Investing in Data for Alzheimer's Disease in LMICs

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Critical global health

- High-income country – Low-income country relationship reflects long, complicated history of colonialism, slavery, exploitation, etc.
- Work involving HIC and LMIC scientists should acknowledge this and strive to improve things
- Lots of work being done on this set of issues, e.g.
  - [When People Come First](#)
  - [Critical Epidemiology and the People's Health](#)
  - [Epidemiological accountability: philanthropists, global health and the audit of saving lives](#)
  - [Time to take critical race theory seriously: moving beyond a colour-blind gender lens in global health](#)
  - [Decolonizing global health: what should be the target of this movement and where does it lead us?](#)

My perspective

- Training: biology, engineering, and demography
- About 20 years working closely with health and demographic surveillance systems in Africa, mostly on data and system design
- About 10 years working with team to update and redesign population estimation and forecasting methods for UN Population Division
- Created group to improve global estimation of U5MR using existing survey data ⇒ led to UNICEF's current method for small-area, longitudinal estimates
- Verbal autopsy to estimate the population *burden of disease*
  - Global standards via WHO - VARG
  - Automated methods - InSilicoVA
  - Robust, generally usable software - openVA
  - Verbal autopsy and minimally-invasive tissue sampling
  - Reference Death Archive

Alzheimer's (and many other) Disease - complicated
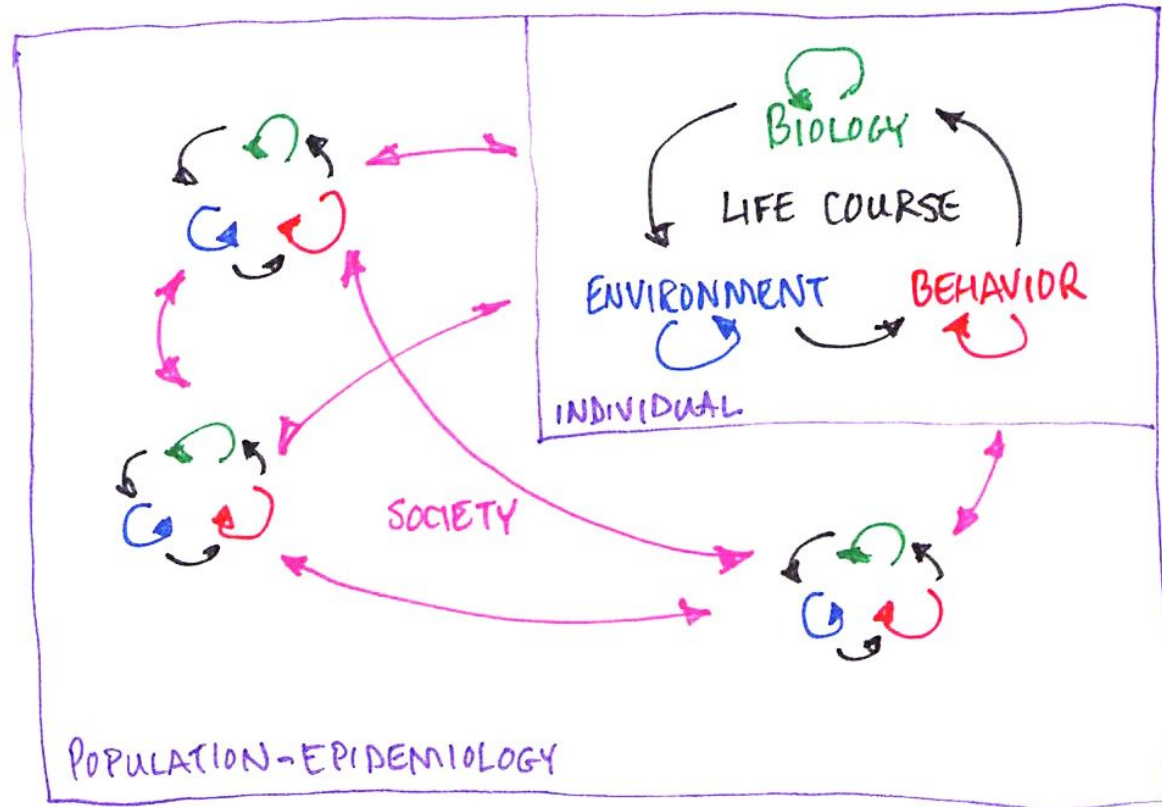
Biology

