Measurement of SED in Child Populations: Design and Estimation Considerations in Multi-phase Studies

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Multi-Phase Survey Design Considerations

- Statistical objectives

- Multi-phase design choices
  - General framework
  - Costs (data acquisition, screening survey, classification survey)
  - Errors (variance of estimates, survey bias, misclassification)
  - Optimal design conditional on existing data

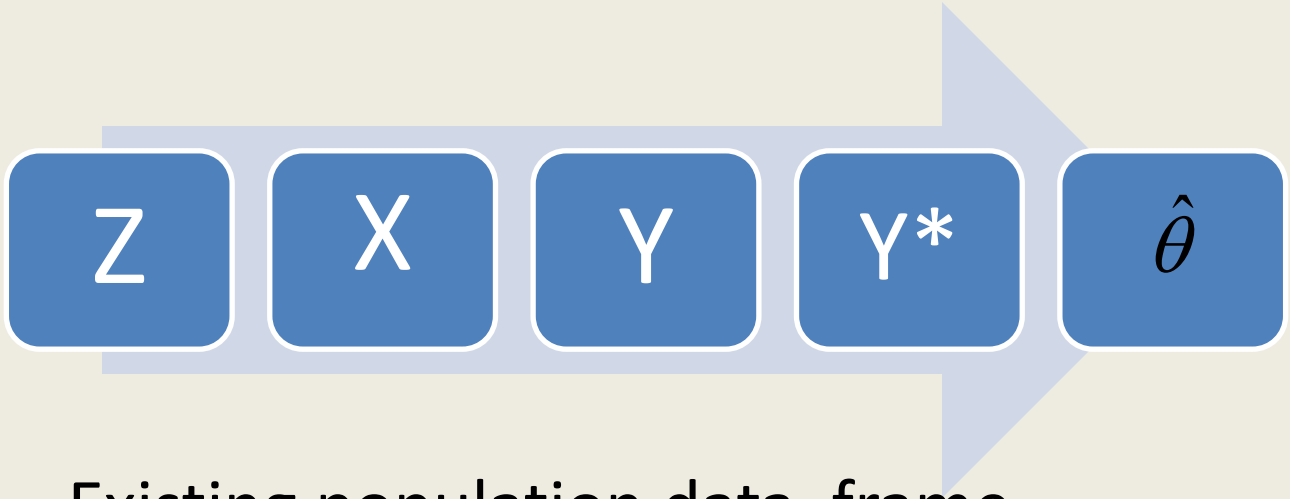
- Measurement error across phases

- Estimation and Inference
  - Direct, design-based methods
  - Model-assisted, model-based

Statistical Objectives of a Screening Study

- Target population
- Estimation of prevalence, population size
- Screening to identify a sample for in-depth subpopulation study
  - Descriptive characteristics, DX types, symptoms
  - Incidence, age of onset
  - Associated factors, causal insights (?)
  - Treatment seeking, treatment compliance

