org/resources/>
- <https://www.deprescribingnetwork.ca/professionals>

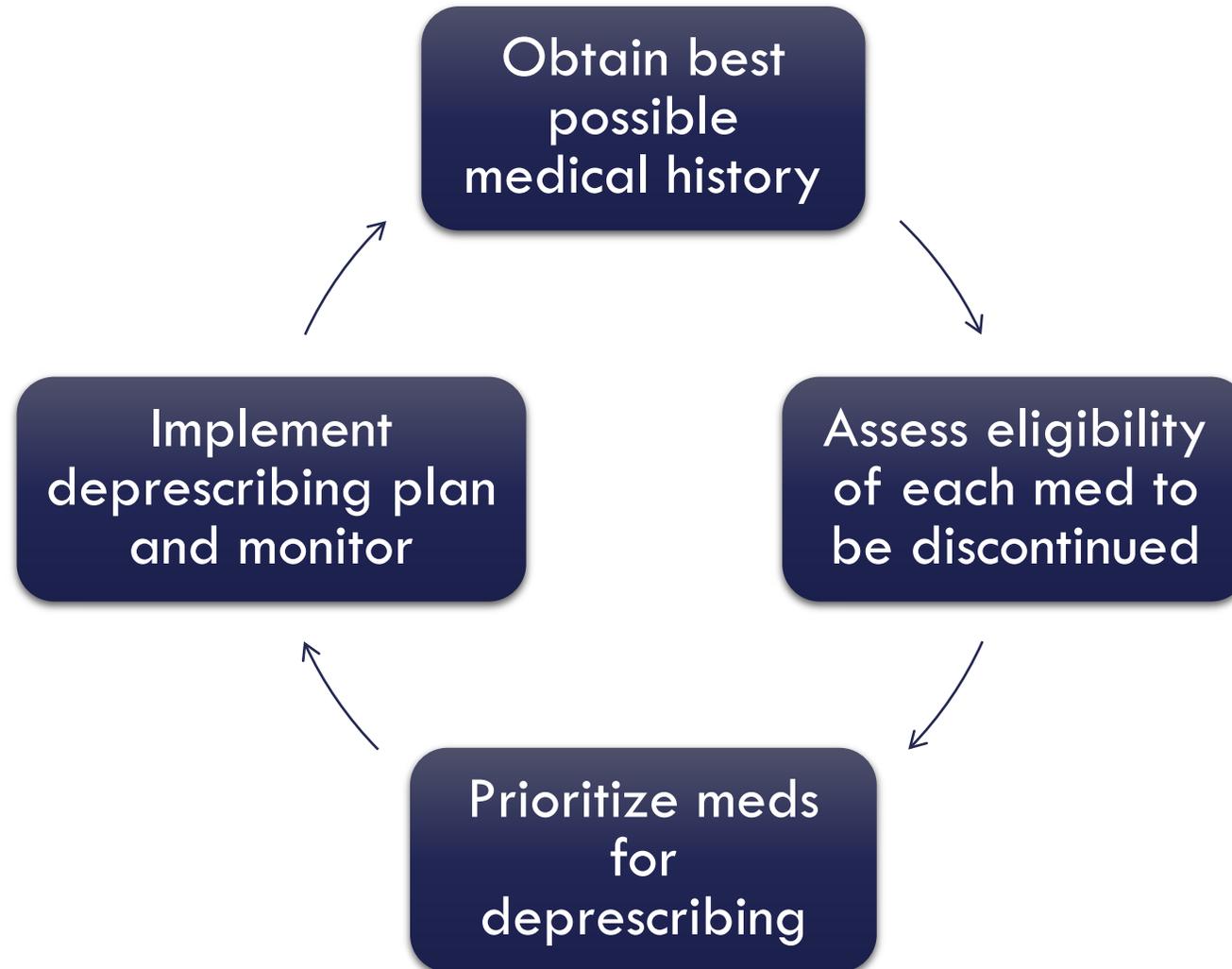
Deprescribing Research Expansion





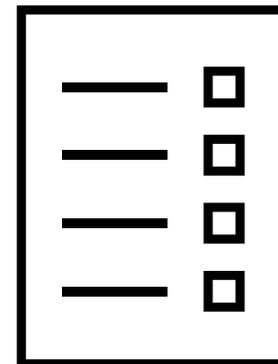
IMPLEMENTING DEPRESCRIBING INTERVENTIONS

Deprescribing Implementation

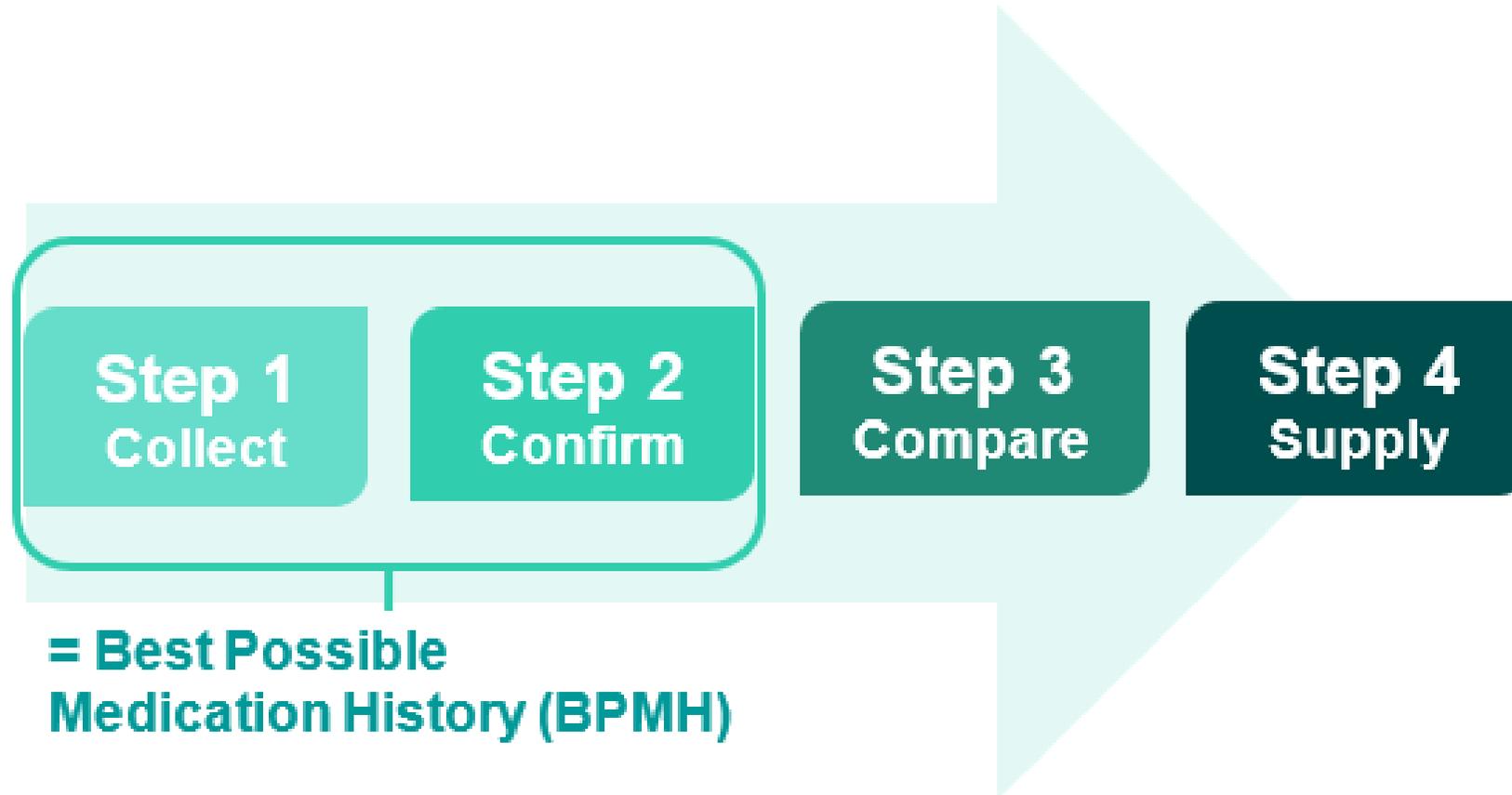


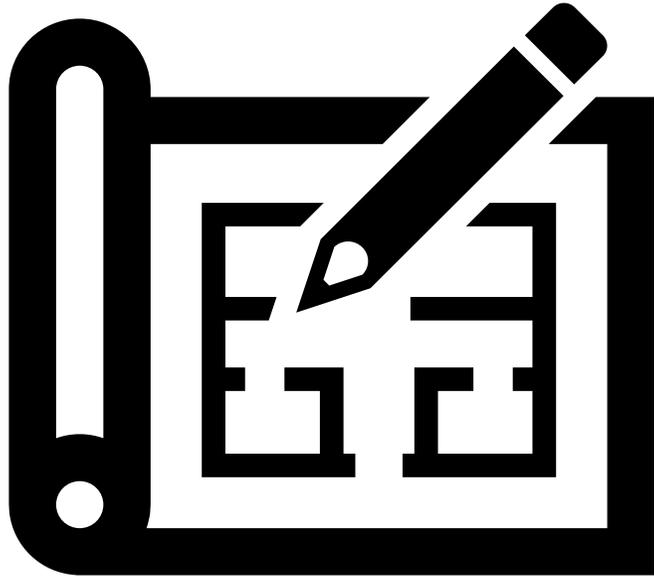
Best Possible Medication History

- A thorough history of ALL regular medication use (prescribed **and** non-prescribed), using a number of sources of information
 - Systematic approach
 - Include prescription medications, OTC and herbal supplements
 - Include dose, frequency, indication, allergies
 - Obtain from multiple sources: patient, family, caregivers, pharmacy records
 - Reconcile between medical records



Steps in Best Possible Medication History





Medication Discontinuation Plan

- Tapering schedule when necessary
- Recommendation for alternative therapies or approaches
- Patient/family education on withdrawal symptoms and follow up
- Monitoring plan

Deprescribing Barriers and Facilitators

Barriers

- Fragmented health care
- Lack of evidence-based guidance
- Provider or patient past negative deprescribing experiences
- Provider's competing priorities
- Uncertainty about which meds to prioritize
- Patient unwillingness

Facilitators

- Availability of non-pharmacologic alternatives
- Shared decision-making
- Integration of a pharmacist in healthcare team
- Educational programs

MEDICATIONS

Name: _____ DOB: / / _____

Medicine Dose Frequency Prescriber

Medicine	Dose	Frequency	Prescriber

Pharmacy: _____

Allergies: _____

Additional Notes: _____

Have an Up-to-Date Medication List

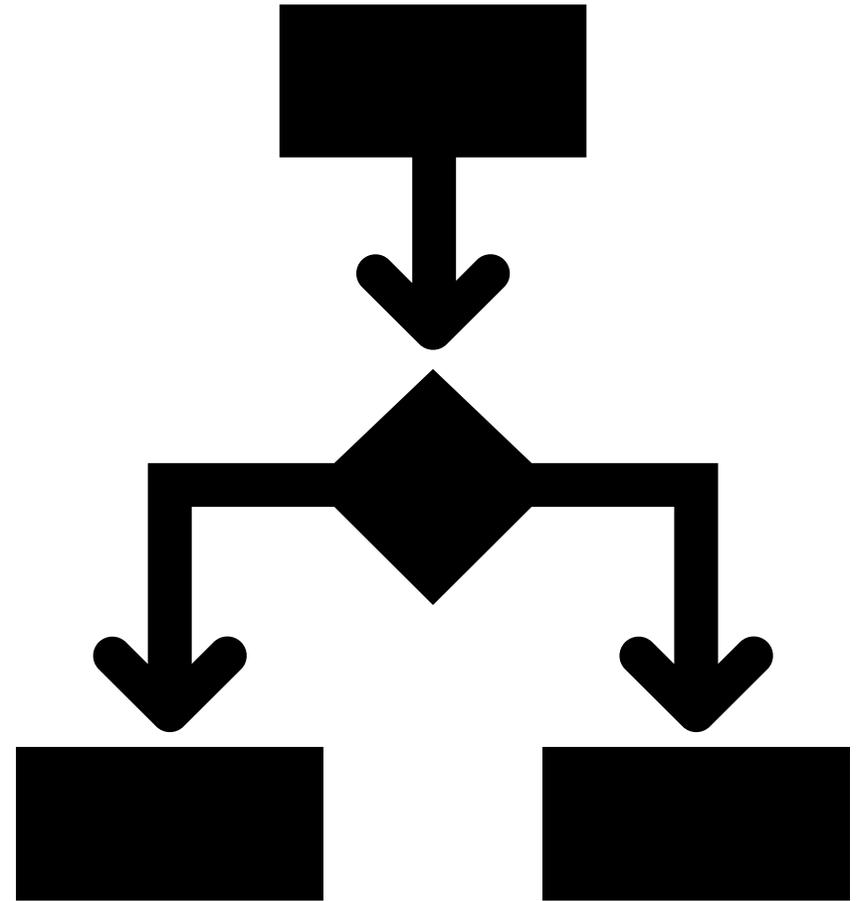
- Include all medications: oral, topical, injectable, ophthalmic
- Include supplements, OTC meds
- Update with every healthcare encounter



MANAGING POLYPHARMACY IN THE FUTURE

Needs for Deprescribing Practice

- Evidence based algorithms for deprescribing
- Algorithms should include monitoring



Technology and Precision Management of Polypharmacy

- Enhancement of drug data analysis and pattern identification with polypharmacy.

MedAware machine learning system

Evaluate clinical validity

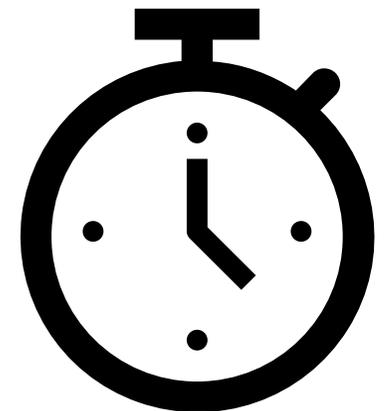
80% of alerts generated were clinically valid

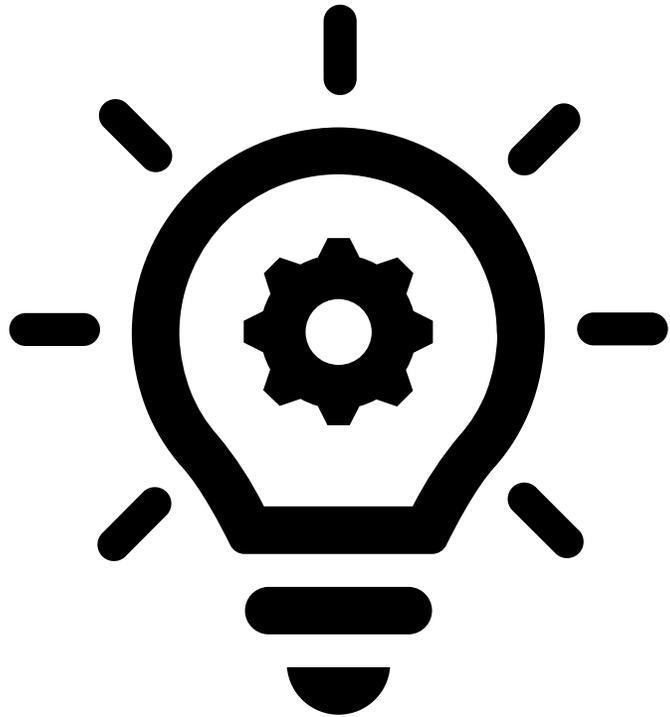
Outperformed traditional rule-based programs

\$1.3 million in saving if extrapolated to whole population

AI Supported Web Application Used to Reduce Adverse Effects of Polypharmacy

- Web-based application took into consideration PIMs from 6 criteria tools.
- AI web-based application saved significant time.
- Identification of drug interactions:
2278 seconds for practitioner vs
33.8 seconds for web-based application; $p < 0.001$

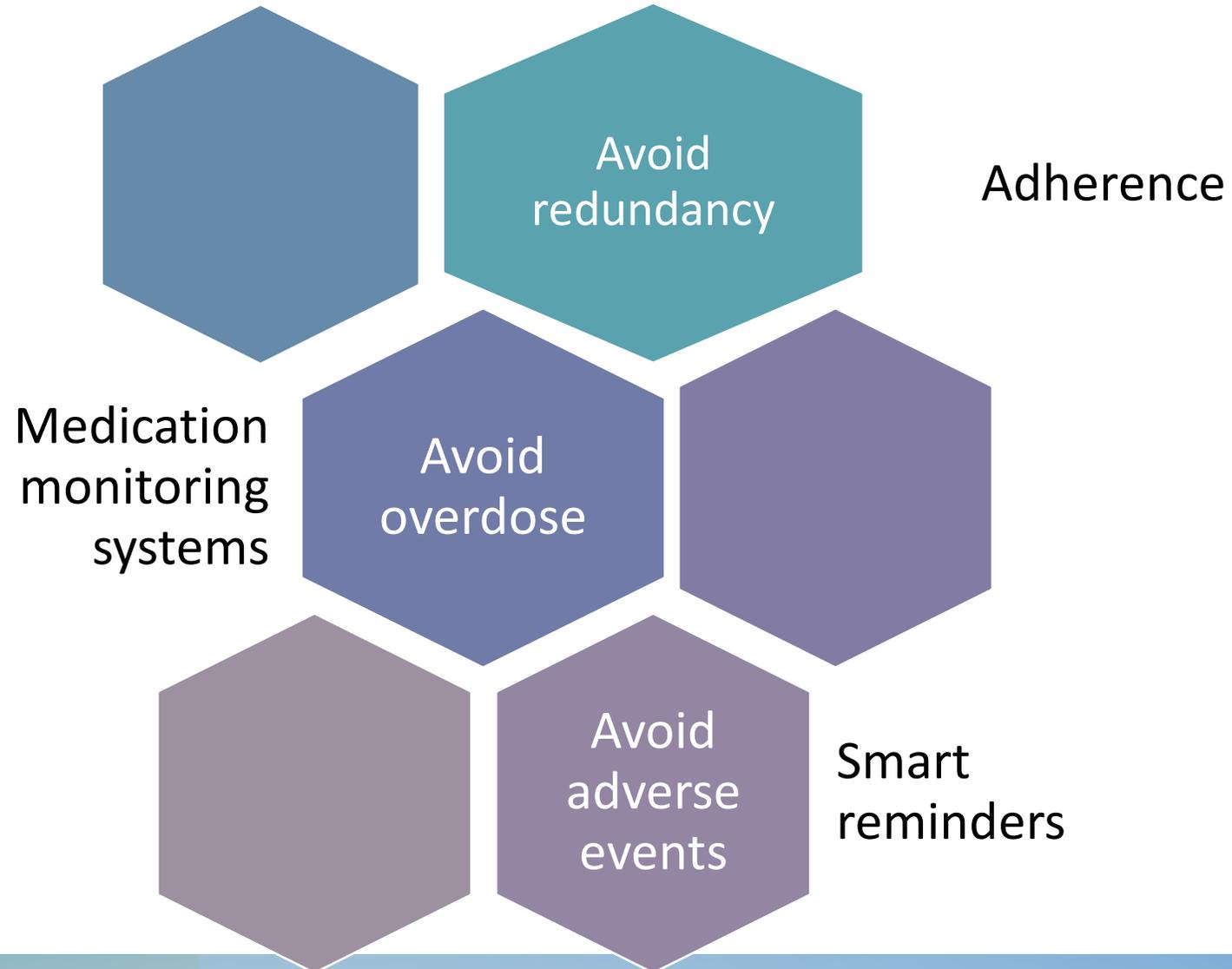




Patient Identification & Precision Dosing

- Future models should predict:
 - Risk for polypharmacy based upon patient and system characteristics.
 - Medication dose adjustments as to avoid adverse drug interactions.
- Research needed to engineer and validate effective machine-learning tool.

Digital Health Tools



Recommendations for Improving Responsible Use of Medication

- Investment in medical audits targeting older patients with multiple medications
- Support for a greater role of pharmacists in medication management and in collaboration with health care professionals for review of therapeutic plans
- Identification of high-risk patients and preparation of targeted medicine management plans for this group
- Establishment of a system for blame-free reporting of medication errors

Summary

Inappropriate polypharmacy poses significant risk to older adults. There is need to better evaluate polypharmacy in older adults.

Identifying inappropriate polypharmacy can include validated tools such as the Beer's Criteria and STOPP/START. Development of deprescribing algorithms and approaches is an opportunity for improved safety.

Research should focus on digital technologies to enhance identification, mitigation of polypharmacy risk and improve patient safety.

**PARTNERING WITH FAMILIES OF HOSPITALIZED
PERSONS WITH DEMENTIA:**

Lessons Learned

Wayne State University
Institute of Gerontology

**2024 ISSUES IN AGING
CONFERENCE
APRIL 29, 2024**



MARIE BOLTZ PhD, GNP-BC, FGSA, FAAN

Elouise Ross Eberly and Robert Eberly

Endowed Chair Professor



Discuss the critical role of family in the life of the person living with dementia and their challenges and rewards

Describe the state of the science related to interventions for family carer partners of persons living with dementia

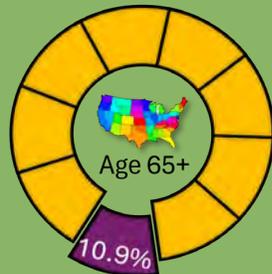
Discuss the family carers' experience and needs when the hospitalized person with dementia is hospitalized.

Discuss emerging issues in research, practice, and policy affecting the family living with dementia

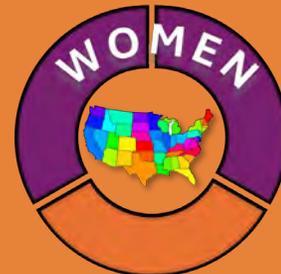
NEARLY 7 MILLION AMERICANS HAVE ALZHEIMER'S

An estimated **6.9 million** Americans age 65 and older are living with Alzheimer's in **2024**. Seventy-three percent are age 75 or older.

About **1 in 9** people aged 65 and older (**10.9%**) has Alzheimer's.



Almost **two-thirds** of Americans with Alzheimer's are women.



Deaths from Alzheimer's have more than doubled between 2000 and 2021.



ONE IN 3 OLDER ADULTS DIES WITH ALZHEIMER'S OR ANOTHER DEMENTIA

OVERVIEW: DEFINITIONS

FAMILY CAREGIVER (CG) – CARE PARTNER (THE PREFERRED TERM)

Any relative, partner, friend or neighbor who has a significant personal relationship with, and provides a broad range of assistance for, an older person or an adult with a chronic or disabling condition

CARE RECIPIENT (CR)

An adult with a chronic illness or disabling condition or an older person who needs ongoing assistance with everyday tasks to function on a daily basis

75-80% OF CARE PROVIDED BY FAMILY / FRIENDS

CARE DELIVERY CARE MANAGEMENT

- ❑ Approximately 15.5 million caregivers provide estimated 17.7 billion hours of unpaid care
- ❑ Higher in African American and Hispanic than White and Asian-American

(Alzheimer's Association, 2024)

MAJORITY OF CAREGIVERS ARE WOMEN (APPROX. 66%)

- ❑ 21% are 65 years old and older
- ❑ average age 42
- ❑ 64% are currently employed, a student or a homemaker
- ❑ 71% are married or in a long-term relationship

ABOUT 25% OF DEMENTIA CAREGIVERS CARE FOR AN AGING PARENT AS WELL AS AT LEAST ONE CHILD



REWARDS OF BEING A CARER

RECIPROCITY

**LEARNING
AND GROWING**

**EMOTIONAL
CLOSENESS**

**ENACTMENT
OF VALUES**



(McGillick & Murphy-White, 2016)

THE CHALLENGES EXPERIENCED BY CARERS

Higher levels of perceived stress

Greater employment complications

Less family time

Disrupted family and social relationships

Less time for leisure

Less self-care

Higher burden, strain, psychological morbidity

Impaired function

- ❑ Cognitive
- ❑ Immune

When depression present

- ❑ Increased vascular inflammation and altered clotting profiles

(Rowe et al., 2016)

ADDRESSING NEEDS . . .



RESPIRE / BREAKS FROM CAREGIVING ARE ESSENTIAL

Maintain a life outside of caregiving



CAREGIVERS NEED TO KNOW THEIR NEEDS / FEELINGS COUNT



- ❑ They need their efforts to be validated
- ❑ Their feelings are important
- ❑ They must take care of their own health
- ❑ They have a right to say what they can do and can't do



THEY HAVE A RIGHT TO ASK QUESTIONS AND TO BE LISTENED TO

- ❑ Get information about community resources
- ❑ Get medical systems to pay attention to them / their concerns



THEY CAN'T DO IT ALONE

HELP THEM identify sources of support

HELP THEM say "YES" to offers of help



Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission

Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

“Triangulation framework”— consistency of evidence from different research lines

Summarize best evidence using quality systematic reviews, meta-analyses, or individual studies

Perform systematic literature reviews and meta-analyses where needed

Present a synthesis of evidence ... balance, strengths, and limitations”

SOME KEY TAKEAWAYS FROM 2020 LANCET REPORT

- ❑ **WELL-BEING** is the goal of much dementia care: How well do we measure this or set this as our goal –in caring and in research?
- ❑ People with dementia have **COMPLEX** problems and symptoms in many domains.
- ❑ Interventions should be **INDIVIDUALIZED, WHOLE PERSON,** and **INCLUDE FAMILY CARERS.**
- ❑ Evidence supports **PSYCHOSOCIAL INTERVENTIONS** tailored to individual needs to manage neuropsychiatric symptoms.

- ❑ Evidence-based **INTERVENTIONS FOR CARERS** can reduce depressive and anxiety symptoms over years and are cost effective.
- ❑ Keeping people with dementia **PHYSICALLY HEALTHY** is important for their cognition and well being.
- ❑ **AVOIDING HOSPITALIZATIONS** is worthwhile as is **PREVENTION OF DELIRIUM.** There is much opportunity for improvement, especially post-COVID
- ❑ **ADVANCE CARE PLANNING** including possibly establishing preferences before dementia impairs judgement and decision making should be promoted.

STIGMA INFLUENCES PERSON LIVING WITH DEMENTIA AND FAMILY CARERS, SUPERIMPOSED UPON AGEISM

IGNORANCE

“WAR” METAPHORS FOR CONFRONTING THIS “EPIDEMIC”

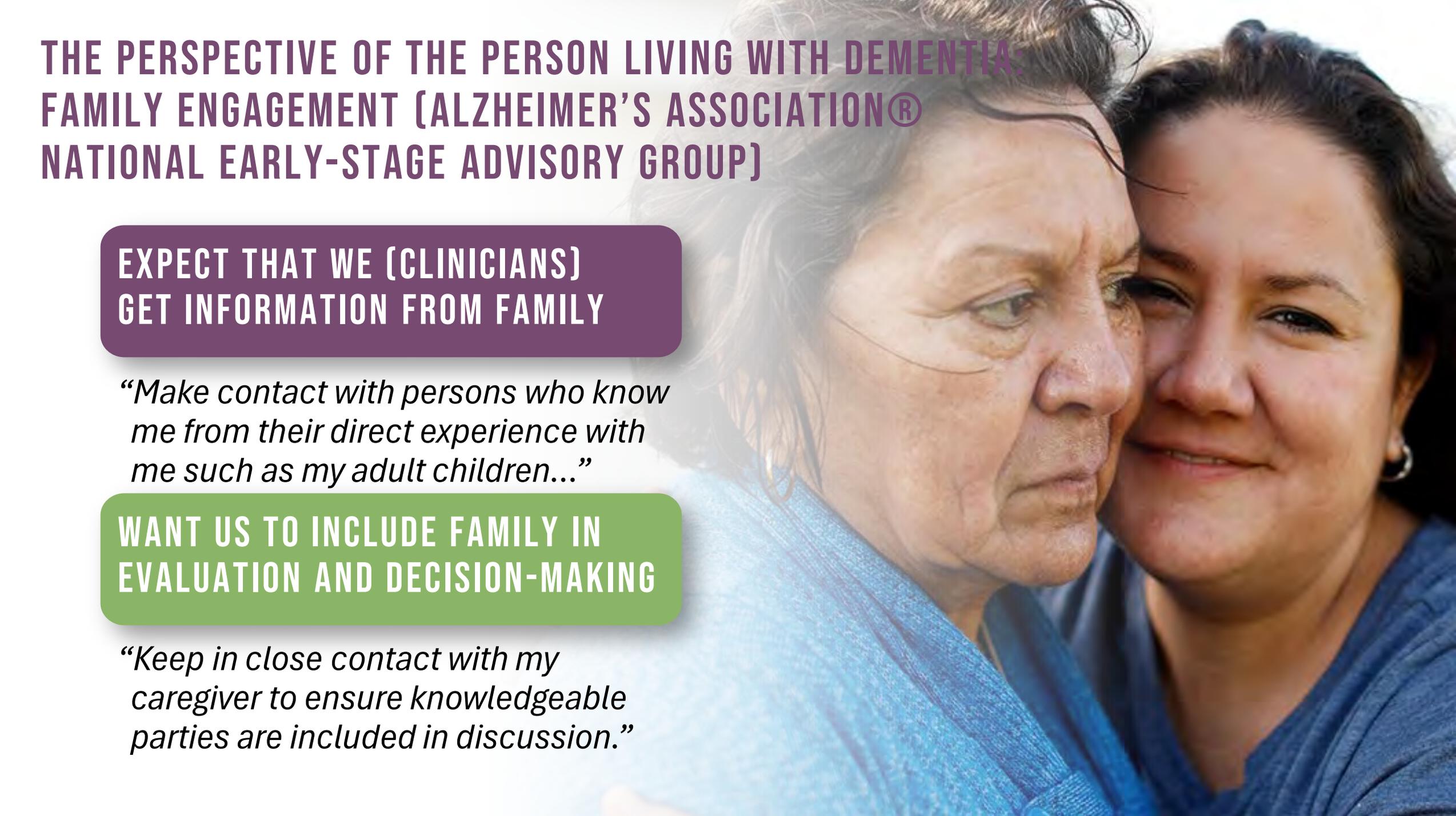
THE “ALZHEIMERIZATION” OF THE DIALOGUE TO SUPPORT EUTHANASIA

DEFINING “SELF” IN RELATION TO COGNITIVE FUNCTION (“I THINK THEREFORE I AM”)

“GETTING DEMENTIA, YOU FEEL THAT YOU HAVE SUDDENLY BECOME A LUNATIC.”



(Desai & Desai, 2016; Johannessen & Moller, 2011)



**THE PERSPECTIVE OF THE PERSON LIVING WITH DEMENTIA:
FAMILY ENGAGEMENT (ALZHEIMER'S ASSOCIATION®
NATIONAL EARLY-STAGE ADVISORY GROUP)**

**EXPECT THAT WE (CLINICIANS)
GET INFORMATION FROM FAMILY**

“Make contact with persons who know me from their direct experience with me such as my adult children...”

**WANT US TO INCLUDE FAMILY IN
EVALUATION AND DECISION-MAKING**

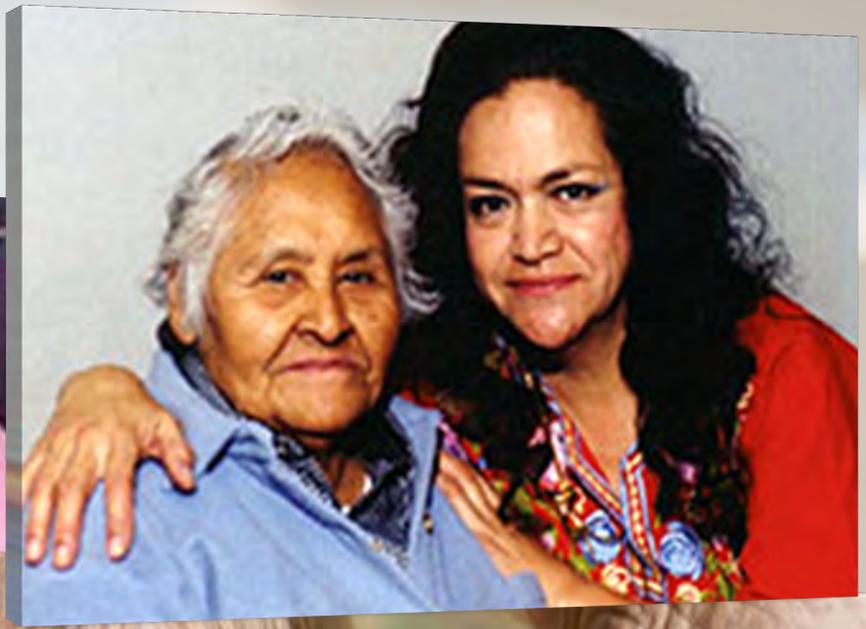
“Keep in close contact with my caregiver to ensure knowledgeable parties are included in discussion.”

EVIDENCE-BASED DEMENTIA CARE:

- ❑ Includes early detection of dementia
- ❑ Prevents, detects, manages complications while managing co-morbidity
- ❑ Focuses on patient function and quality of life
- ❑ Is family-centered- addresses patient and family needs

Supporting the patient without due consideration of the family can result in increased carer distress and poorer overall outcomes for both patient and carer.

Burns R et al. Primary Care Interventions for Dementia Caregivers: 2-Year Outcomes From the REACH Study. *Gerontologist* 43(4):547–555



WHY A DYADIC APPROACH?

