

ACTU19 Renewal: Project meeting

Paul K. Crane, MD MPH

Andrea LaCroix, PhD

Linda McEvoy, PhD

MPIs, ACTU19

Outline

- Brief intro to ACTU19
- Data collection in ACT
- The Cores
- Very brief intro to current Projects as examples
- The LOI request
- Lots of time for questions

ACTU19

- Cooperative Research Program
- NIH scientists have an active interest
- Cores and Projects
- ACT builds on a U01 x many cycles; currently starting Y4 of the U19 mechanism
- Prospective cohort study of older adults enrolled from a healthcare delivery system
- “Secret sauce” is combination of research data collected by ACT (and ancillary studies) with data from care delivery

Enrollment waves

- Original cohort 2581 enrolled 1994-1996
- Expansion cohort 811 enrolled 2000-2003
- Continuous enrollment 2371 2005-March 2020 (Covid)
 - Total up to then = 5763
- New enrollment strategy 2022-onward, enrolled 350+ so far
 - New enrollment is diverse, will return to this
- Data Query Tool includes data up to March 2020; tremendous resource
- 5763 with data. 3388 had died, 36 disenrolled, 2015 active participants. 3343 females. 2420 males. Mean 7.69 years of follow-up (44,317 person-years of follow-up)
 - Building on these data and adding something new is a terrific strategy for a compelling Project proposal

Diverse new enrollment: 12% to 64%!

	Established cohort (n=1,480)		New enrollees (n=346)	
	N	%	N	%
Non-Hispanic white	1308	88	126	36
Asian	46	3	90	26
Black	42	3	41	12
Hispanic	42	3	55	16
PI/NA	4	<1	6	2
Multiple	12	1	20	6
Other	11	1	19	5
Unknown	20	1	5	1

Projection for when we reach n=3,000

	Established cohort (n=1,200)		New enrollees (n=1,800)		Total cohort (n=3,000)	
	N	%	N	%	N	%
Non-Hispanic white	1,058	88	655	36	1,713	57
Asian	37	3	468	26	505	17
Black	34	3	213	12	247	8
Hispanic	34	3	286	16	320	11
PI/NA	3	<1	31	2	34	1
Multiple	9	1	104	6	113	4
Other	8	1	98	5	106	4
Unknown	16	1	26	1	42	1

ACT study data collection

ACT study visit

Qs on risk factors, medical history
Measure cognition with CASI, now CASI+
Measure physical performance
Height, weight, BP, a few others

Low CASI score: dementia eval

Further testing

Clinician eval

Medical record reviews

Consensus conference

Dementia – special

Not dementia-return

Moving to tablet-based cognitive data collection

ACT study visit

ACT study data collection



ACT study visit

Devices

ACT study visit

Devices

As of U19: accelerometer, position monitor, and sleep watch

1 week wear time

Participants invited to consider, somewhat more than half do (consistent with other studies)

Packet of additional information on wear logs, self-reported sleep quality and activity, etc.