Notation for the Sequence: Design, Observation, Measurement and Estimation



Z – Existing population data, frame

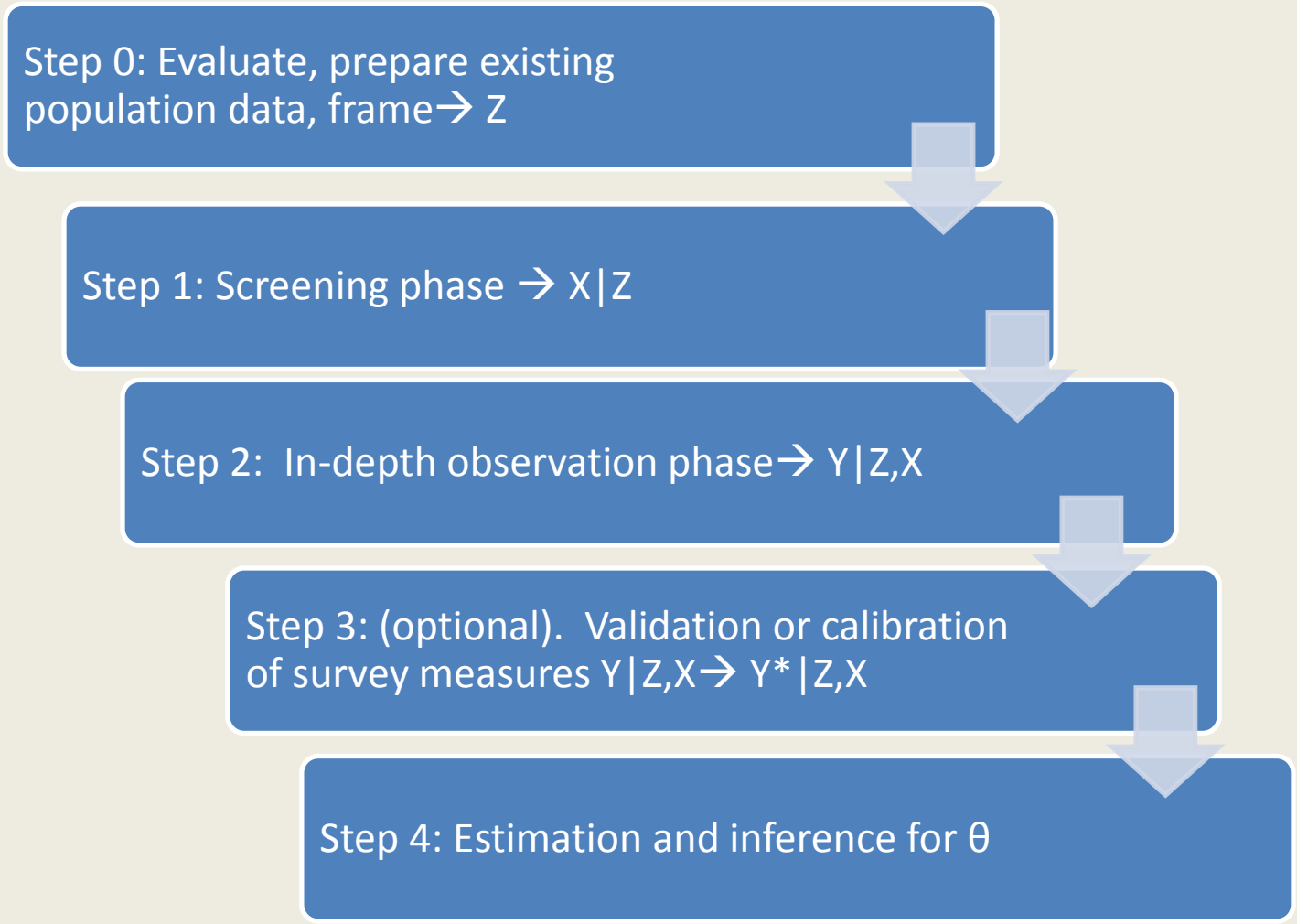
X - Phase 1 Screening data

Y - Phase 2 measurement of outcome of interest

Y*- Validated, calibrated outcome of interest

$\hat{\theta}$ - Estimate of population parameter

Multi-phase Design Framework



Cost Factors in Optimal Multi-phase Design

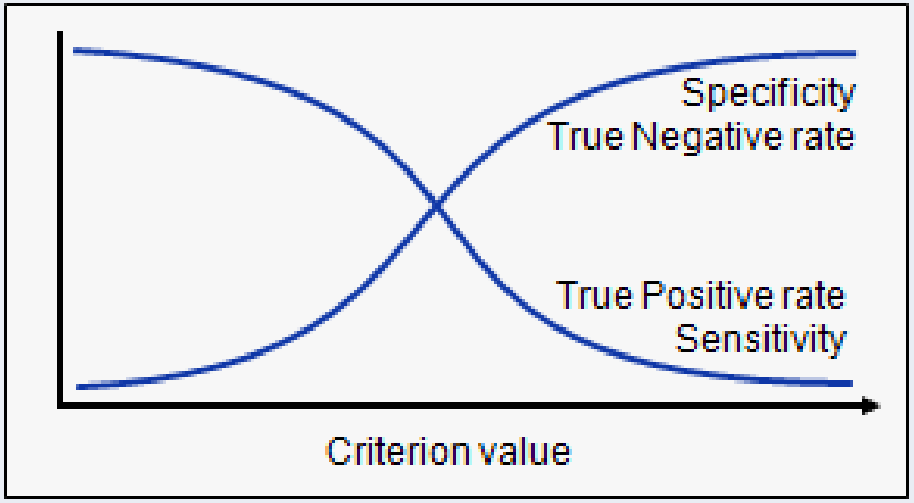
- Prevalence of target population
  - Prevalence estimation, drives n for estimating P
  - Subpop study, drives n to achieve eligible sample of size m
- Need for new Step 1 survey screening (alternative is to assign screener status using existing data source).
- Ratio of phase-specific unit costs: C(2)/C(1)
- Sensitivity of Step 1 screener
  - High false positive rate requires larger Phase 2 follow-up sample size to identify eligible case sample of size m.
- Need for validation, calibration for Y→Y*