PATIENT FACTORS INFLUENCE CAREGIVER STATUS

(Rowe et al., 2016)

MECHANISMS INFLUENCING PHYSIOLOGIC CHANGES IN CAREGIVERS:

- ❑ Poor sleep, sustained vigilance, and interference with caregivers' health promoting behaviors

MECHANISMS INFLUENCING PSYCHOLOGICAL CHANGES IN CAREGIVERS:

- ❑ Being a spouse, female, with poorer perceived health, smaller social network
- ❑ Role overload, captivity, or burden associated with depression

CARE RECIPIENT CHARACTERISTICS THAT ARE ASSOCIATED WITH CAREGIVER DEPRESSION AND BURDEN INCLUDE:

- ❑ poorer cognitive function
- ❑ higher dependence in activities of daily living
- ❑ behavioral manifestations of distress

**FAMILY
CAREGIVER
FACTORS
INFLUENCE
PATIENT
OUTCOMES**

Caregiver strain affects ability to support the ADL needs of the person with dementia.
(Tao et al, 2012; Boltz et al., 2015a)

Higher family efficacy support associated with better functional status.
(Tao et al, 2012)

Baseline function, depression, dementia severity, and *caregiver strain* were associated with preadmission loss of function.
(Boltz et al., 2018)



**THE FAMILY CARE
PARTNER (CAREGIVER)
AS THE UNIT OF CARE**



NEED TO CONSIDER THE INTERRELATIONSHIP OF CARE-RECEIVER AND CAREGIVER NEEDS AND RESPONSES WHEN PLANNING, PROVIDING, AND EVALUATING CARE . . . AND REFLECT ON

**OUR PERSONAL VIEW
OF PATIENTS AND
FAMILIES**

**THEIR EXPOSURE
TO OTHERS' VIEWS**

**OUR RELATIONSHIP
WITH THEM**

OLDER PERSONS WITH ALZHEIMER'S DISEASE AND RELATED DEMENTIAS (ADRD) ARE 2-3 X'S MORE LIKELY TO BE HOSPITALIZED AS THEIR PEERS WHO ARE COGNITIVELY HEALTHY (ALZHEIMER'S ASSOCIATION, 2024)

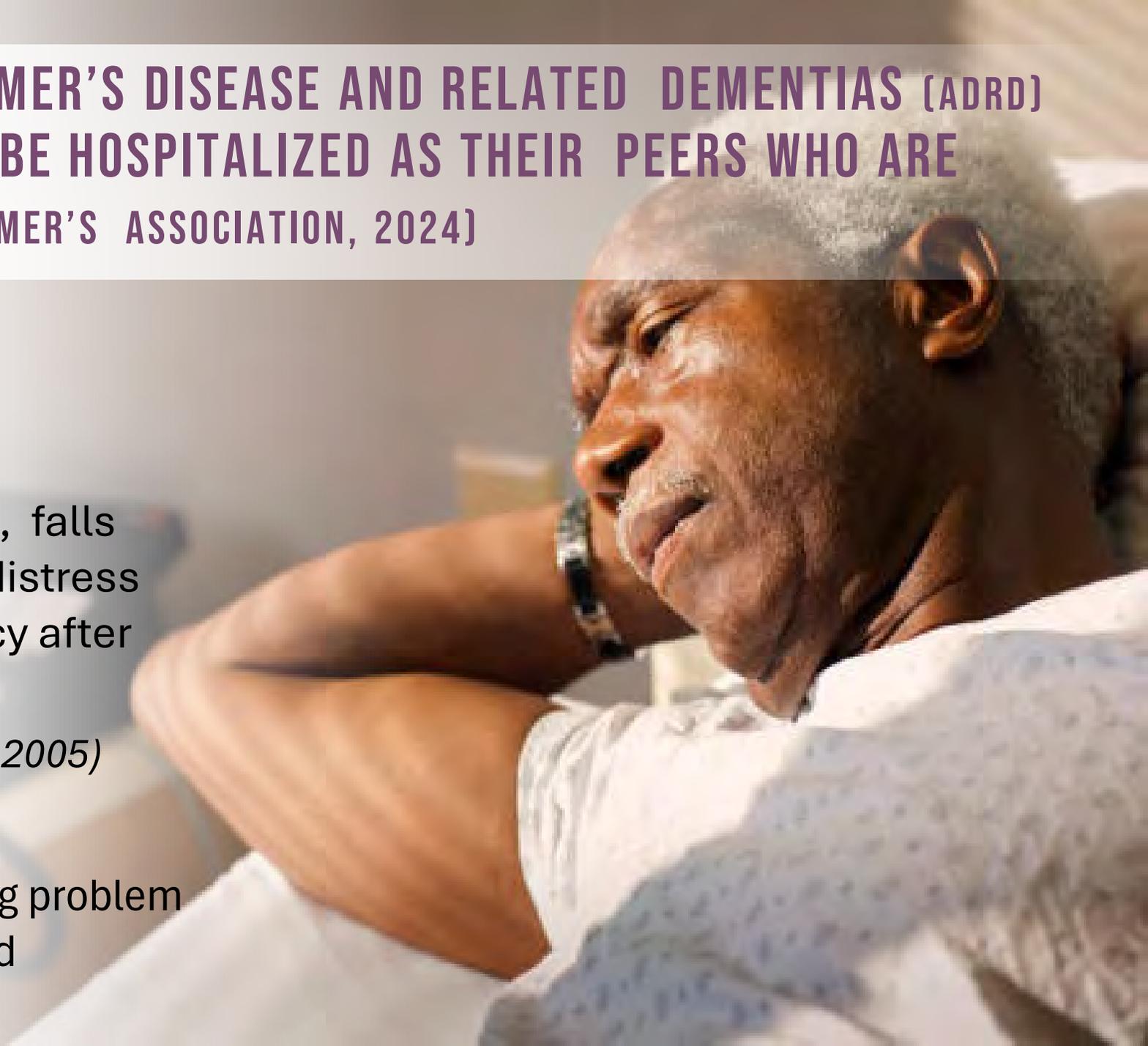
THEY ARE AT GREATER RISK FOR:

- ❑ Functional decline
- ❑ Delirium
- ❑ Nutritional problems, pain, falls
- ❑ Emotional/psychological distress
- ❑ Increased care dependency after discharge

(Fick et al, 2002; Mecocci et al, 2005)

CONTRIBUTING FACTORS

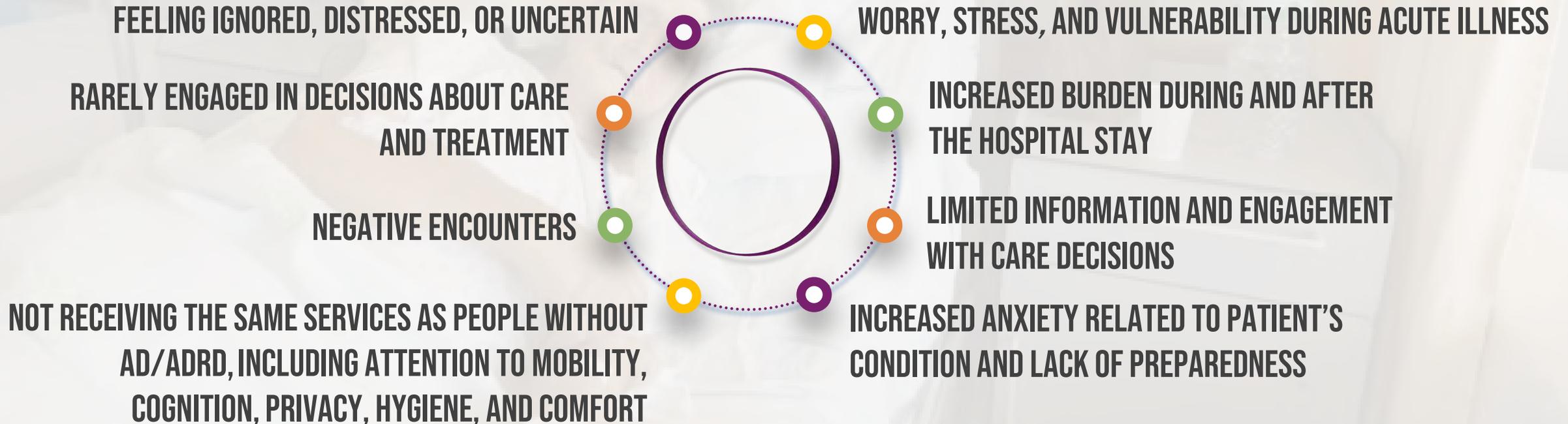
- ❑ Focus on the acute, admitting problem
- ❑ Dementia is rarely recognized



EXPERIENCES OF HOSPITALIZATION

PERSONS LIVING WITH DEMENTIA

FAMILY CARERS



(Boltz et al, 2015; Goldberg & Harwood, 2013; Innes, Kelly, Scerri, Abela, 2016; Hung et al, 2017)

WHY ENGAGE CARE PARTNERS IN ACUTE CARE ?

**OFTEN HAVE BASELINE
PHYSICAL AND
PSYCHOLOGICAL
MORBIDITY**

**PROVIDE 75-80% OF
CARE TO PERSONS
LIVING WITH DEMENTIA**

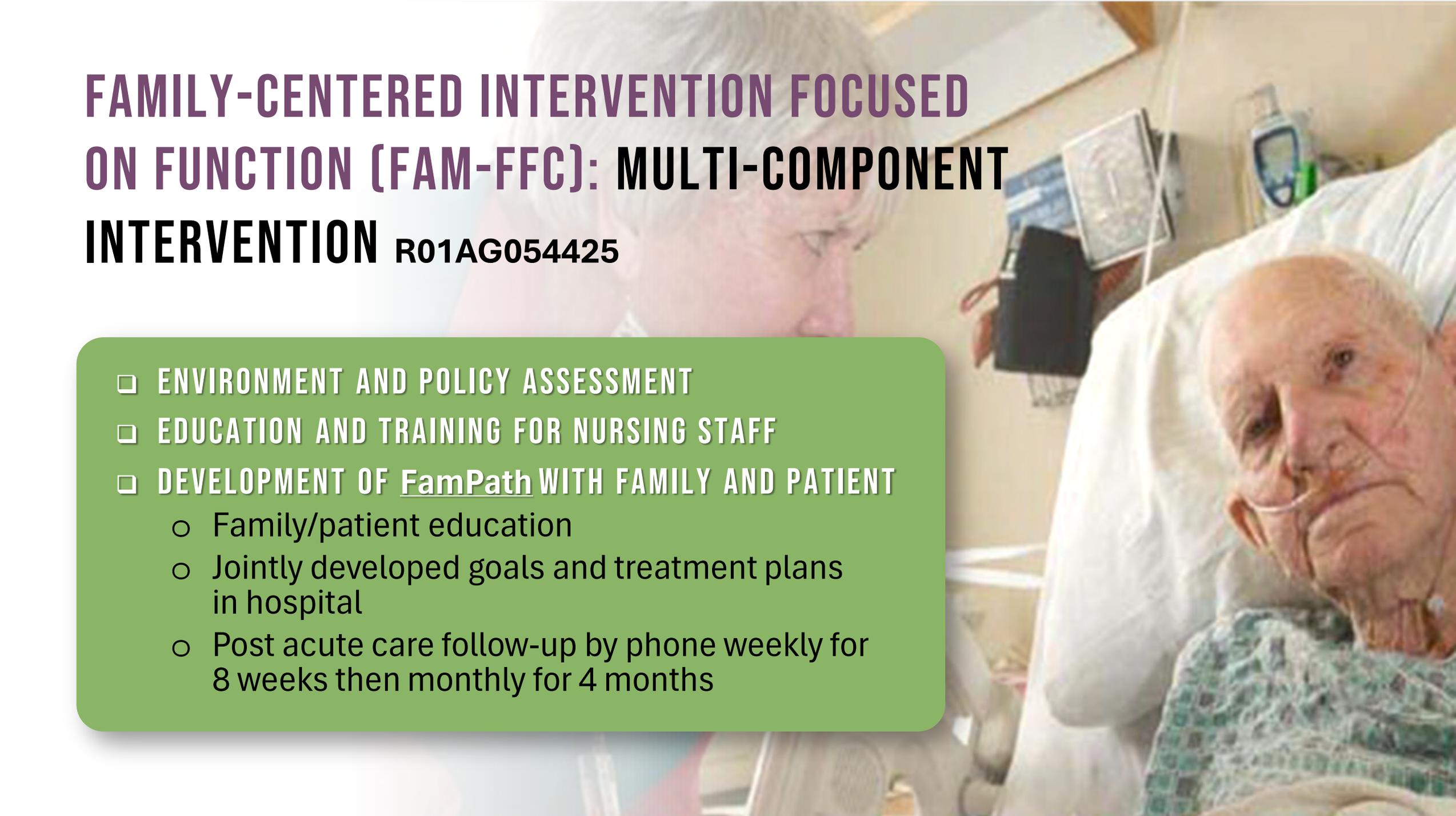


**CAN PROVIDE VITAL
INFORMATION, EMOTIONAL
SUPPORT, MOTIVATION, AND
ASSUME RESPONSIBILITY IN
VARYING DEGREES FOR POST-
ACUTE CARE DELIVERY AND
COORDINATION.**

(Li, 2005; Boltz et al, 2015, 2016)

Can goals of promoting functional recovery (cognitive and physical) align with improving family caregiver preparedness and sense of well-being?





FAMILY-CENTERED INTERVENTION FOCUSED ON FUNCTION (FAM-FFC): MULTI-COMPONENT INTERVENTION R01AG054425

- ❑ ENVIRONMENT AND POLICY ASSESSMENT
- ❑ EDUCATION AND TRAINING FOR NURSING STAFF
- ❑ DEVELOPMENT OF FamPath WITH FAMILY AND PATIENT
 - Family/patient education
 - Jointly developed goals and treatment plans in hospital
 - Post acute care follow-up by phone weekly for 8 weeks then monthly for 4 months

FAMILY ENGAGEMENT WITHIN A PREPARED PHYSICAL AND SOCIAL ENVIRONMENT

ENVIRONMENTAL / POLICY ASSESSMENT

- ❑ Safety of environment
- ❑ Access to supplies:
sensory, mobility, nutrition
- ❑ Bed height/toilet height
- ❑ Policy regarding visitation
- ❑ Inclusion of patient/family in rounds



STAFF EDUCATION

- ❑ Experience of patient /family
- ❑ Communication
- ❑ Cognitive and functional assessment
- ❑ Evidence-based approaches to prevent functional decline, delirium and complications
- ❑ Function-focused care
- ❑ Partnership with families

IMPLEMENTING FamPath

IN-HOSPITAL ENGAGEMENT WITH PATIENTS AND FAMILIES

- ❑ Education – delirium, function, sleep, nutrition, family caregiver role in dementia care
- ❑ Conduct assessment/interview focusing on caregiver role, patient's typical activities
- ❑ Co-Create function-focused goals (typically 2-4 goals)
- ❑ Daily follow-up

NURSE INTERVENTIONIST ENGAGEMENT WITH STUDY CHAMPIONS AND NURSING STAFF

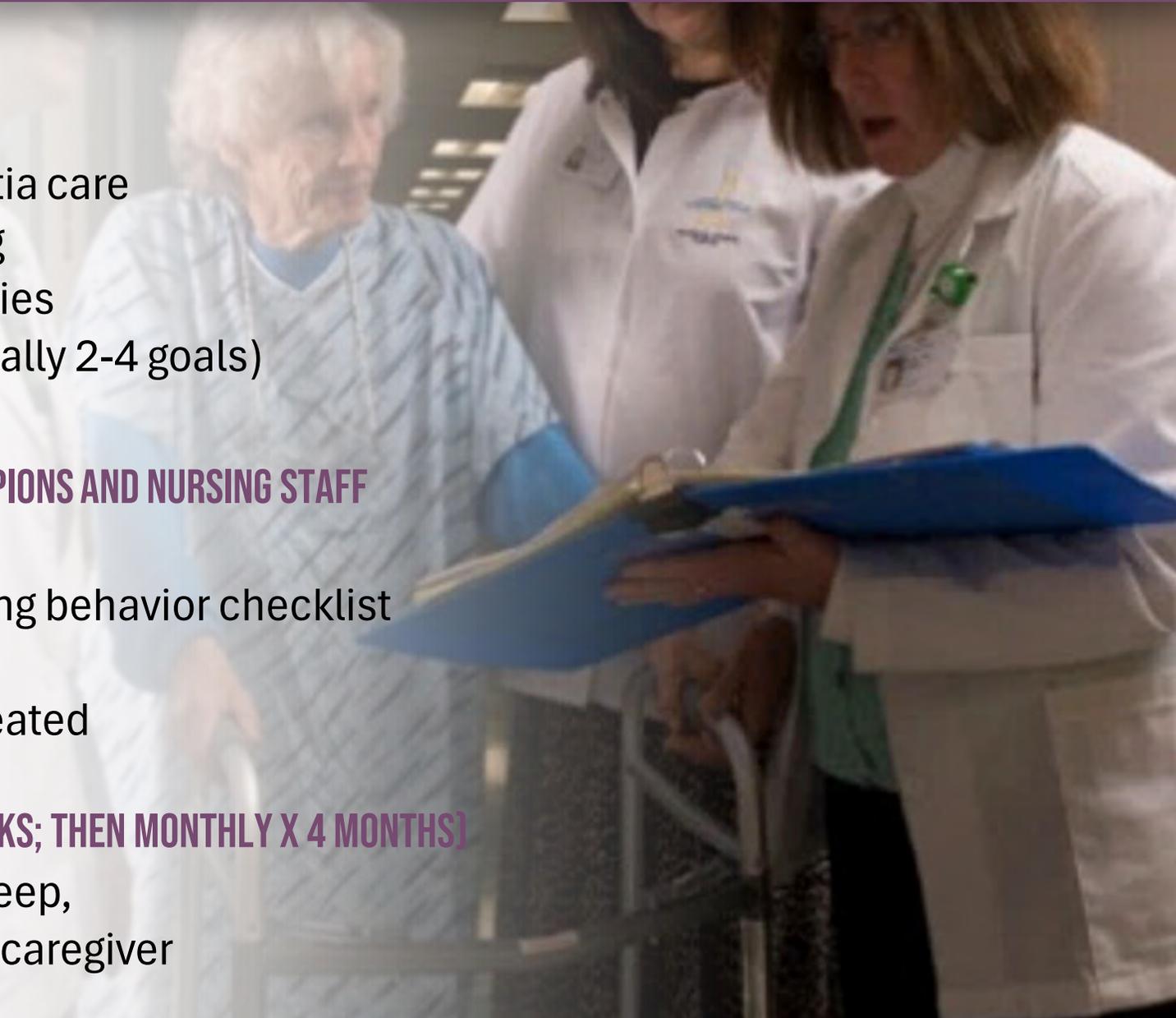
- ❑ Coaching and clinical support
- ❑ Observed nurse/patient interactions using behavior checklist

DISCHARGE ASSESSMENT AND GOAL PLANNING

- ❑ Evaluated progress toward goals and created function-focused home plan

FOLLOW-UP PHONE CALLS TO CAREGIVER (WEEKLY X 8 WEEKS; THEN MONTHLY X 4 MONTHS)

- ❑ Used goals to guide the conversation; sleep, nutrition, function and falls; check in on caregiver



PARTNERING WITH FAMILY CARE PARTNERS



FamPath Information for Patients and Families

Patients and Families guide the decision-making and play an active role!

INFORMATION

SLEEP & REST

NUTRITION

FUNCTION,
STRENGTH,
ABILITY

SKIN CONDITION

WHAT YOU
CAN DO

DELIRIUM

FALLS

DISCHARGE
PLANNING

INFORMATION to share with the health care team:

- Medical and surgical history
- Normal abilities (examples include: transferring, ambulating, feeding, toileting, bathing, dressing, shopping, preparing food, doing laundry, medication administration)
- History of memory or thinking problems
- Daily routine at home
- Signs of stress (including behaviors and functioning)
- Ways to prevent or help cope with stress
- Use of health care or support services
- Living situation and plan for assistance at discharge

WHAT YOU CAN DO as the Family Caregiver while in the hospital:

- Find out who the physician and nurse are and introduce yourself
- Always have paper/pen to write down information and any questions
- Arrange to meet (in person or on the phone) with patient and members of the healthcare team on a regular basis
- Have a friend or family member with you during conversations as support
- The bedside FamPath is a guide to prevent complications and discharge the patient in the best possible condition – please review, provide feedback, and keep current!
- Use the “Family Caregiver Report” with the FamPath to document any changes
- Provide as much information as you can about your loved one!



FamPath Assessment and Plan

Name:

FAMILY ROLES	
The family member or friend who is designated by the patient and /or legally authorized status to help make decisions and guide care planning is:	
Name Relationship:	
Telephone number:	_____
Email:	
Other family members who will be involved in care: if the patient is upset, this is the person to call:	
Name:	
Telephone number:	_____
Email:	
Advanced directive information:	

FAM-FFC OUTCOMES

Family care partners showed increased preparedness

Goal attainment was associated with delirium abatement and less hospital readmissions

Patients exposed to Fam-FFC were more likely to **RETURN TO BASELINE FUNCTION** over time when compared to those exposed to routine care.

- ❑ Results are consistent with goals set by FCPs which focused on mobility and self-care (Boltz et al., 2023)

Fam-FFC patients showed **FEWER BEHAVIORAL SYMPTOMS OF DISTRESS** as compared to the control group at 6 months.

- ❑ FCPs were helped to provide function-focused care, provided in tandem with a structured daily routine and meaningful activities post-hospitalization

PSYCHOSOCIAL SUPPORT

E.g., staying connected to others, managing behaviors

MANAGING SYMPTOMS

- ❑ Delirium Detection
- ❑ Sleep hygiene

PHYSICAL ACTIVITY/ COGNITIVE STIMULATION

E.g., helping activities, sit to stand, walks, leisure activities

ADVOCACY

Get involved in activities, walking, discontinuing an offending medication, getting and giving information

WHAT DO FAMILIES SAY THEY NEED AFTER CARE RECEIVERS' HOSPITALIZATION?

CAREGIVER STRESS

E.g., referral to Aging Services and support programs supportive listening

CULTURAL APPROPRIATENESS OF THE INTERVENTION

CAREGIVER IDENTITY

- ❑ Do not identify as caregivers, did not express need for additional assistance
 - Prefer to be considered just family members
- ❑ Expressed joy and privilege
 - Their responsibility as a spouse, child, family member

SPIRITUALITY

- ❑ Not typically asked about or discussed (by staff)
- ❑ Deemed as important by the care partner / or not important at all
- ❑ Spirituality helps get the care partner cope with stress
- ❑ Requests for community activities that “engage the spiritual mind”

CARE PARTNER VIEWS

MEASURES

- ❑ Need for positive measures

CULTURAL APPROPRIATENESS OF THE INTERVENTION: CAREGIVER VIEWS

- ❑ Additional research is needed on care partner identity and the relationship to help-seeking.
- ❑ Individualized family-centered care may benefit from supports for family spiritual preferences.
 - How about the non-religious?



OPERATIONAL APPROACHES ALIGNED WITH FAMILY-CENTERED CARE

- ❑ Assessing family role(s) upon admission
- ❑ Liberal visiting hours
- ❑ Facilities (overnight accommodations, showers, nutrition stations)
- ❑ Patient and Family Advisory Programs
- ❑ Bedside rounds that include patients and families
- ❑ Partnering with family in evaluation and research



WORKING WITH PERSONS LIVING WITH DEMENTIA & FAMILIES

Leadership “buy in” is important

Hospitalists are key to promoting function of the patient and family engagement

Role of nursing assistants is critical yet under-recognized



Feedback mechanism promotes staff engagement

Rounds are important to support:

- Family engagement
- Follow-through



WORKING WITH PERSONS WITH DEMENTIA AND FAMILIES: LESSONS SO FAR . . .

INFORMATION ON PREFERRED COMMUNICATION
NEEDED TO SUPPORT ON-GOING ENGAGEMENT

- ❑ Back-up contacts

CONCEPT OF “**CAREGIVING**” MAY NOT BE
CONCORDANT WITH CARE PARTNERS’ VIEWS

ISSUES THAT WE HAVE NOT/SHOULD HAVE
CONSIDERED:

- ❑ Spirituality as a source of strength
/resource
- ❑ Food insecurity
- ❑ Inclusion of care partner network



MORE WORK NEEDED



- ❑ Interventions co-designed with people with dementia and care partners
- ❑ Interventions that provide education and support *when care partners need them*
- ❑ Address inequities in dementia care - people in rural areas, ethnic minorities, sexual minoritized, people with disabilities, people living alone
- ❑ Measuring what is important to family carers
- ❑ Additional research is needed on care partner identity and the relationship to help-seeking.
- ❑ Individualized family-centered care may benefit from supports for family spiritual preferences.
 - How about the non-religious?

MORE WORK NEEDED



Need for orientation of staff, patients, and families to acknowledge the role of care partners as patient advocate

Need for caregiver assessment across service areas

Policy that goes beyond supporting the needs of the persons with dementia: supporting care partners to flourish (*Beach et al. 2022*)

TAKE HOME POINTS

When working with persons with dementia and care partners language is important

Hospitalization can be a life-changing event for the person with dementia and their care partner



The needs of both need to be addressed in tandem – during and during the post-acute period

- An under-researched period**
- Simple operational approaches are helpful**
- Goal setting is valuable**

THANK YOU

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Issues in Aging 2024:

Navigating Challenges in Aging

Monday, April 29



CAPABLE

Community Aging in Place-Advancing Better Living for Elders

*an evidence-based program developed
by Johns Hopkins School of Nursing*

Tricia Ford
Sr. VP of Operations

Amanda Goodenow MS, OTR/L
Strategic Partnership Specialist



The Facts on Aging

Statistics on AGING in the United States?



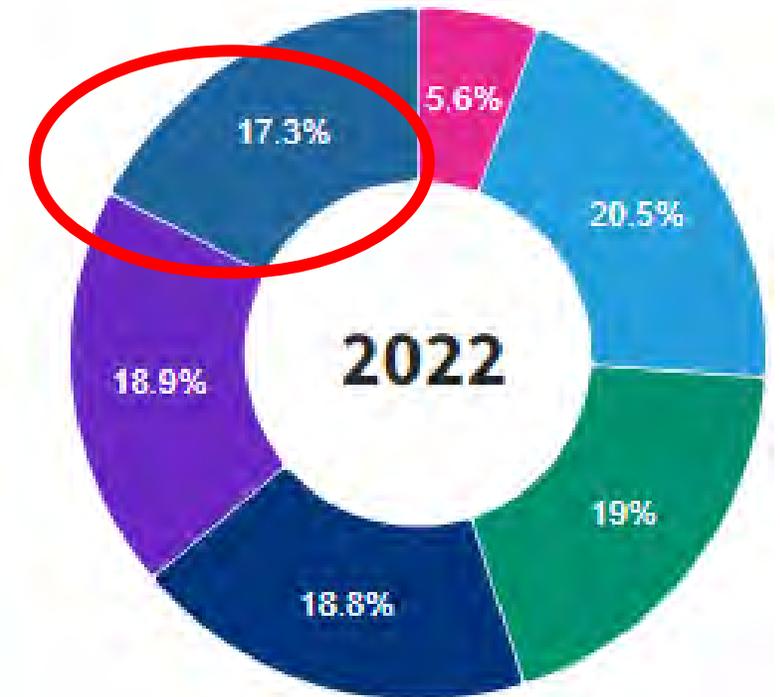
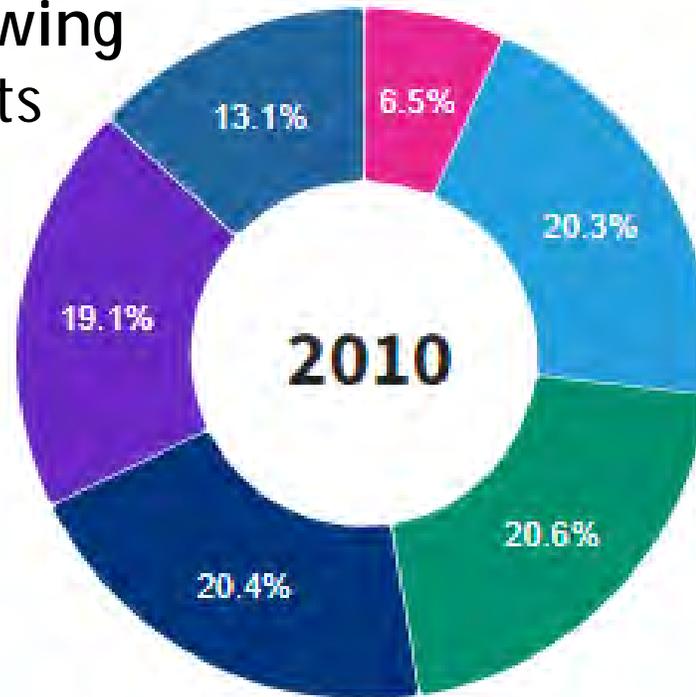
Aging Population

65+ group was the fastest growing between 2010 and 2022 with its population increasing 42.8% ¹

65+ population in 2022 in the US was 57,794,852 or 17.3% of the total population ²

In 2022, another 62,892,984 in population was attributed to ages 50-64 ³

The death rate for people ages 65 or older declined 24% between 2000 and 2019 ⁴



Total Population 333,287,557



The Facts on Aging

Statistics on AGING in the United States?

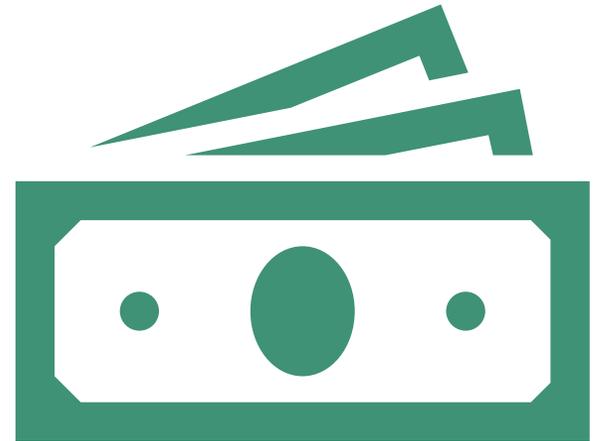


Income and Poverty Levels

Roughly 1 in 3 older adults aged 65+ are **economically insecure**, with incomes below 200% of the Federal Poverty Level (FPL). ⁵

Among Social Security beneficiaries age 65+, **Social Security** represents 50% or more of their income for 37% of men and 42% of women, and **90% or more of their income** of 12% of men and 15% of women. ⁶

Of retirees 65+ surveyed in 2021, **93% said Social Security** was a source of income in the previous 12 months, and 68% said a pension was. ⁷



The Facts on Aging

Statistics on AGING in the United States?

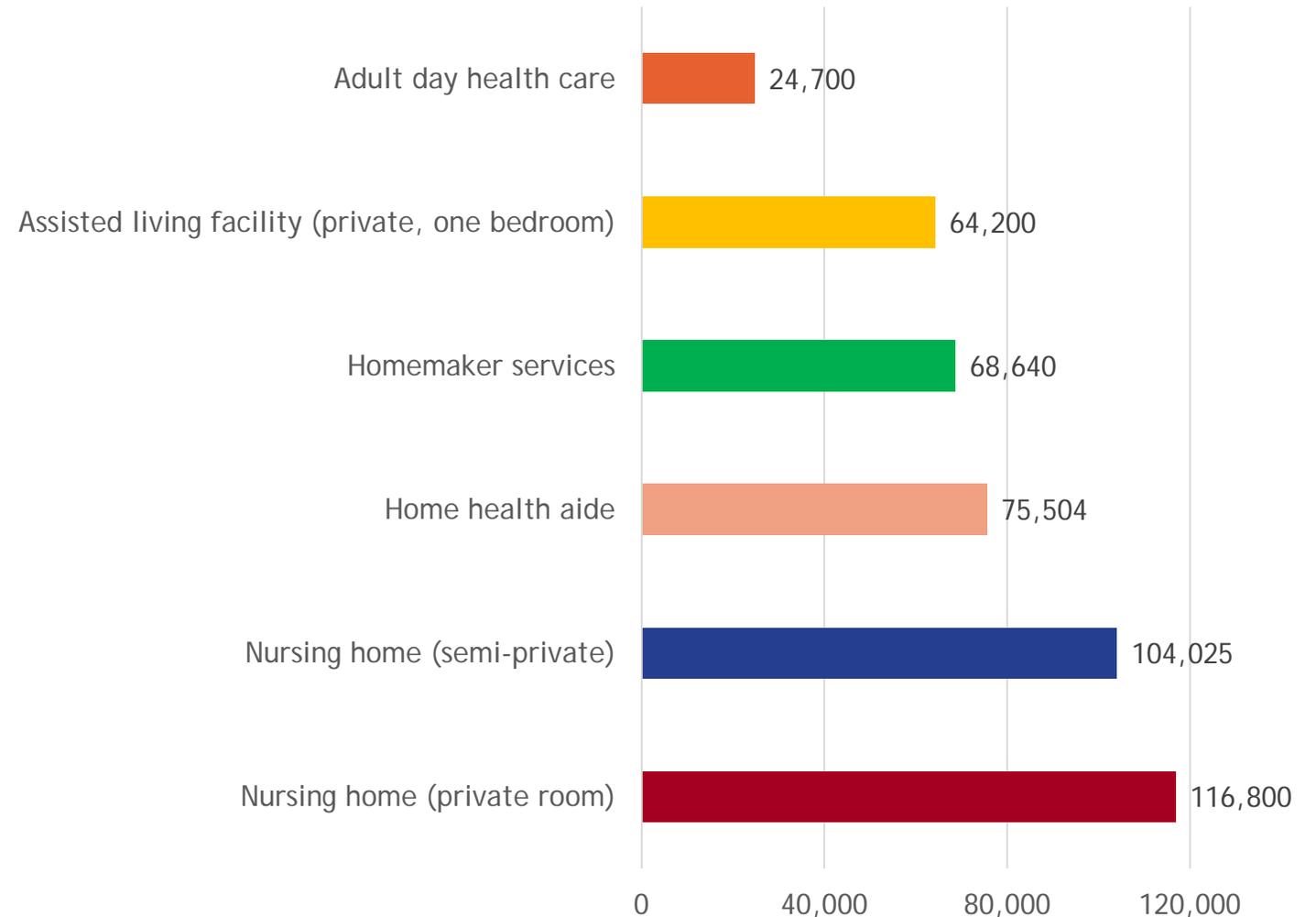


Housing

Housing-related expenses cost adults 55+ an average of \$16,219 per year, or 33% of their yearly budget. ⁸

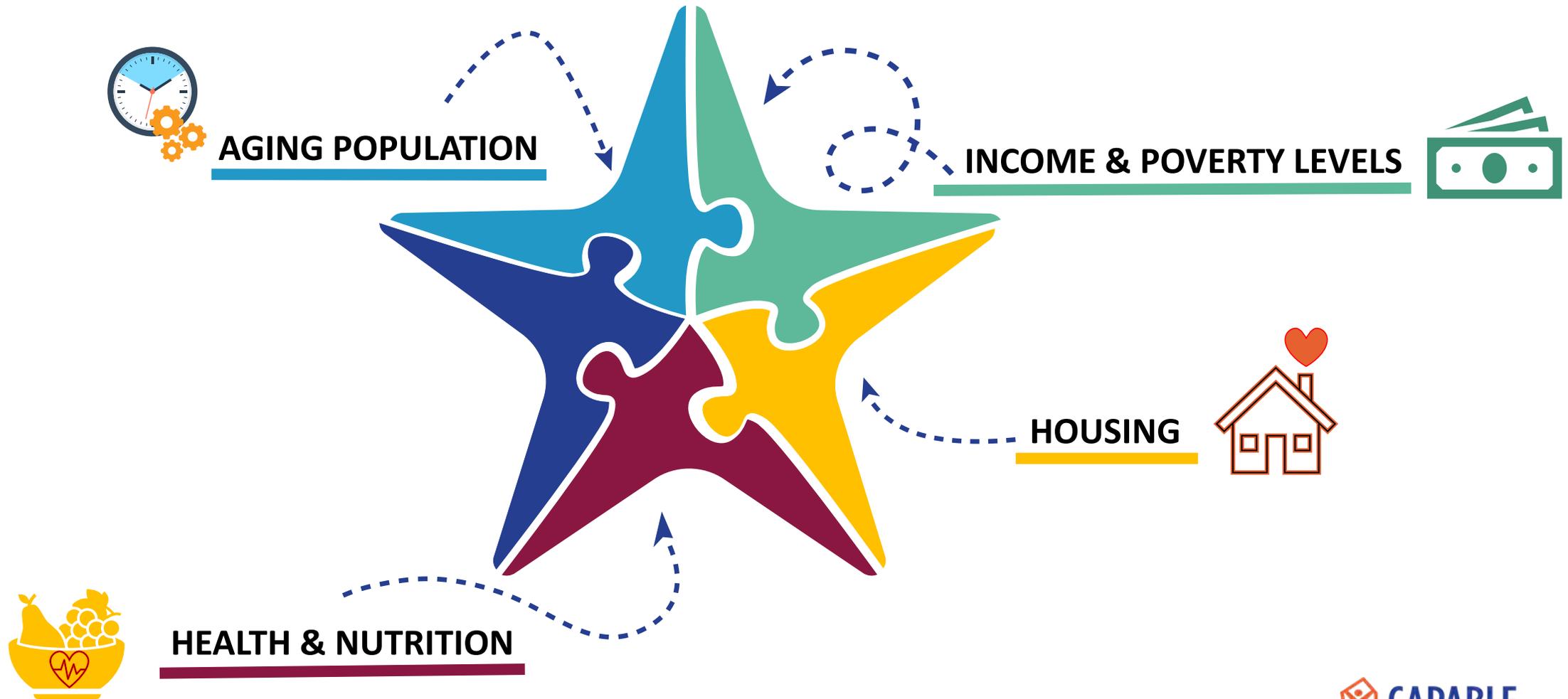
About 75 million or 60% of U.S. homes don't have the most basic, aging-ready features — a step-free entryway into the home and a bedroom and full bathroom on the first floor. ⁹

Median Annual Rate in US Dollars



The Facts on Aging

Statistics on AGING in the United States?

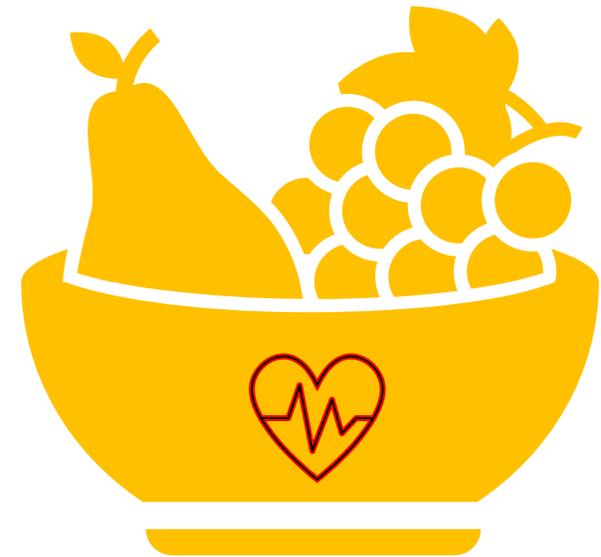


Health and Nutrition

About one in four older adults 65+ scrimp on food, utilities, clothing, or medication due to health care costs. In 2022, 37% of older adults were worried about affording health care in the coming year. ¹⁰

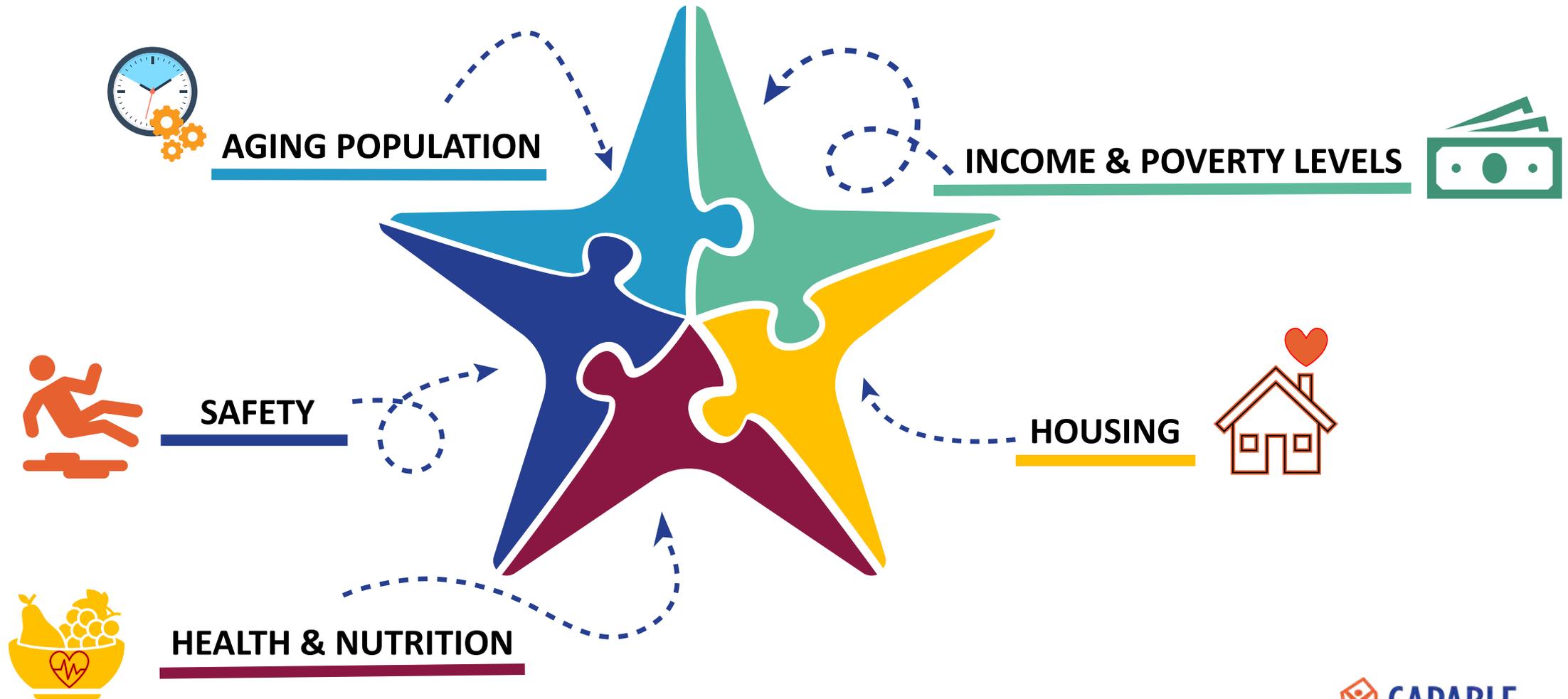
All types of **disabilities increase with age**, and 55% of those age 80 and over report at least one disability. ¹¹

In 2020, 5.2 million older Americans faced the threat of hunger, representing 6.8% of adults age 60+ in the U.S. Hunger is more likely for older Americans who are Black, Hispanic, or Native American, who have lower incomes, or who have a disability. ¹²



The Facts on Aging

Statistics on AGING in the United States?