Dori Rosenberg, Sue McCurry

of people offered the Actiwatch in the first year of data collection,

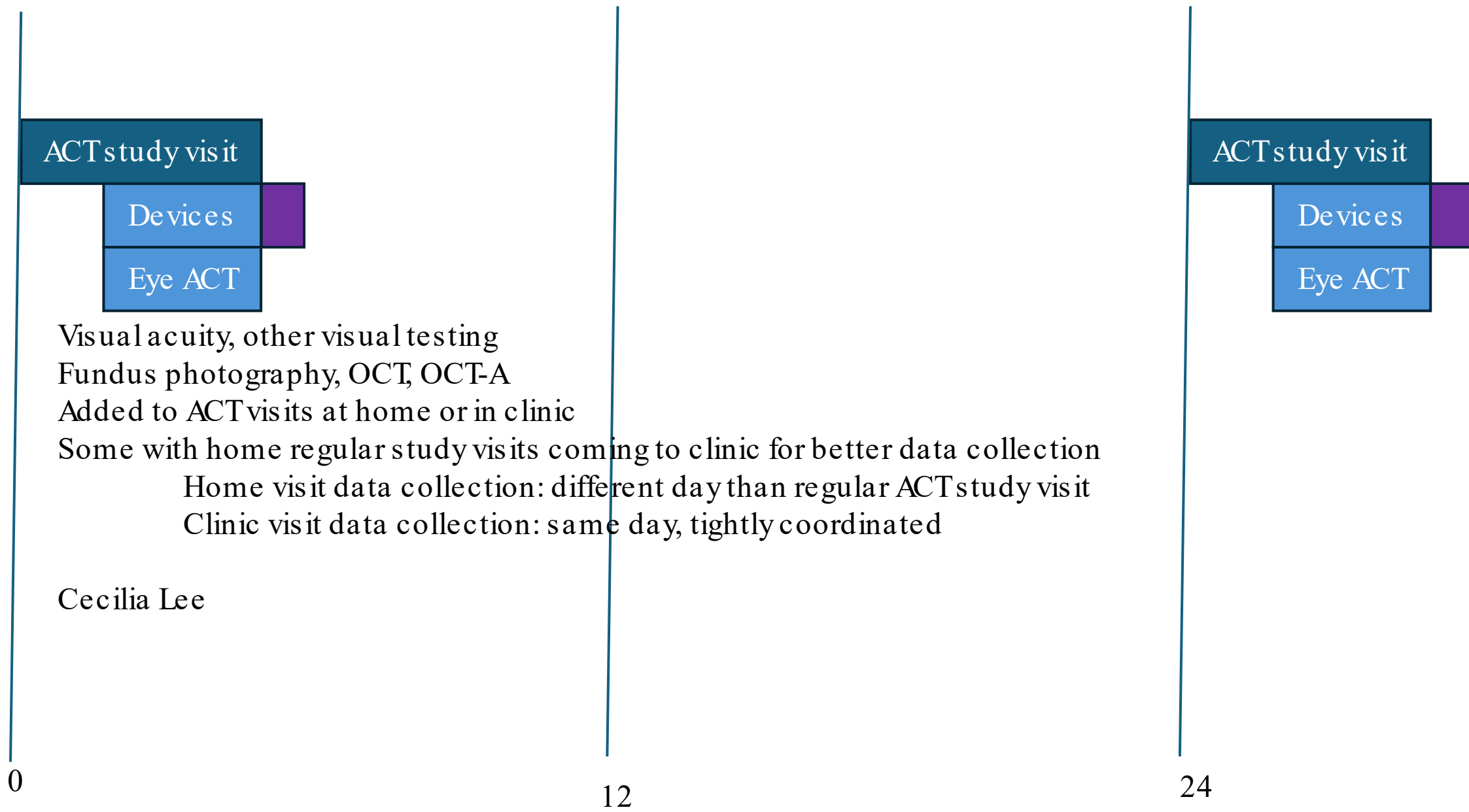
37% consented to wear them,

33% (of the original # offered) actually put them on/took them at the enrollment or biennial visit, and