- **Objective**: *biological mechanisms*
- **Level**: molecules, individual humans, and population genetics
- **Cause/effect** established through experiments
  - Few human experiments; mostly cell lines or animal models
- Genetics - important alleles of apolipoprotein E (*APOE*) gene that confer significant risk
- Largely generalizable and transferable, i.e. all humans have very similar biology, with nuances
- Often effectively deterministic
- *Biology interacts with behavior and the environment over the lifecourse to create individual disease outcomes*

Behavior

- **Objective:** *behavioral effects +/- on risk of disease, disease progression, and disease outcomes*
- **Level**: individual humans, and groups of humans
- **Cause/effect** established through observational studies and various forms of randomized study
- *Sometimes* generalizable and transferable, i.e. in some circumstances humans share behavior, but in many there are nuanced differences
- Measurement affected by circumstances and quality of human interactions, e.g. interviews, participant observation, etc.
- *Behavior interacts with biology and the environment over the lifecourse to create individual disease outcomes*

Environment

- **Objective**: *describe physical environment and its effects on disease dynamics and individual disease outcomes*
- **Level**: physical environment experienced by individual humans and populations of humans
- **Cause/effect** established through combination of observational studies and experiments, both intentional and accidental
- Generalizability depends on exact nature of environmental factor, e.g. biology-level or socio-cultural
- Measurement both deterministic/precise and statistical (estimates, distributions, uncertainty/confidence)

Population - epidemiology

- **Objective**: *population-level description of burden of disease, disease dynamics, and cause/effect*
- **Level**: well-defined (large-ish) populations of human beings
- **Cause/effect** established through observational and various forms of randomized study
- Essential measures:
  - Burden of disease
  - Disease dynamics: incidence, prevalence
- *Identify and rank important health challenges*
- Describe/infer how many, where, when, and who at various levels of granularity (disaggregation)
- Usually population/circumstance-specific and often difficult to completely generalize
- Most often statistical, i.e. estimates of distributions, uncertainty/confidence

Society - behavior sciences

- **Objective:** _group-level_ behavioral _effects on burden of disease, disease dynamics, individual disease progression, and individual disease outcomes_
- **Level**: _connections_ between individual humans, groups of humans
- **Cause/effect** established through _observational_ studies and various forms of randomized study
- _Maybe_ generalizable and transferable, but often context-specific
- Measurement affected by circumstances and quality of human interactions, e.g. interviews, participant observation, etc.
- How to individual humans affect each other's behavior?
- Effects of social institutions on disease processes, e.g. _government interventions_

Where are we now in LMICs?

Biology

- Biology is essentially universal
- We can largely borrow what we know from HIC settings
- *However,* need to replicate and check key findings in LMIC populations and ensure that original work included all types of people, e.g. both sexes
- **Need:** biomarkers, biobanks, labs, animal models, cell lines, etc.

Behavior

- Lots of work still necessary in HICs
- Because behavior is circumstantial/cultural, behavioral results are not necessarily generalizable or transferable
- Behavioral studies must be done in LMIC settings, accounting for the socio-cultural, contextual circumstances of LMICs
- Cultures and languages must be handled carefully; western medical concepts cannot be directly transferred to many LMIC contexts
- There's **a lot** to do

Environment

- Most environments in LMICs have not been described or investigated with respect to Alzheimer's or other diseases of aging
- This is particularly true for people who live in rural communities or informal urban areas - i.e. a great many people
- **Need:** to initiate this work in most areas
- Much to do!