Error Factors in Optimal Multi-Phase Design

- Prevalence of target group – drives sampling variance
- Strength of associations: Step 1 (X|Z), Step 2 (Y|Z,X)
- Specificity of screener
  - Coverage of all true cases requires Step 2 subsampling of negative screens
  - High false negative rate based on Step 1 screener implies need for variable weighting of true cases in positive screen and those in subsample of screen negative cases
  - Variable subsampling and weighting of Step 1 +/- screens
    - Increases variance of estimates of population prevalence
    - Inflates variances of estimates for analyses of true subpopulation cases
- Validity of Y for Y*- potential for classification bias

Measurement:
Sensitivity/Specificity of Step 1 Screening

Step 1 Screening or Model Assignment, g(Z,X)	Step 2 Observed Status (Y)	
	NO	YES
NO		
YES		



Measurement Example: Sensitivity/Specificity of Step 1 Screening (Example: true prevalence=.20)

Step 1 Screening or Model Assignment, g(Z,X)	Step 2 Observed Status (Y)		
	NO (0)	YES (1)	Total
NO (0)	P_{00}=.64	P_{01}=.04	P_{0+}=.36
YES (1)	P_{10}=.16	P_{11}=.16	P_{1+}=.64
Total	P_{+0}=.80	P_{+1}=.20	P_{++}=1.00

Screener Sensitivity=P_{11}/P_{+1}=0.8 Screener Specificity=P_{00}/P_{+0}=0.8

Approximate % Increase in Variance of Estimated Prevalence Based on Step 2 Sample

$$L_{percent} \approx \left[\frac{\sum_{r=0}^{1} n_r^{(2)} \cdot W_r^2}{\sum_{r=0}^{1} \left(n_r^{(2)} \cdot W_r \right)^2} \cdot (n^{(2)}) - 1 \right] \cdot 100 = \frac{Var(W_i)}{\bar{W}^2} \cdot 100$$

$=$ Relvariance of Step 2 design weights for all cases in Step 2 sample.

Example of Weighting Loss in Variance of Estimates of Population Prevalence Due to Step 2 Subsampling of Step 1 Negative Screens (true prevalence, P=.20)

f_{pos}	$f_{neg,\ sub}$	% Increase in Var(p)
1.0	0.5	8%
1.0	0.33	22%
1.0	0.25	36%
1.0	0.10	130%

Expected Disposition of Step 2 Eligible Cases in a Two-Phase Design

Step 1 Screening or Model Assignment, g(Z,X)	Step 2 Expected Eligible Cases .	
	Expected sample size. Eligible true cases	Relative Design Weight. Step 1 is epsem.
NO (0)	$E(m_{01}) = \frac{n \cdot (1-P)}{K} \cdot (1-Spec)$	$W_i = K = 1/f_{neg,\ sub}$
YES (1)	$E(m_{11}) = n \cdot P \cdot Sens$	$W_i = 1.0$

Approximate % Increase in Variance of Mean Estimates for Phase 2 Eligible Subpopulation Sample

$$L_{percent} \approx \left[\frac{\sum_{r=0}^{1} m_{r1} \cdot W_r^2}{\sum_{r=0}^{1} \left(m_{r1} \cdot W_r \right)^2} \cdot (m_{+1}) - 1 \right] \cdot 100 = \frac{Var(W_i)}{\bar{W}^2} \cdot 100$$

= Relvariance of Step 2 design weights for true cases in Step 2 sample.