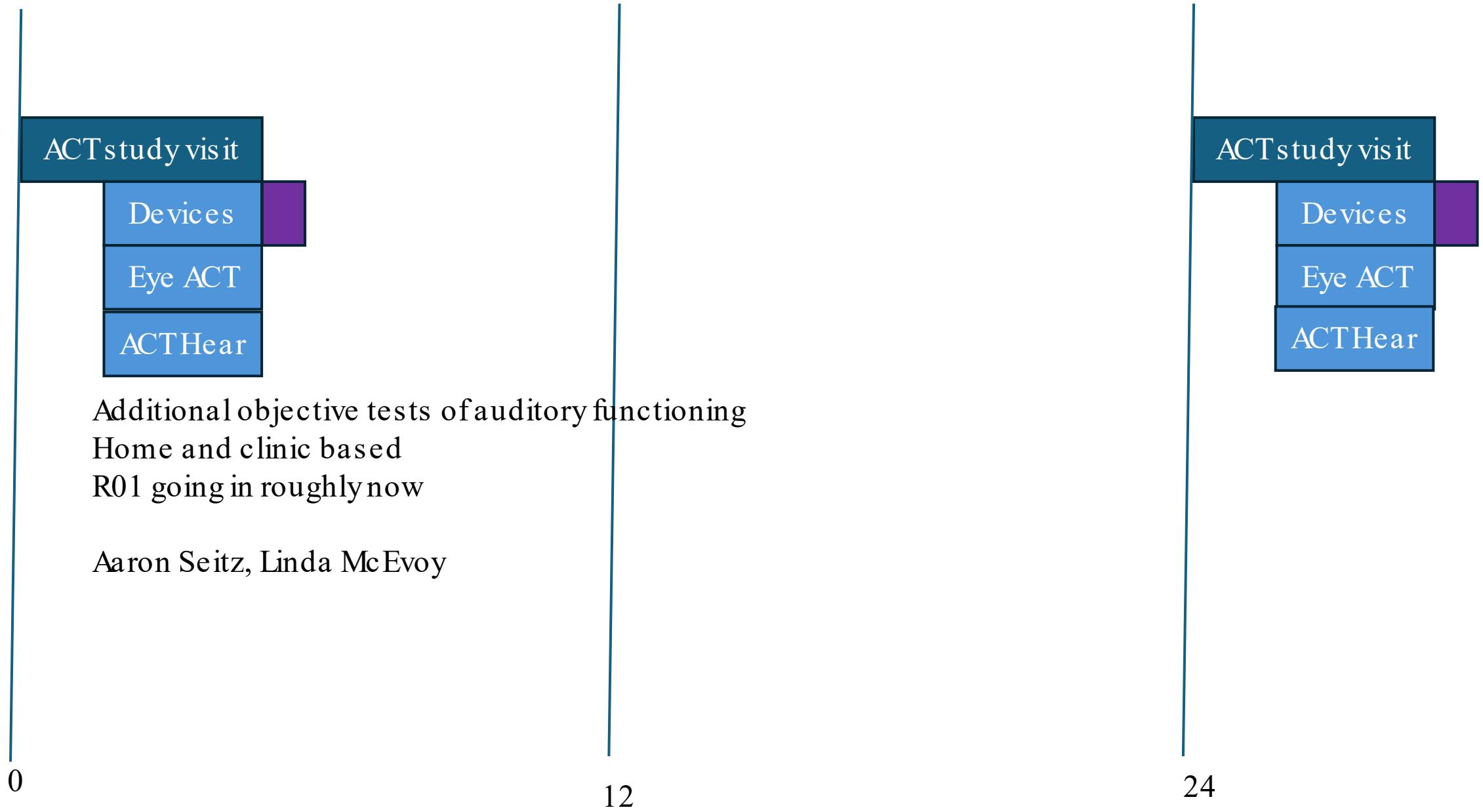
30% returned them with usable data,

meaning only 3% of the devices are either lost or returned with data that are bad for some reason (device failure, participant wear problem)