Safety

More than one out of four Americans age 65+ falls each year. ¹³

The cost of treating injuries caused by falls is projected to increase to over **\$101 billion by 2030.** ¹⁴

Falls result in more than 3 million injuries treated in emergency departments annually, including over **800,000 hospitalizations.** ^{15, NIH}

Bedrooms (25% Overall)

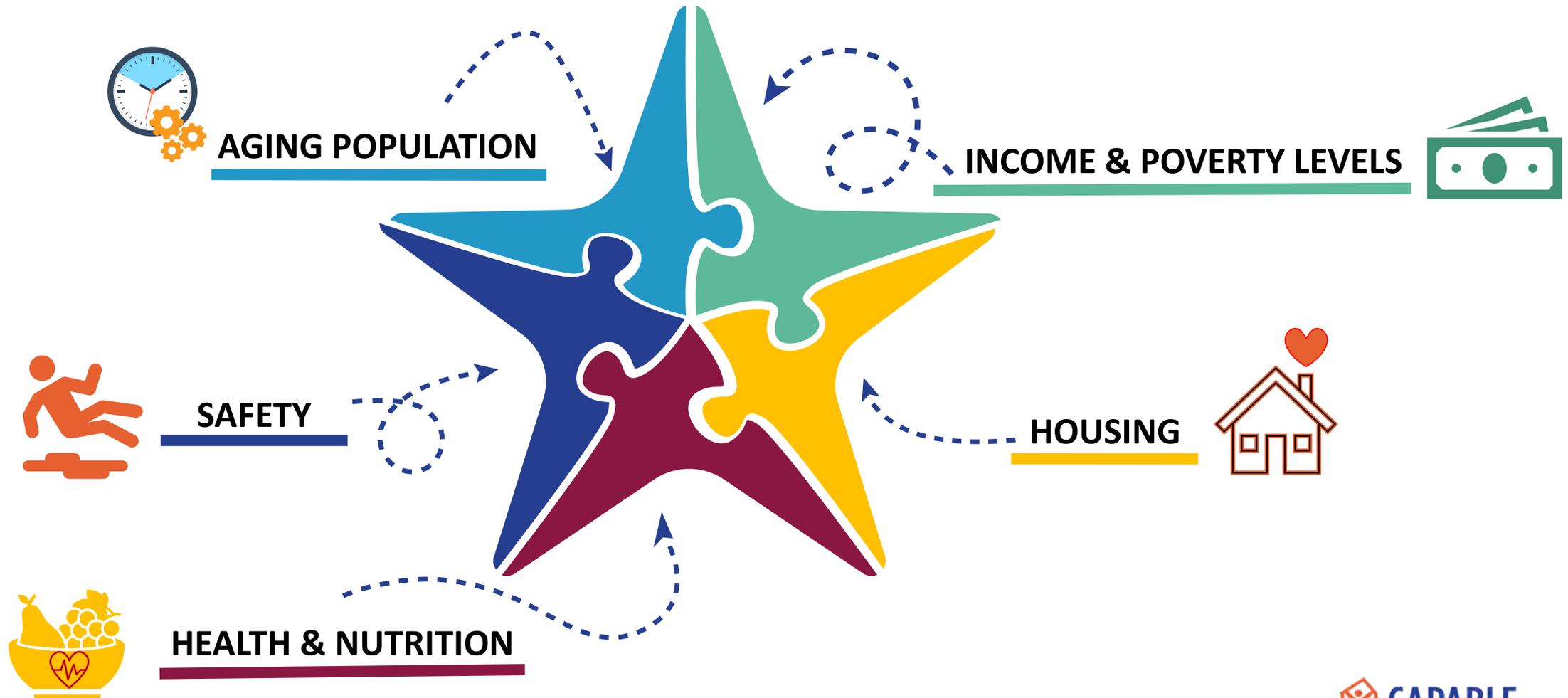
Stairs (22.9% Overall)

Bathrooms (22.7% Overall)



The Facts on Aging

Statistics on AGING in the United States?



© Cartoonbank.com



"There's no easy way I can tell you this, so I'm sending you to someone who can."



CAPABLE

The View of the Client and the Clinician



Courtesy of St. David's Foundation in Austin, TX

What is CAPABLE?



Evidence-based



Home-based



Client-Directed



Interprofessional



Long-term impact



Behavioral change

How CAPABLE works



Participant

- Self-assessment
- Readiness to change
- Drives own goals and priority settings
- Brainstorms options/solutions; Develops Action Plan in own words
- Makes progress between visits; Exercises, reads material, practices within home
- Practices tips for safe, independent living
- Uses new skills and equipment

An interdisciplinary team uses motivational interviewing, active listening, and coaching communication methods to enable the participant to achieve their self-prioritized goals



Occupational Therapist

- Functional/Mobility assessment
- Home risk; modifications & equipment needs
- Fall prevention, equipment guidance



Registered Nurse

- Medical history, current healthcare providers
- Key health issues/risks
- Pain, medication review



Handy Person

- Receives work order; confers with participant
- Obtains and installs equipment
- Makes minor home repairs/modifications

CAPABLE at a Glance

CAPABLE is delivered in the home during 10 visits over 4 months through an inter-professional team including the participant:



Occupational
Therapist



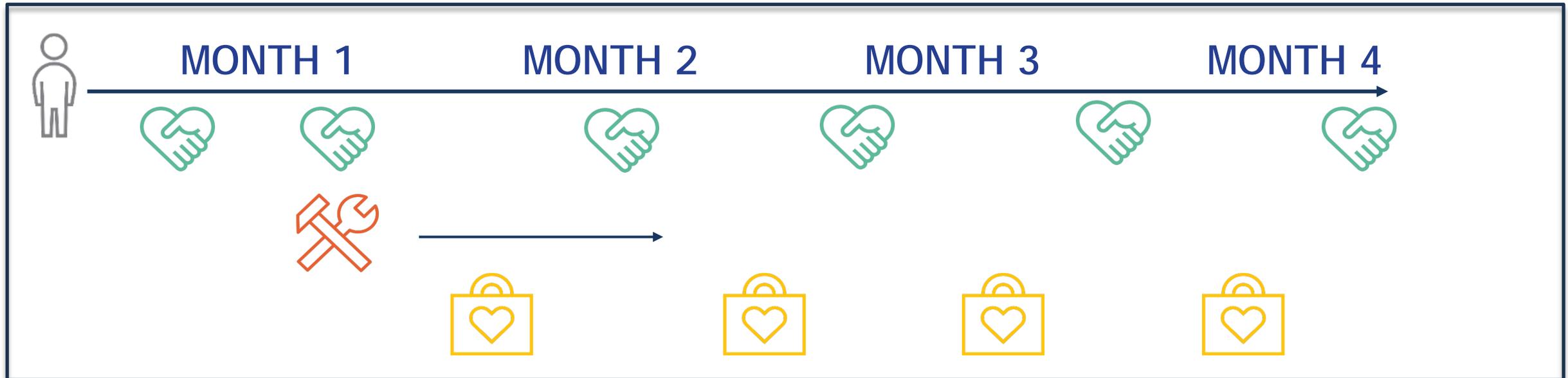
Registered
Nurse



Handy-worker



Participant



CAPABLE Participants



Adults - age 50+



With functional limitations



Living at home or in an apartment



Cognitively intact

Participant Learns:



Goal Setting
Brainstorming
Action Planning
Trying
Doing
Achieving



"The single best thing is they do it in a style that is not directive or confrontive. It is collaborative. What it does is gives such room for thought."
Baltimore, MD 2022

CAPABLE Client: Mrs. R

Daily activities have become harder due to advanced arthritis and lung disease.

She works with her CAPABLE team - an occupational therapist, nurse, and handy worker - to identify goals and address challenges.



Mrs. R's Goal

Be able to bathe with less effort.





1

The handy worker smooths out the bathroom entry threshold so Mrs. R can push her rolling walker with ease.



2

The shower doors and frame are removed and a secure shower curtain rod is installed, allowing more room to access the tub area safely.

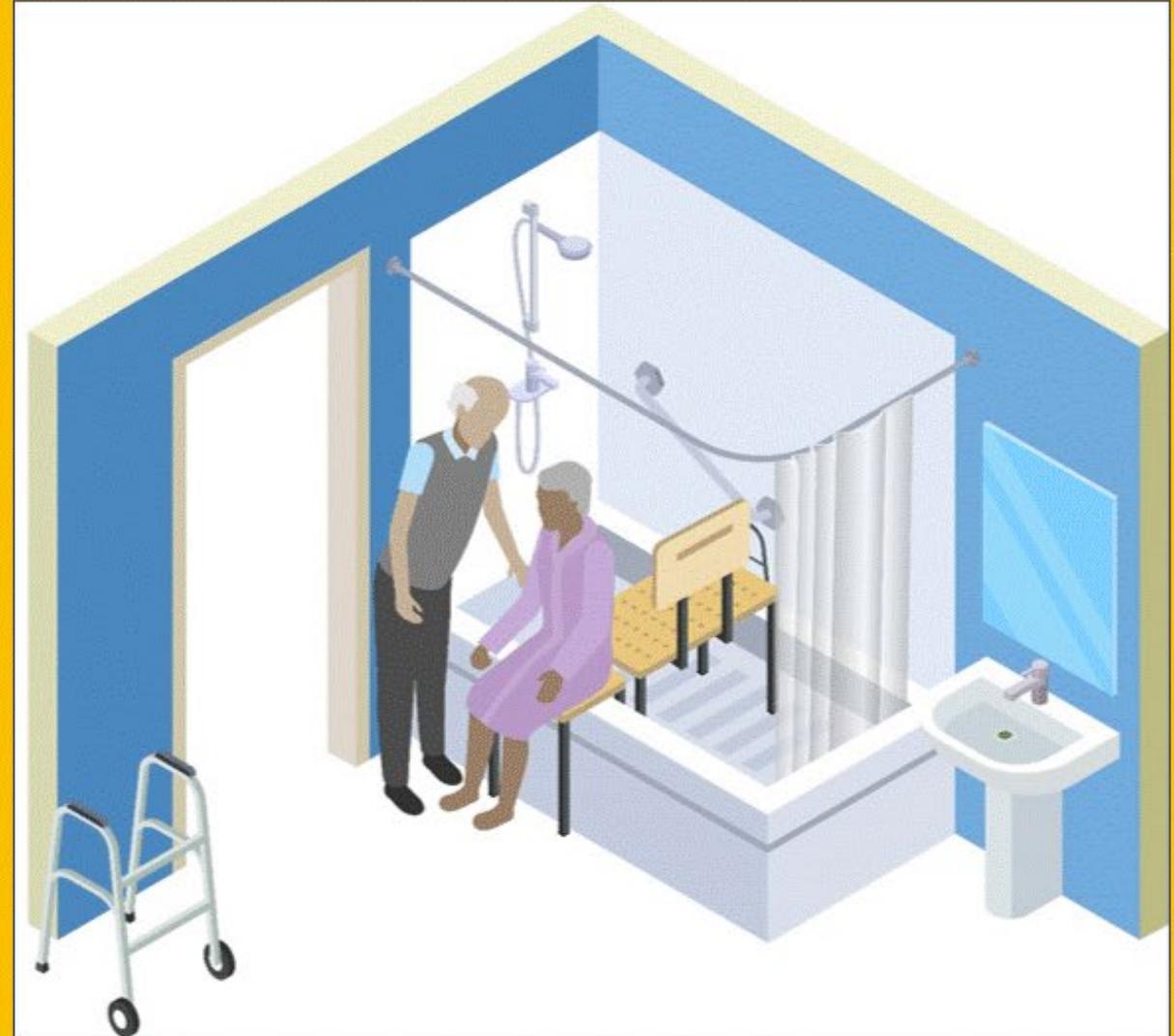


3

The new tub transfer bench allows Mrs. R to get in and out of the tub safely and reduces her husband's assistance.

GOAL ACHIEVED!

Mrs. R is able to bathe with less effort.



CAPABLE Client: Mrs. R

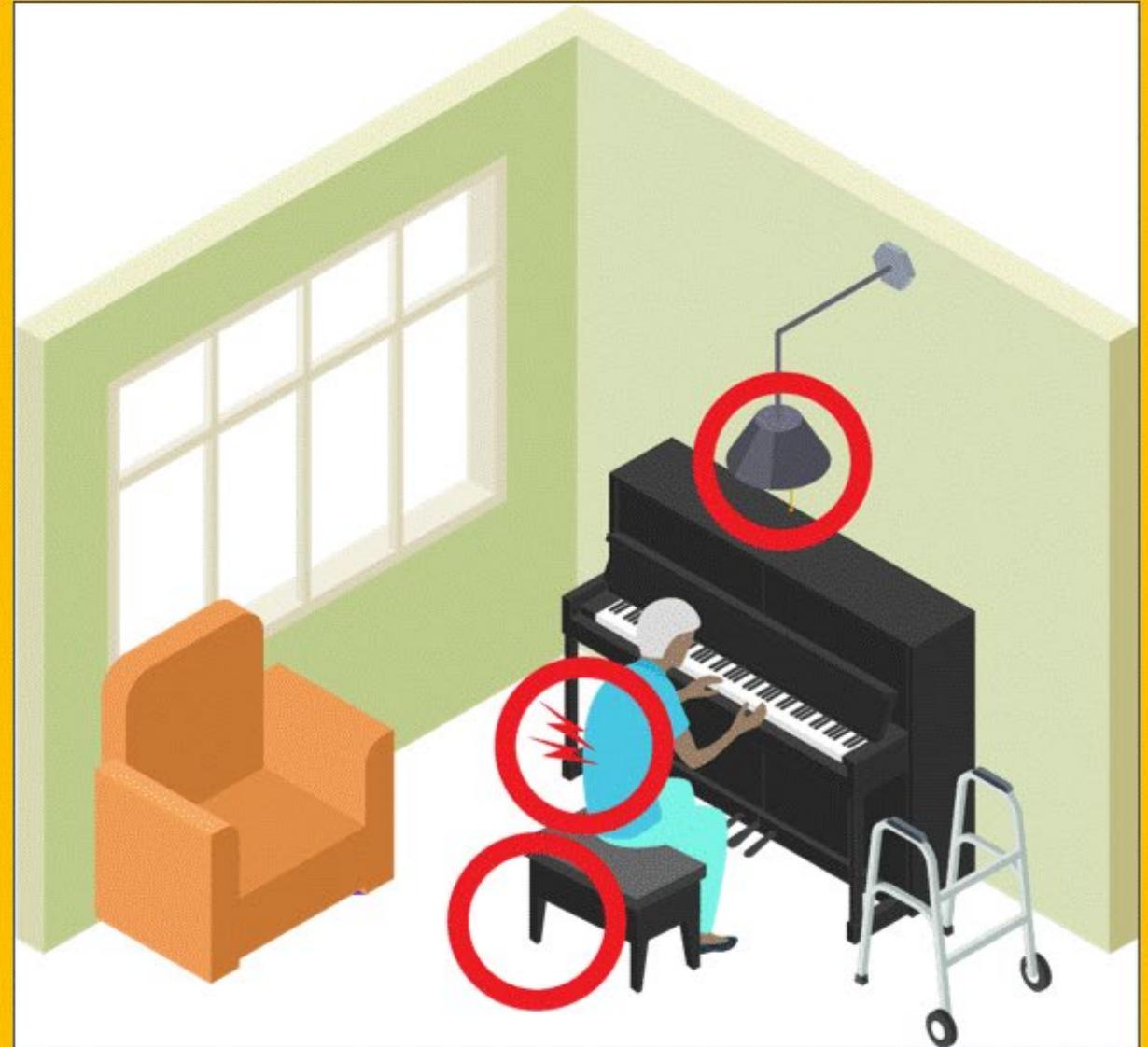
Daily activities have become harder due to advanced arthritis and lung disease.

She works with her CAPABLE team - an occupational therapist, nurse, and handy worker - to identify goals and address challenges.



Mrs. R's Goal

Feel less pain
while playing the
piano.





1

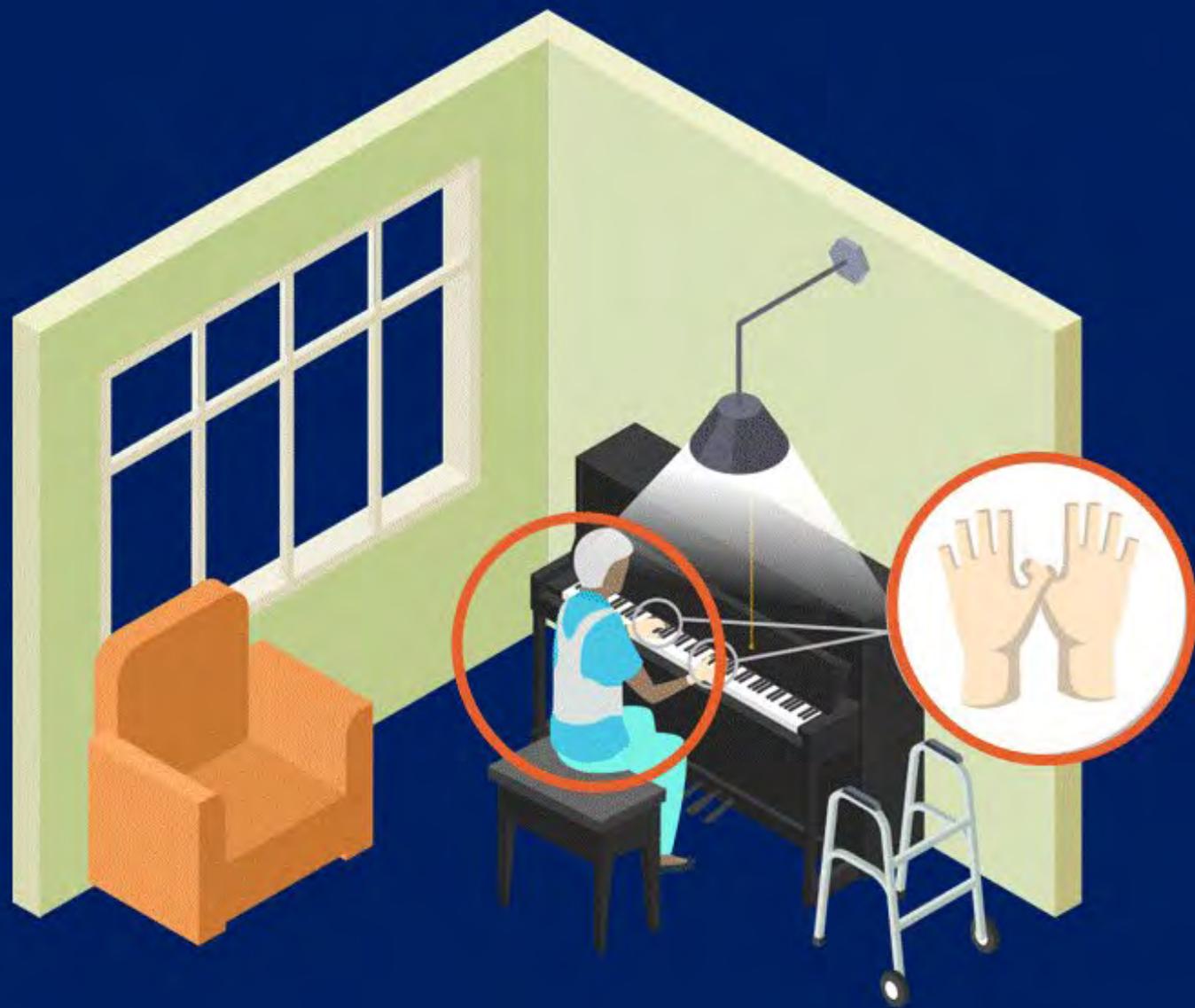
The handy worker added an extended chain to her light and switched the light bulb to an LED.

Mrs. R can now operate the light herself and read the sheet music better.



2

The handy worker constructed a higher bench to prevent back pain when playing the piano.

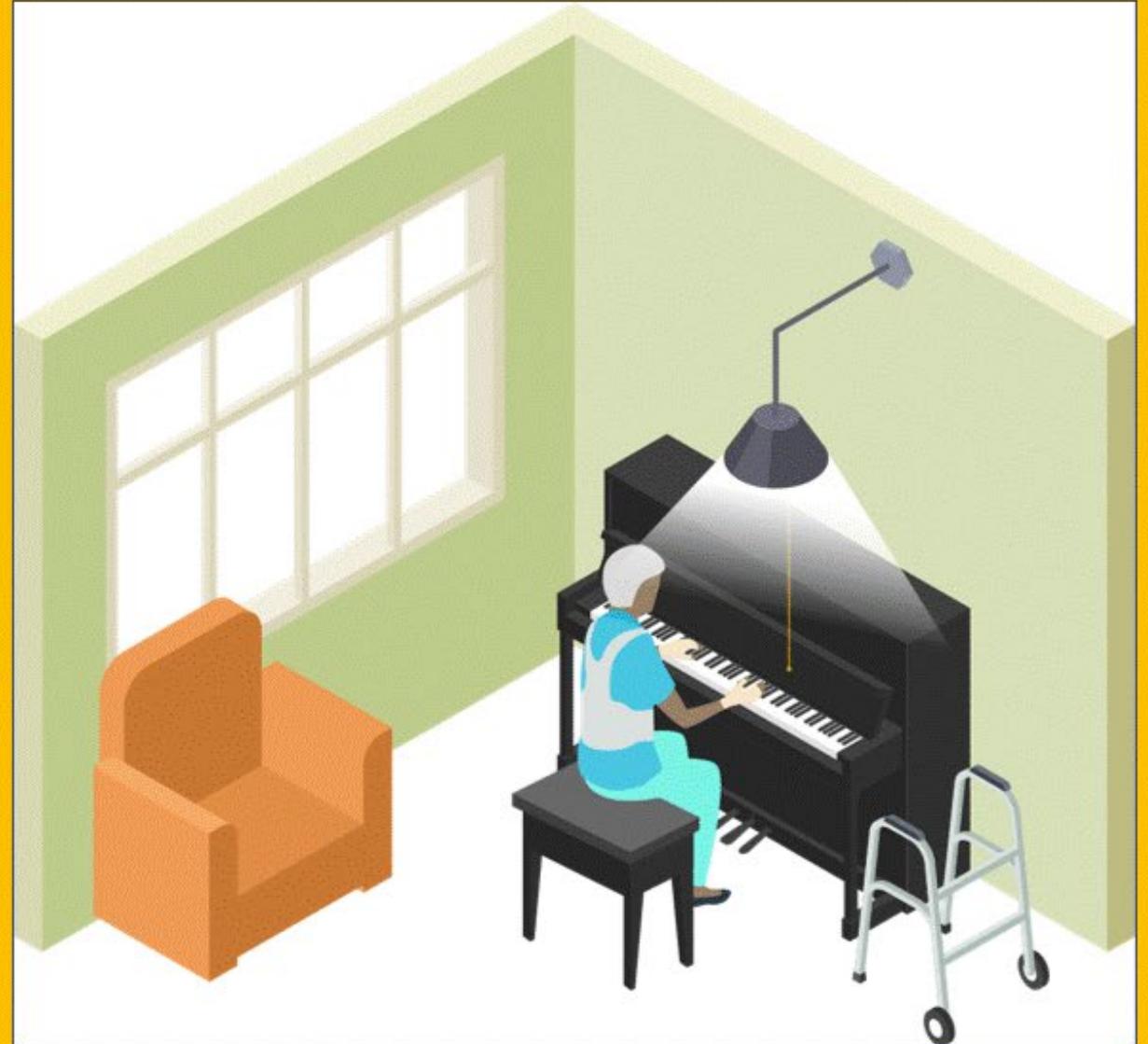


3

Wearing arthritis compression gloves and a back brace decreases her pain.

GOAL ACHIEVED!

Mrs. R feels less pain while playing the piano.



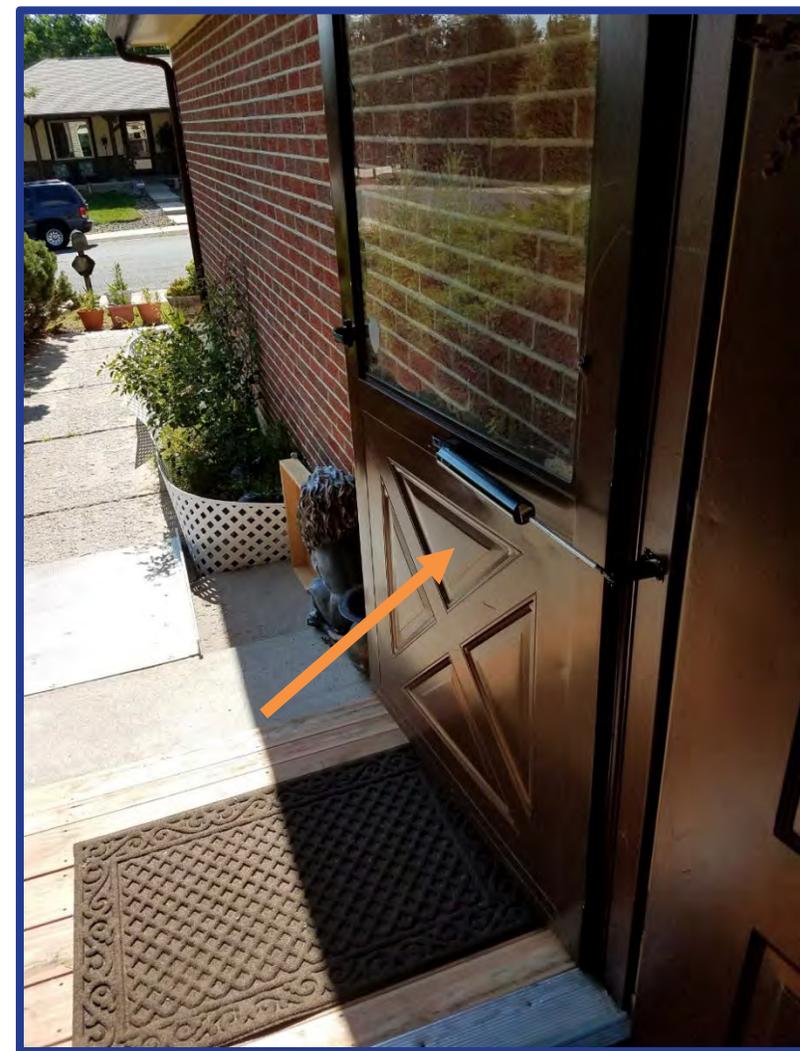
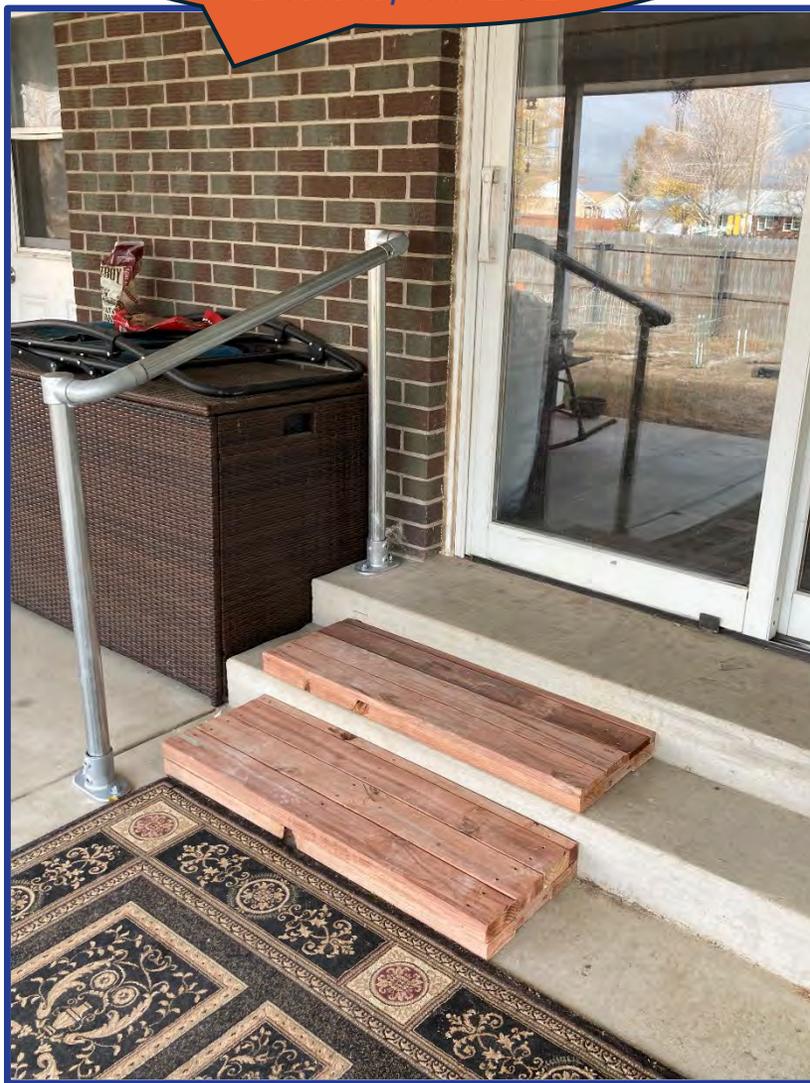
GOALS – Set by the participant

Examples:

- *I want to: make my own meals/cook at stove/oven vs. frozen microwave food*
- *I want to take a shower by myself*
- *I want to: clean better (bathroom, kitchen), make my bed*
- *I want to declutter and reach things in my cabinets*
- *I want to get stronger; avoid falls-especially on stairs and in bathroom*
- *I want to be able to talk with my doctor and get some things changed with my meds*
- *I want to manage my bladder*
- *I want to be less tired all day long*

I have been homebound for so long. The program has really helped me get out.

Denver, CO 2024



I feel cleaner from head to toe.
I must have stayed in here for an
hour the first time.
Denver, CO 2024



Common Supplies & Installations

DME:

1. Shower chairs
2. Tub transfer benches
3. Rollators
4. Reachers

Non DME supplies:

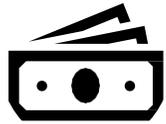
1. Rubber bathmats
2. Non-sliding rugs (bath and kitchen)
3. Tub safety strips
4. Heating pads
5. Ice packs
6. Knee braces
7. Back braces/sciatica belts
8. Max Freeze (topical pain relief)

Home Modifications:

1. Interior railings
2. Grab bars
3. Flexible shower hoses
4. Exterior railing
5. Motion sensor lighting and other lighting
6. Door-bells
7. Door lock sets
8. Lever door handles

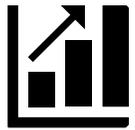


Program Benefits



6 to 7 x return on investment

Roughly \$3,000 in program costs yielded more than \$30,000 in savings in medical costs driven by reductions in both inpatient and outpatient expenditures.*



Improved physical function

Participants had difficulty with an average of 3.9 out of 8.0 Activities of Daily Living (ADLs) at baseline, compared to 2.0 after five months. 74.8% participants had less difficulty with ADLs.



Improved motivation

The change in physical environment further motivates the participant. Addressing both the person and the environment in which they live allows the person to thrive. 77.6% of participants had less home hazards.



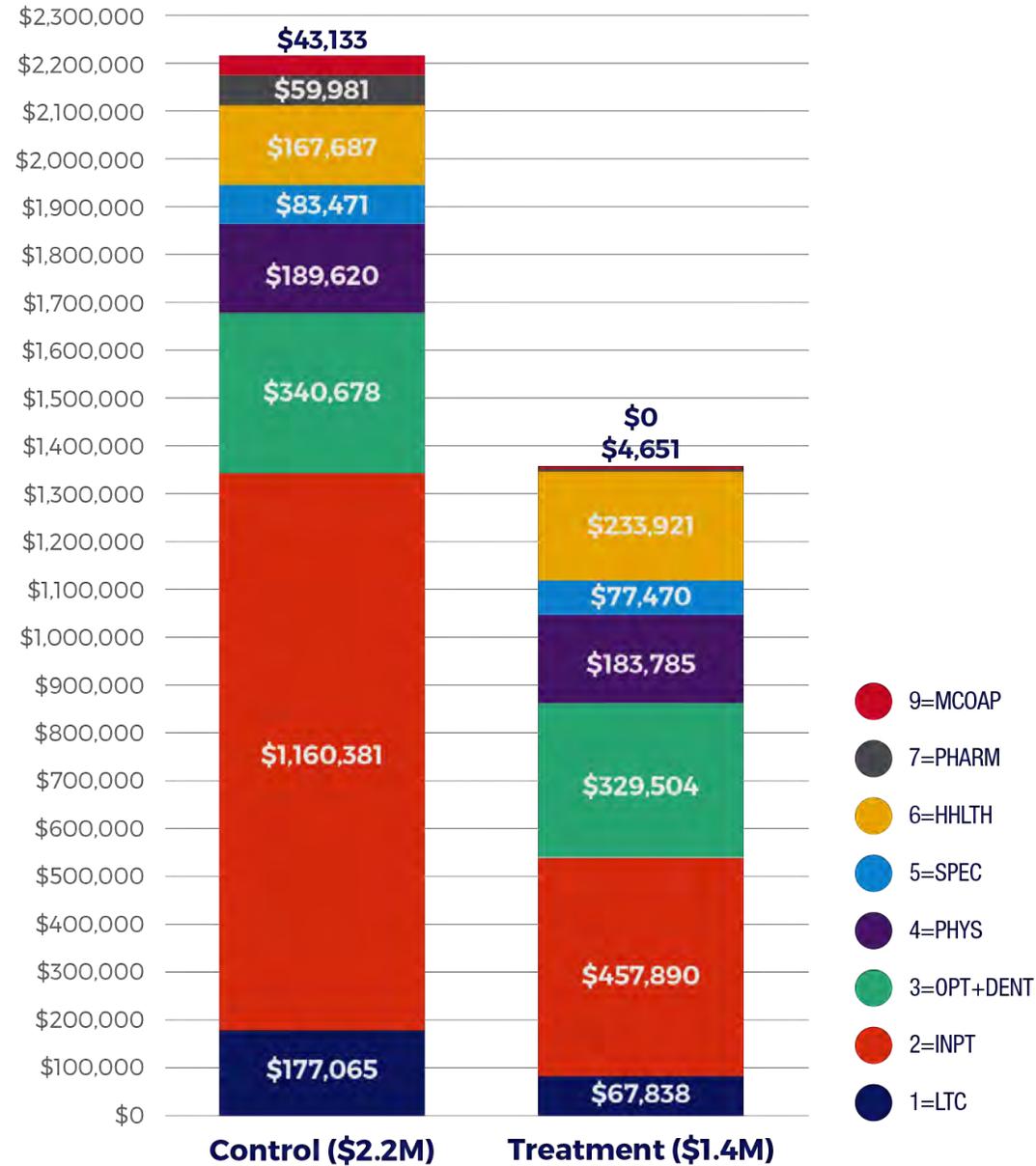
Reduced symptoms of depression

52.9% of participants had less depressive symptoms and ability to do important tasks. 65% of participants improved in such tasks as grocery shop and manage medications.