Example of Approximate % Weighting Loss in Variance of Estimated Means for Phase 2 Eligible Subpopulation Sample (true prevalence=.20, sensitivity=0.8)

f_{pos}	$f_{neg,\ sub}$	Step 1 Screen Specificity					
		1.0	0.9	0.8	0.7	0.6	0.5
1.0	0.5	0%	11%	13%	12%	11%	10%
1.0	0.33	0%	30%	34%	33%	30%	20%
1.0	0.25	0%	50%	56%	54%	50%	46%
1.0	0.10	0	180%	203%	194%	180%	265%

Measurement:
Reliability and Validity in True Case Identification

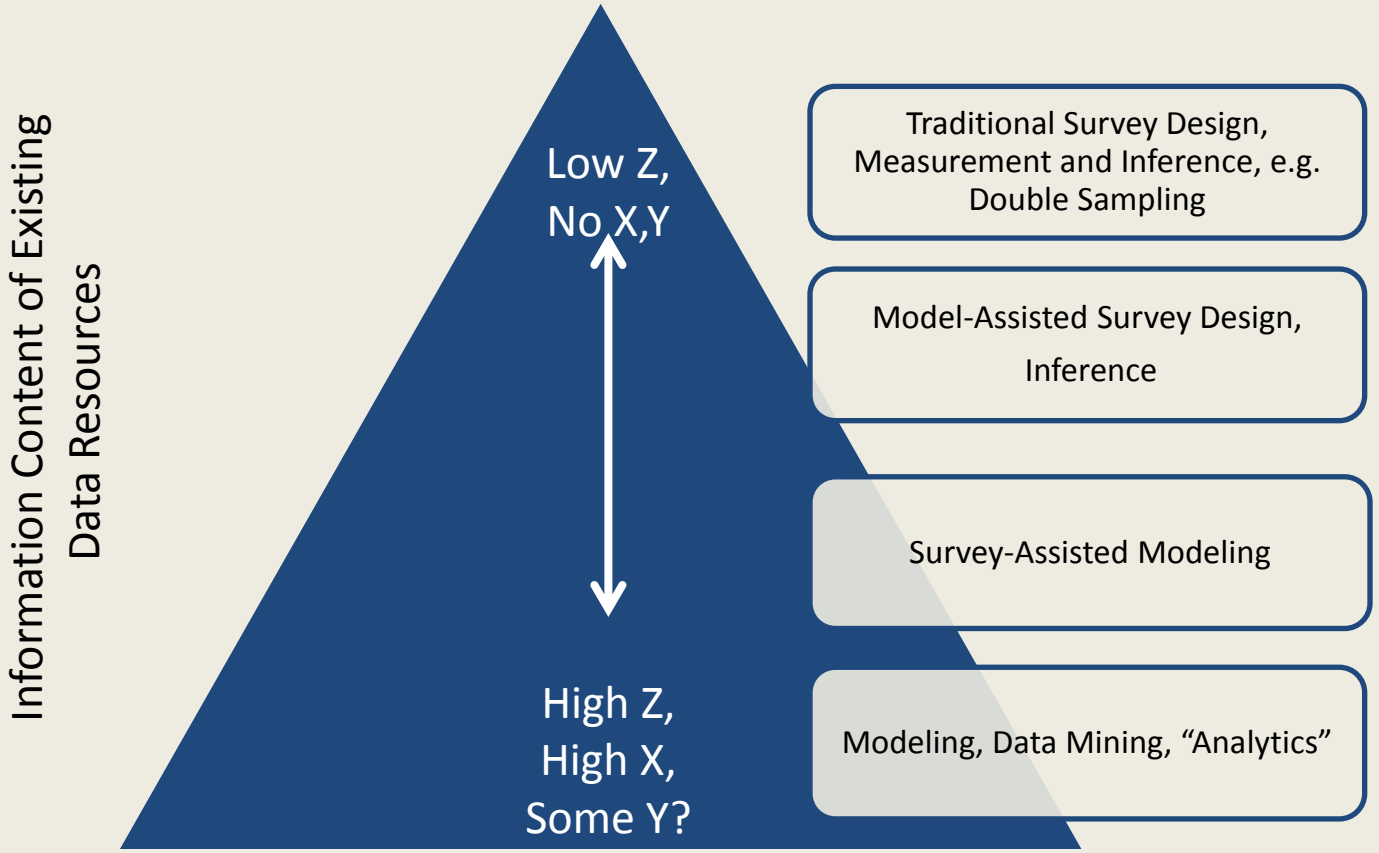
Kessler, et al. (2009). The National Comorbidity Survey Adolescent Supplement (NCS-A): III. Concordance of DS<-IV/CIDI diagnoses with clinical reassessments. *J Am Acad Child Adolescent Psychiatry:* 48(4):386-399