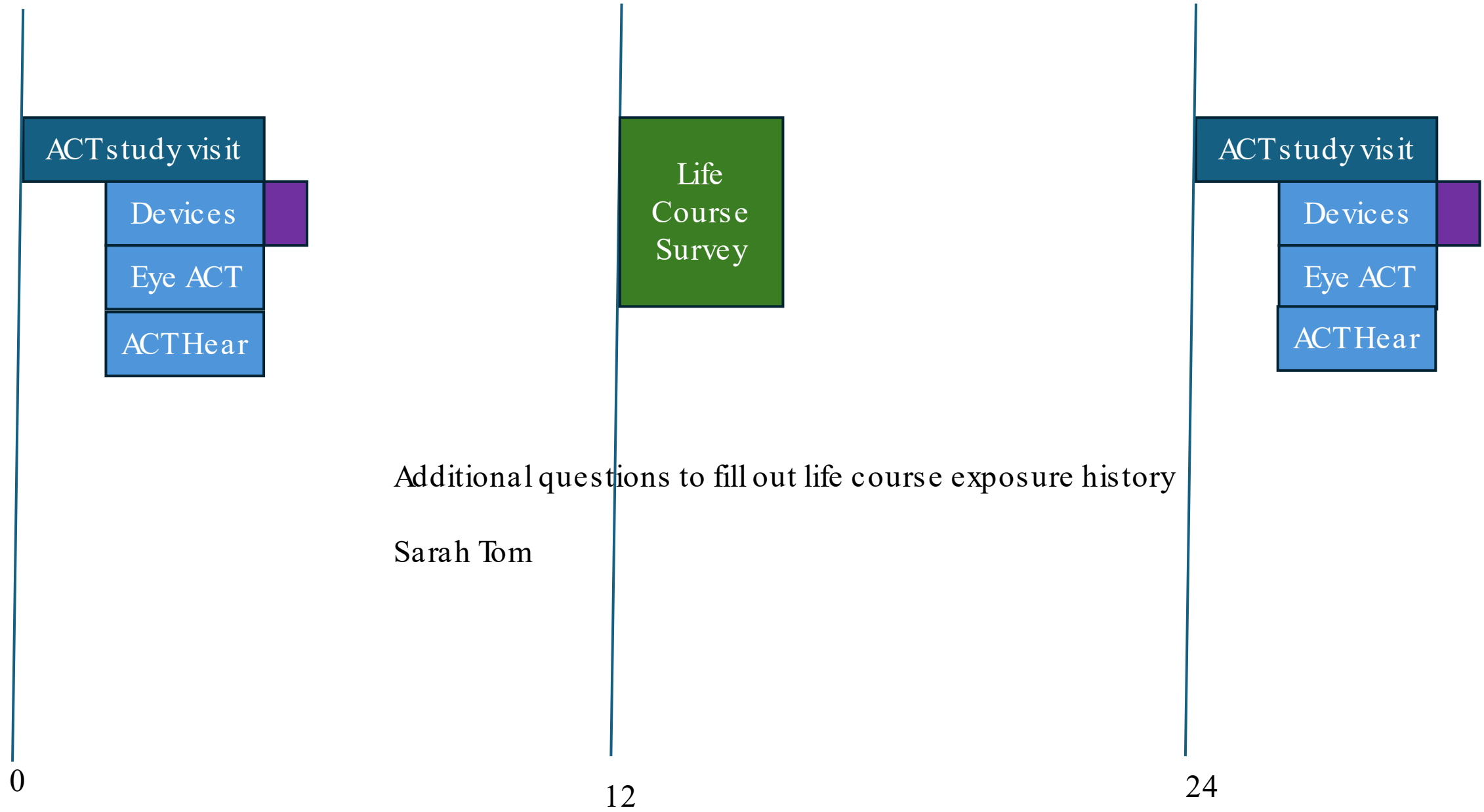
ACT study data collection



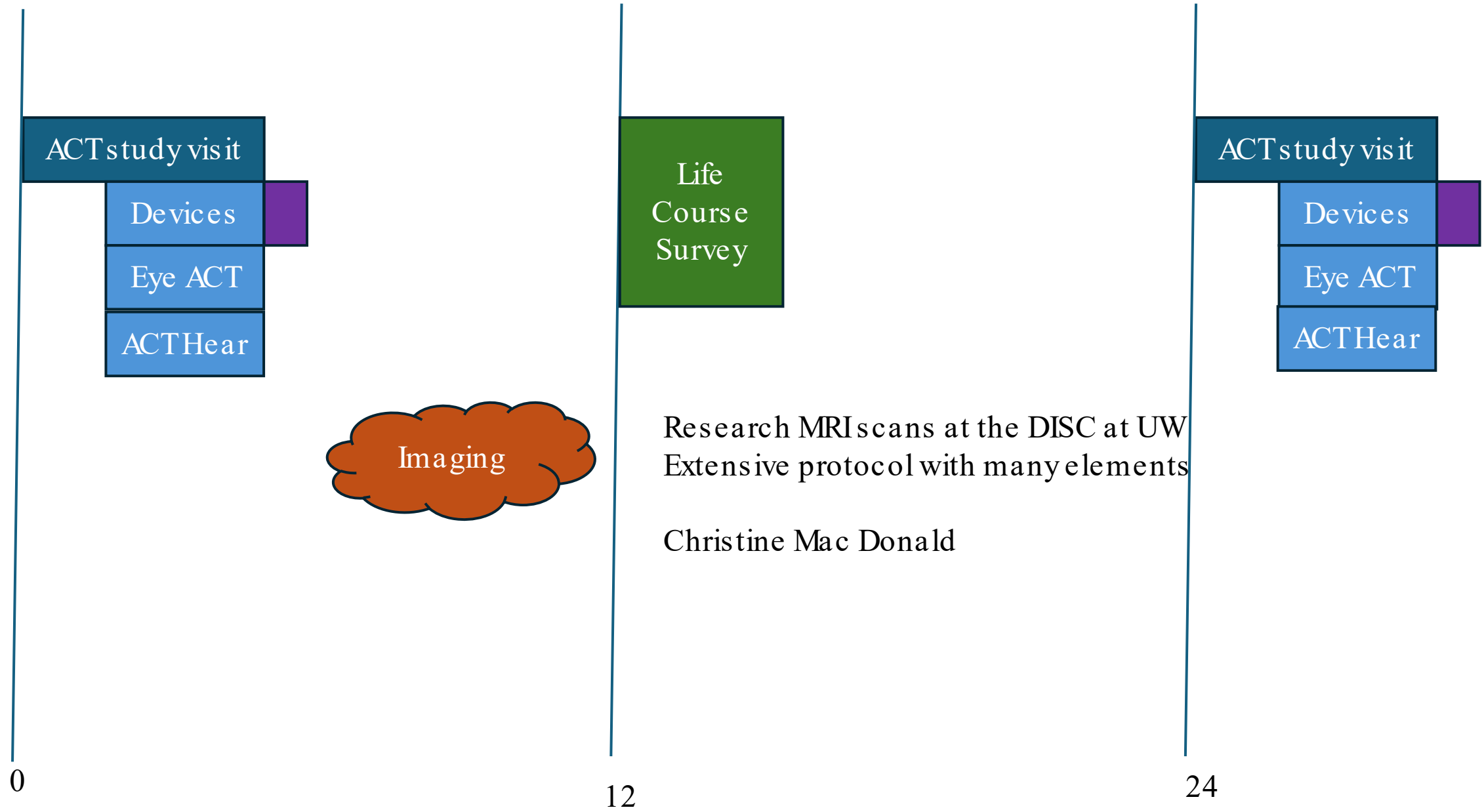
ACT study data collection



ACT study data collection



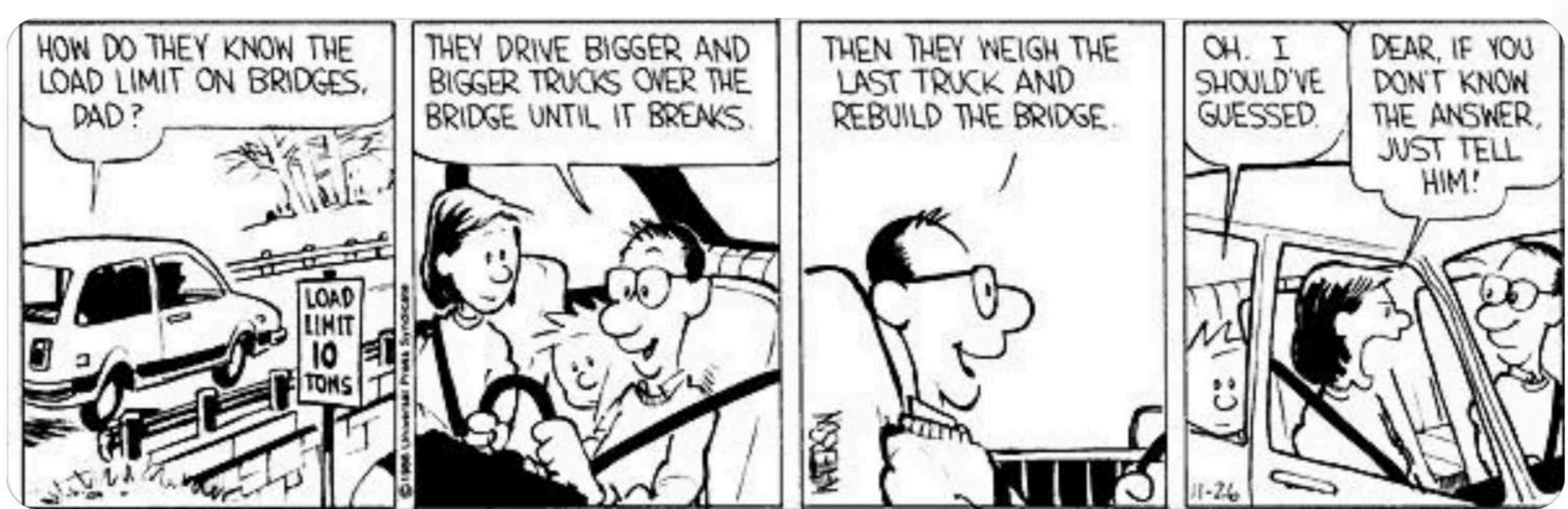
ACT study data collection



Thoughts on proposing additional new data collection activities

- Competition for the ACT study visits is fierce
 - New collection there would need to be mission critical
 - Time and burden considerations are critical
- Enrolling interested people in additional data collection is proving to work well for Eye-ACT, high interest in hearing
- Wearables has gone well, integrated nicely
- Life Course Survey is new for us and pretty well accepted
 - Offloads data collection from the ACT study visit cycle
- Imaging works well, has taken some coordination and effort
 - Imaging at a central site, transportation and communication challenges
- Definitely good to discuss and brainstorm about burden