Epidemiology

- Some work done on people who live in urban areas and are accessible
- Very little done in rural areas or informal settlements
- Population burden of cognitive disorders of aging not directly measured in most LMICs
- Only direct measurements for special populations
- **Need**:
  - Describe basic burden of disease
  - Increase coverage to whole populations
  - Create measurement systems with ability to operate at fine(r) levels of granularity - subpopulations, disaggregation
  - Longitudinal surveillance
  - Routine, population-scale, continuous monitoring

Society

- Variety of work done at this level
  - General assessments based on fragmentary and flawed data
  - Intervention design and testing/monitoring
  - Monitoring of accessible subpopulations, mainly in context of research
- **Need**:
  - Research to define what to focus on here?
  - Do HIC concepts translate to LMICs?
  - I'm not sure!

Ideas for how to proceed

- To improve and increase research in LMICs
  - **TRAINING**
  - **Decolonize global health** → will lead more context relevant research with better chance of driving change
  - **Public funding**, 'open-access' funding for researcher-initiated projects, prioritize mutual partnerships between HIC and LMIC scientists, and LMIC scientists in general
  - **Avoid foundation-driven work** that narrowly adheres to foundation's view of what to do → help foundations move to more open-access, researcher-initiated approaches
- **New data, methods, approaches** adapted to LMIC settings

Training

- **Survey, trial, and research design**
- Electronic data capture
- Data management
- Data ethics
- **Bayesian statistics**
- Machine learning
- General (frequentist) statistics
- Emphasize **sampling design, generalizability**
- **Longitudinal** research design, data management, analysis, etc.
- *General programming*, not just stats packages

Training

- Socio-cultural systems and language - **human interaction**
  - Interviewer effects are *very* imporant!
  - **Interview design**
  - **Interviewing in specific socio-cultural settings**
- **Translation** - policy, implementation, sustainability
- Conduct training in LMICs as much as possible
- Utilize existing field sites/stations/laboratories to build in apprenticeships
- Aim for wider cross-field training, at least including
  - Biology
  - Behavior
  - Methods
  - Culture/Society

Data & Methods

- **Build and support widely-used, public data resources**
    - **Data standards (harmonization), standards setting and maintaining committee(s)**
    - **Trusted, programmable archives, full documentation/metadata**
- Build and maintain high performance computing centers
- Whole population and subgroup burden of disease
- Build basic surveillance into routine administrative systems
    - Civil registration and vital statistics
    - Regularly occurring, standard surveys that represent whole population and important subgroups
- Lots of data already exist, use them, invent new ways of using them!
    - Example is new small-area methods for traditional DHS surveys → UNICEF U5MR estimates
- Explore use of unanchored data streams (aka 'big data')
    - Develop approaches to calibrate or ground truth
    - Potentially very valuable longitudinal monitoring, possibly very cheap too

Data & Methods

- Build on health and demographic surveillance systems
  - Hawthorne effect
- Build and strengthen vital statistics
- Incorporate traditional healers to develop effective interventions
- ***Design and build hybrid vital statistics + survey + health and demographic surveillance longitudinal monitoring systems***
  - Potentially much more efficient and accurate
  - See Hyak for a start on this idea
  - Potential for routine monitoring at all important levels/aspects of the Alzheimer's/cognitive disease system: individual, group of individuals, biology, behavior, environment, whole population, etc.
  - *Need completely new methods for collection and analysis*
- **New, creative methodological thinking that goes beyond traditional statistics and data sources: *requires cross-trained individuals and interdisciplinary teams***

Interesting initiatives/organizations - <u>Africa</u>

- [African population cohort consortium](#)
- [DS-I Africa](#)
- [APHRC](#), Kenya and Senegal
- [AHRI](#), South Africa
- [Regional Institute for Population Studies (RIPS)](#), Ghana
- Many more!

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