- Any disruptive behavior disorder, AUC = .84

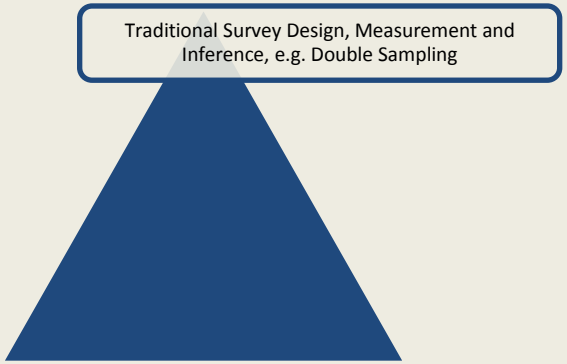
Observed/Assigned Case Status, Y	**True Case Status (Y*)**	
	NO	YES
NO	Specificity: 90.9% Sensitivity: 77.9%	
YES		
Total		

Integrating survey and administrative data.

Adaptation to Information Content of Available Data



Multi-phase Data Collections: Double Sample



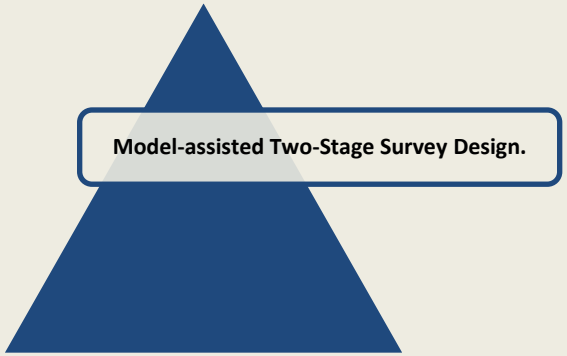
- Probability sample selected on the basis of Z
- Step 1 screening ascertains X for full sample
- Step 2 in depth interview or clinical follow-up for subsample ascertains Y or Y*.
- Optional: Calibration study after Step 2 determines Y→ Y*

Flint Men's Health Study

- Heeringa, SG., Alcser, KH., et al. (2001), "Potential Selection Bias in a Community-Based Study of PSA Levels in African-American Men," *Journal of Clinical Epidemiology*,54(2),142-148.

- Multi-phase design
  - Step 0: Area probability sample frame for Flint, MI disproportionately allocated to efficiently identify African-American households.
  - Step 1: Screening of new household sample to: 1) identify African-American males age 40+, 2)conduct health history interview, 3)obtain blood sample for PSA test (X|Z).
  - Step 2: Sample of Step 1 participants stratified by measured PSA level. Urologist clinical visit for clinical tests and transrectal ultrasound (TRUS) to determine probable cancer→ Y|X,Z.
  - Step 3: Biopsy to confirm cancer in detected growths, Y→Y*

Multi-phase Data Collections: Model-Assisted Survey Design



- Z, X^0 known for the population or existing probability sample
- Model of $f(Y^*|Z,X^0)$ is assumed
- Step 1: Under the assumed model, near optimal sample is selected directly based on $f(Y|Z,X)$ and known values of Z, X^0
- Step 2: In depth interview or clinical follow-up for the subsample ascertains Y or Y*, $f(Y|Z,X)$ is estimated and used in population estimation.
- Optional: Calibration study after Step 2 determines properties of Y→ Y*
- Standard estimation of θ from sample data