We won't be doing this!



https://www.reddit.com/r/calvinandhobbes/comments/j7c201/thats_how_they_know_the_weight_limit_on_bridges/?rdt=46559

Clinical data resources

- Pharmacy data 1977-
- Lab data 1988-
- Billing codes e.g. ICD9, ICD10 codes, CPT codes
 - Combinations of these e.g. Parkinson's disease
- Address data from billing (augmented with Life Course Survey)
- EMR around 2003
- Paper medical records for decades
- Gold mines like OCT, other legacy computerized data
- Definitely good to discuss and brainstorm
 - These resources may require \$ but do not add burden

Core structure

- Administrative Core (Katie Rose Johnson, Nicole Gatto, Paul Crane, Andrea LaCroix, Linda McEvoy)
- Clinical Core (Linda McEvoy)
- Life Course Core (Sarah Tom)
- Neuropathology Core (Dirk Keene)
- Neuroimaging Core (Christine Mac Donald)
- Data and Analysis Core (Pam Shaw and Rod Walker)

Life Course Core

- Broad thinking about exposures across the entire life course
 - Early life exposures, area-based exposures, census data
 - Adversity, social determinants of health
 - ...Many others.
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- Sarah Tom

Neuropathology Core

Dirk Keene
Caitlin Latimer
Amber Nolan

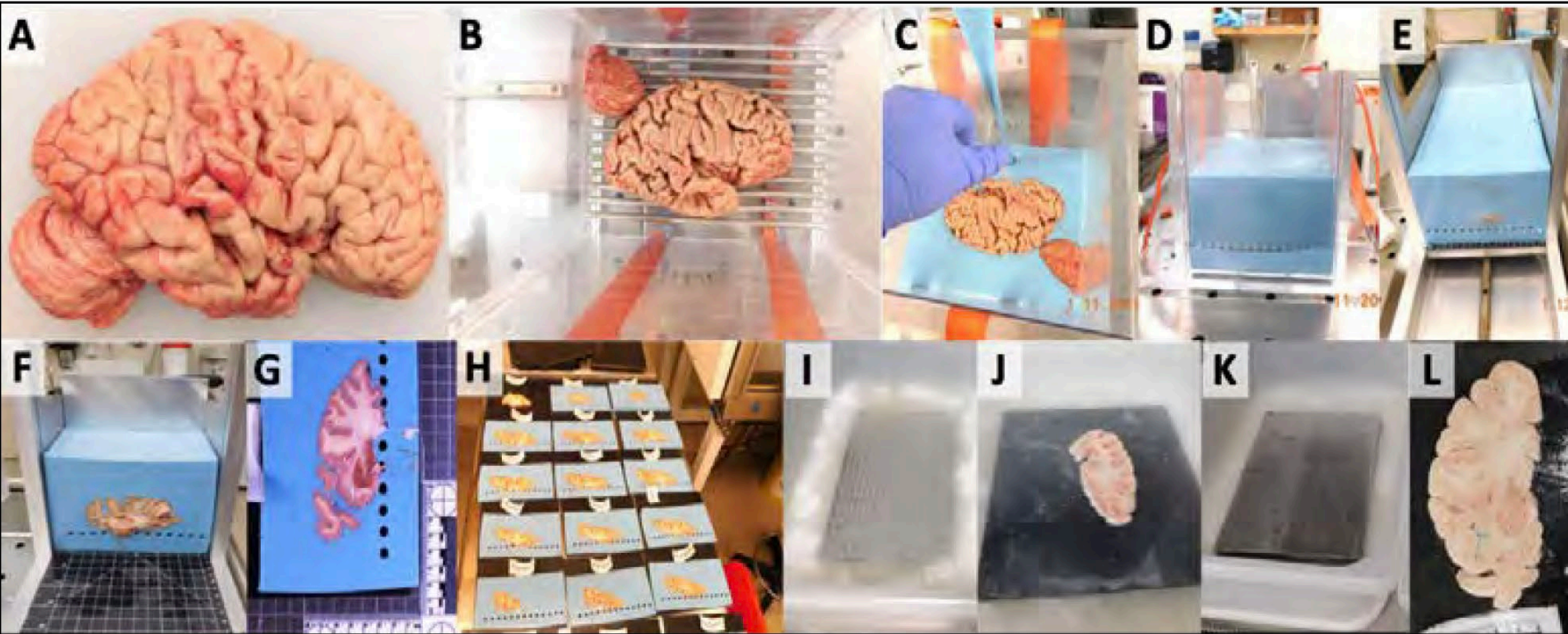


Figure 3. Rapid Autopsy for Integrated Neuropathology. ACT participant hemiserebrum stripped of meninges (**A**) is dissociated from brainstem/cerebellum and placed on crossbars (**B**) followed by addition of liquid alginate (**C**) which sets in <5 minutes to form alginate-brain block (**D**) and is placed in slicing sled (**E**), cut into uniform 4mm thick coronal slices (**F** – brain is normally stabilized at cut edge with Teflon plate which was removed for photograph). The alginate-brain slices are photographed with a fixed, high resolution digital camera (**G**), laid out (**H**), placed in dry ice-isopentane slurry (**I**) on Teflon plate (**J**) then sandwiched with second Teflon plate, and flipped to ensure even, rapid freezing to protect cytoarchitecture (**K**) resulting in optimally frozen thin coronal slices (**L**) that are vacuum sealed and stored at -80°C. Alternating coronal slices are fixed for pathology.

Neuroimaging Core

- Historical and ongoing clinical scans ~2000
 - Read by neuroradiologists and CDEs determined
 - Freesurfer pipelines when possible and they often are
- Research scans ~400
 - Lots of research sequences not used in clinical care alongside structural
- In situ cadaveric scans in the autopsy suite
- Post-mortem imaging

Data and analysis is core

- Lots of cool puzzles we enjoy trying to solve!
- Selection and generalizability
- Missing data
- Longitudinal data
- Psychometrics

Current Project 1: sleep, activity, 24 hour cycle

- Leverages study data and data from wearable devices
- Statistical approaches to 24 hours in a day (“ipsative”)