*Ruiz et. al, 2017

*Szanton et al, June 2016

Monthly Medicaid Cost for a Hypothetical Cohort of 1,000 People Per Service Type and Study Arm

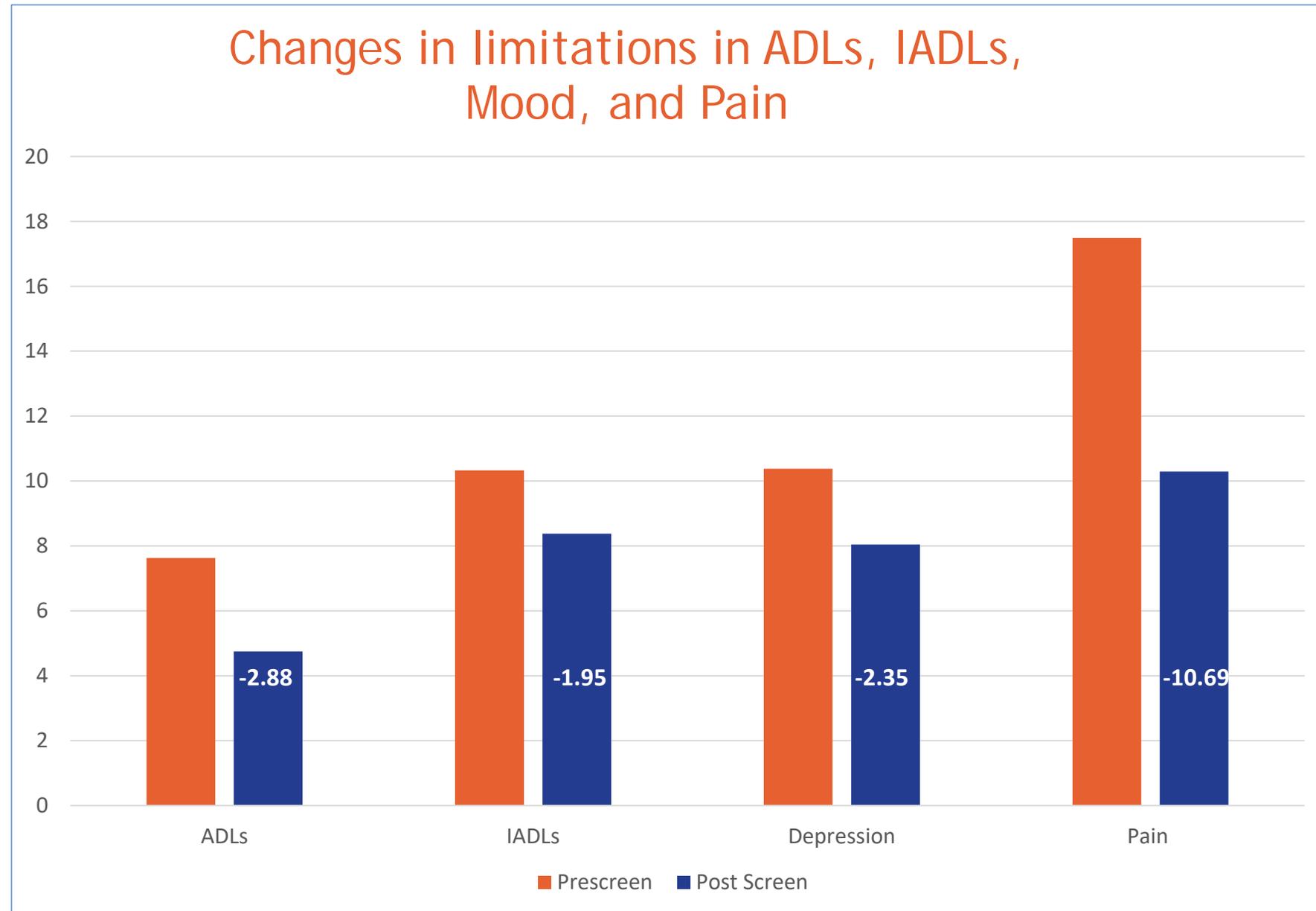


State Example – Colorado Preliminary Data

Two Implementation sites:
Home Health Agency
Housing Organization

A goal of 400 Medicaid
members to receive
CAPABLE Services for this
demonstration pilot

Number of members served,
300 members
and 180 have graduated
(through March 2024)



Keys to Success



Strengths and goals developed by participant



Clinicians provide resources to achieve those goals



Unleashes participant's motivation



Person/environmental fit



Helps demonstrate that function can be improved/is not lost



Builds self-efficacy for new challenges

CAPABLE Intersections



Program Costs — \$3,500 to \$4,500 per participant



Occupational
Therapist



Nurse



Handyworker



Supplies, Mileage

Indirect costs also include:

- Program administration
- Marketing and outreach
- Database
- Communications
- Evaluation

Adoption & Implementation Key Considerations



Purpose

Why are we doing this and why now?



Strategy

How does it align with our mission and services?



Scope/Scale

How many participants, covering what area, and in what timeframe?



Funding

Do we have a source of funds to test/pilot?

What are our options for ongoing funding?



Will this require partners to implement?

How will we define and assess our success and impact?

How will we sustain this if it works?

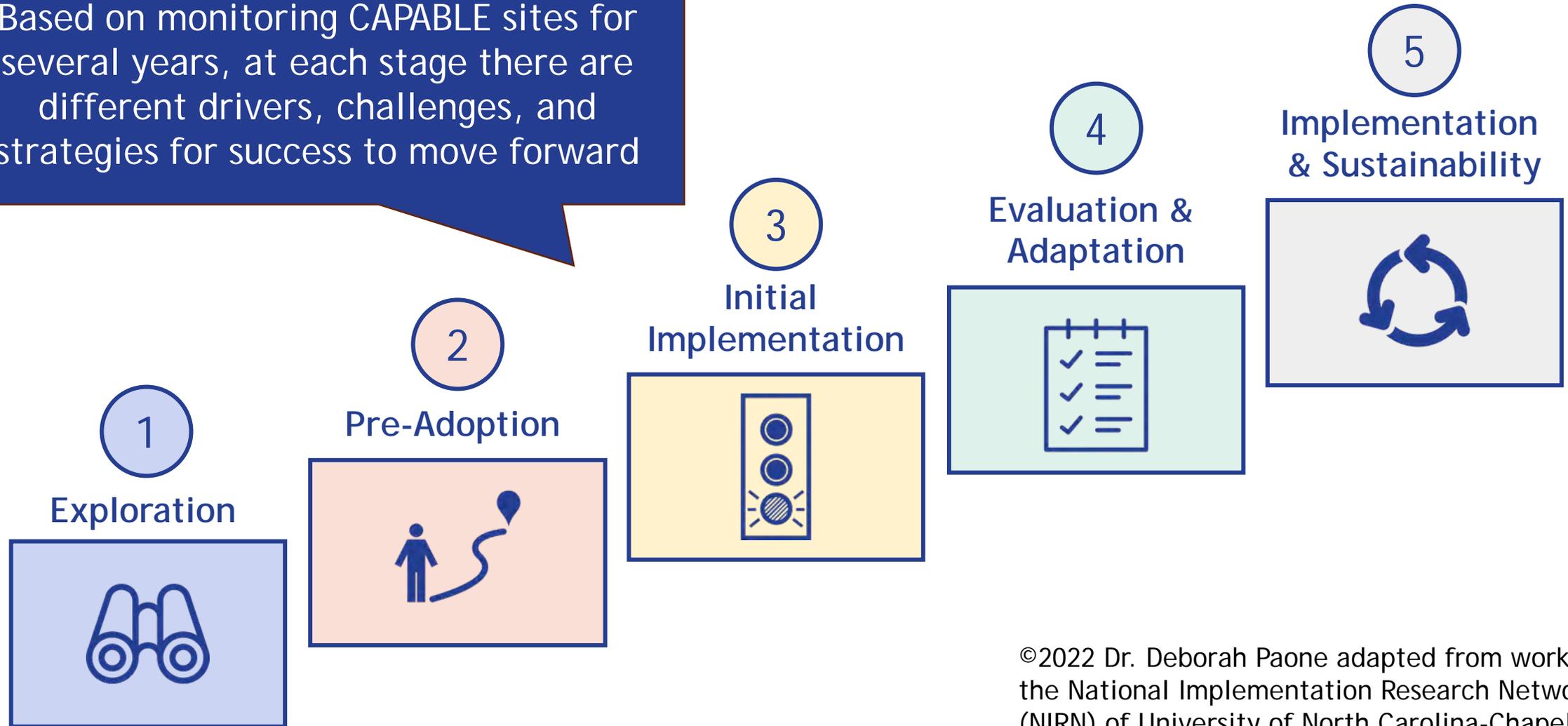


Program Components

Do we have or can we develop the capacity to follow the CAPABLE model?

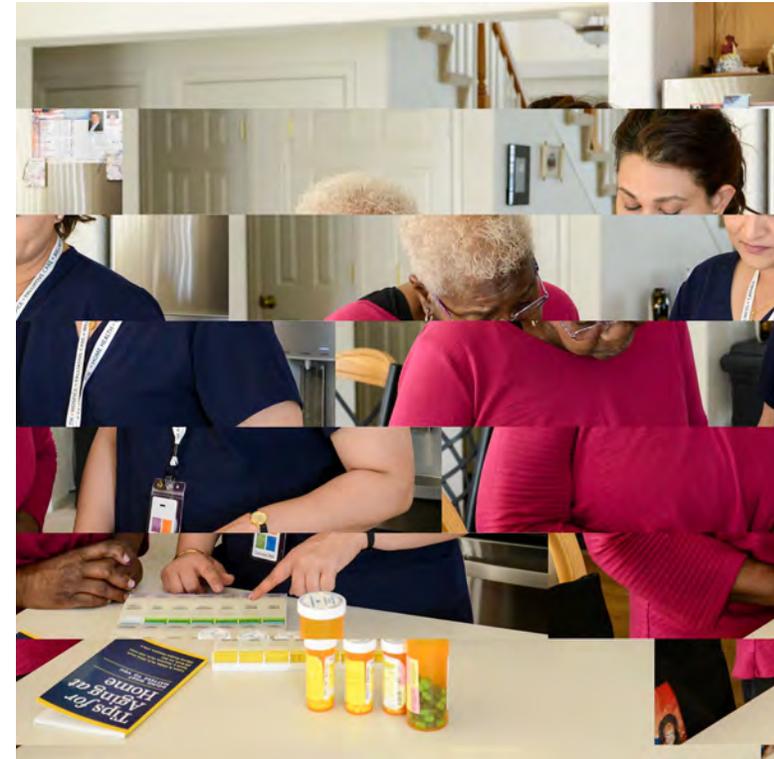
5 Implementation Stages

Based on monitoring CAPABLE sites for several years, at each stage there are different drivers, challenges, and strategies for success to move forward



Perspectives on Value Equation

STAKEHOLDER	TOP VALUE of CAPABLE
Potential Participant	<i>Improved quality of life</i>
Organization offering CAPABLE Leadership (Board, C-Suite)	<i>Service, mission, reputation, cover costs, strategic direction</i>
Partners	<i>Service, mission, payment, long-term partnership interest/strategic</i>
OT, RN, and Handy-worker	<i>Service excellence and satisfaction</i>
Local senior service providers	<i>Ability to refer their clients to a proven, effective program</i>
Private Philanthropist or Foundation	<i>Proven effectiveness, Health Outcomes & Community impact</i>

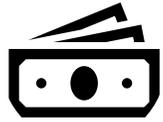


Perspectives on Value Equation



STAKEHOLDER	TOP VALUE of CAPABLE
Primary care providers	<i>Fewer patient falls/calls; improved patient health and self-care at home</i>
Hospital & ED (in value-based arrangement)	<i>Fewer hospital readmissions; fewer ED visits</i>
Managed care organization	<i>Reduced hospital/ER costs and improved member satisfaction</i>
Federal Medicare Program	<i>Reduced Medicare costs due to avoided hospital/ER costs; better quality outcomes</i>
State Medicaid Program	<i>Reduced Medicaid costs due to avoiding early admissions to a nursing home; better quality outcomes</i>
City/Town Services (EMT, Fire)	<i>Reduce "pick up from floor calls"</i>

Variety of Program Funding Options



GRANTS/
PHILANTHROPY

Grants are the most frequent source of funding for CAPABLE; Several programs have sustained foundation funding or special initiatives from private philanthropy



Reserves

Self-funded programs (organizational reserves)



VB Payment

Value-based payments are used by MA & ACOs (St. Louis MA program)



Municipal/Tax

City or other gov't unit funding that comes from taxes (e.g., City of Chicago)



ARPA or Waiver
programs

ARPA \$ and State waiver or demonstration - (e.g., Colorado; Massachusetts)

The CAPABLE Difference

What makes **CAPABLE *work*** - in a population where so much *doesn't*?

Typical disease prevention/management intervention	 CAPABLE
Designed to prevent a single event or focuses on a single disease (e.g., a fall, post-hip surgery rehab, CHF)	Designed to maximize independence, which has positive effects across an individual's daily life, which decreases risk factors for hospitalization.
Provider-driven (i.e., "you should do this")	Client-driven (i.e., "I want to do this.")
Focuses on narrow risk factors or on the equipment ("we put in grab bars")	Focuses on person-environment fit, addressing physical function, the home environment, and social drivers through a wholistic approach
Does not last (the effect ends when the intervention ends)	Self-sustaining for long-term impact

Questions?

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"I have enjoyed the CAPABLE National Center office hour meetings. They have been helpful."
Savannah, GA



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12 Feeding America. Facts about senior hunger in America. Found on the internet at <https://www.feedingamerica.org/hunger-in-america/senior-hunger-facts>

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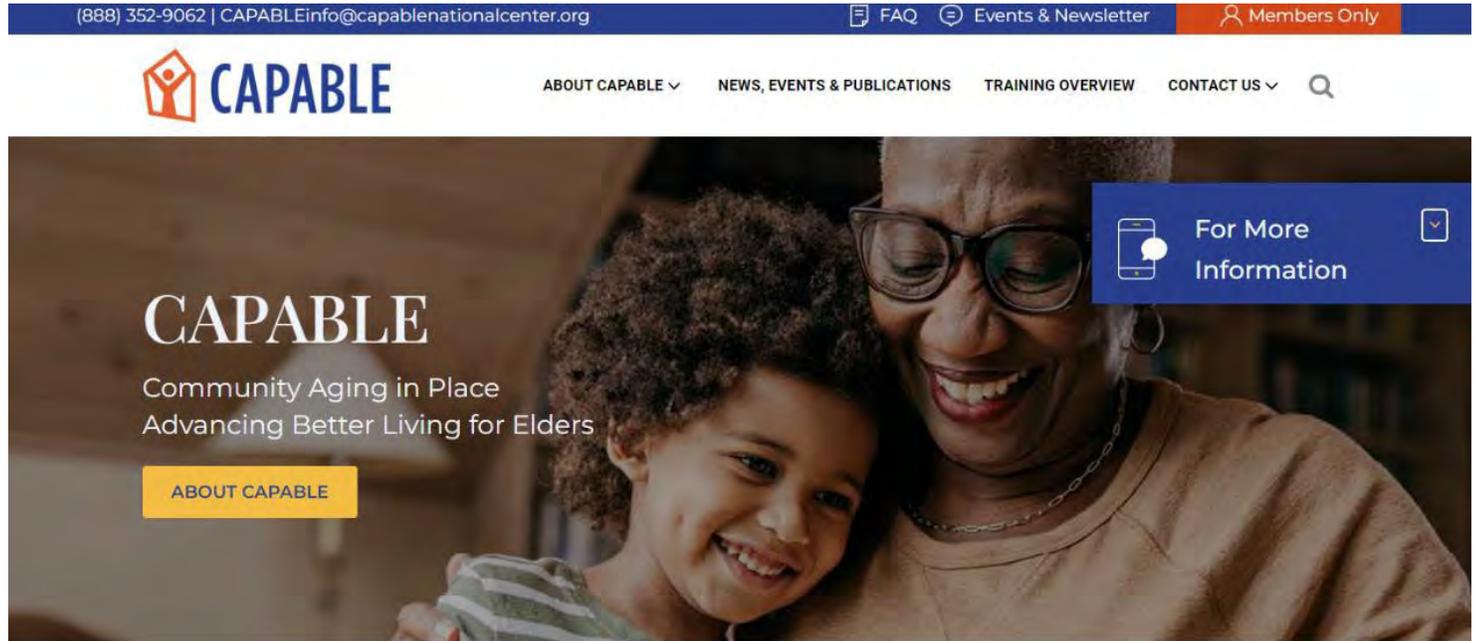
14 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4681302/>

15 Facts About Falls. Centers for Disease Control and Prevention. Found on the internet at <https://www.cdc.gov/falls/facts.html>

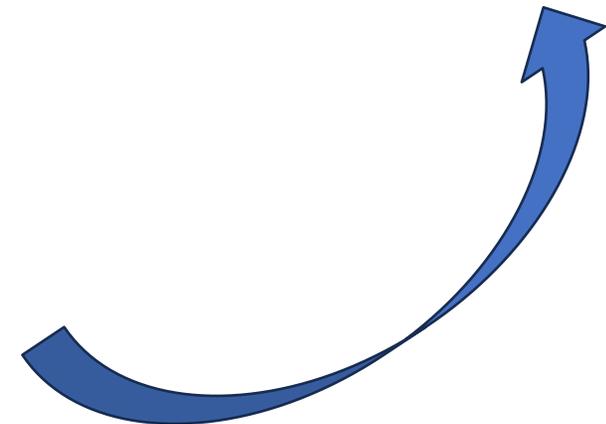
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<https://www.ncoa.org/article/evidence-based-program-capable>

<https://capablenationalcenter.org/news-events-publications/>



For more information:
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CAPABLEinfo@capablenationalcenter.org
<https://capablenationalcenter.org/>







Structural insights into the neuropathology of frontotemporal dementia and ALS

Sami Barmada
Department of Neurology
University of Michigan



Amyotrophic lateral sclerosis (ALS)

“Lateral sclerosis”
Upper motor neuron
Weakness
Muscle stiffness

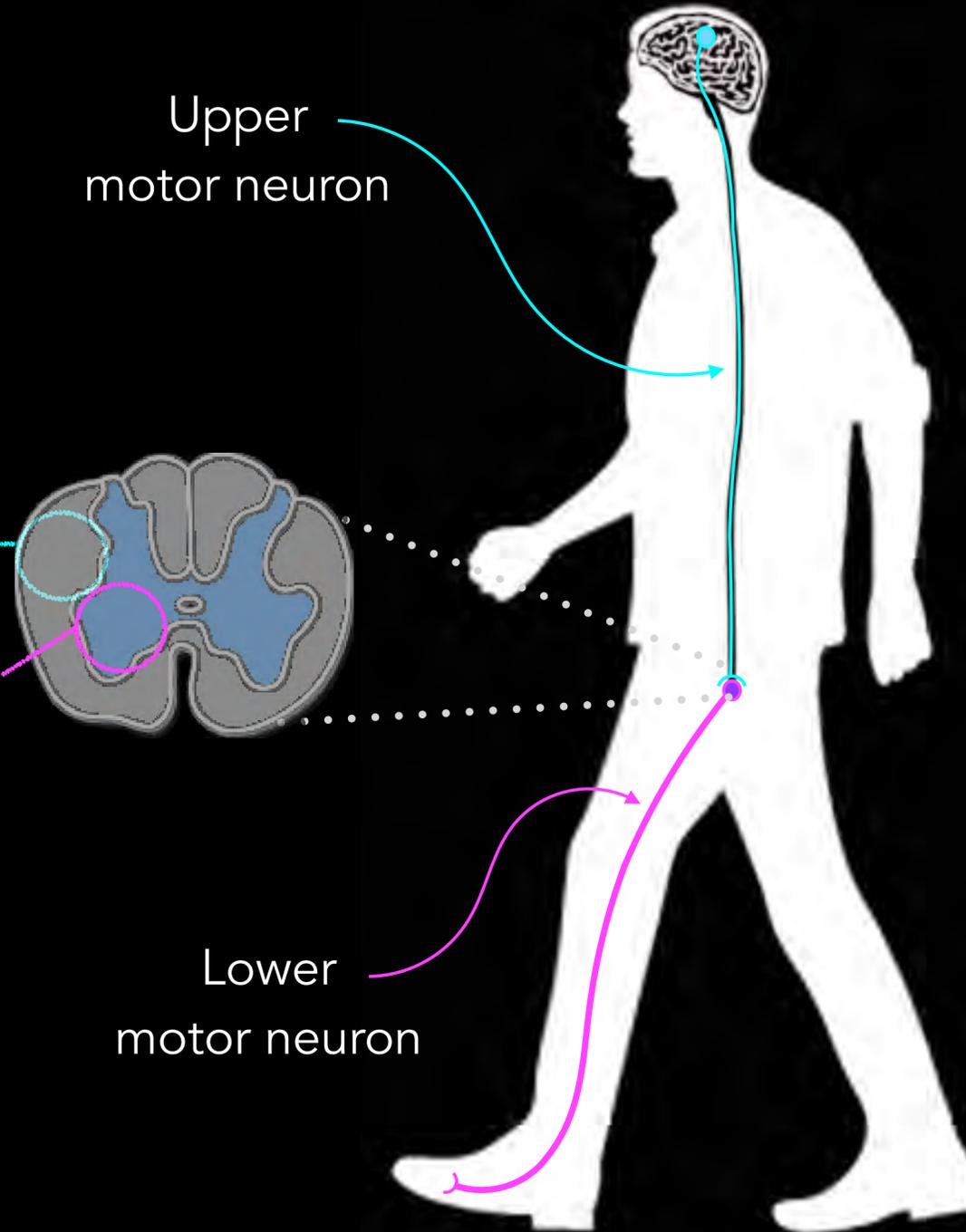
Upper motor neuron

Lateral corticospinal tract

Anterior horn

“Amyotrophic”
Lower motor neuron
Weakness
Muscle shrinkage

Lower motor neuron



Amyotrophic lateral sclerosis (ALS)

“Lateral sclerosis”
Upper motor neuron
Spasticity
Hyperreflexia

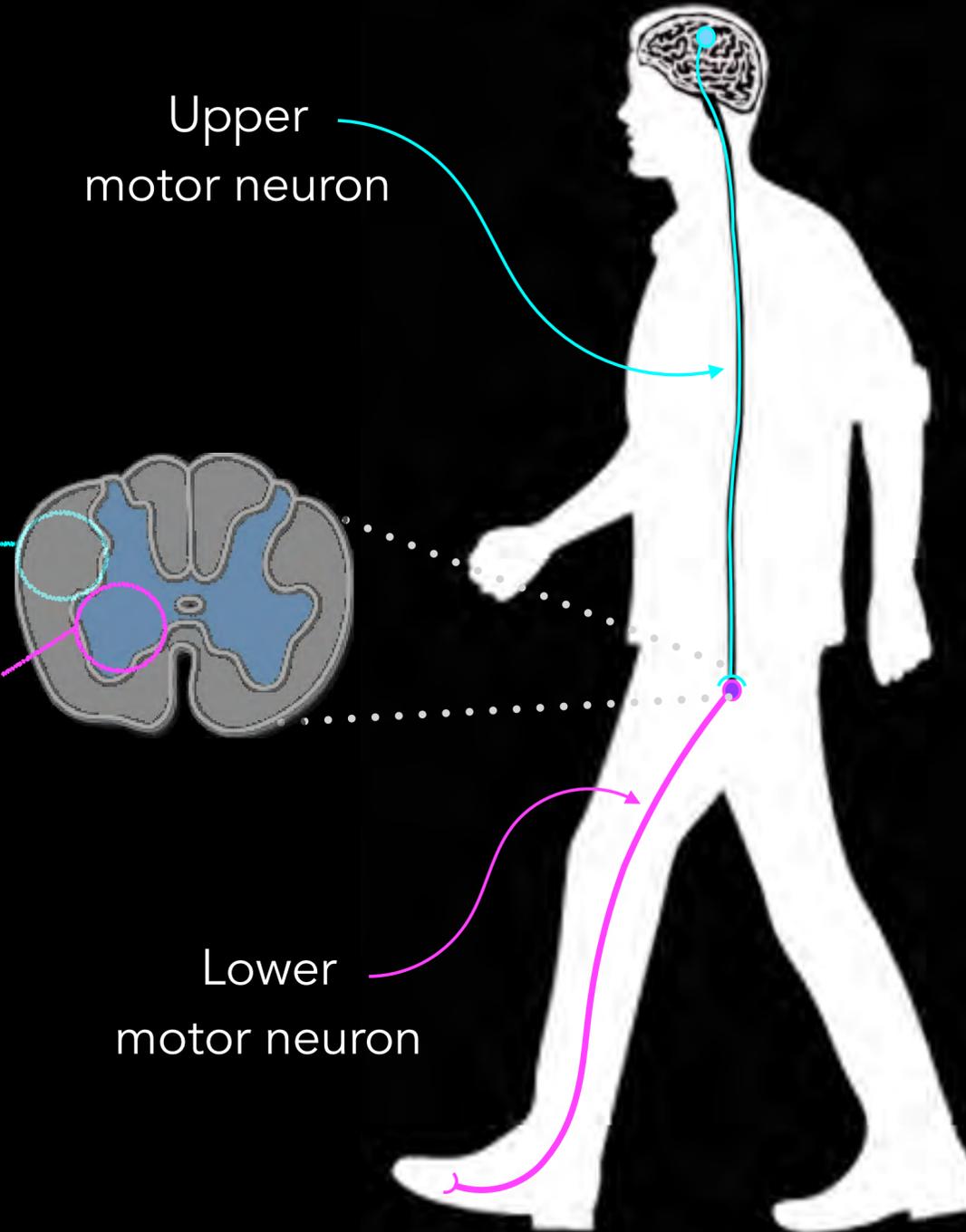
Upper motor neuron

Lateral corticospinal tract

Anterior horn

“Amyotrophic”
Lower motor neuron
Hypotonia
Hyporeflexia

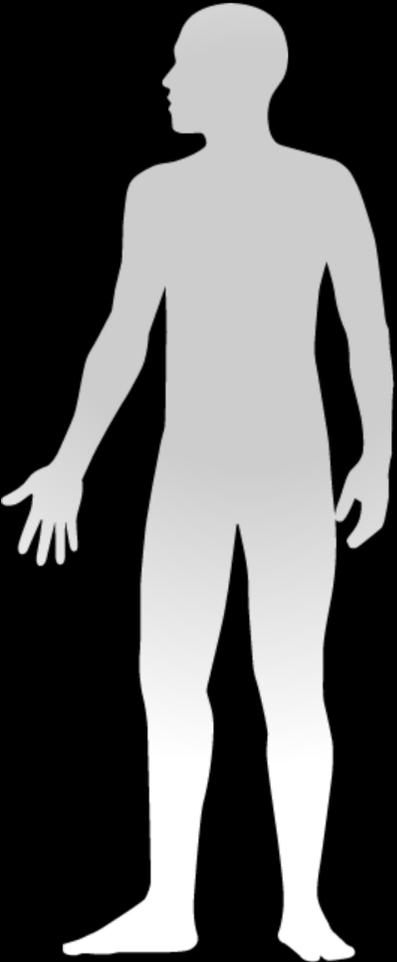
Lower motor neuron



Amyotrophic lateral sclerosis (ALS)

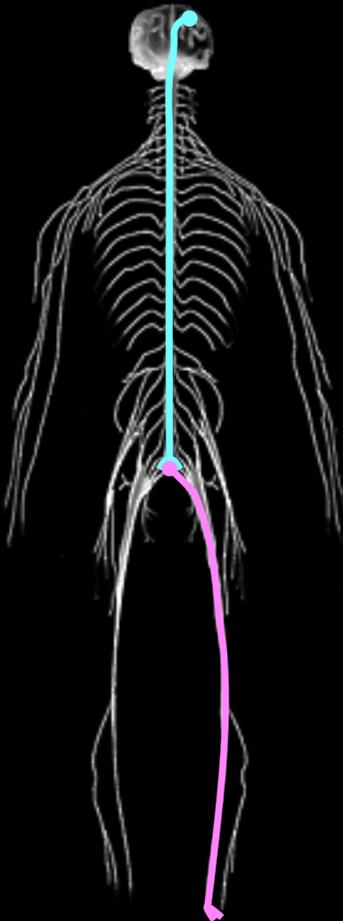
Symptoms

Spasticity
Hyperreflexia



Hypotonia
Hyporeflexia

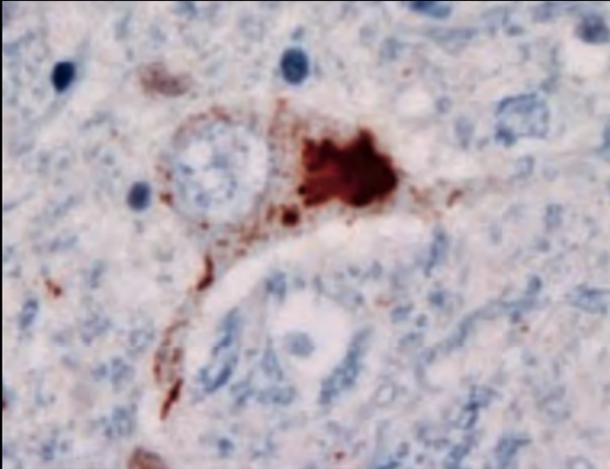
Localization



Diagnosis

Amyotrophic
lateral sclerosis

TDP43



Frontotemporal dementia (FTD)

Behavioral variant FTD (bvFTD)

Apathy

Social withdrawal

Disinhibition

Lack of empathy

Obsessions / compulsions

Eating disorder

Poor judgment



Frontotemporal dementia (FTD)



Language variants (primary progressive aphasia, PPA)

Reduced output

Reduced vocabulary

Effortful speech

Substitutions / combinations

Perseveration

Frontotemporal dementia (FTD)

Symptoms

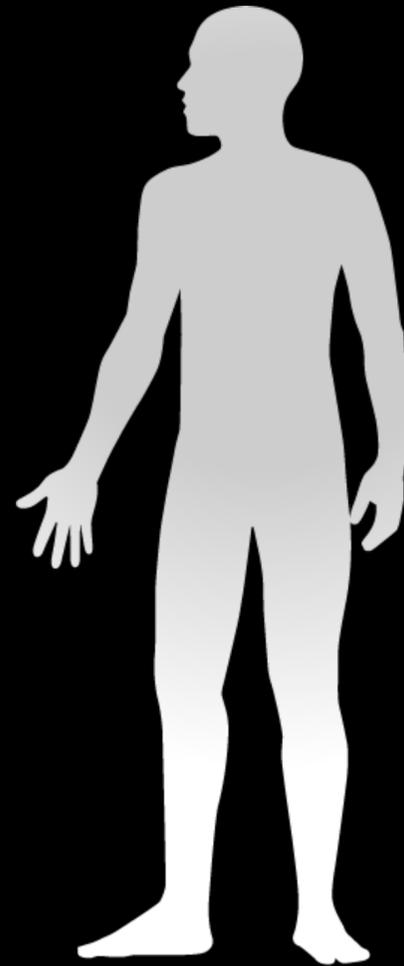
Localization

Diagnosis

Personality change

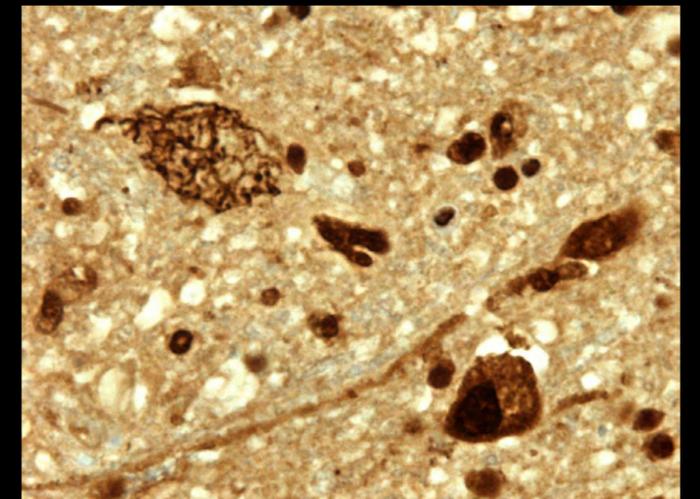
Word-finding
difficulties

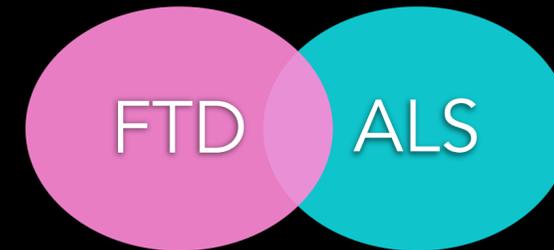
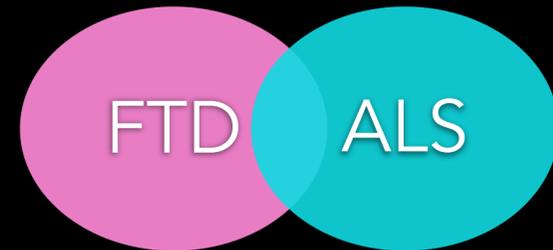
Lack of motivation



Frontotemporal
dementia

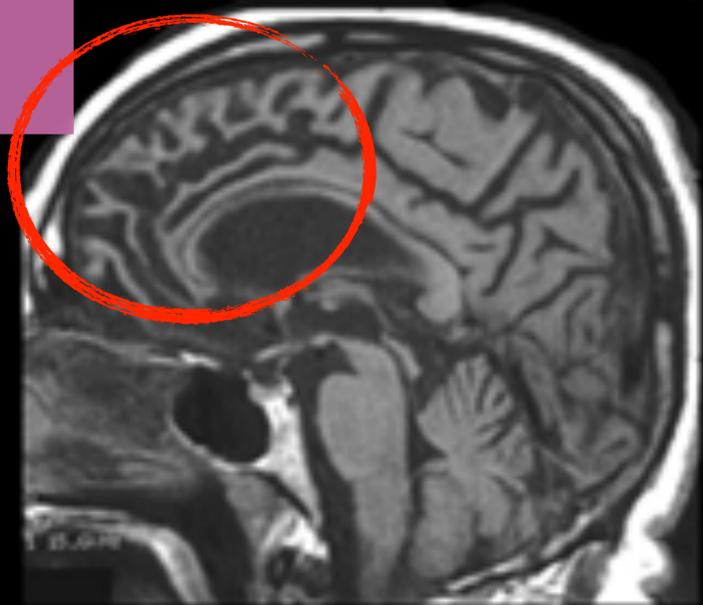
TDP43



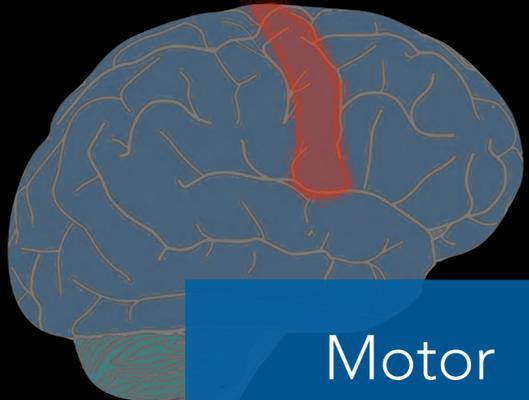


FTD

?



