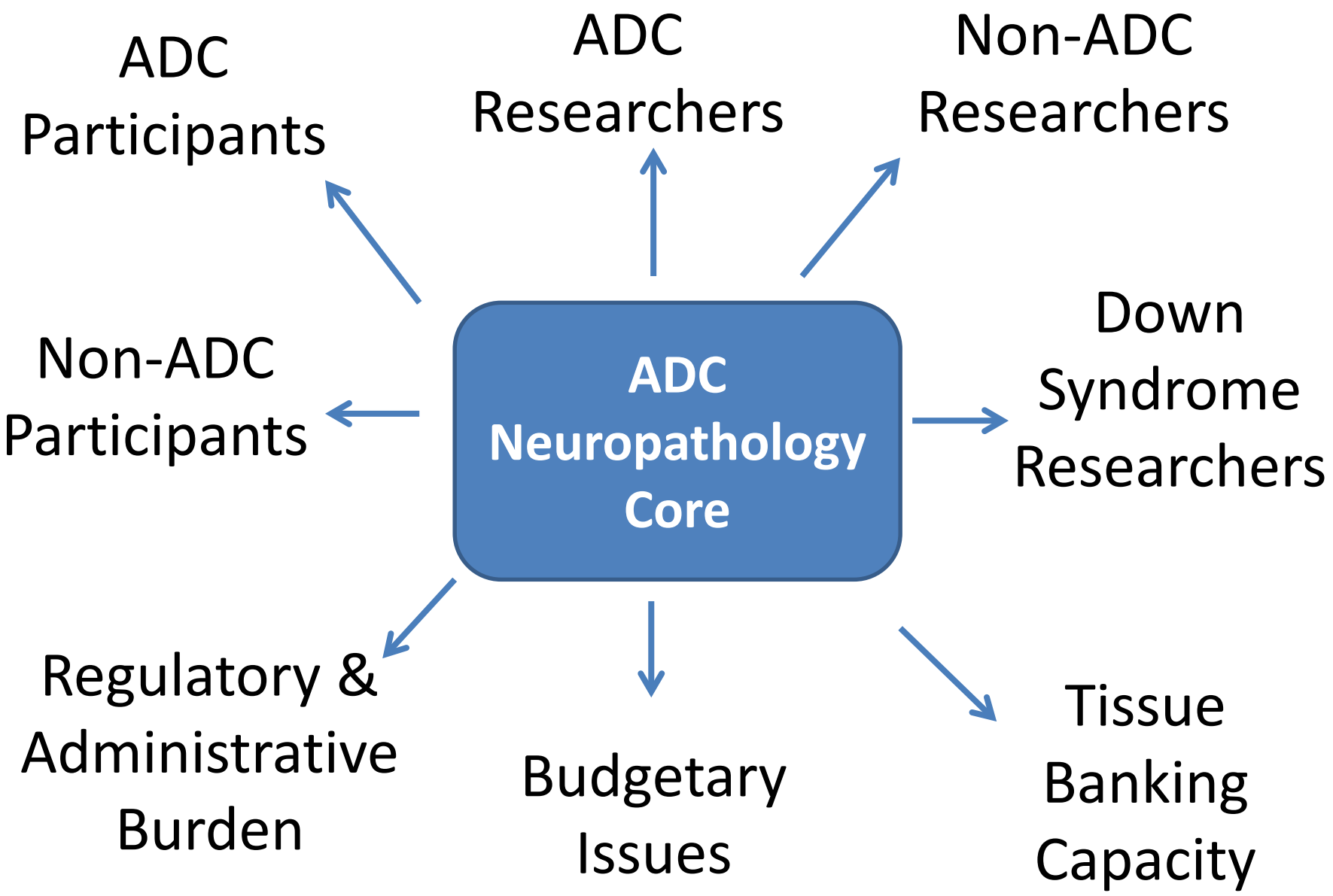
ADC NP Core Leaders Survey 2017

Survey Overview

- Several issues raised with the ADC NP Core Steering Committee and the NIA
- Survey of ADC NP Core Leaders covering 7 topics.
- Input from steering committee (C Dirk Keene, Matthew Frosch), NIA program officers (Cerise Elliott, Nina Silverberg), Down Syndrome research community.
- ***29 responses corresponding to a 94% response rate***


ADC Participants
ADC Researchers
Non-ADC Researchers
Non-ADC Participants
ADC Neuropathology Core
Down Syndrome Researchers
Regulatory & Administrative Burden
Budgetary Issues
Tissue Banking Capacity

ADC NP Core Leaders' Survey

1. Non-ADC Autopsies
2. Central repository/database
3. Support of non-ADC research
4. Down syndrome research
5. Clinical trial cases
6. CLIA certification
7. Other

Survey Response Themes

- How do ADC NP Cores deal with over-commitment of limited resources?