- Coordinated with other studies around the world with similar sorts of data
- Amazing leap in the data available for sleep and for activity with objective measures
 - Collaborative efforts with others around the world collecting similar data
- Address selection with analyses

Current Project 2: Cognitively-defined AD subgroups

- New thinking about heterogeneity among people with AD, maybe AD is not just one thing
- Aim 1: Imaging
- Aim 2: Neuropathology
- Aim 3: Lived experience of people with AD and their caregivers.
 - Anthropologists, economists, computational linguists (NLP)
 - Qualitative data – providers, caregivers, people living with dementia...

Current Project 3: Pharmacoeconomics and stem cells

- Leverages extensive pharmacy data
- Fundamental issue: not RCTs
- Generating stem cells from ACT autopsies, can grow into neurons (and other things)
- Expose one set of clones to Drug A, a second set to Drug B, compare and contrast
 - Novel matching up of disparate fields to address limitations of each
 - Mechanisms and molecules up to epidemiology

The LOI request

We encourage LOIs for ideas that are in the early stages of development as we are looking for the best possible projects to include and will work with you to help develop your proposal. Investigators and teams from diverse backgrounds and/or including junior investigators are encouraged to apply.

LOI Required Information:

- Investigative team (if current ACT investigators are not included, we will work to connect you to ACT investigators with relevant expertise).|
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- Draft specific aims, addressing significance of proposed work and how it leverages ACT's unique resources and utilizes all cores.
 - Description of potential participant or clinical staff burden (if any).

Criteria for review: Relevance to brain aging and dementia and compatibility with current ACT data and cores. We will select projects that best align together to create a cohesive U19 when added to the cores, fitting within our life course theme. Projects that utilize multiple cores are preferred, as are those that will enrich ACT resources. Lead investigators should have strong experience in the field of aging and dementia, with experience leading an R01 or equivalent award.

Evaluation:

LOIs will be evaluated by ACT's executive committee. Investigators may be invited to present to the executive committee during the evaluation process. Final selection will occur by May 1st, 2024.

If selected: ACT will work closely with the investigative teams selected to develop the strongest possible proposal to include in the U19 renewal. Investigators will be expected to attend the ACT symposium in May 2024 to discuss their proposals with ACT investigators.

If not selected: For meritorious projects, ACT will encourage investigators to [propose an ancillary study](#).

QUESTIONS?