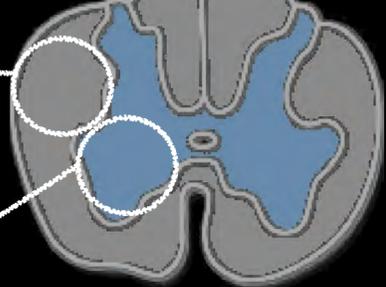
ALS

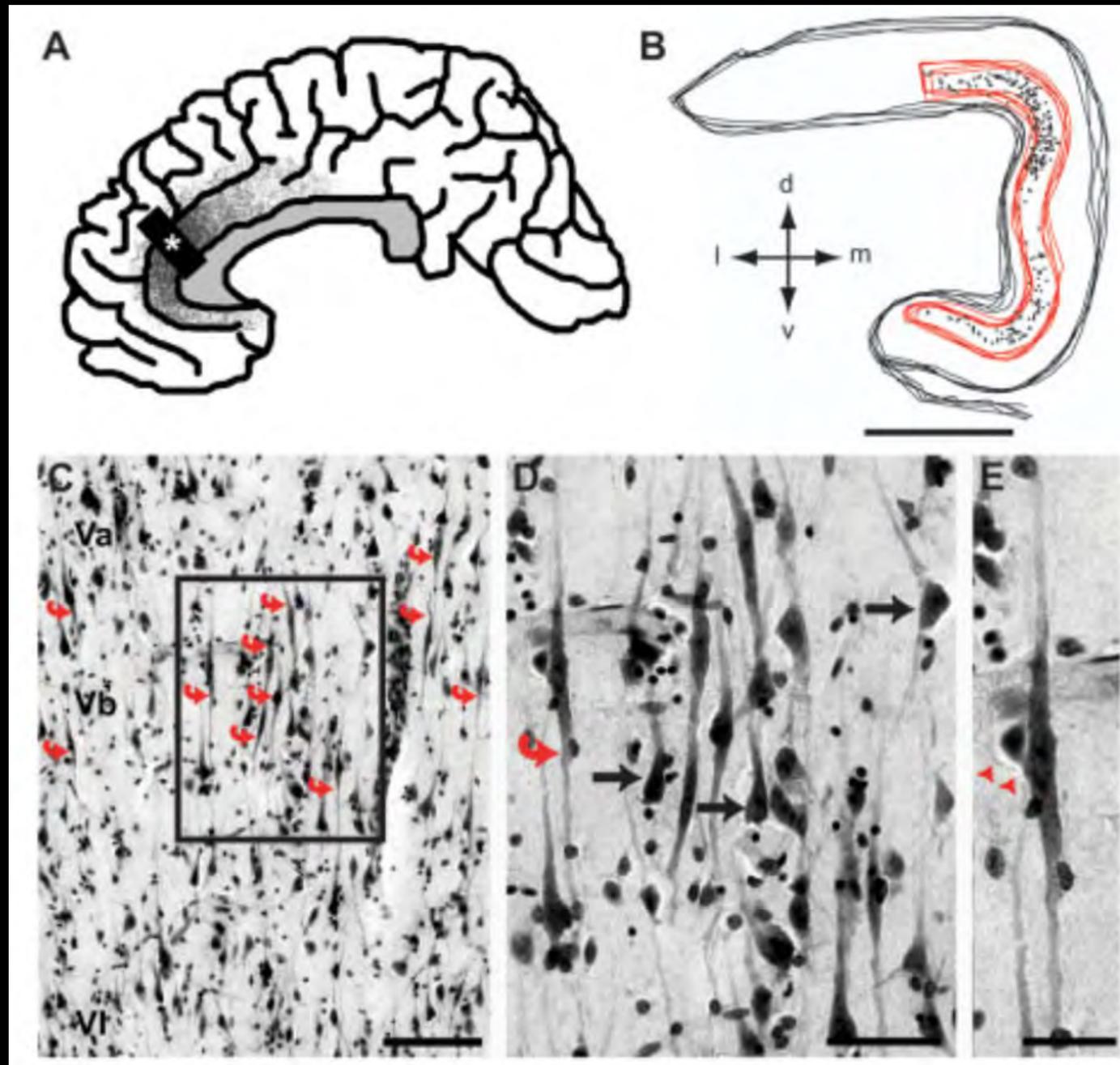


Motor neurons

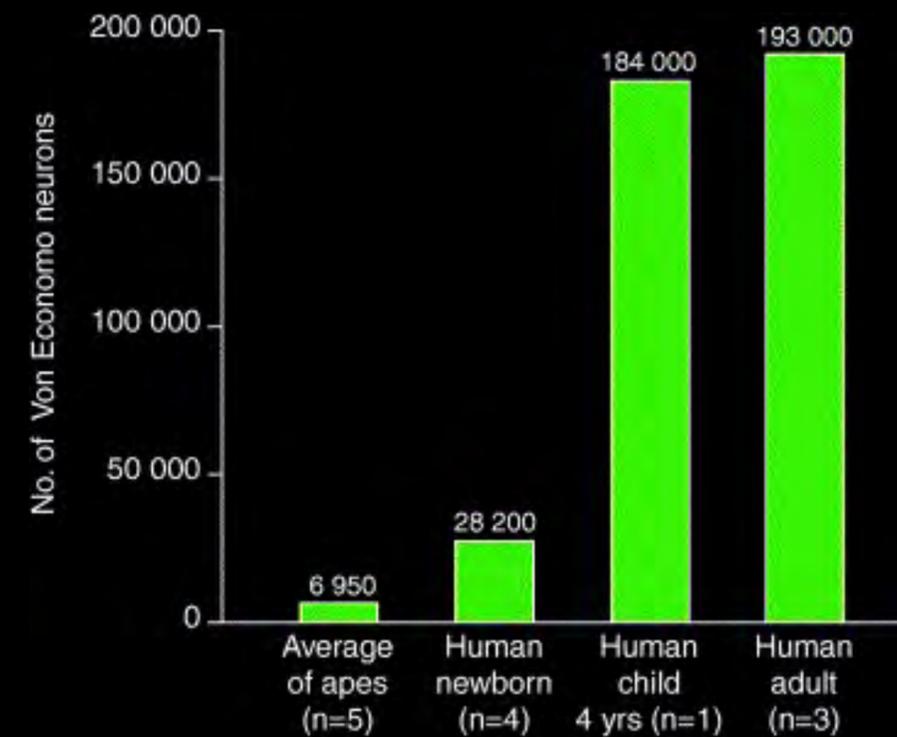
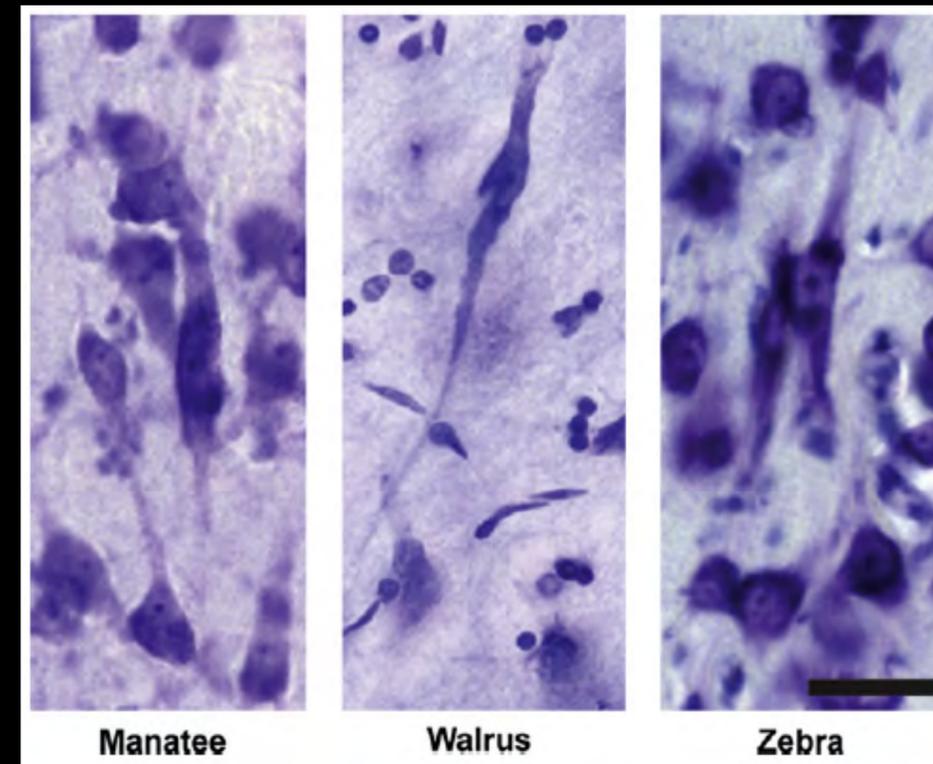
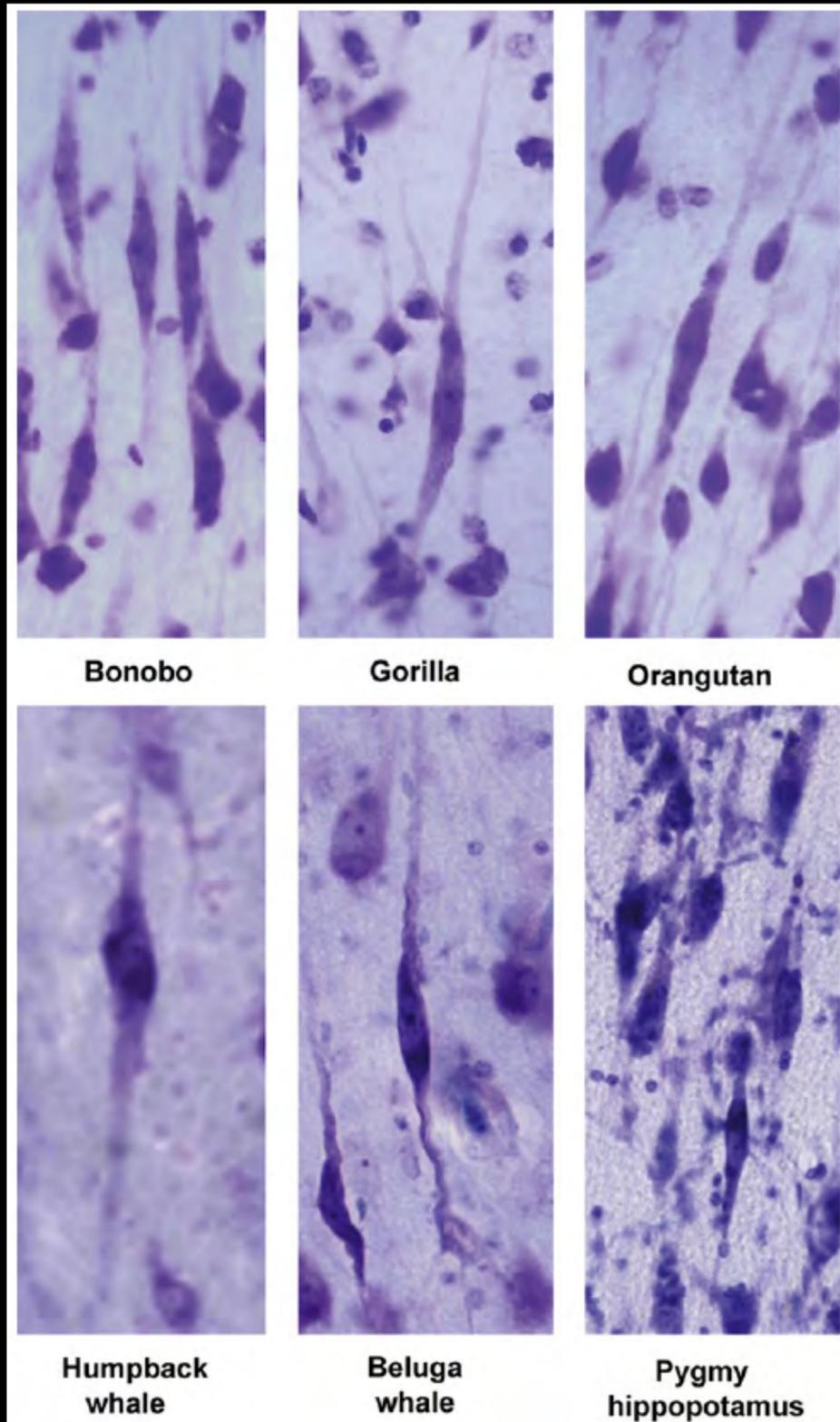
Lateral corticospinal tract

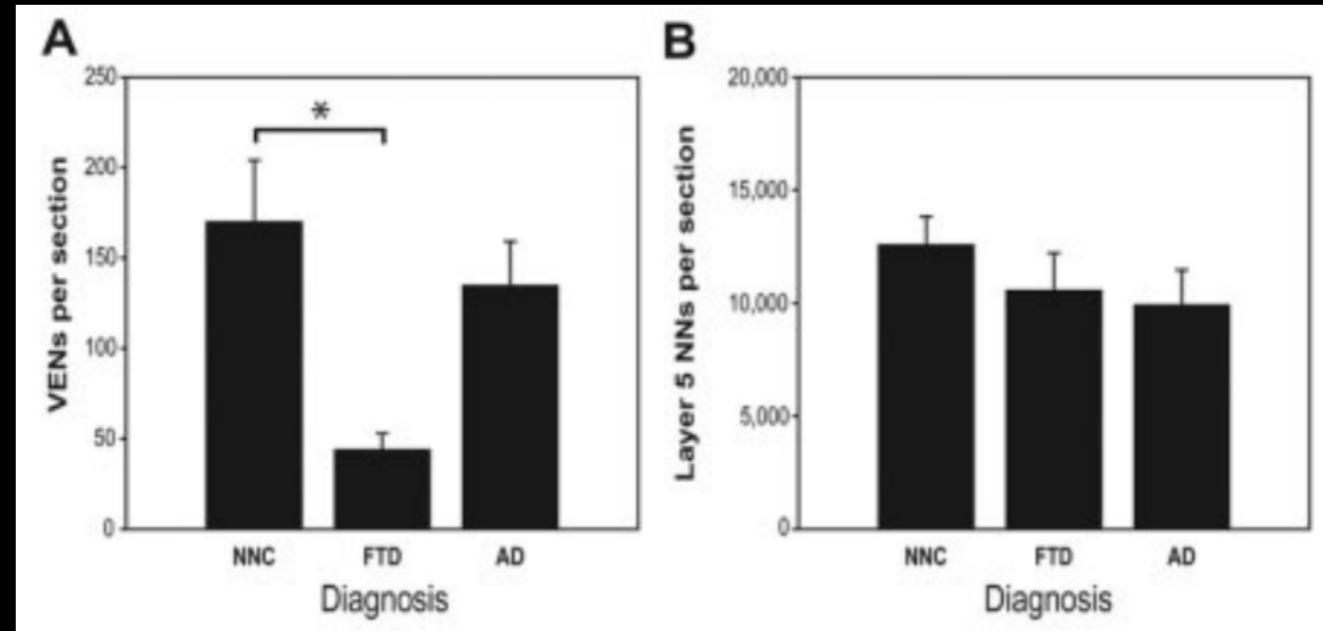
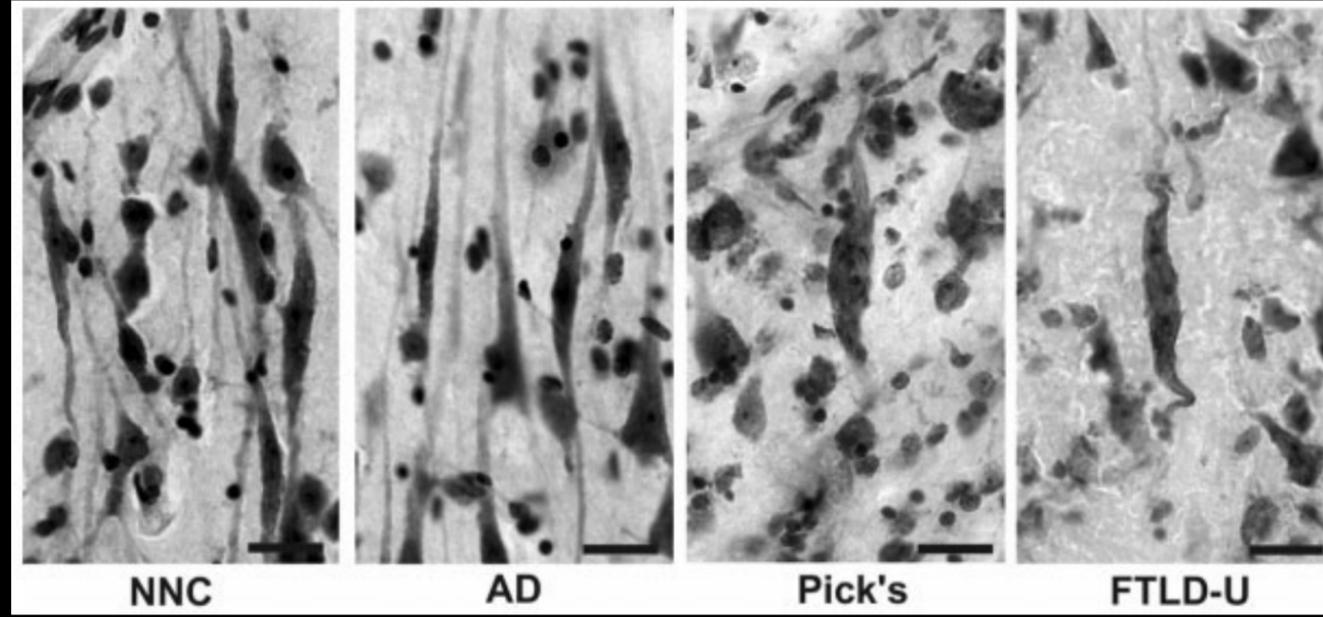
Anterior horn



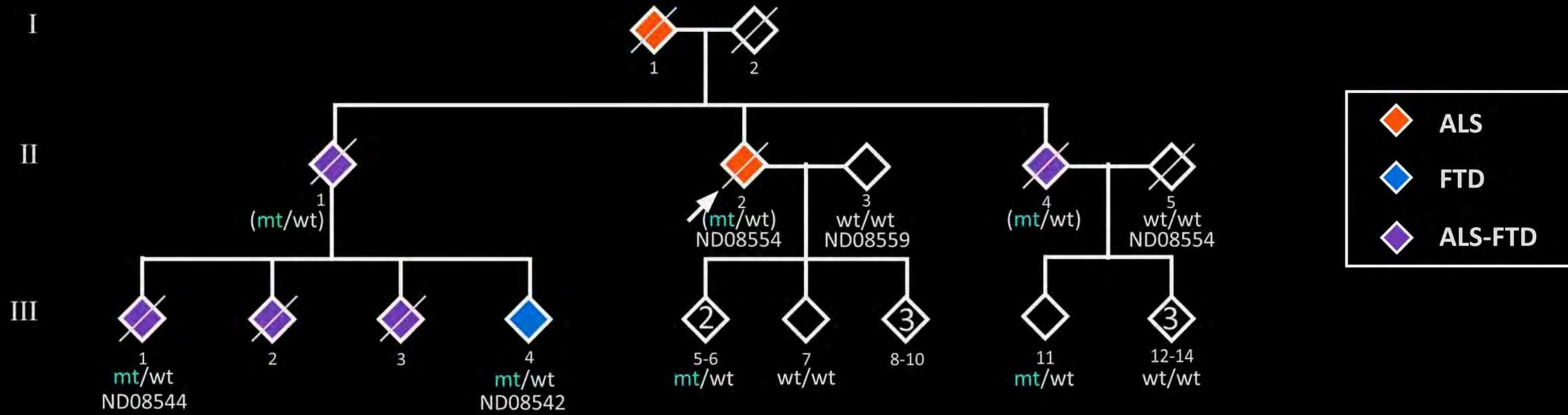


Von Economo neurons
(VENs)





Genetics of ALS and FTD



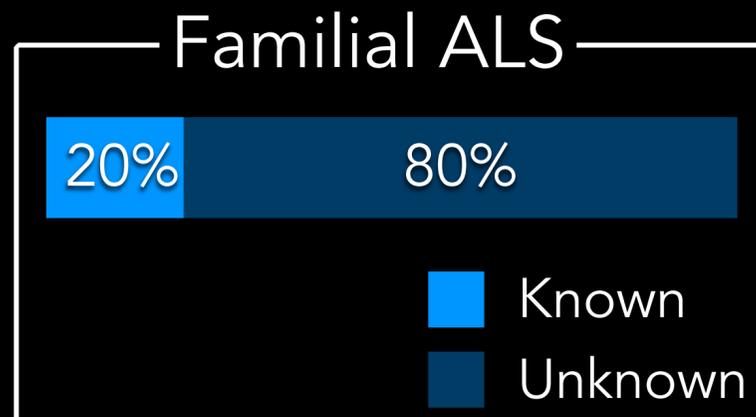
Genetics of ALS and FTD

2004

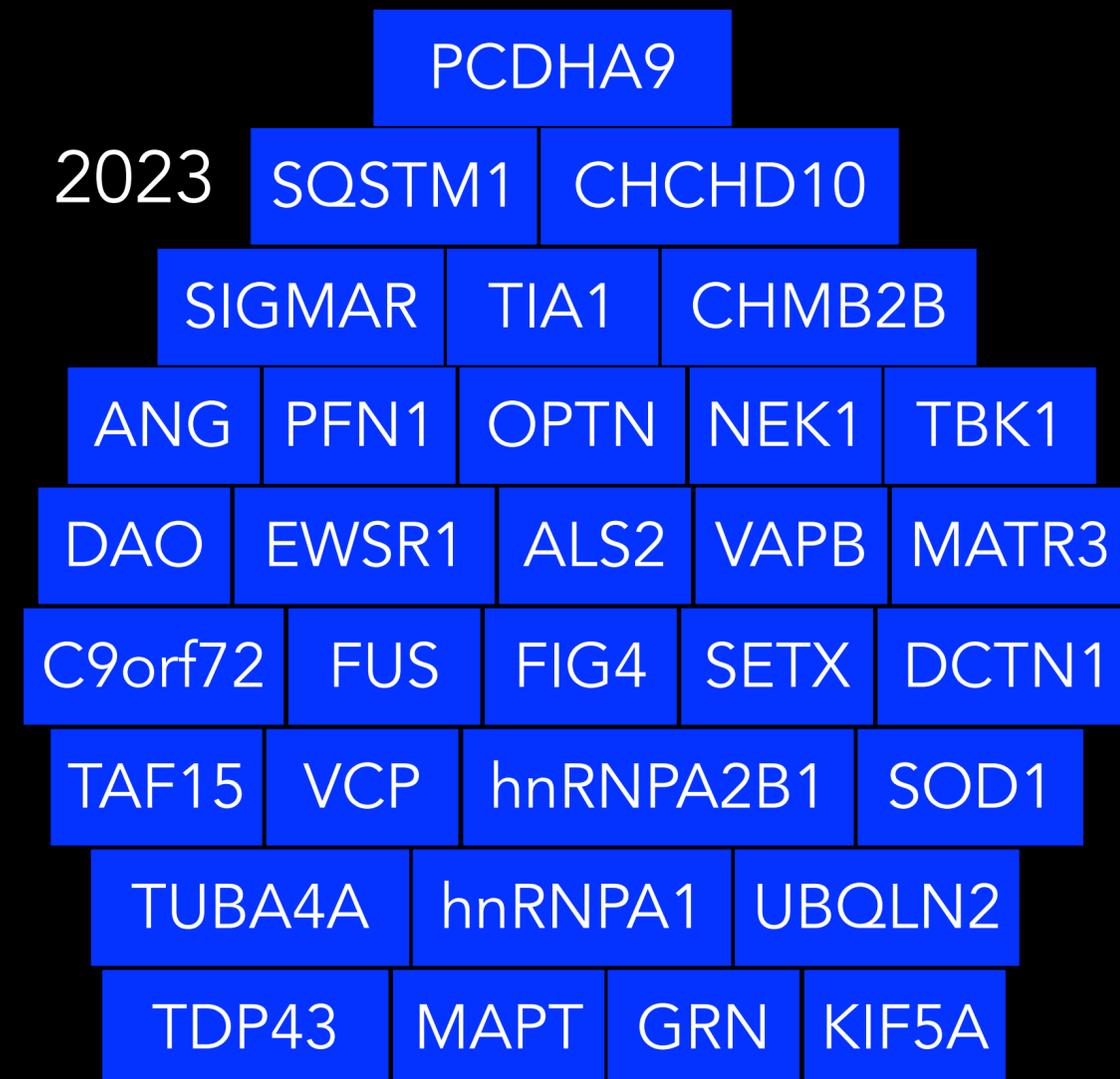
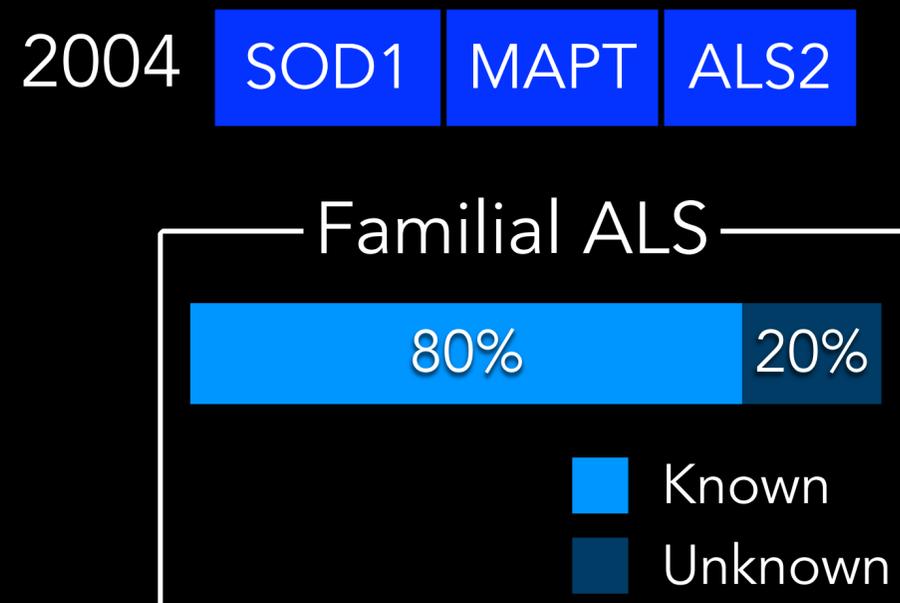
SOD1

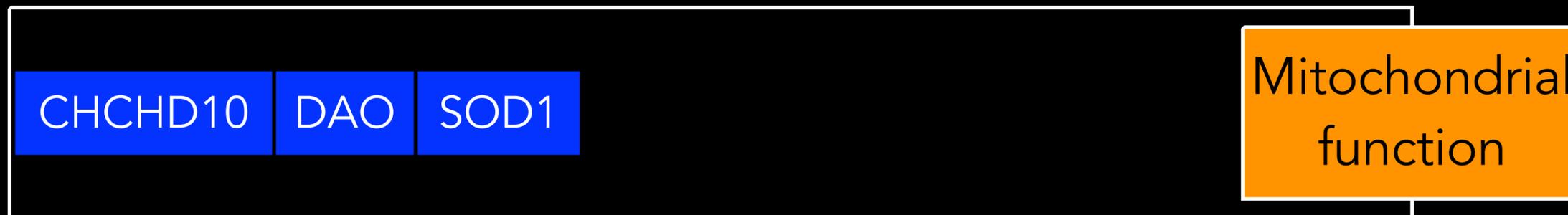
MAPT

ALS2



Genetics of ALS and FTD





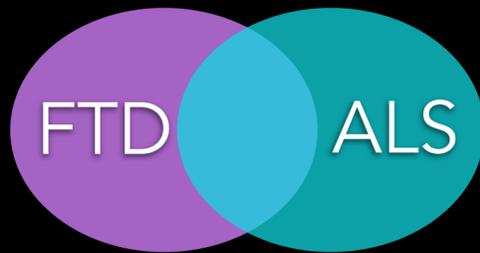


- | | | | | | | | |
|------|------|-------|--------|-------|-------|--------|--------|
| PFN1 | FUS | TAF15 | SETX | EWSR1 | DCTN1 | TUBA4A | PCDHA9 |
| DAO | FIG4 | ANG | SIGMAR | SOD1 | ALS2 | NEK1 | KIF5A |

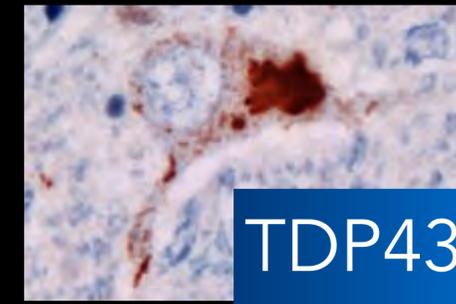
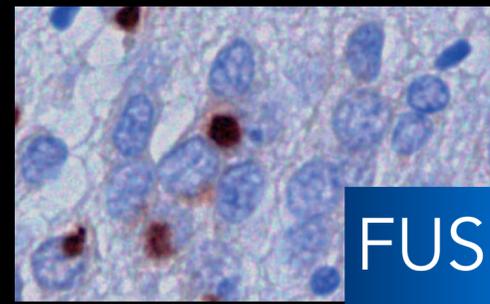
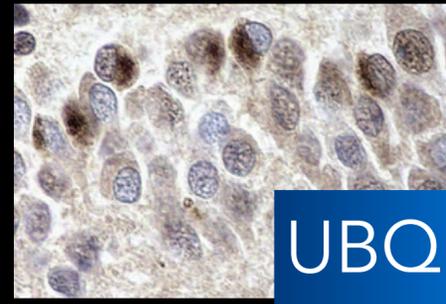
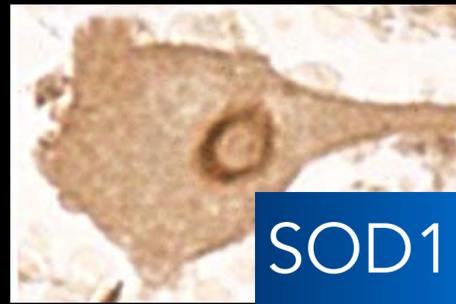
FTD



ALS



- | | | | | | |
|-------|-----------|---------|---------|-------|------|
| MATR3 | VCP | OPTN | SQSTM1 | GRN | TIA1 |
| VAPB | UBQLN2 | CHMB2B | C9orf72 | TDP43 | MAPT |
| TBK1 | hnRNPA2B1 | hnRNPA1 | CHCHD10 | | |



SOD1

CHMB2B

FUS

SETX

VAPB

DAO

EWSR1

UBQLN2

TDP43

MATR3

TAF15

VCP

GRN

ALS2

C9orf72

OPTN

hnRNPA1

SIGMAR

FIG4

TBK1

SQSTM1

PFN1

TIA1

CHCHD10

KIF5A

ANG

DCTN1

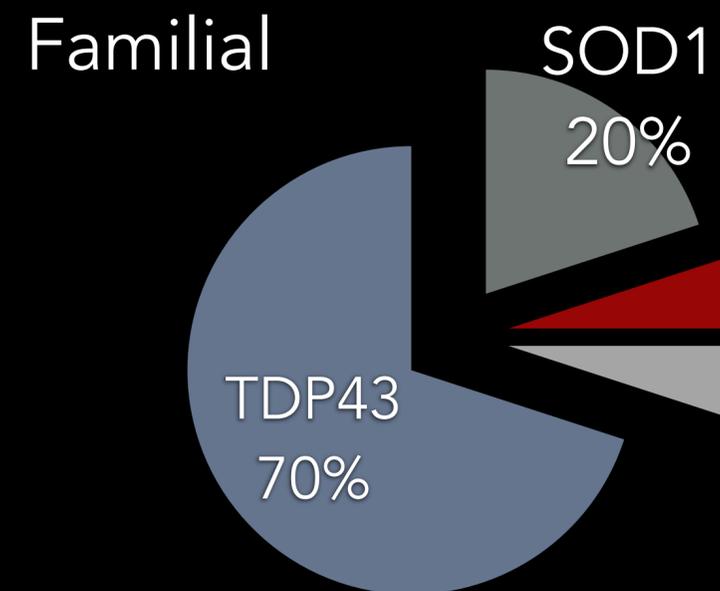
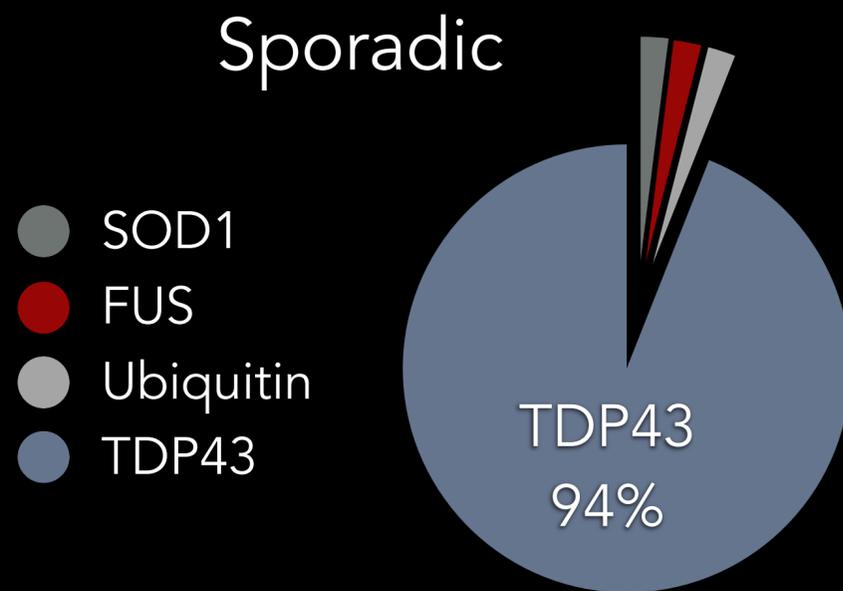
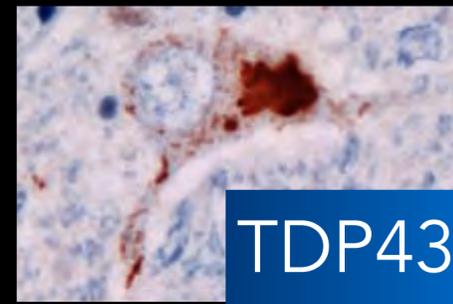
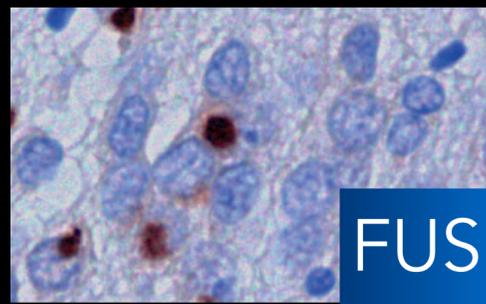
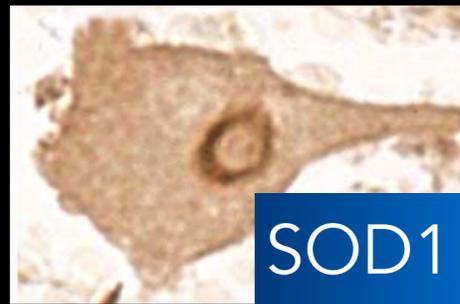
PCDHA9

TUBA4A

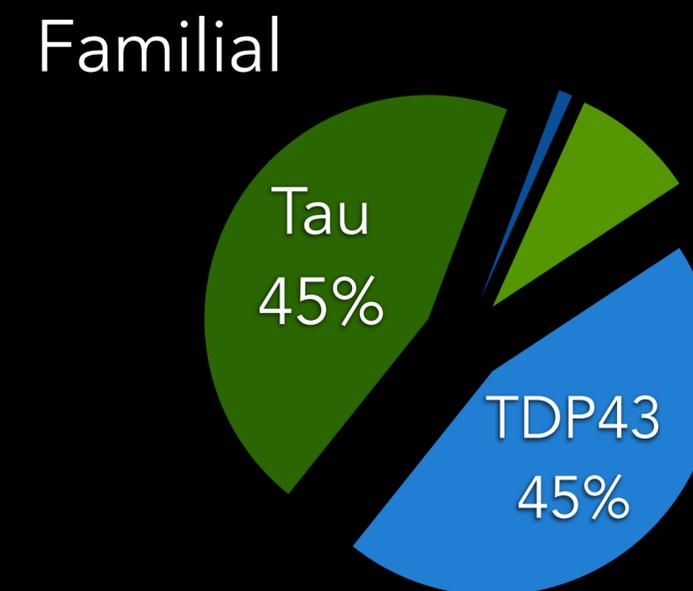
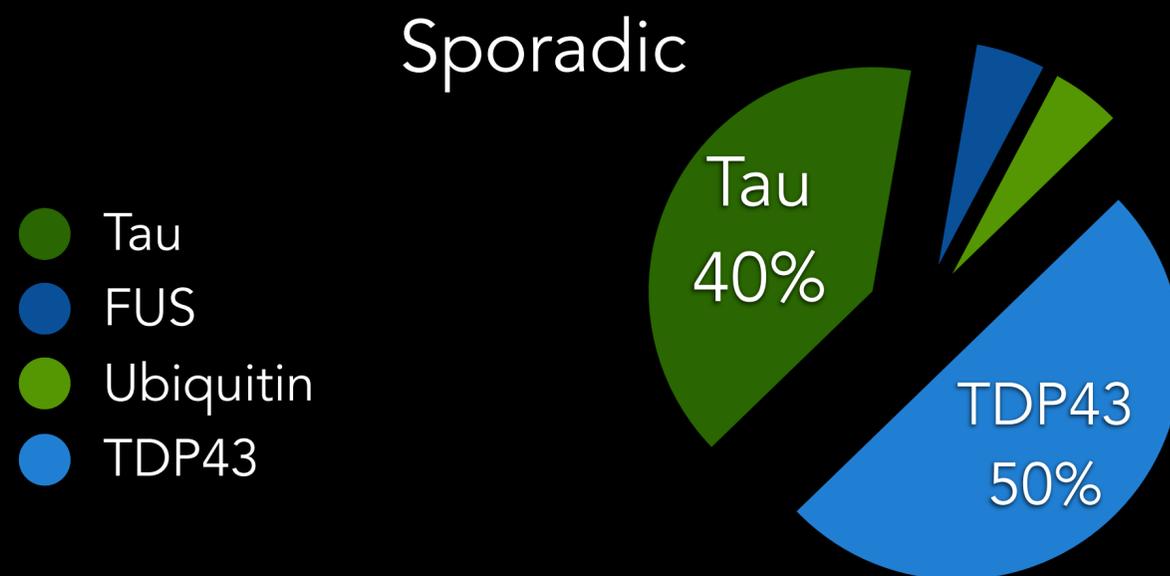
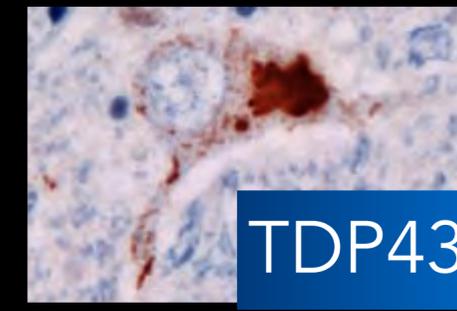
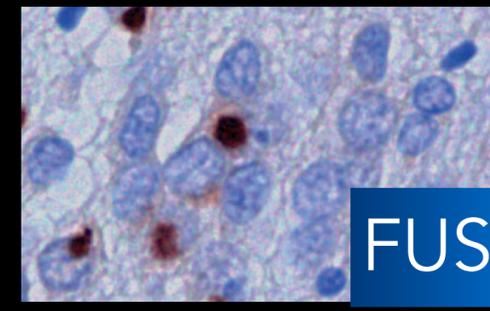
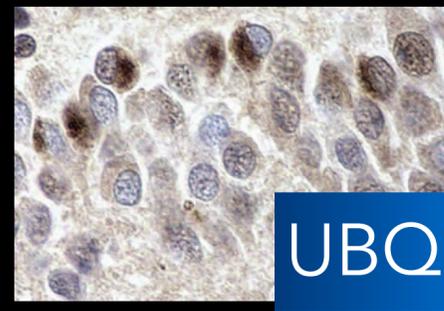
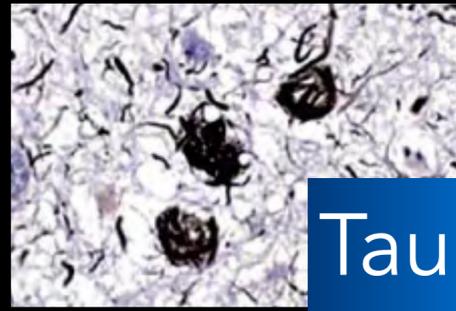
hnRNPA2B1

33 genes associated with ALS/FTD
3/4 (25) result in TDP43 pathology

How common is TDP43 pathology in ALS?