- Balance between national coordination & standardization versus maintaining the strengths and unique abilities of individual ADC NP Cores.

ADC NP Core Leaders' Survey

1. Non-ADC Autopsies
2. **Central repository/database**
3. **Support of non-ADC research**
4. Down syndrome research
5. Clinical trial cases
6. **CLIA certification**
7. Other

Issue #2. ADC brain banks are committed to banking AD tissues including many end-stage brains. The following questions center on your opinions regarding various national/central resources or initiatives.

Would a central frozen tissue database/bank be helpful?

- 18 of 29 No
- 3 database but not repository
- 6 yes with provisions, or maybe
- 2 yes

- Rare/unusual cases
- Cost, effort, limited resources better spent on existing ADC brain banks
- NACC already exists as database
- Repository OK but only if optional
- Administrative burden (deposits/retrievals)
- Non-standard/heterogeneous banking procedures

Central database/bank for other tissues?

- 13 of 29 No
- 4 database but no repository
- 7 maybe
- 5 yes
- 1 “I don’t know”

- Useful for rare/unusual cases
- NACC already exists, add to NACC (3)
- Cost, management, limited resources (7)
- Few centers collect such tissues (1)

Central tissue request mechanism?

- 10 No
  - One size does not fit all, need local review, need consultation for tissue type/fesibility/experimental design
- 3 NACC already exists
- 5 Yes provided final decision lies with parent ADC, low administrative burden/inertia (strong system to evaluate requests, ease of use)
- 6 Yes

Issue 2: Central Bank

- Many centers do not support for a central repository with a somewhat mixed response regarding a central database.
- NACC fulfills much of this role already.
- Worry about funding and administrative burden for NP Cores that are already stretched thin.

- Some NP Cores see a central database/repository as a means to streamline and homogenize brain banking

Issue #6. There is inherent variability from center to center in terms of the performance, analysis and reporting of research brain autopsies, including whether brain banks are operating with CLIA certification.

Is you NP Core CLIA certitifed?

- 18 of 29 No
- 7 Yes
- 3 Mixed/hybrid

- One center: “big problem”
- Another center: mistake to require CLIA certification due to increase costs (one-third), paperwork, admin costs

Department's clinical lab vs. running an independent lab?

- 15 of 29 ADC NP Cores run an independent lab
- 6 use department's clinical laboratory
- 8 us a mixture (clinical lab + their independent lab)

- Prefer to develop their own technology, lack of available stains in clinical lab, institutional barriers between research/clinical labs, ADC NP Cores are superior (fast food vs. four star restaurant)

Barriers to CLIA certification?

- 14 of 24 Money and resources
  - Higher staff salaries, validation requirements, controls
- 6 Administrative burden
- 3 Not sure or have not considered

Against CLIA

- “I would rather not have to deal with the additional documentation and “paperwork.”
- “We want to do science and not to spend valuable time in ever increasing regulation”
- “We don’t need additional levels of regulation. What purpose would this serve? Is there an existing problem that would be addressed by this? What might be the unintended consequences of this?”

For CLIA

- “We are interested in this”
- “We believe that NIA should establish a working party to investigate the transition from a purely research funded NP core to one which is administratively and functionally integrated with clinical services within the hospital.”
- “We have skated around this issue for years, but the CLIA law states that any studies done for diagnosis (i.e., reported to the family or clinician) must be done in a CLIA-certified lab; it doesn’t matter whether you charge or not. This issue may come to a head at some point.”

Discussion of Issue #6: CLIA Certification

Issue 3: The resources of the ADC are meant to be used within and outside of the ADC network. How can we leverage the resources of the ADC to augment science/other research studies that have a brain autopsy component?

How do you support science outside of the ADC network?

- 20 of 29 provide tissues to non-ADC investigators locally, nationally and internationally (including industry)
- 9 also discuss collaborations, advice/education & grants with non-ADC investigators.
- 7 highlighted the magnitude of non-ADC interactions (lots, >1000 samples, most requests are non-ADC, extensive sharing, etc.)

- ADNI, DIAN, NACC, NCRAD
- non-AD dementias, PD, ALS, HD, metabolism
- Not easy given over-commitment of personnel and cost limitations

Can you identify non-ADC investigators who can use ADC NP Cores?