Aging Demographics and Memory Study (ADAMS) - Direct Estimation

- Langa, K.M., Plassman, B.L., Wallace, R.B., Herzog, A.R., Heeringa, S.G., Ofstedal, M.B., Burke, J.R., Fisher, G.G., Fultz, N.H., Hurd, M.D., Potter. G.G., Rodgers. W.L., Steffans, D.C., Weir, D.R., Willis, R.J. (2005). "The Aging, Demographics and Memory Study: Study Design and Methods". *Neuroepidemiology, 25,* 181-191.

- Multi-phase design
  - Step 0: Health and Retirement Survey (HRS) longitudinal panel of U.S. adults born prior to 1949. Rich longitudinal data including cognition test measures from HRS 2000, 2002. Ability to estimate a logit model of the probability of dementia from an external data set. Based on existing information in the HRS and a model the HRS panel "frame" was stratified by age, gender and cognitive score.

Dementia Probability Model (VSMA)*

$$logit\left\{ p(dementia \mid X) \right\} = \beta_0 + \beta_1 \cdot Age + \beta_2 \cdot Educ + \beta_3 \cdot CogScore$$

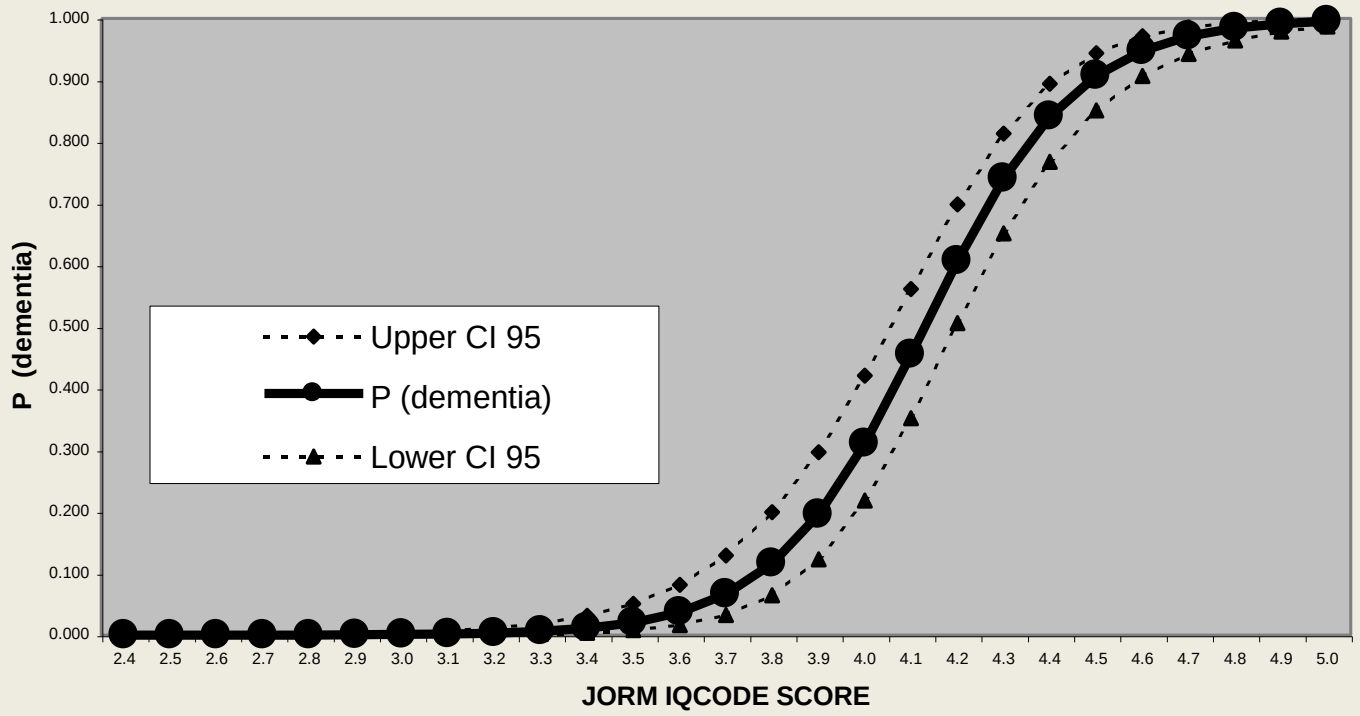
where:

CogScore = TICS 10 for HRS Self-reporters

= JORM IQ Code Score for Proxy Reports

* Source: Veterans Study of Memory and Aging

Figure 1: Predicted Probability of Dementia. Model Estimated from VSMA Data



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- Multi-phase design (continued)
  - Step 1: "Screening" and stratified subsampling for follow-up of HRS panel based on a stratification that used an externally estimated model relating probability of dementia to: age, education level , and TICS/JORM cognition test scores (2000 or 2002).
  - Step 2: In-home neurocognitive assessment, medical records collection, followed by consensus diagnostic conference review by expert medical panel to assign diagnosis category: normal, CIND, possible dementia, probable dementia, ALZ
  - Step 3: Two year follow-up to refine probable/possible dementia into CIND and dementia categories. Y→Y*

Aging Demographics and Memory Study (ADAMS) - Direct Estimation

$$\hat{p}_{dementia} = \frac{\sum_i w_i \cdot y_i}{\sum_i w_i}$$

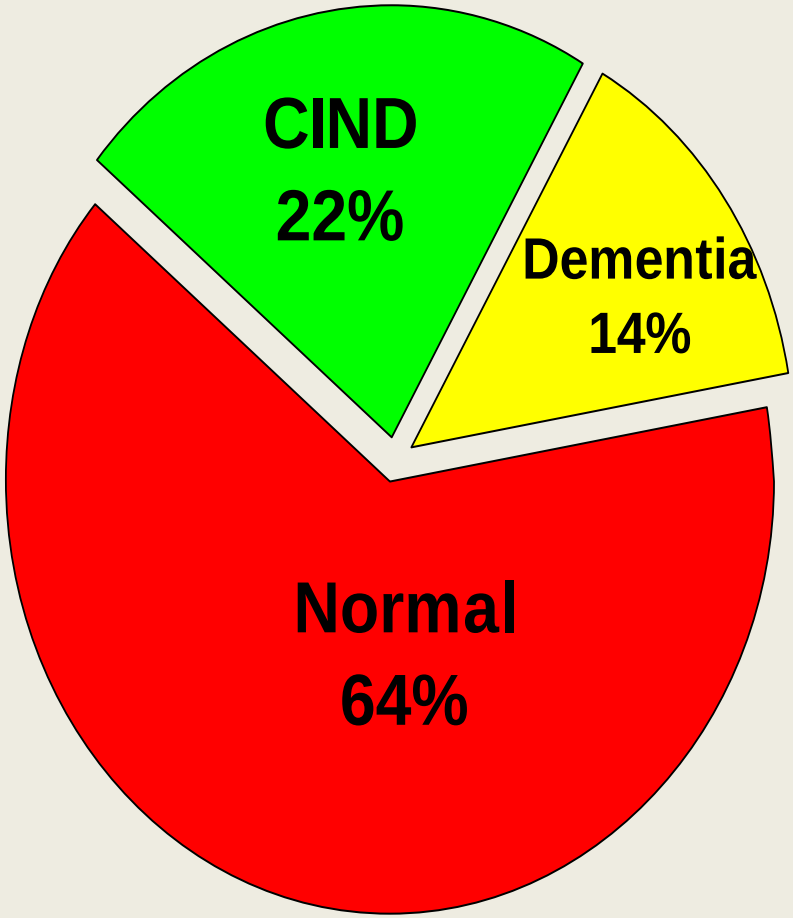
where:

$y_i = 1$ if ADAMS respondent i=1,...,n is classified as dementia, 0 otherwise;

$w_i =$ a case specific (population) weight to reflect sampling probabilities and nonresponse in the HRS panel and the ADAMS subsample.