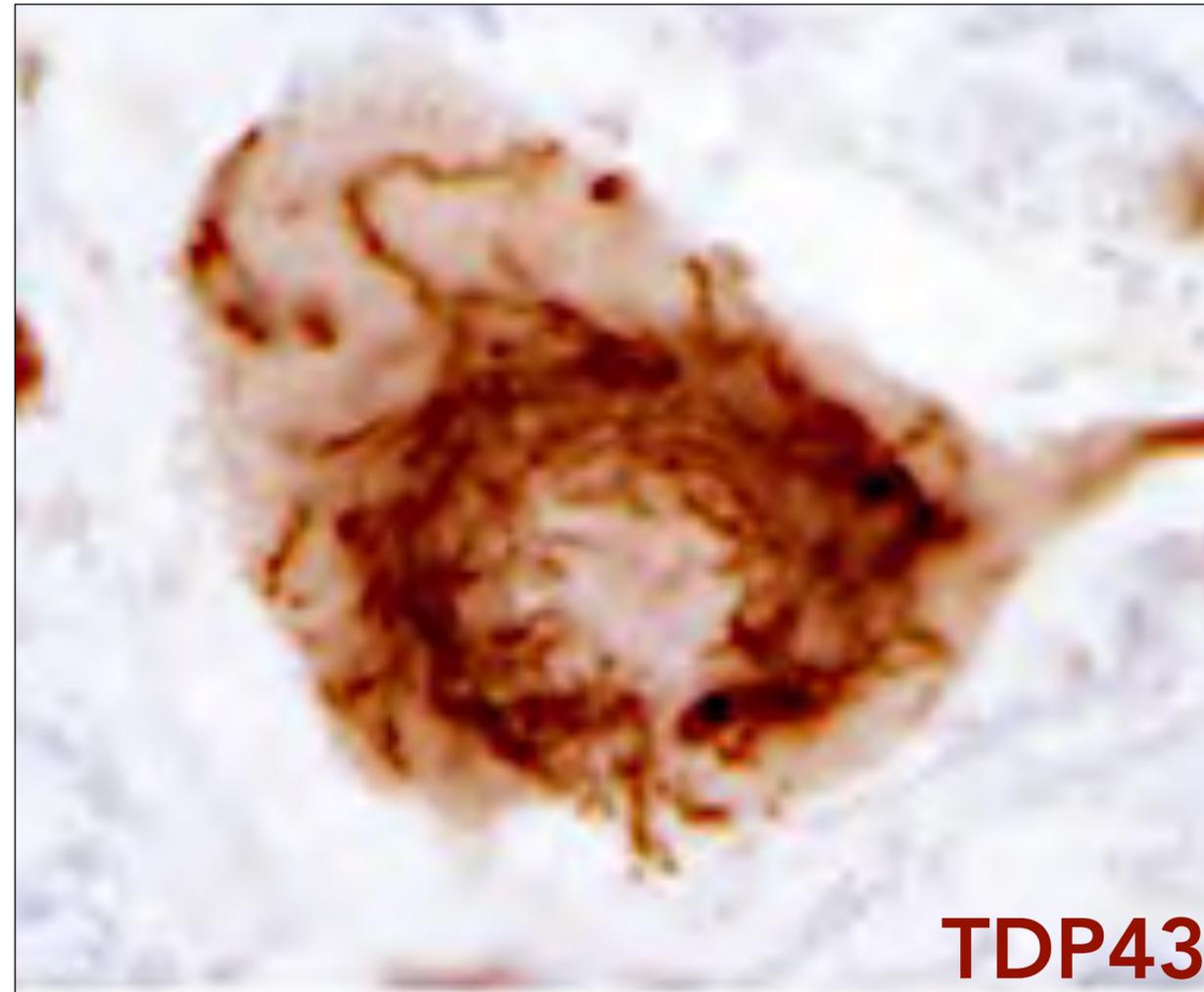


How common is TDP43 pathology in FTD?



Summary and next steps (1)

- ALS and FTD are related disorders
 - Clinical overlap
 - Genetic overlap
 - Pathologic overlap (TDP43)
- TDP43-based biomarkers and treatments are *severely* lacking



Amyotrophic lateral sclerosis (ALS)
Frontotemporal dementia (FTD)

What are the triggers for TDP43 pathology?
What are the consequences?

Humans have ~100,000 genes

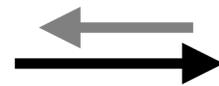
Approximately 1/3 (**30,000**) are recognized by TDP43

TDP43 pathology → RNA misprocessing

Humans have ~100,000 genes

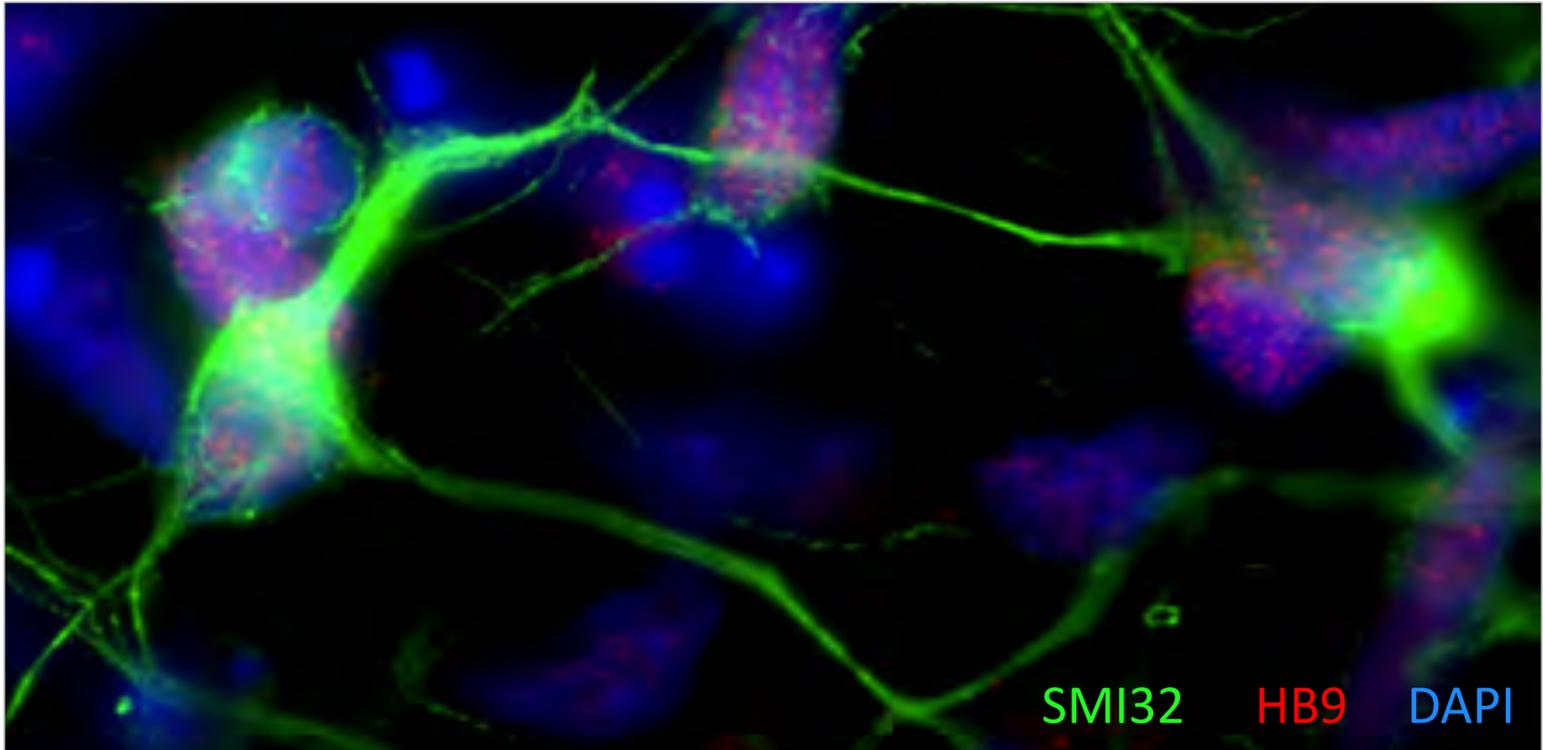
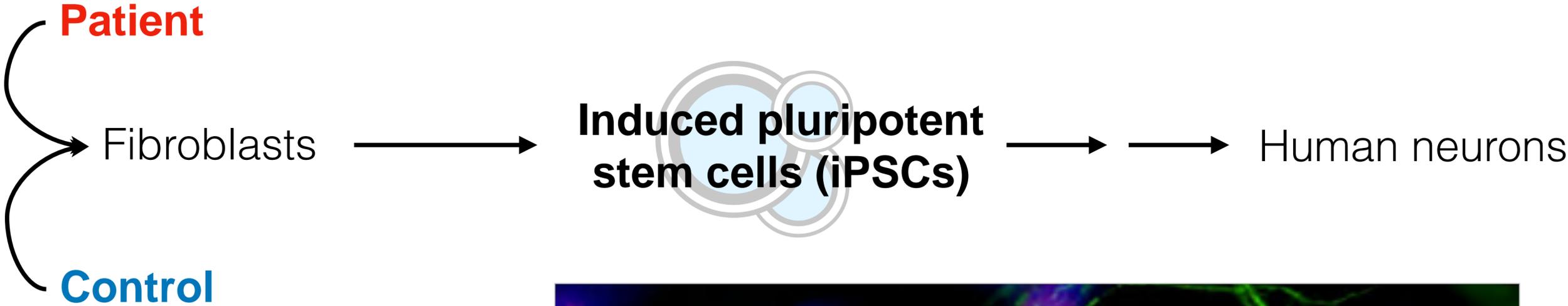
Approximately 1/3 (**30,000**) are recognized by TDP43

RNA misprocessing



TDP43 pathology

Human neurons



RNA dependent TDP43 mislocalization

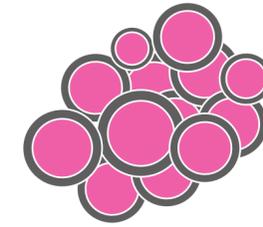
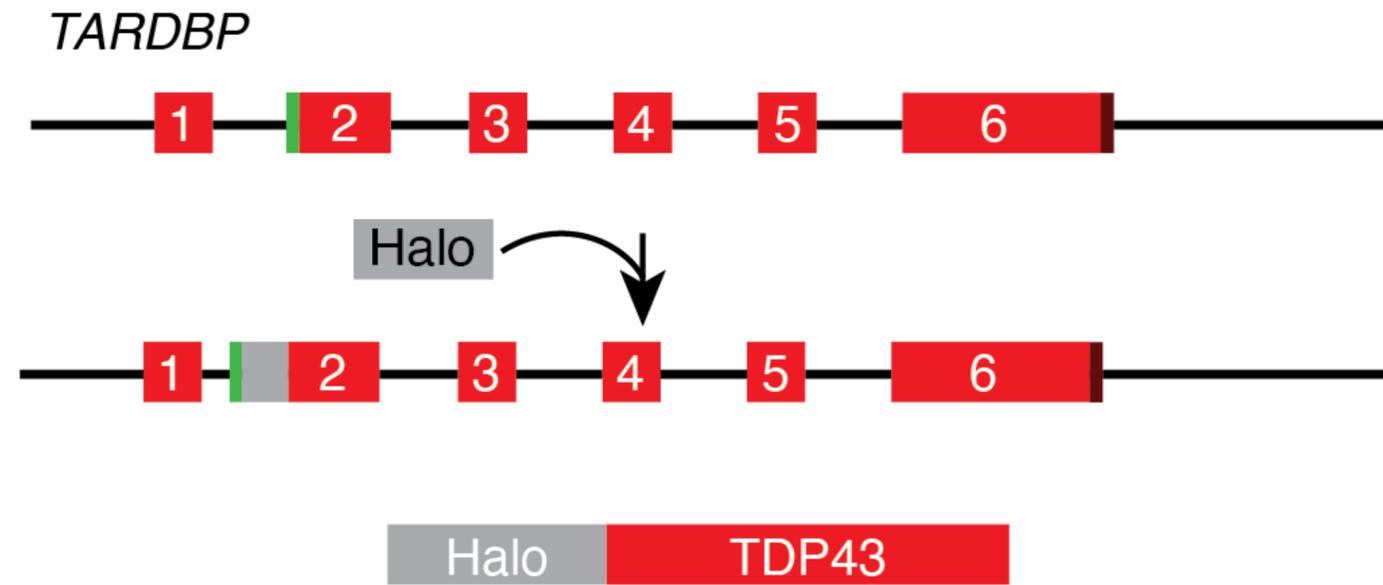


Shyamal Mosalaganti

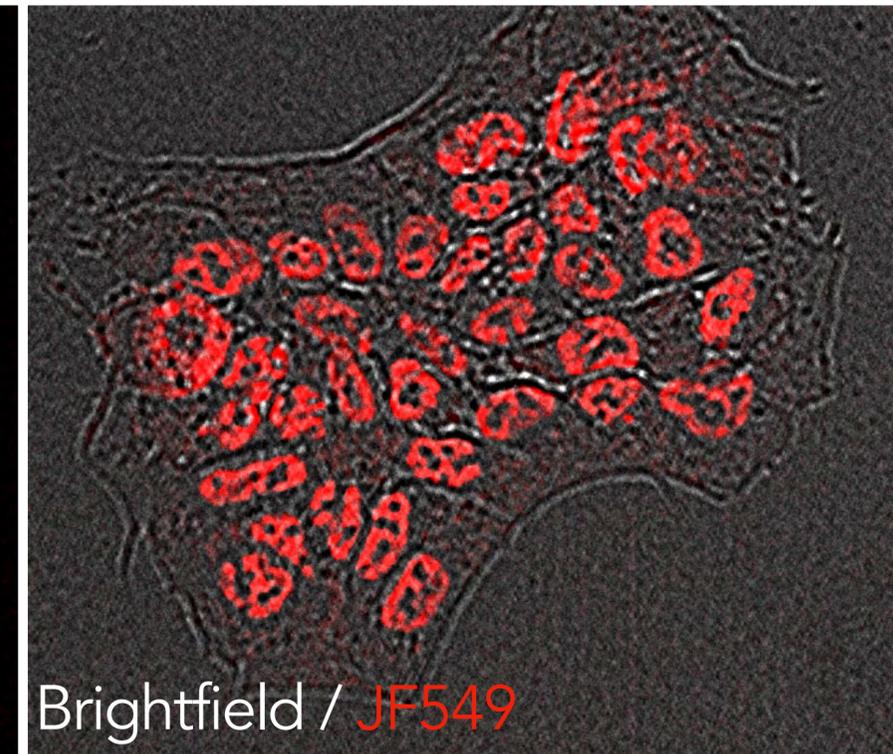
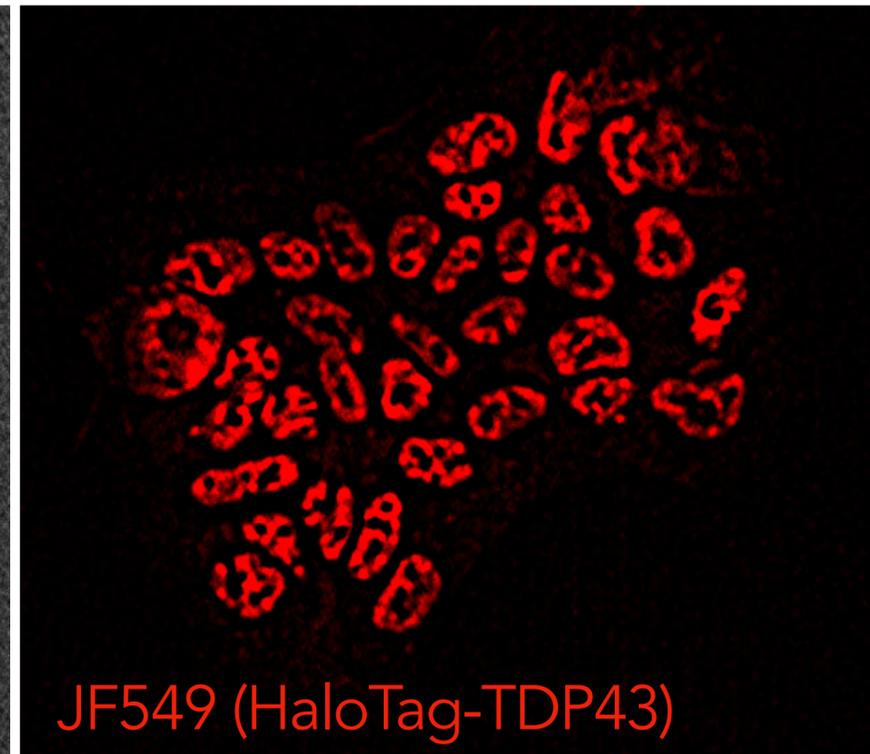
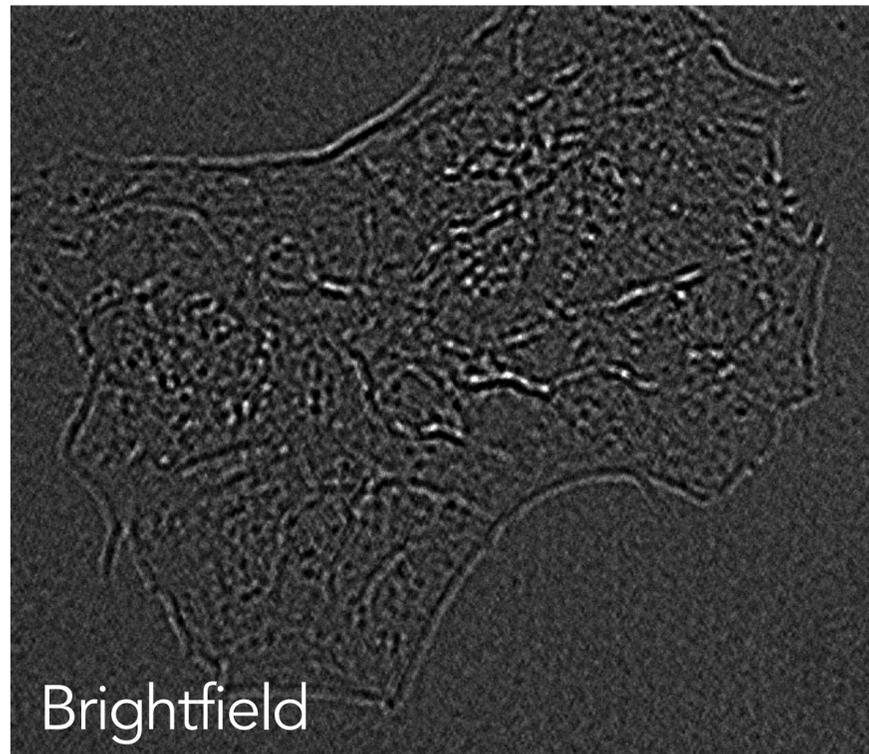


Amanda Erwin

RNA dependent TDP43 mislocalization

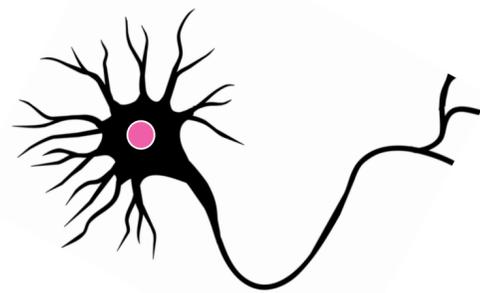
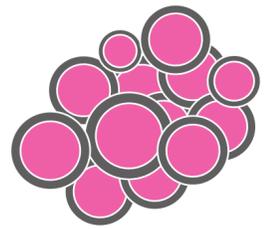


HaloTag-TDP43
iPSCs

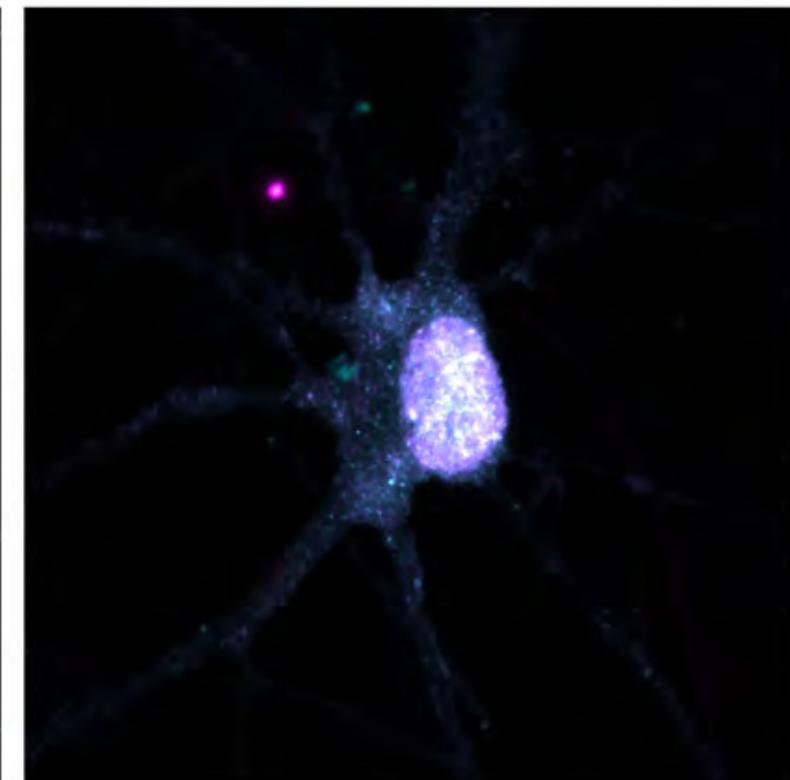
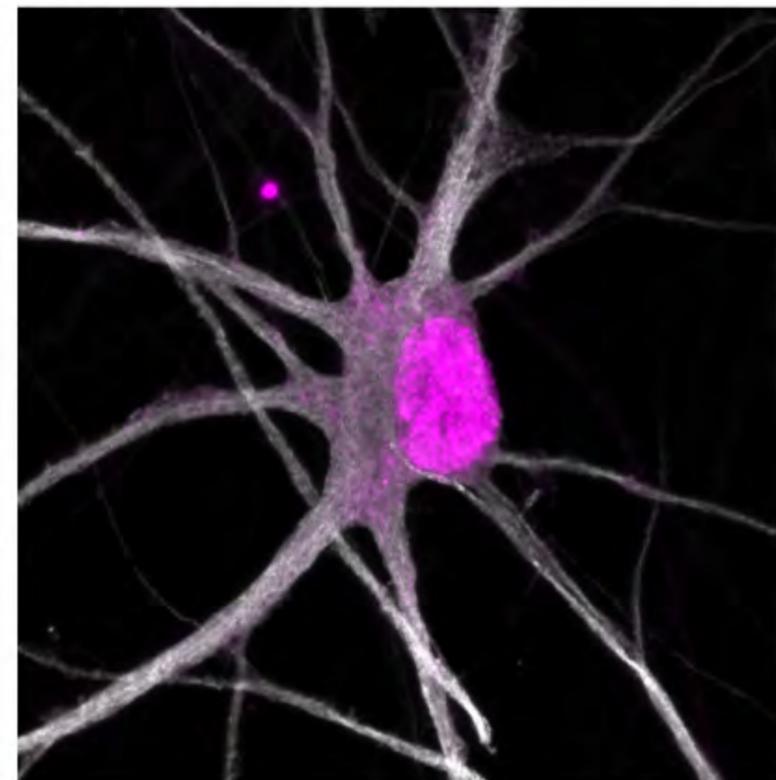
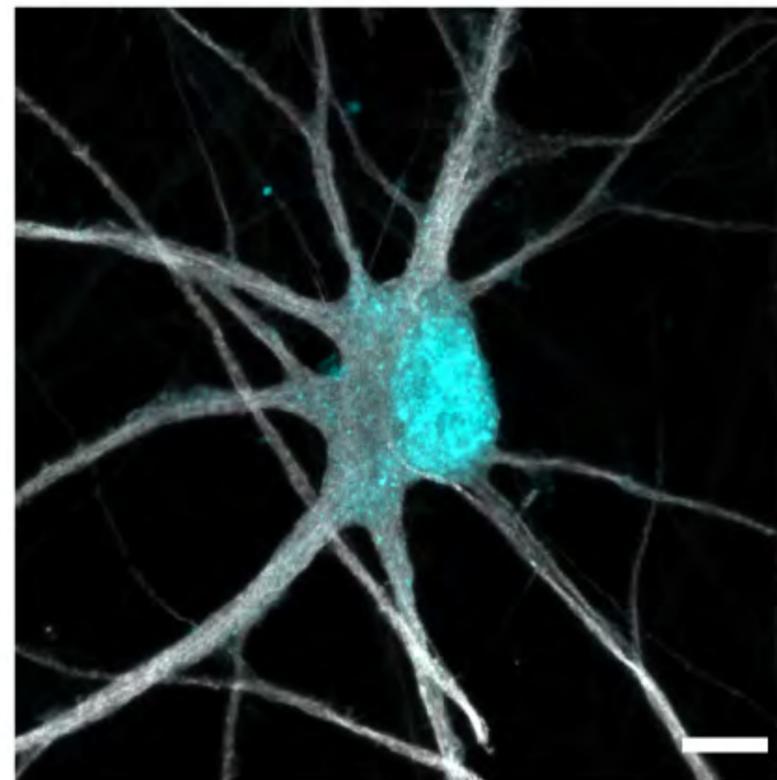
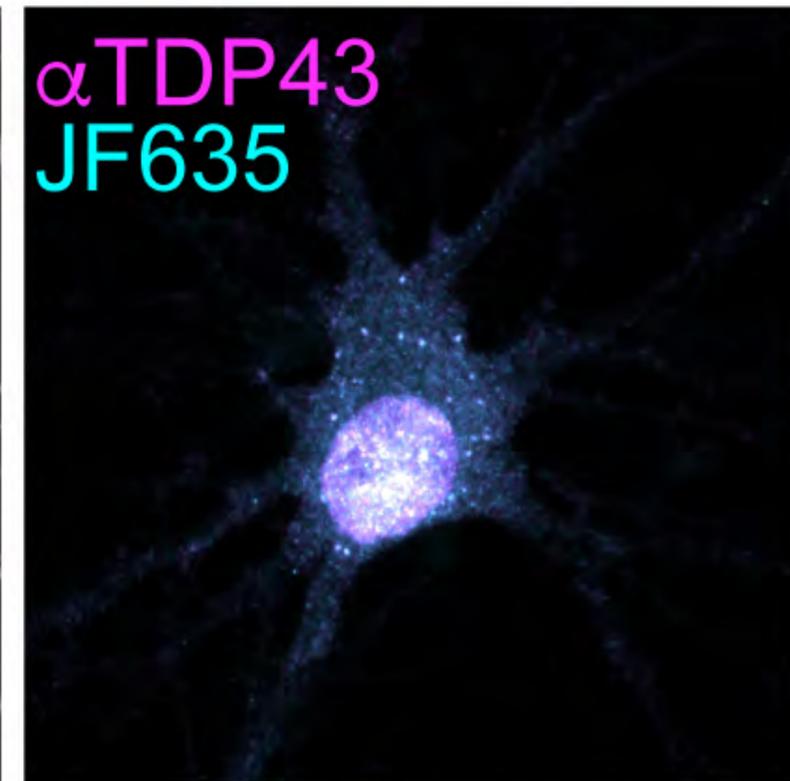
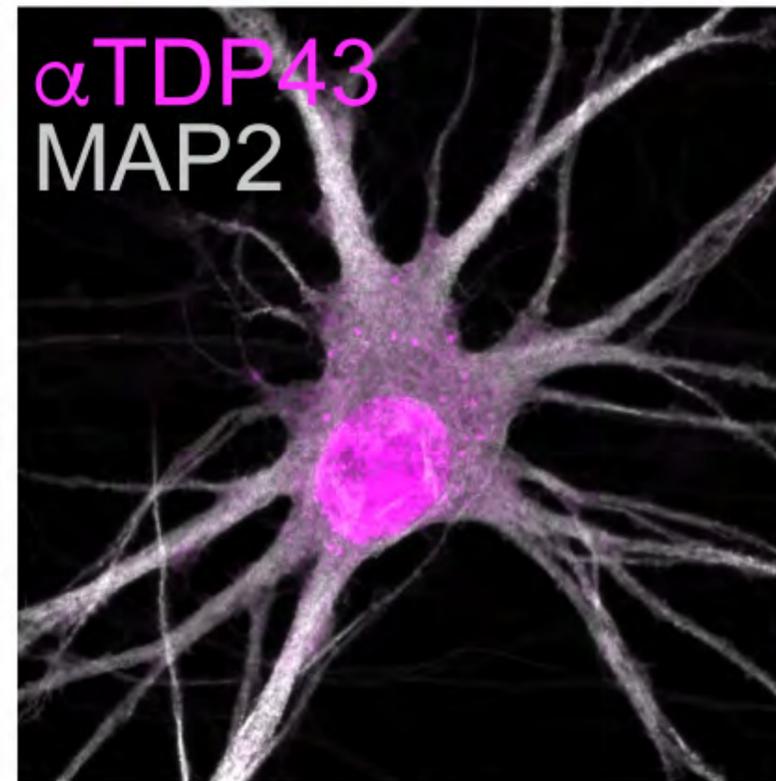
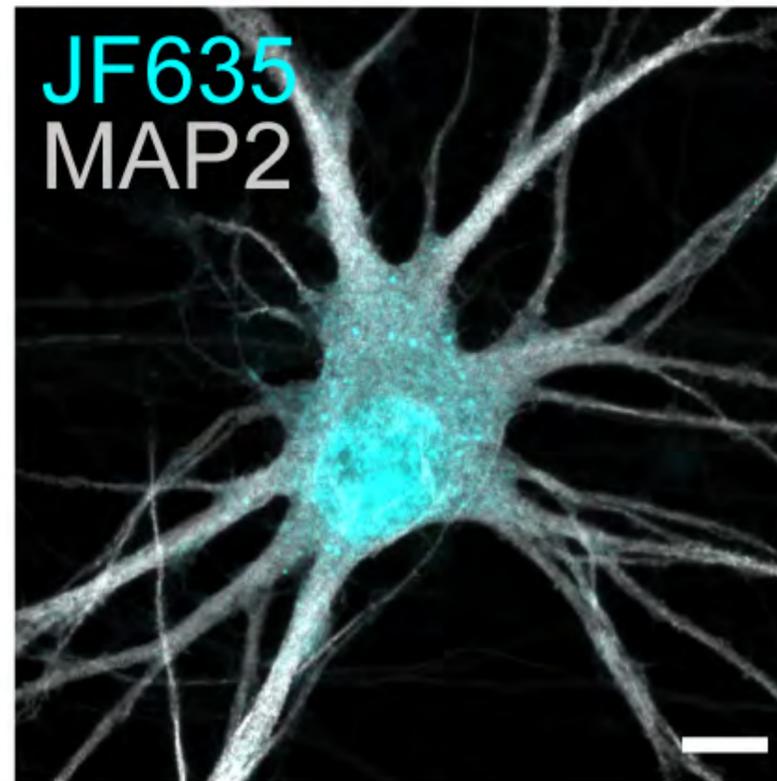


HaloTag-TDP43 iNeurons

HaloTag-TDP43
iPSCs



HaloTag-TDP43
iNeurons

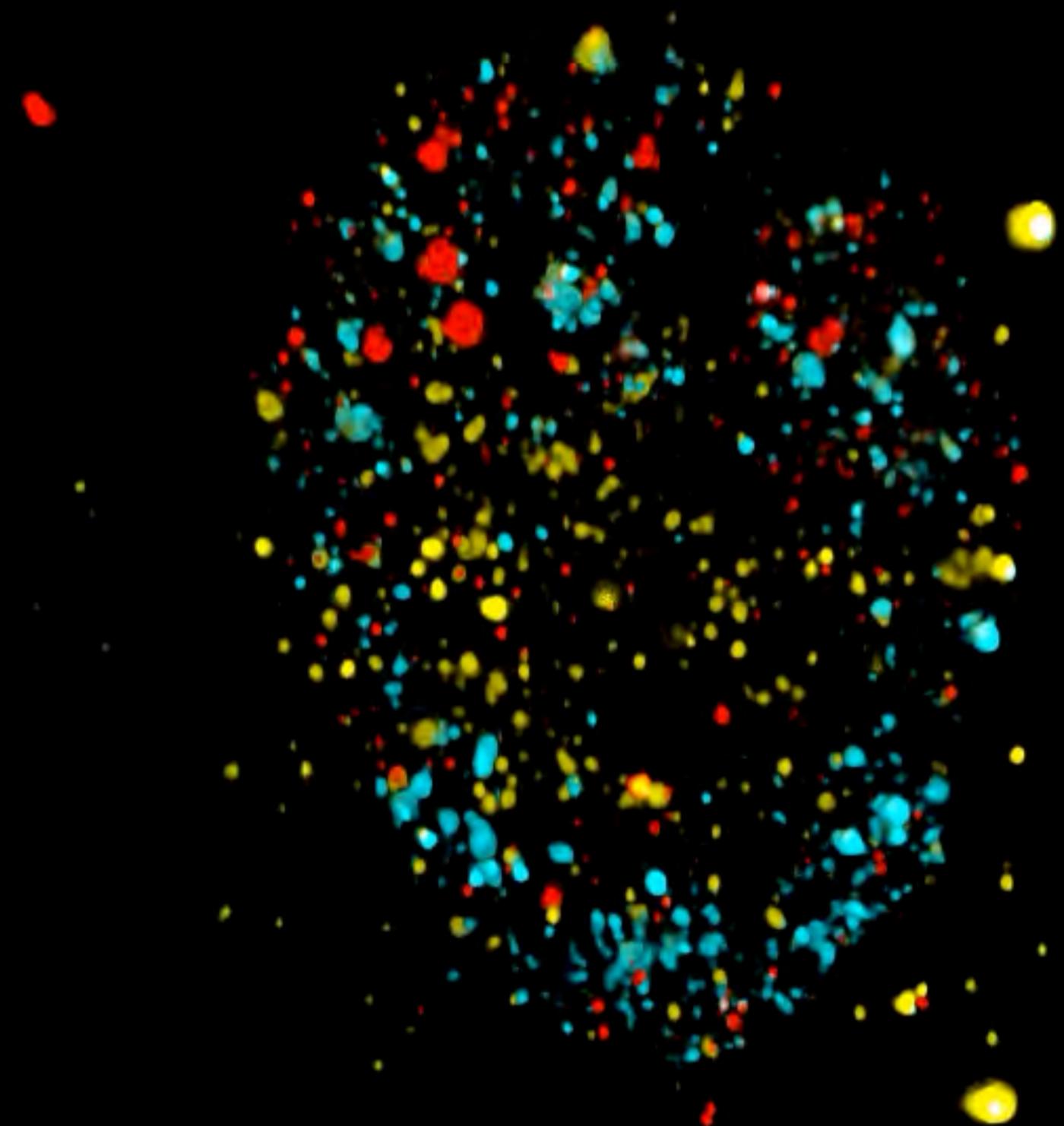


MAP2

HaloTag-TDP43

LC3B

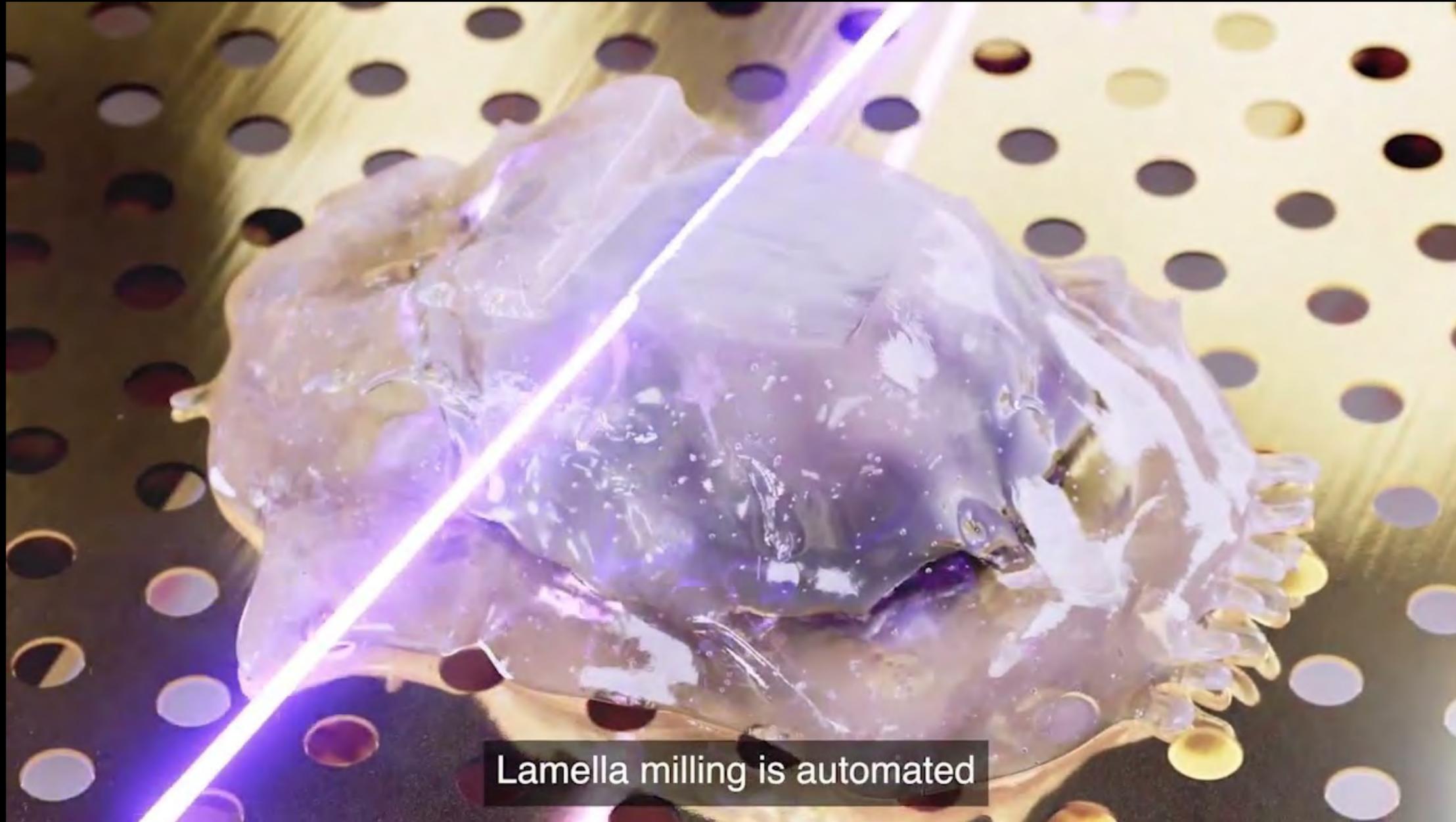
LAMP1



Structure of mislocalized TDP43 - Cryo-scanning electron microscopy (SEM)