- 26 out of 26 Yes, not a problem, easy
- 3 core over-committed

  busy as is, overabundance of requests, underfunded, backlog, no problem attracting results

- Neuroimaging, genetics, psychology
- ALS groups (Target ALS, Answerl ALS, NEALS)
- PD groups (MJ Fox)
- Other NIA investigators
- SFN, ASCB

What is needed to leverage NP Cores for broader scientific use

- 16 of 29 support in the form of money (11), resources (6) and/or personnel (4)
  - Existing budget insufficient, small fraction, reliant on philanthropy/discretionary funds, do not want to charge for samples
- 5 Education/dissemination of information
- Other suggestions: committee, less admin burden, innovative use, more normals, publish quality papers, coordinate with other research groups, coinvestment in neuropathology cores

Guildelines for NP cores to leverage existing infrastructure?

- 13 of 29 “Yes” to “maybe helpful”
  - Guidance for charges, develop a central repository, need additional funds to support new guidelines
- 12 of 29 “No”
  - Need resources/funding/support, Unfunded mandate, already stretched thin, not necessary, not one size fits all, individual core strengths may be compromised
- 3 intermediate: needs discussion, committee, “I don’t know”

How many annual requests inside/oustide the ADC network?

ADC Requests	non-ADC Requests	Number of samples	ADC vs. non-ADC Requests
Do not know	Do not know		
Few	None		
3			
3	3	276 frozen, 1558 blocks	Approximately Equal
3	15		Non-ADC
5	13	1414	Non-ADC
4-6	2-4		Approximately Equal
4	1-2	Dozens per request	Approximately Equal
<10	Very few		ADC
10	40		Non-ADC
10	17	2623 over 2 years	Non-ADC
10	20		Non-ADC
10-15	10-15		Approximately Equal
12-24	100's		Non-ADC
15	15	Few to 100's per request	Approximately Equal
~15			
20-30	120-150		Non-ADC
30	31		Approximately Equal
42	9		ADC
50	20		ADC
>50			>6000
Too many	Too many		
60-80 per year	25-40%		ADC
~100	10%		ADC
Several 100	Several 100		

Discussion of Issue #3: Supporting non-ADC Research

- ADC NP Core Leaders are already supporting non-ADC researchers
- Additional use of ADC NP Core resources is possible in theory, but there is a strong sentiment from several centers that they are underfunded as is, warning against an "unfunded mandate"

Issue #1: Autopsy requests from non-ADC participants

Do you accept/deny such cases?

- 14 of 29 do not accept non-ADC cases except for rare occasions (for unusual/rare cases of potentially high scientific yield).
- 9 centers will accept non-ADC cases if they were seen previously at their institution or part of an ancillary research group at their institution.
- 4 accept non-ADC cases.
- 1 “occasionally”
- 1 decision made by clinical core

If you accept, do you charge?

- 12 out of 26 do not charge
- 5 charge autopsy/transportation fees only if not seen at their institution
- 4 charge transportation fees
- 2 partially subsidize transportation fees
- 1 decides transportation fees case-by-case
- 3 charge autopsy and transportation fees

How do you report such cases?

- Autopsy report or letter (25 out of 25)
- Family or next of kin (16 out of 17)
  - 3 by telephone and report/letter
- Physician (6 out of 17)
- Clinical core only (1 out of 17)

- One center indicates their report is for research purposes only and not for medical decision making

Do you make tissue available for distribution?

- 22 of 26 Yes
- 4 No

Discussion of Issue #1: Non-ADC Brains

- Generally not accepted with some exceptions for local, rare/unusual cases.
- Variable costs associated with non-ADC brain autopsies

Issue #5. What role do the ADC NP cores have in terms of evaluating individuals who have participated in prior or ongoing clinical trials?

Should clinical trial participant brains be collected systematically?

- 23 of 29 Yes/absolutely
- 2 Depends on details of clinical trial
- 1 Depends as systematically sometimes means "lowest common denominator"
- 2 Already being banked
- 1 Considered doing this, no SOP yet

What resources would be required?

- 18 or 29 Personnel, resources and/or money
- 2 Industry financial support
- 2 database of participants (with clinical data)
- 2 usual banking resources
- 1 high administrative burden, esp with industry/access/subject identity
- 5 Depends, need more details
- 2 Already banking these brains

How should these cases be recorded for availability to the community?

- 9 Database (7 NACC)
- 5 Treat per usual ADC methods
- 4 Data should be made available
  - Perhaps after initial clinical trial studies completed
- 8 Depends/Not sure
  - Need more details regarding trial/target, need to understand research question, understand needs/requirements of industry partners
- 1 Separate repository

Discussion of Issue #5: Clinical Trial Cases

Issue #7. How can/should autopsies contribute to science? Can we develop a rating scale, can we get telephone clinical data, can we get data on participation in other studies, etc.? Can/should centers get "credit" for providing service to the research community?