$se(\hat{p}_{dementia}) \sim$ computed using variance estimation methods appropriate to the ADAMS complex sample.

ADAMS Estimates of 2002 Population Prevalence, Age 71+



US Population, Age 71+:

Dementia	**3.4 million**
CIND	**5.4 million**
Total Pop	**24.3 million**

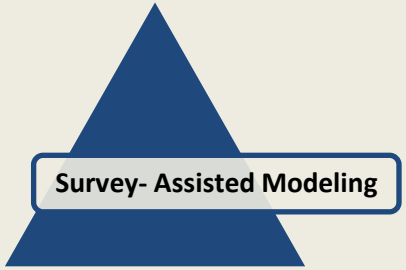
Sources : Plassman B, Langa K, Fisher G et al, 2007, 2008.

ADAMS Direct Estimates of Overall Prevalence of Dementia by Age Categories

Age	Adams Direct
70-79 years	4.95
	(1.27)
80-89 years	24.13
	(2.22)
≥ 90 years	38.18
	(3.79)
Total	13.67
	(1.29)

Percentages and Complex Design Corrected Standard Errors (parentheses) .

Multi-phase Data Collections: Survey-assisted Modeling



- Z, X^0 known for the population or existing probability sample that represents the full population
- Y* is not known. Model of $f(Y^*|Z,X^0)$ is assumed but parameters cannot be estimated from existing data.
- Step 1: Under the assumed model, sample is selected based on known values of Z, X^0. Sample design is optimized to estimate f(Y|Z,X).
- Step 2,3: In depth interview or clinical follow-up for the subsample ascertains Y or Y* and concurrent values of X, Z.
- From the survey data (training set), a "best" predictive model, f(Y|Z,X) is estimated
- The predictive model estimated from the survey is used to predict Y for each element in the existing frame (e.g. population reference, large baseline survey).
- Estimation and inference are based on model-predictions, properly reflecting the uncertainty associated with the modeled values of Y*.

Multi-phase Data Collections: Survey-assisted Modeling

- Predictive modeling approaches assign classification probabilities to all elements in the population frame (or weighted sample):

  Gertrude: "I hear the average American family now has 1.5 automobiles."

  Heathcliffe: "I bet that half a car is tough to drive."

  Red Skelton (ca. 1968)

- Decision is needed to analyze on probability scale or use probabilities to impute discrete classification.

- Inference should reflect prediction (imputation) uncertainty inherent in modeled values.

Estimation and inference: Predicted probability or discrete classification?

- Option 1: Use probability of dx classification directly in analysis

$$\hat{p}_i = \text{ predicted value drawn from } p(Y=1|X, Z_{obs}, \hat{\theta})$$

- Option 2: Impute discrete classification

$$\hat{Y}_i \in (0,1)$$

$$= \text{draw from } B(\hat{p}_i \mid Z, X, \hat{\theta})$$

ADAMS- Survey Assisted Modeling. Estimating the prevalence of dementia in the U.S. household population, age 70+ (2002)*

Statistic	ADAMS Direct Estimate	Predictive Modeling Method Using ADAMS to predict dementia for full HRS.				
		Logistic Regress w/MI	Lasso	Random Forest	Boosting	BART
$\hat{p}_{dementia}$	0.137	0.141	0.156	0.156	0.157	0.155
$se(\hat{p}_{dementia})$	0.013	0.004	0.004	0.004	0.004	0.004

* Covariate data base: HRS 2002. Predictive models fitted based on ADAMS sample data.

HRS: Logistic Regression Model for Overnight Stays in Hospital during the Past Two Years*

	2002	2004
Dementia*	1.30	1.32
	(1.11 - 1.53)	(1.09 - 1.60)
Age	1.03	1.03
	(1.02 - 1.04)	(1.02 -1.04)
White	1.22	1.08
	(1.01 - 1.46)	(0.94 - 1.25)
Female	0.92	0.87
	(0.82 - 1.04)	(0.79 – 0.96)
Odds Ratios, with 95% CI in parentheses		

*Dementia predictor is predicted value from ADAMS dementia logistic prediction model. Multiple imputation of predicted probabilities is used to reflect imputation uncertainty in the model predictions.