Structure of mislocalized TDP43 - focused ion beam (FIB) milling

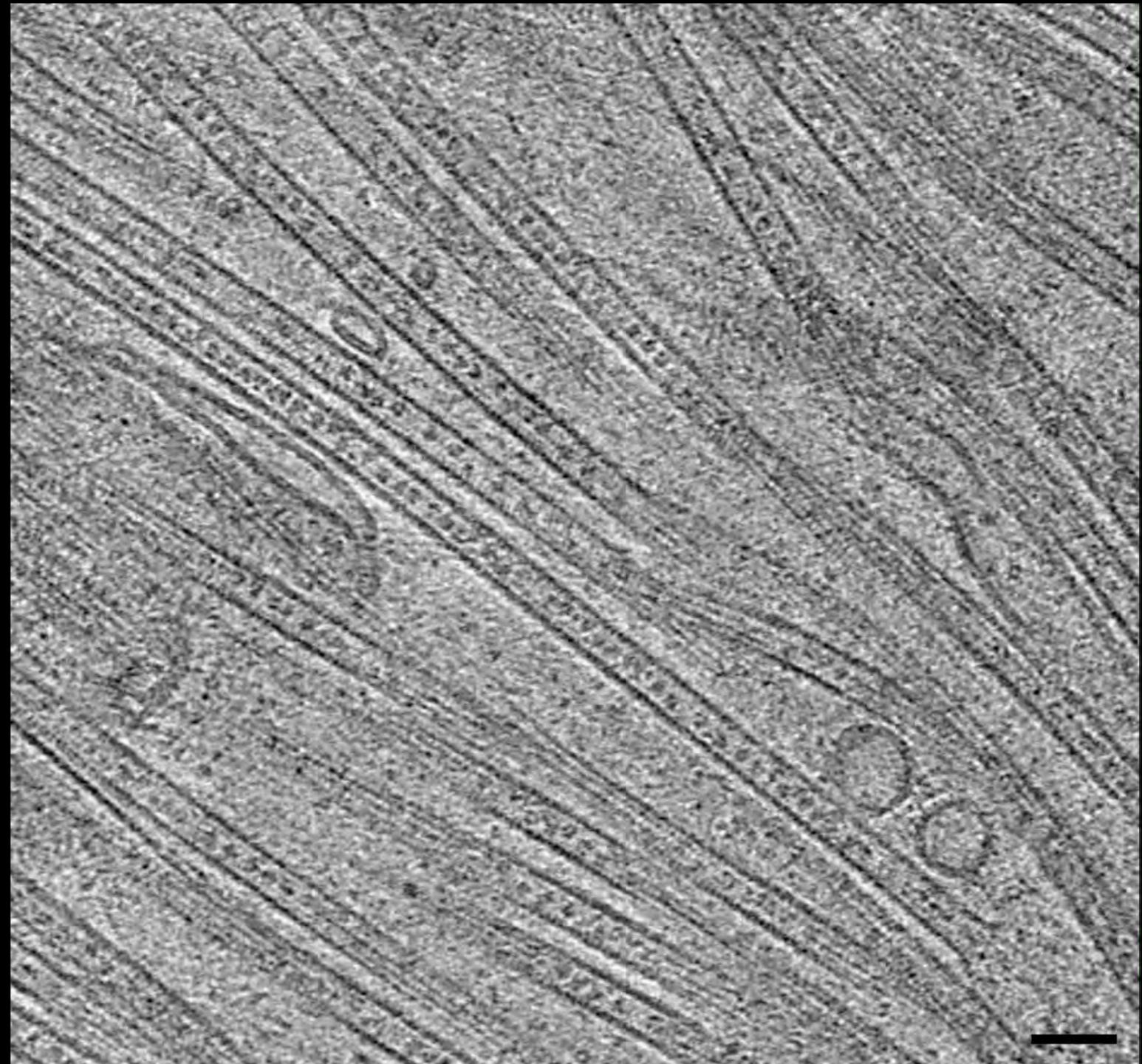
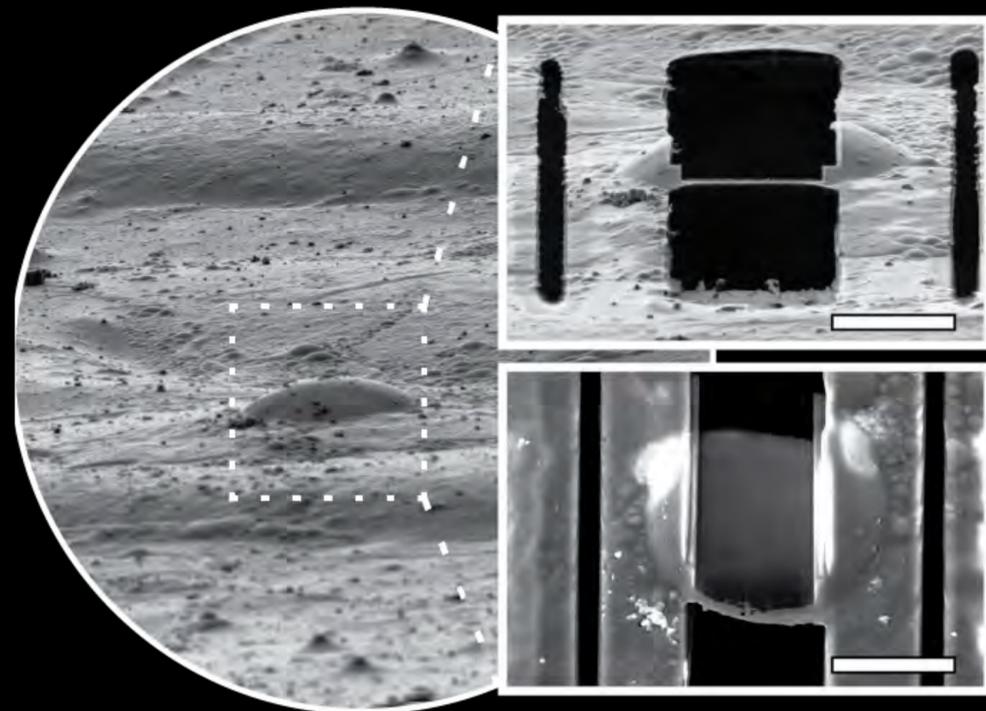


Structure of mislocalized TDP43 - Cryo-transmission electron microscopy (TEM)

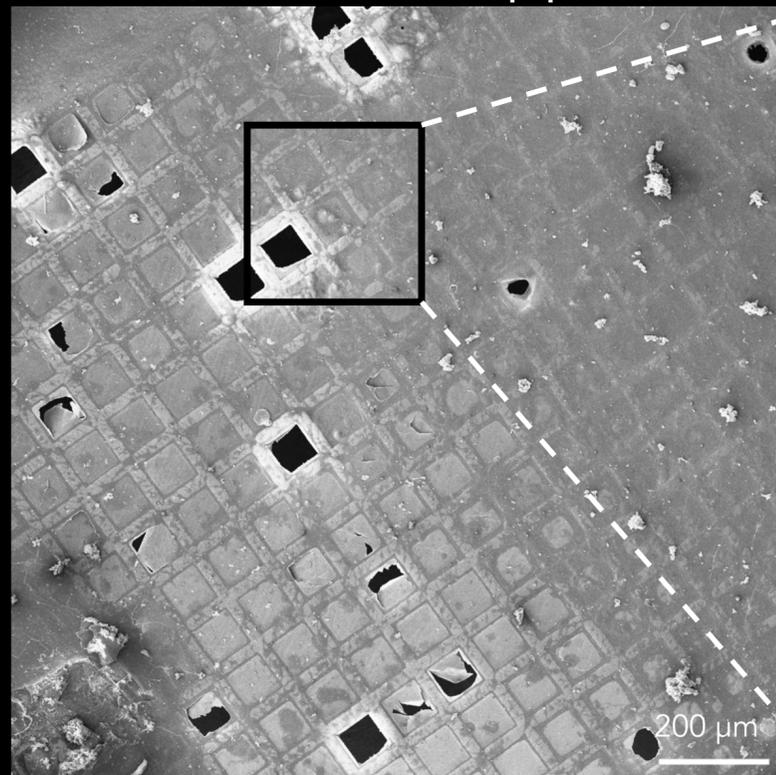
Cryo-SEM



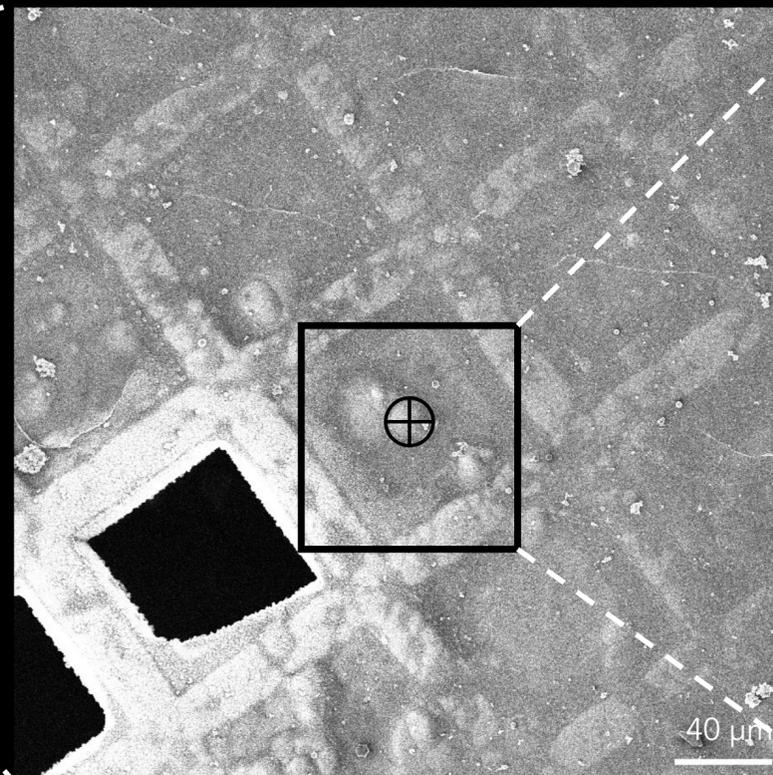
Cryo-FIB
milling



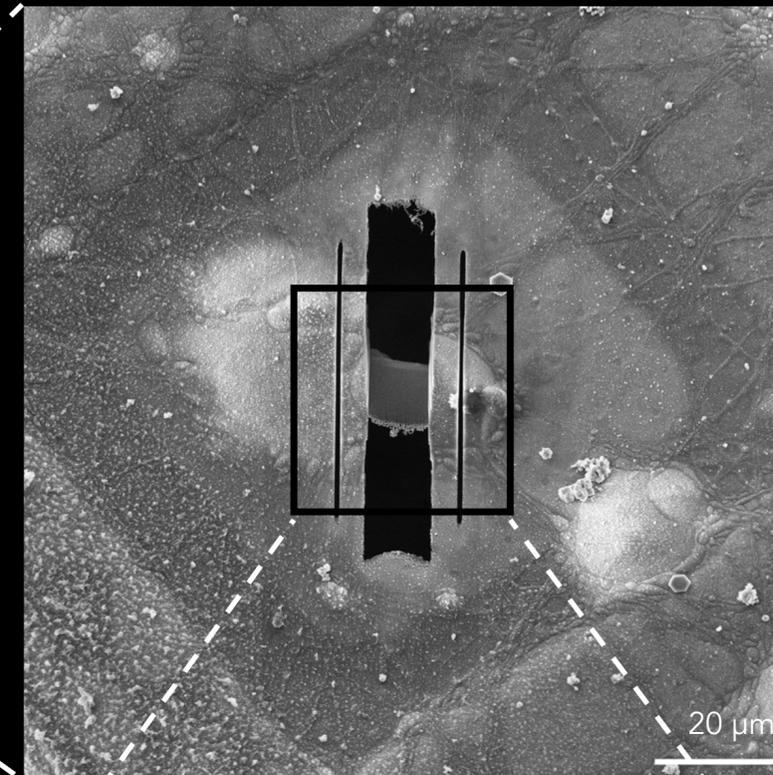
Cryo-SEM mapping



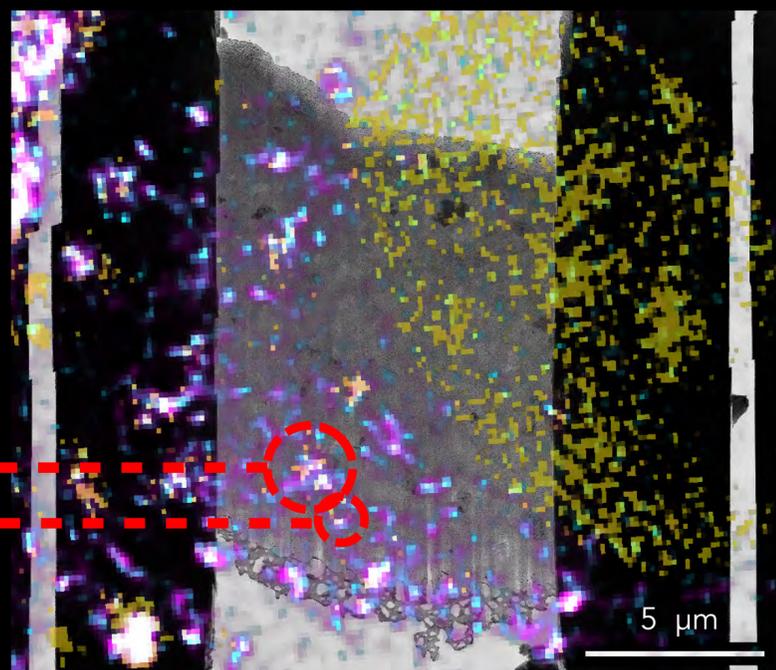
Lamella site identification



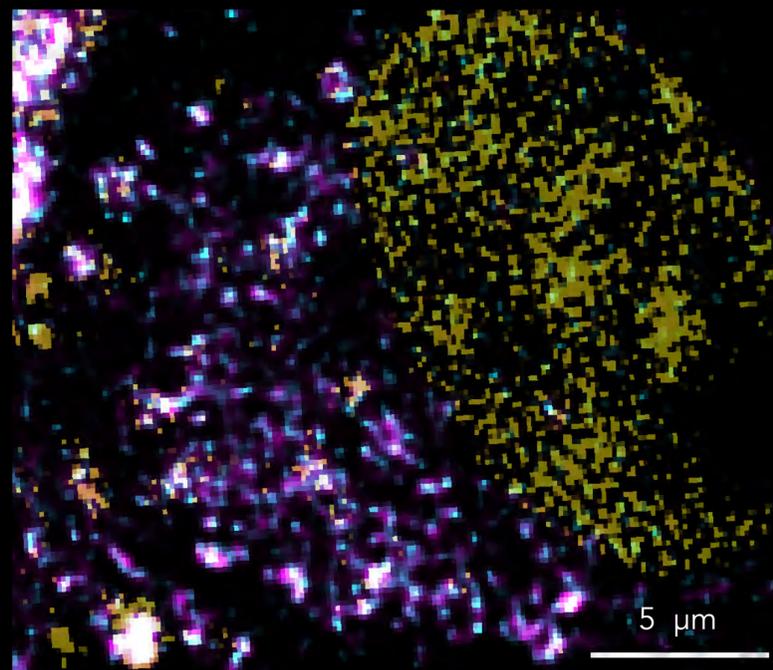
Cryo-FIB milling



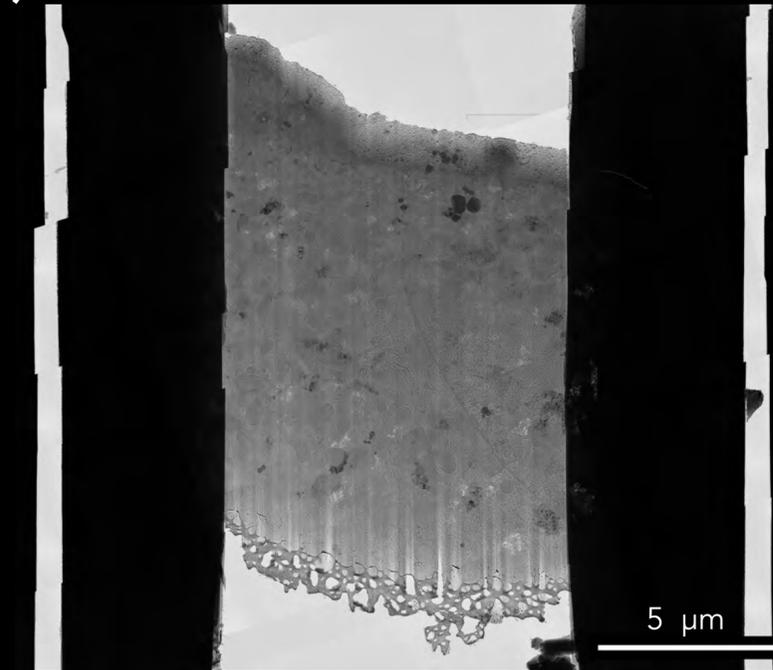
Cryo-CLEM overlay



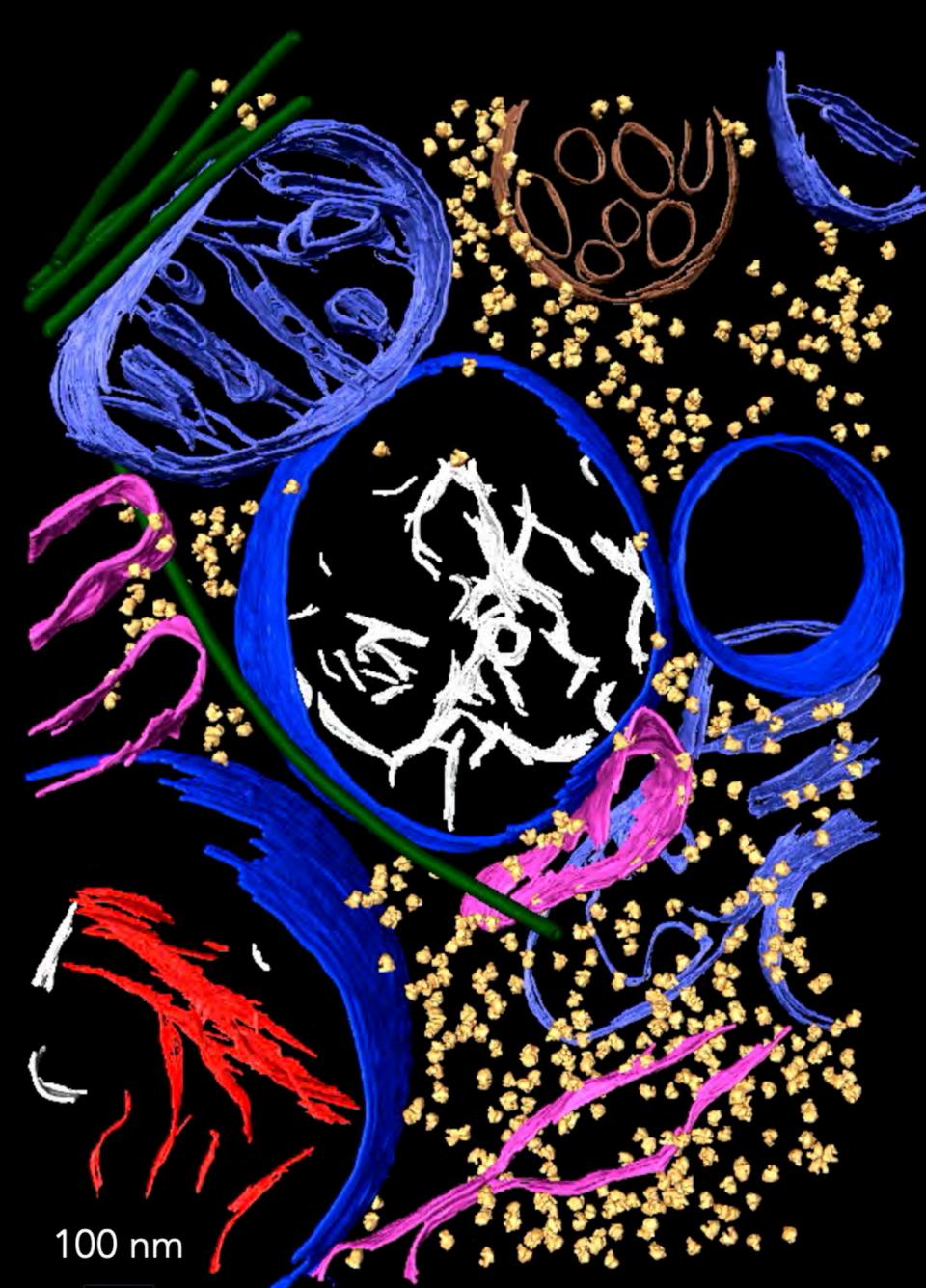
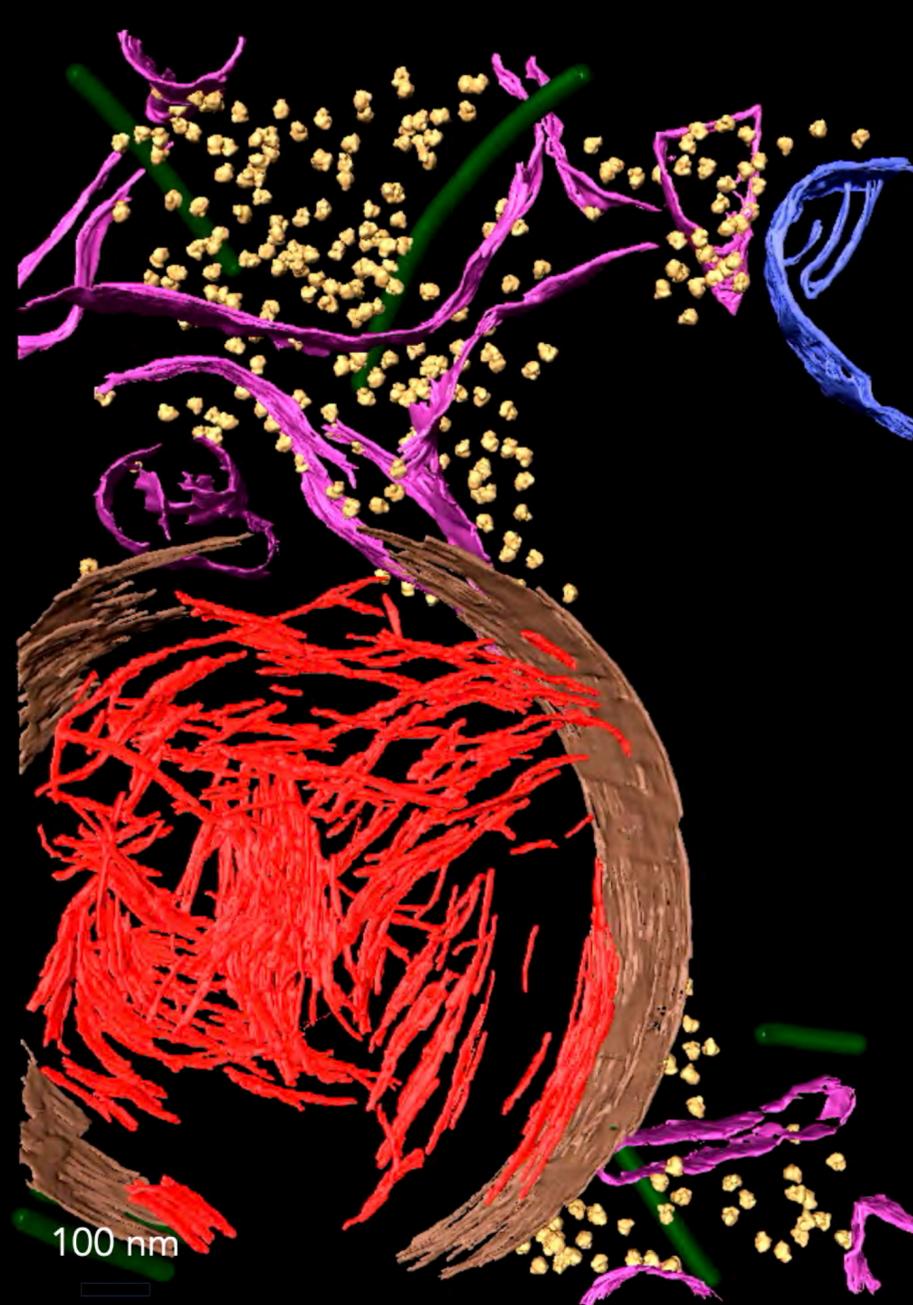
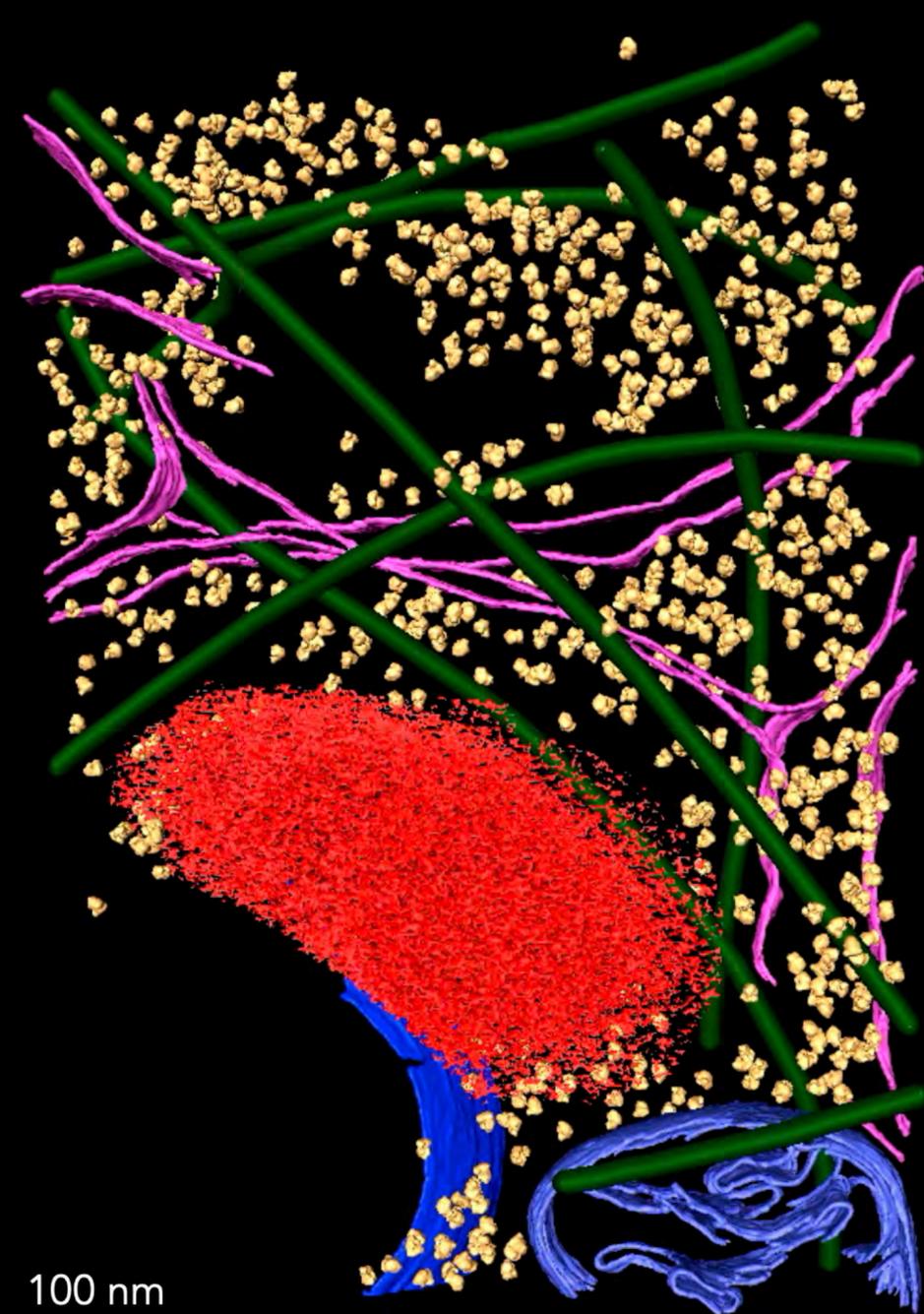
Cryo-confocal



Cryo-TEM



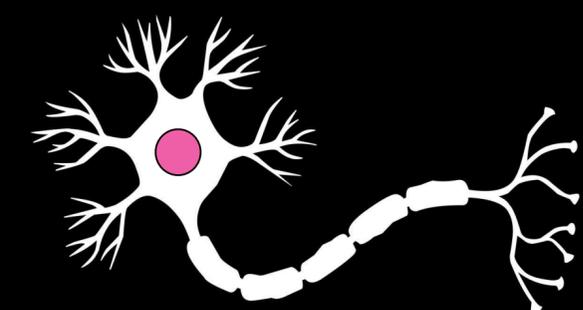
large ←
small ←



100 nm

100 nm

100 nm



Nuclear
TDP43

RNA

mislocalization



cytosolic
droplets

?

internalization

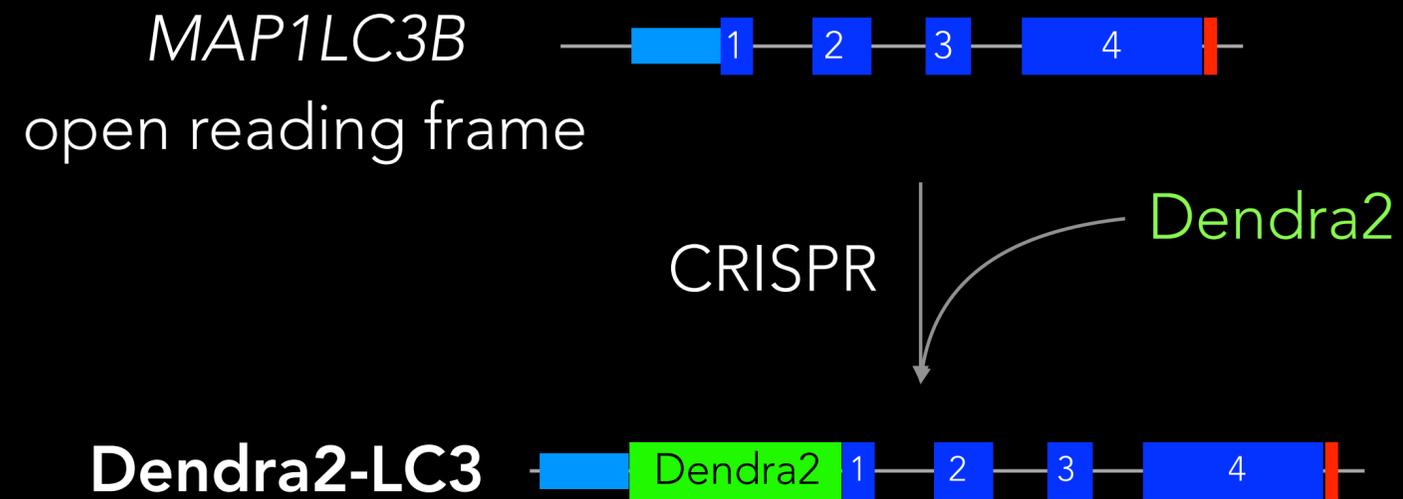


fibrils

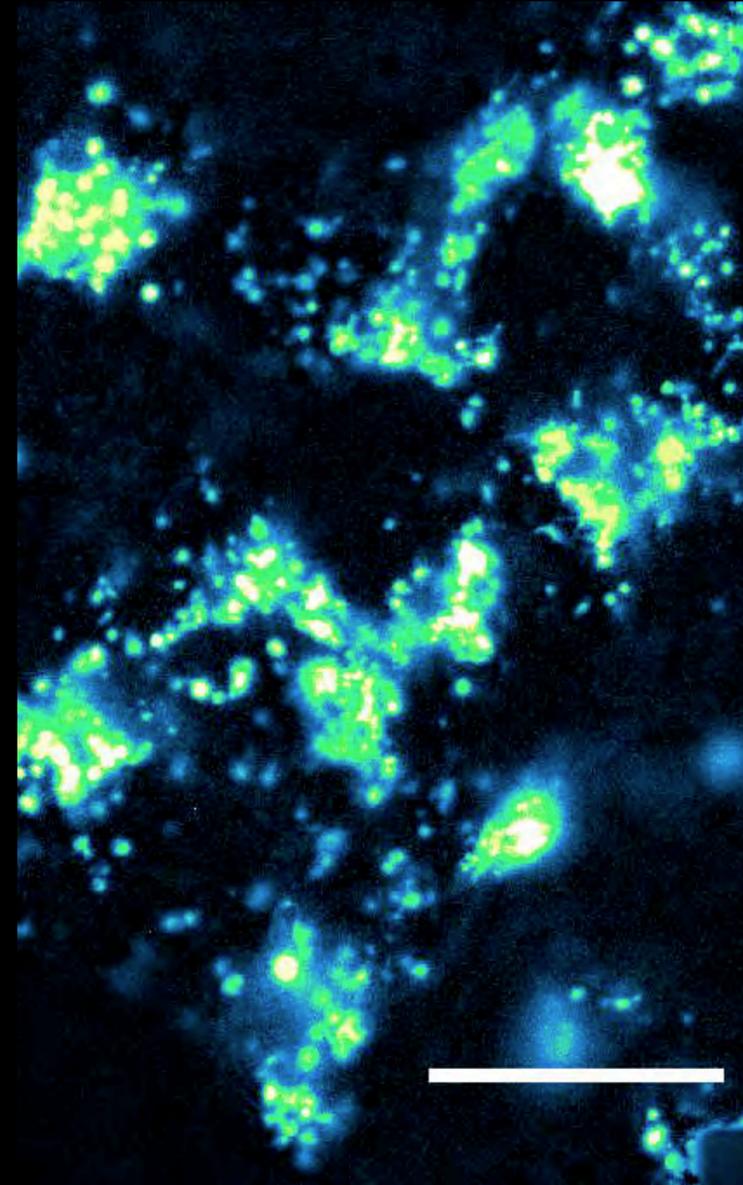
Endoplasmic
reticulum
Mitochondria
Autophagosome
TDP43

Ribosomes
Microtubules
Lysosomes
Membranes
MVB

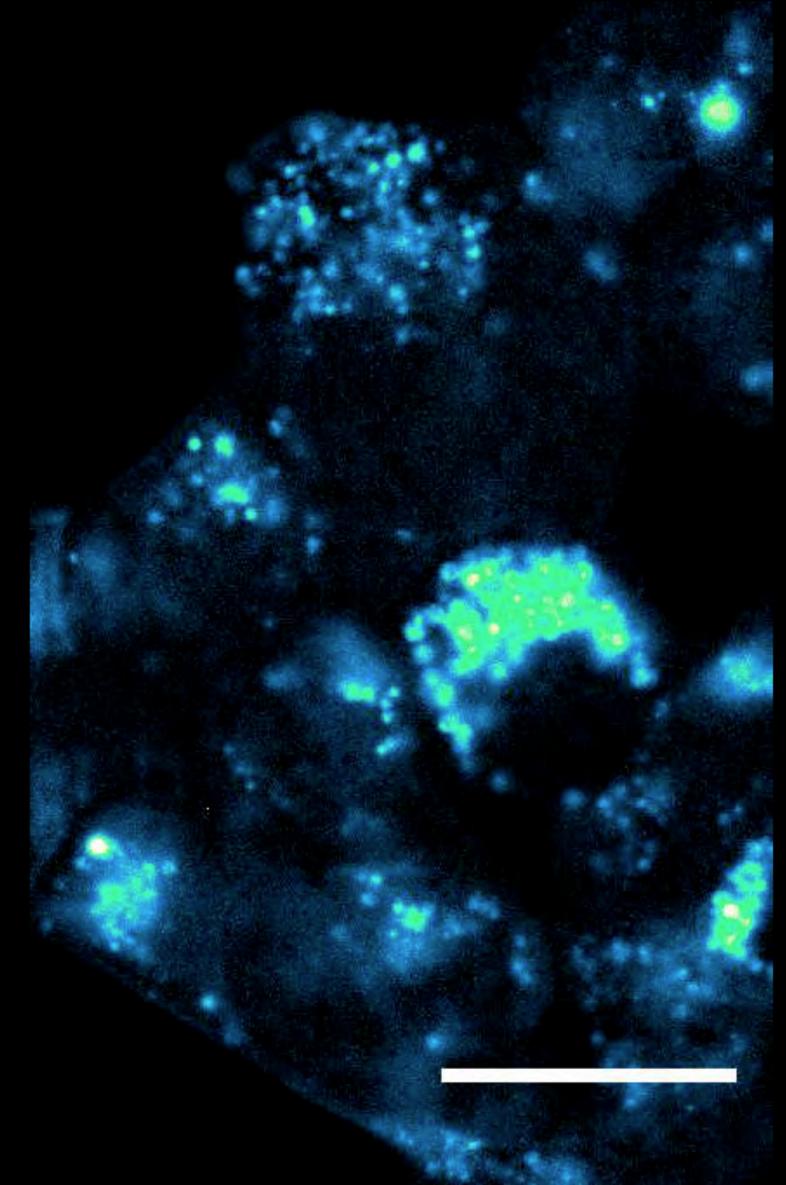
Confirming autophagosomal/lysosomal TDP43 mislocalization



+Torin1

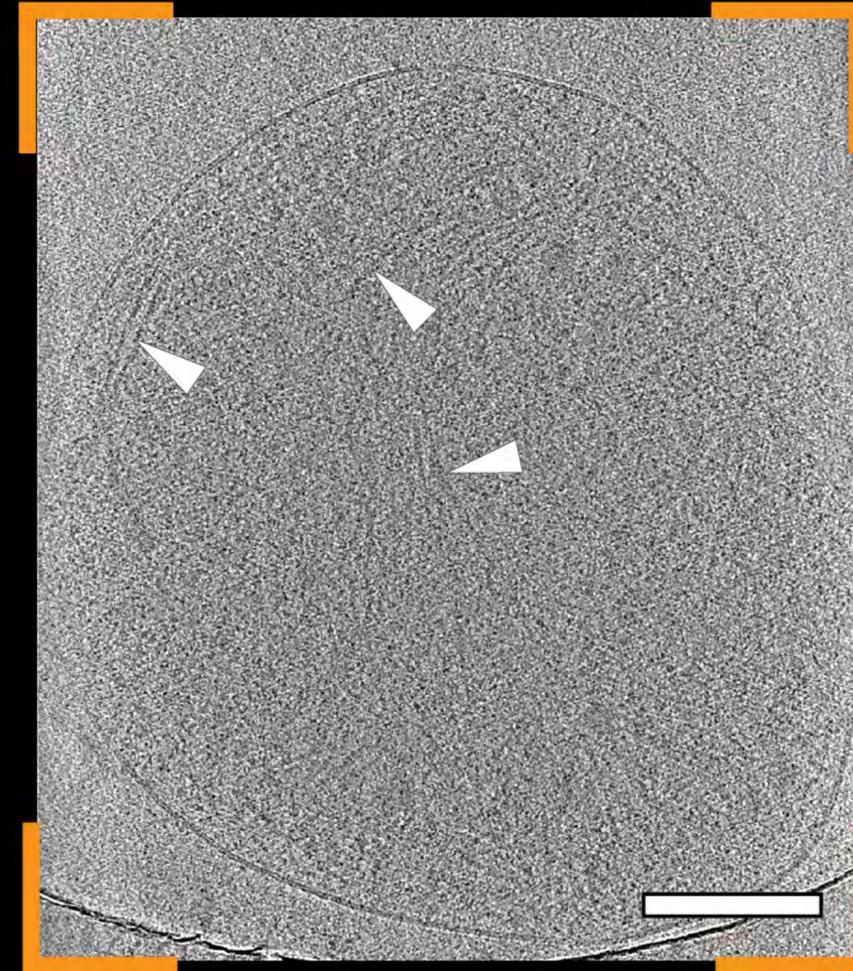
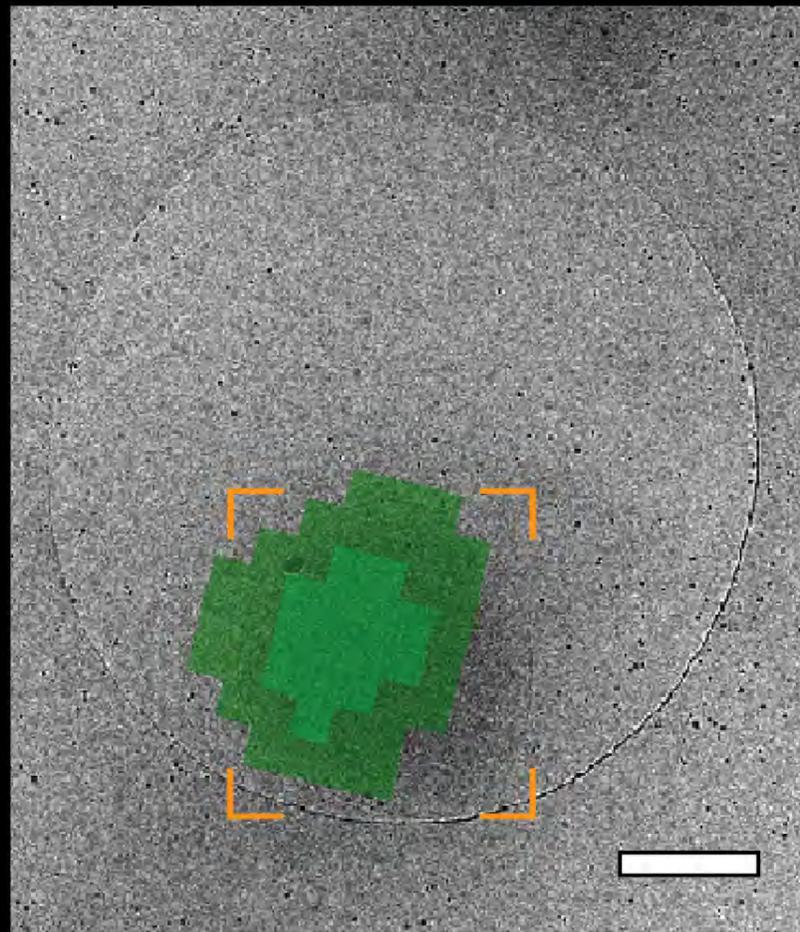


+BafilomycinA1

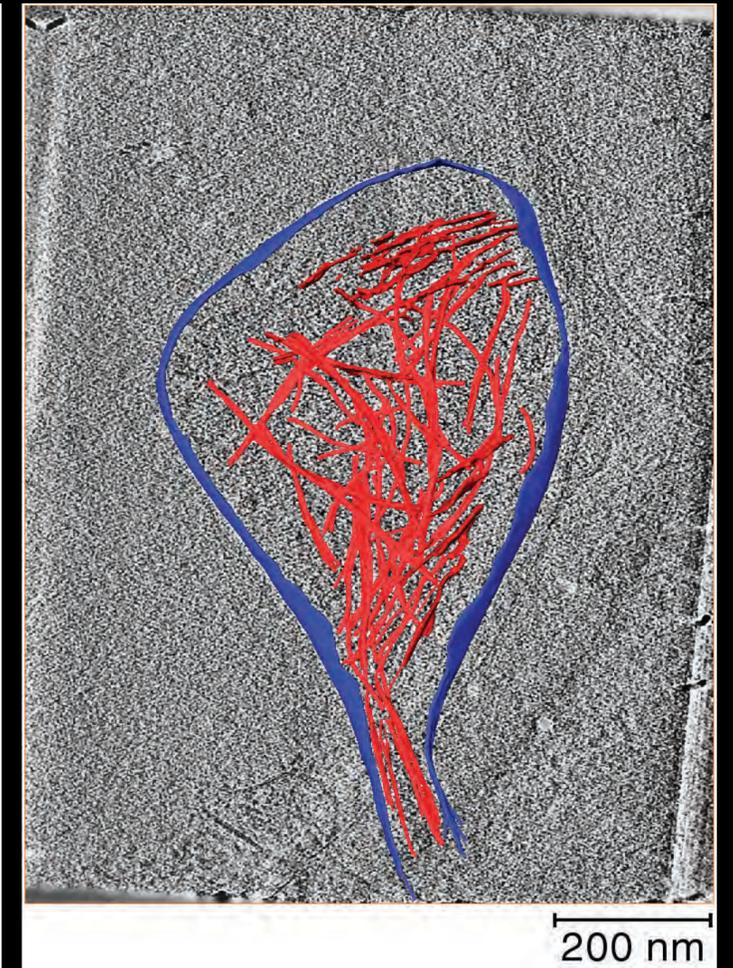
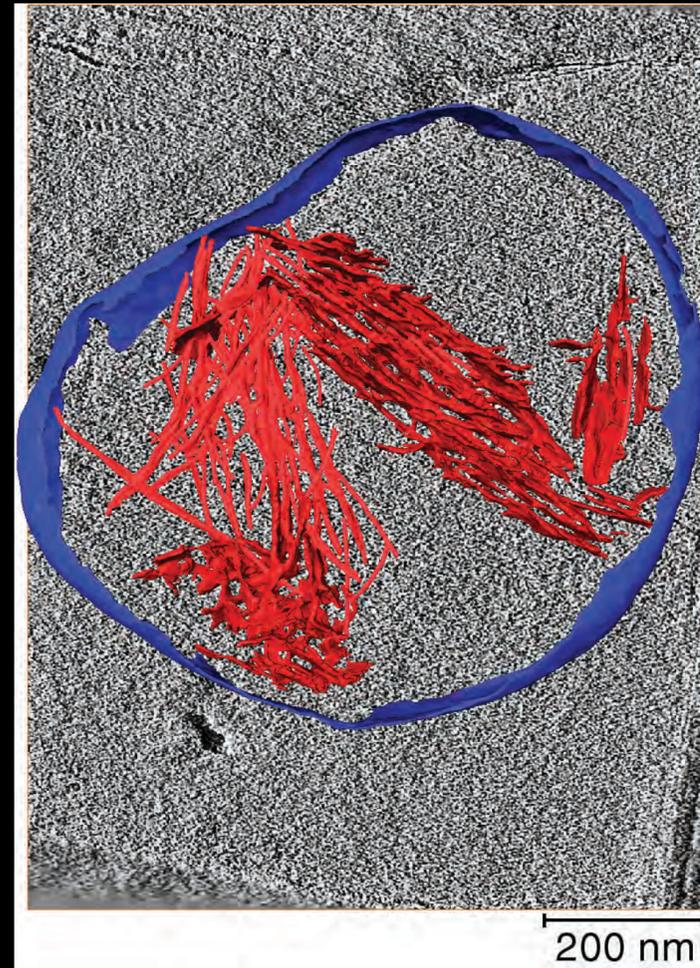


Confirmation of TDP43 mislocalization by correlative light-EM microscopy

LC3-Dendra2

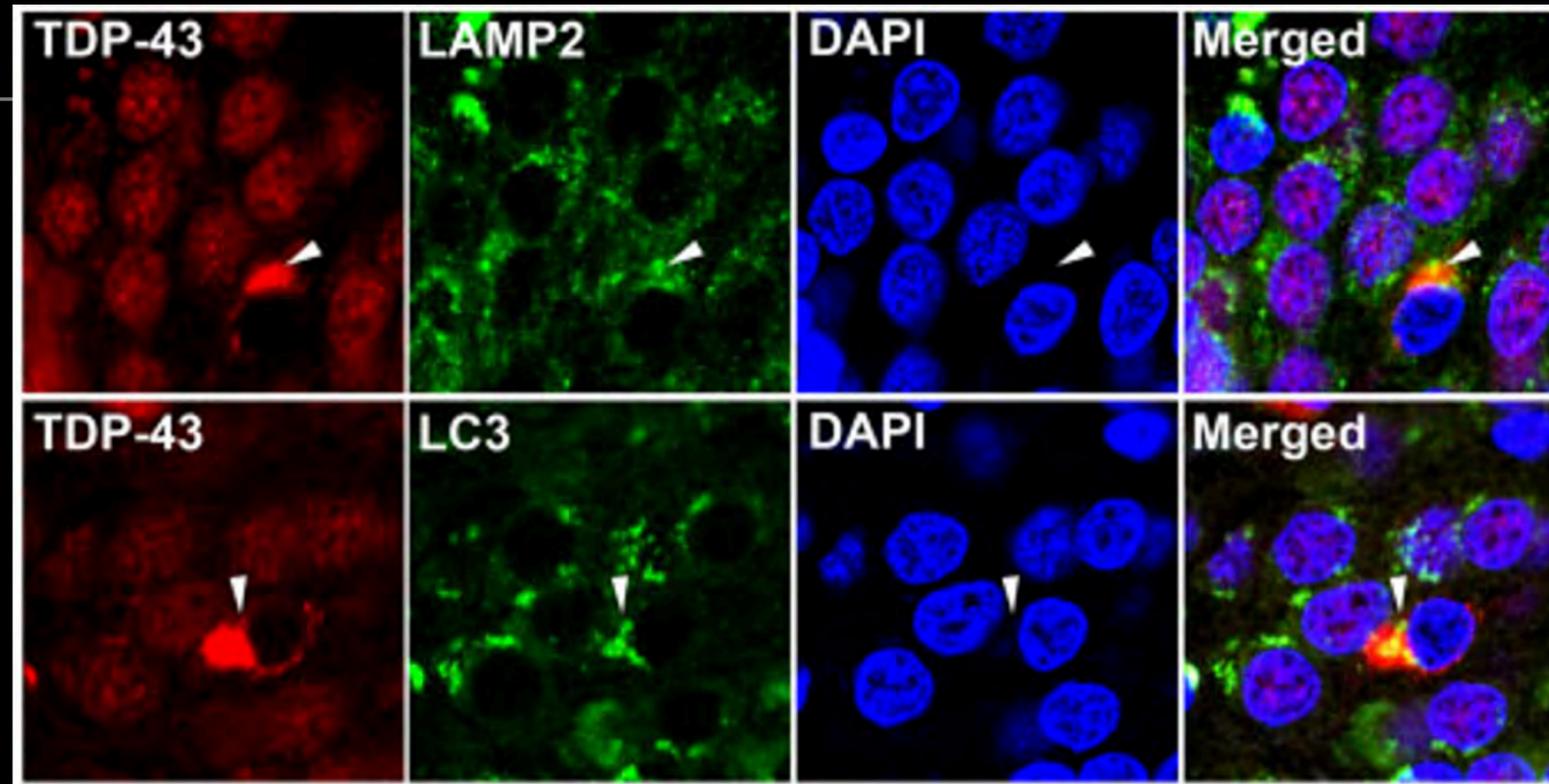


Confirming autophagosomal/lysosomal TDP43 mislocalization

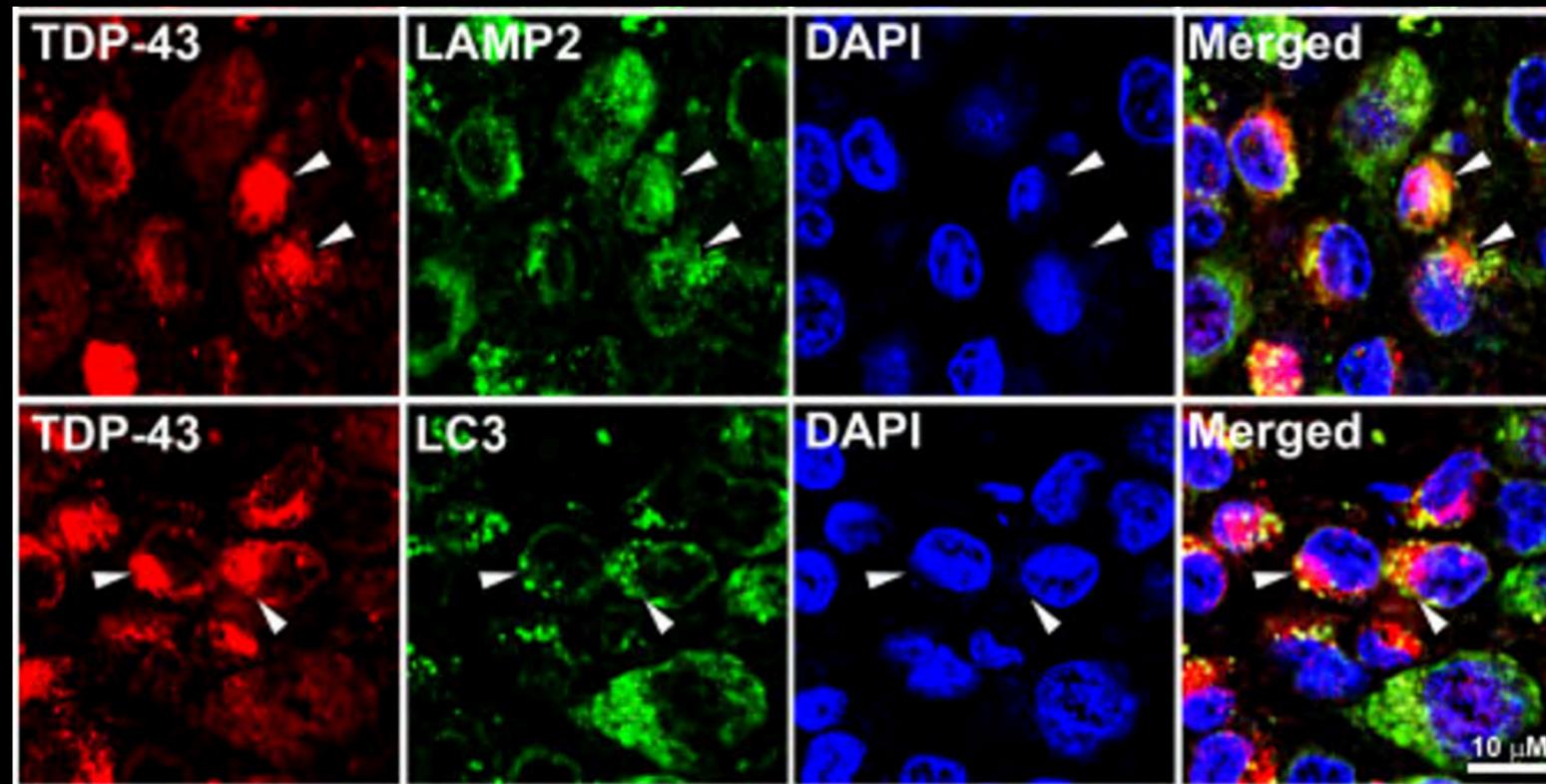


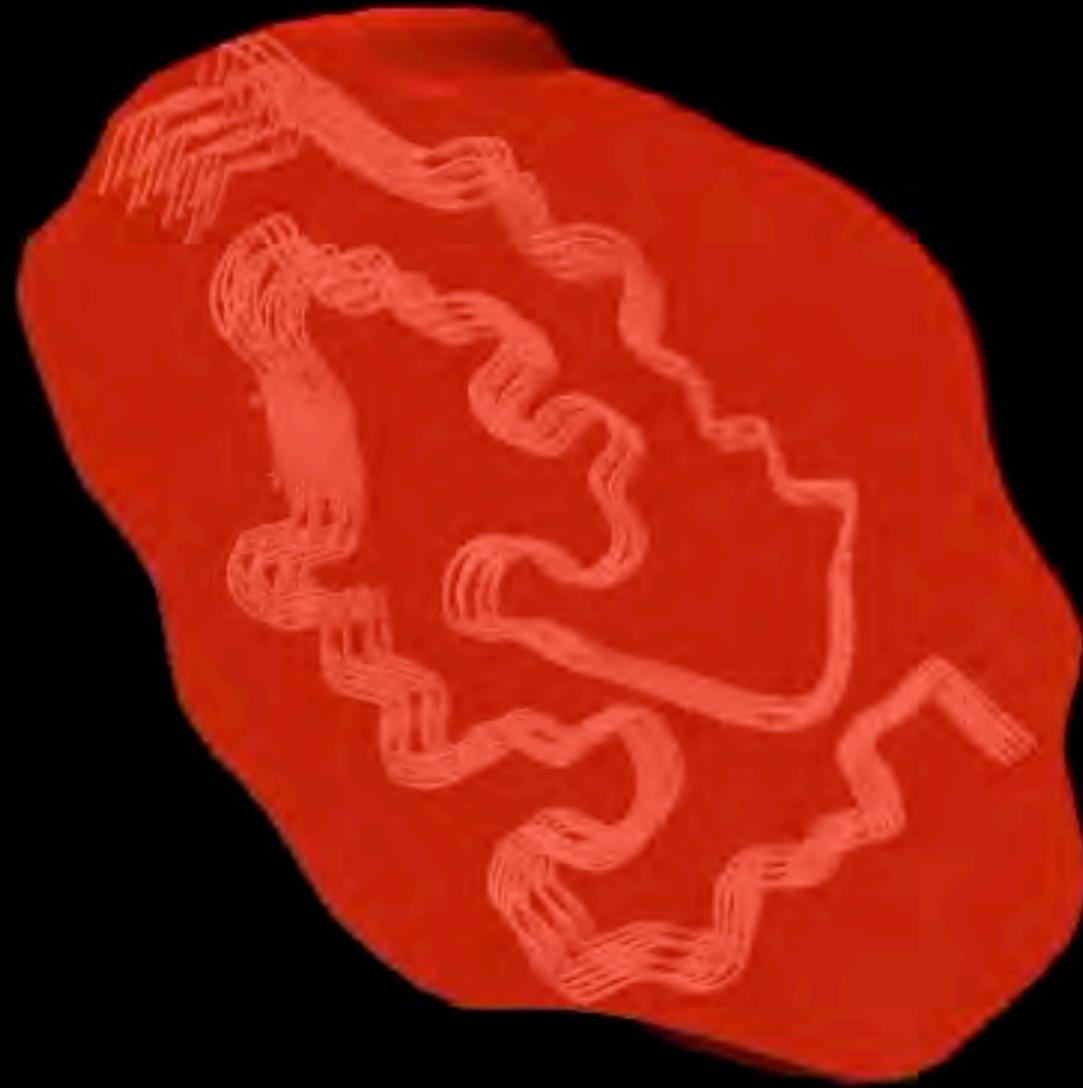
How relevant is this?

C9ORF72-related
ALS



Sporadic
ALS



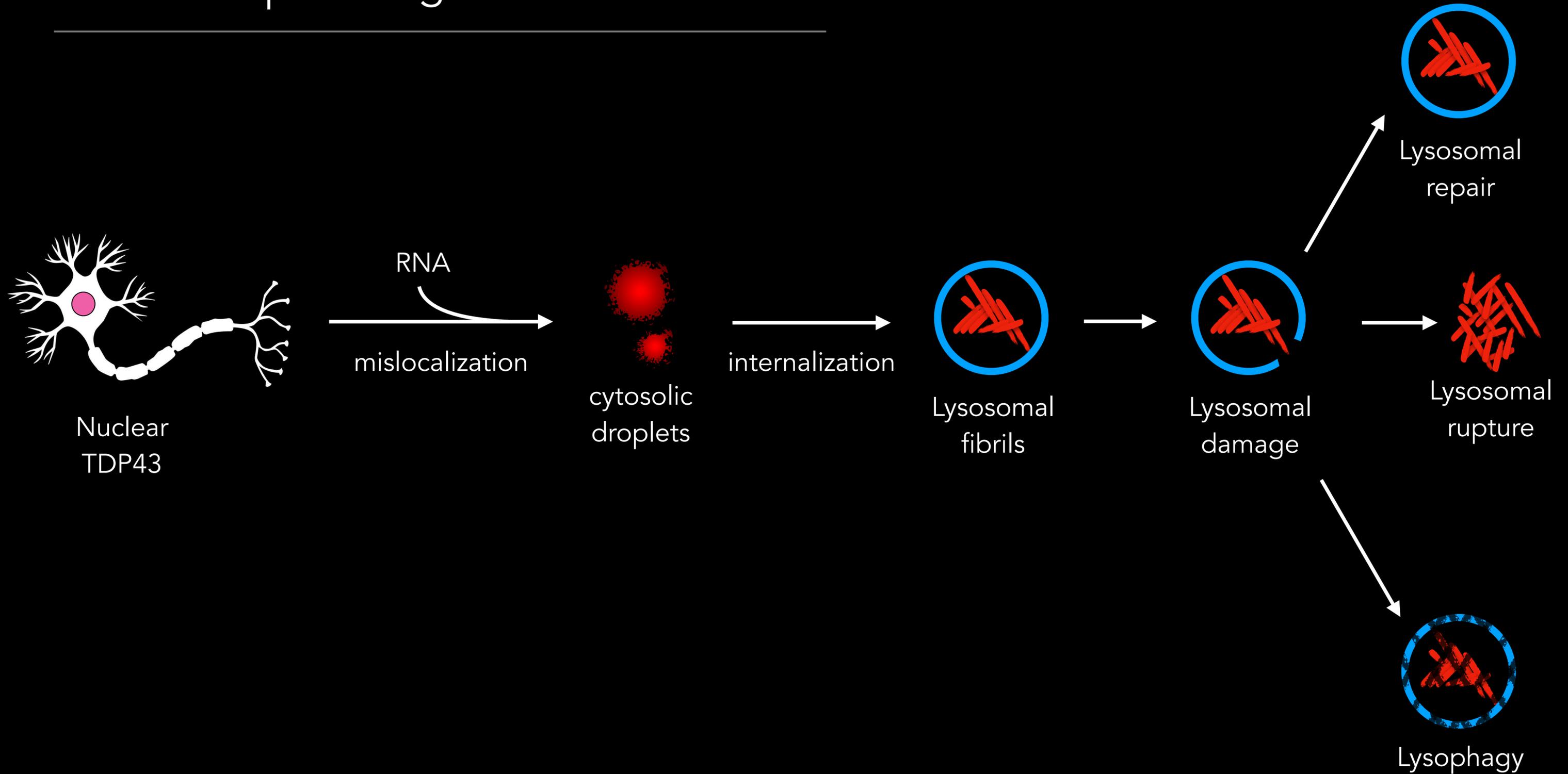


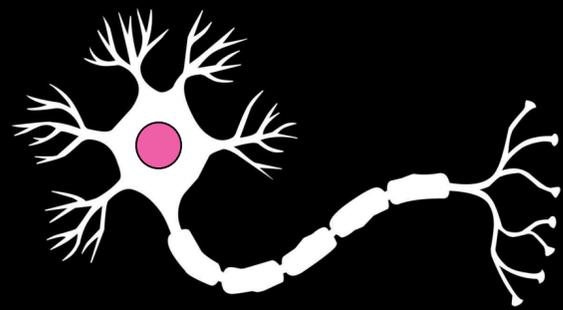
Cryo-EM map of
TDP43 fibrils from
FTLD-TDP brain
(Arseni et al., *Nature*, 2021)

FIT WITH PDB MODEL

S. Mosalaganti, A. Erwin, M. Chang, M. Fernandez

Model for pathological TDP43 mislocalization





Nuclear
TDP43

RNA

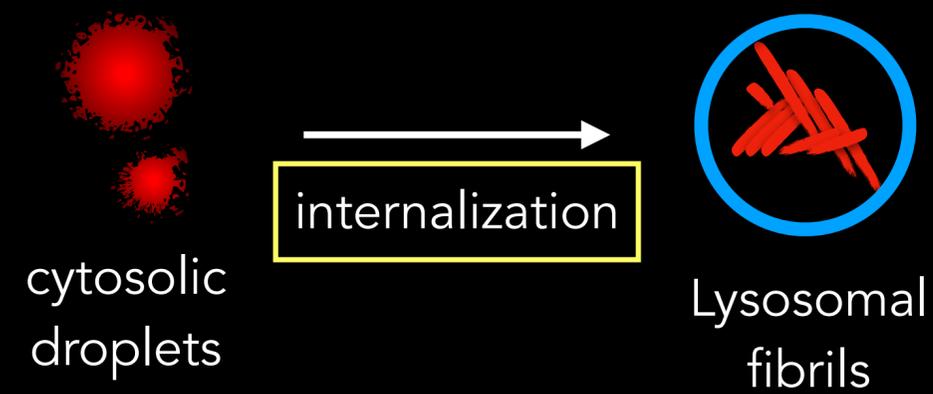


mislocalization



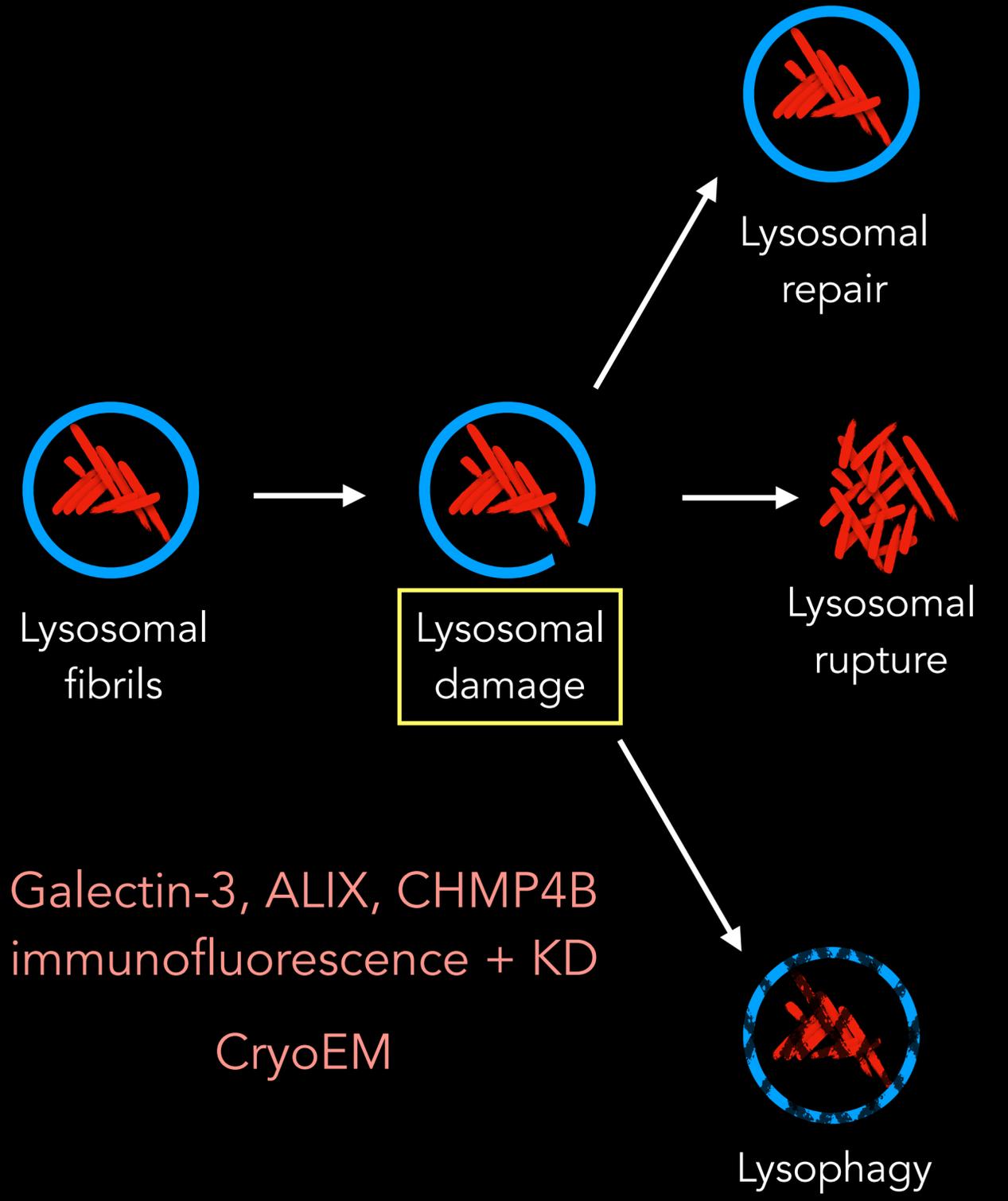
cytosolic
droplets

- RNA length
- GU content
- Spacing of GU motifs
- Other RBP motifs
- Secondary structure
- Methylation (m6A)
- m6A-GU proximity
- Other modifications
- Stoichiometry



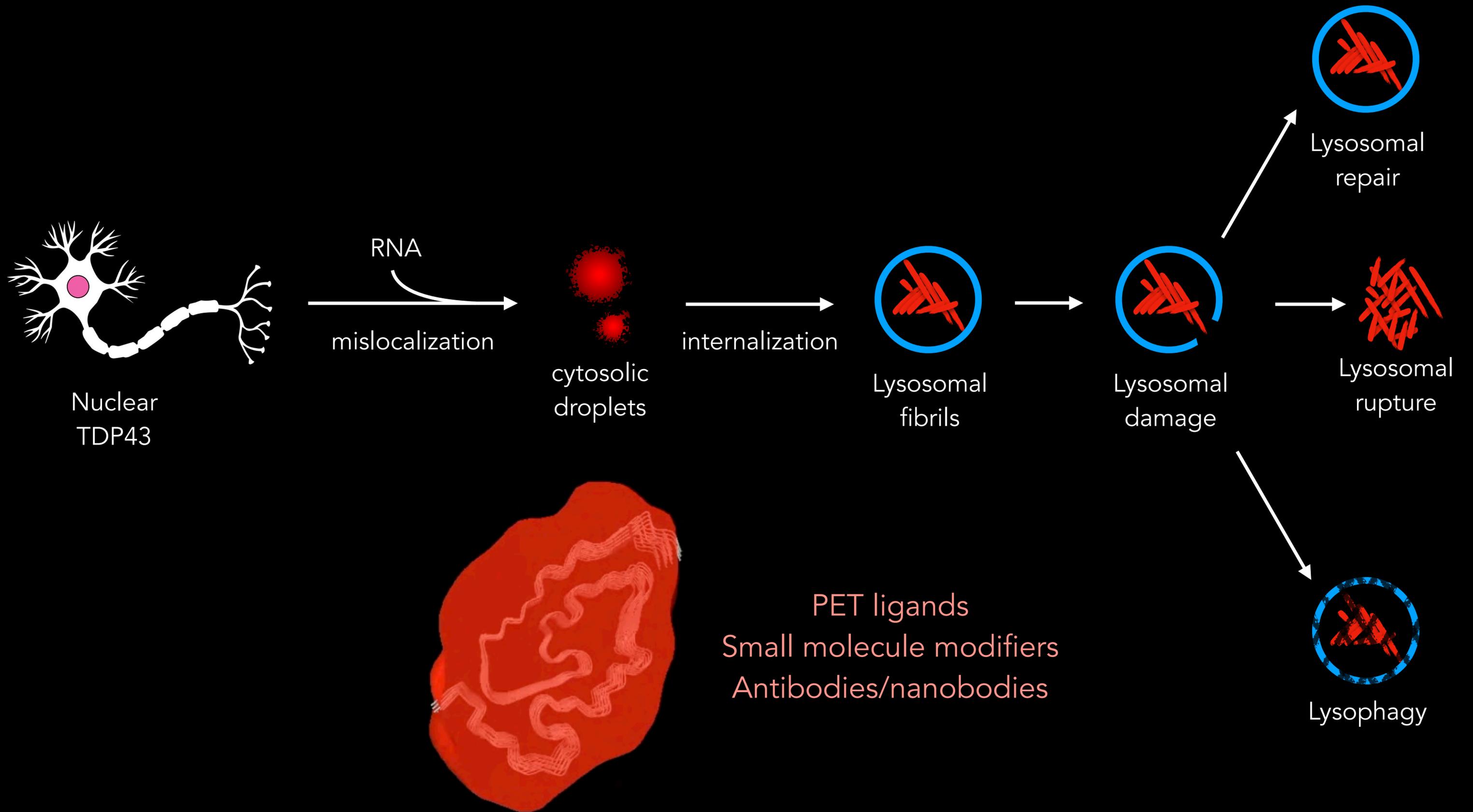
Proximity labeling of
HaloTag-TDP43

Mass spectrometry



Galectin-3, ALIX, CHMP4B
immunofluorescence + KD

CryoEM



Summary and next steps (2)

- **TDP43 pathology** can be recapitulated by RNA introduction
 - Nuclear mislocalization
 - Cytosolic fibril formation
 - Lysosomal origin of TDP43 aggregates?
- Search for small molecule **TDP43 ligands**
 - Selective for TDP43 fibrils
 - Biomarkers (PET)
 - Therapeutics?

Sami Barmada
Elizabeth Tank
Xingli Li
Michael Bekier
Amanda Erwin
Durga Atili
Babhru Roy
Emile Pinarbasi
Christopher Altheim
Ataur Rahman
Genesis Rodriguez
Megan Dykstra
Caroline Hsieh
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Terry Hahn
Jen Bai

Shyamal
Mosalaganti
Martin Fernandez
Matthew Chang



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Nils Walter
Peter Todd
Hank Paulson
Hayley McLoughlin
Eva Feldman
Stephen Goutman
Vivian Cheung

Mayo Clinic
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St. Louis University
Yuna Ayala

WashU in St. Louis
Tim Miller

Mayo Jacksonville
Veronique Belzil
Wilfred Rossol

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Department of Defense
Robert Packard Center
Ann Arbor Active Against ALS
Angela Dobson, Lyndon Welch & family

