Rural-Urban Differences in Stroke Risk

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I have nothing to disclose

Why Focus on Health Disparities?

- **Health disparities are immense, and it is just the right thing to do!**

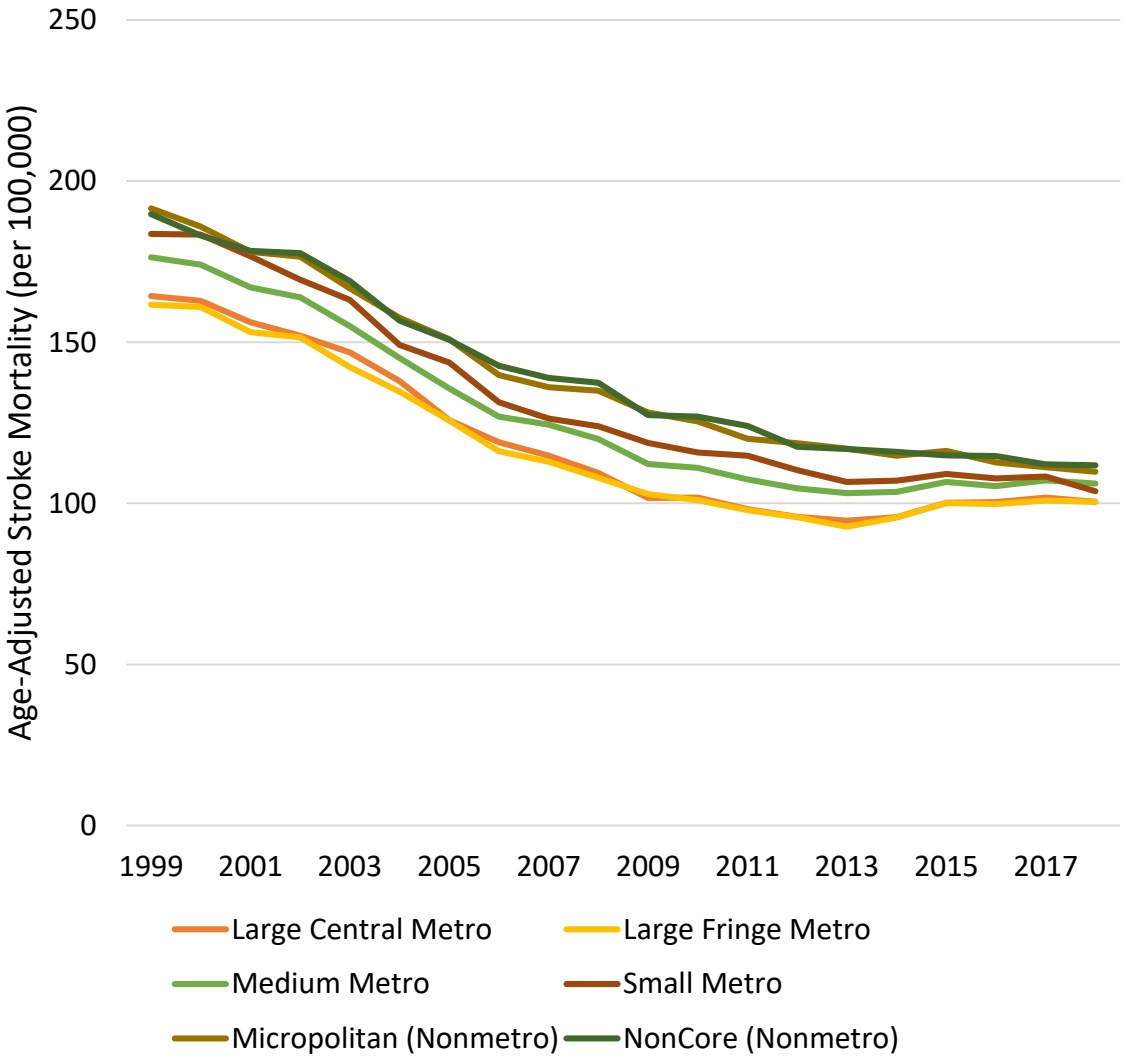
  … but also the *Minority Health and Health Disparities Research and Education Act* (*United States Public Law 106-525;*2000, p. 2498) instructs NIH to assess disparities, with a focus on:

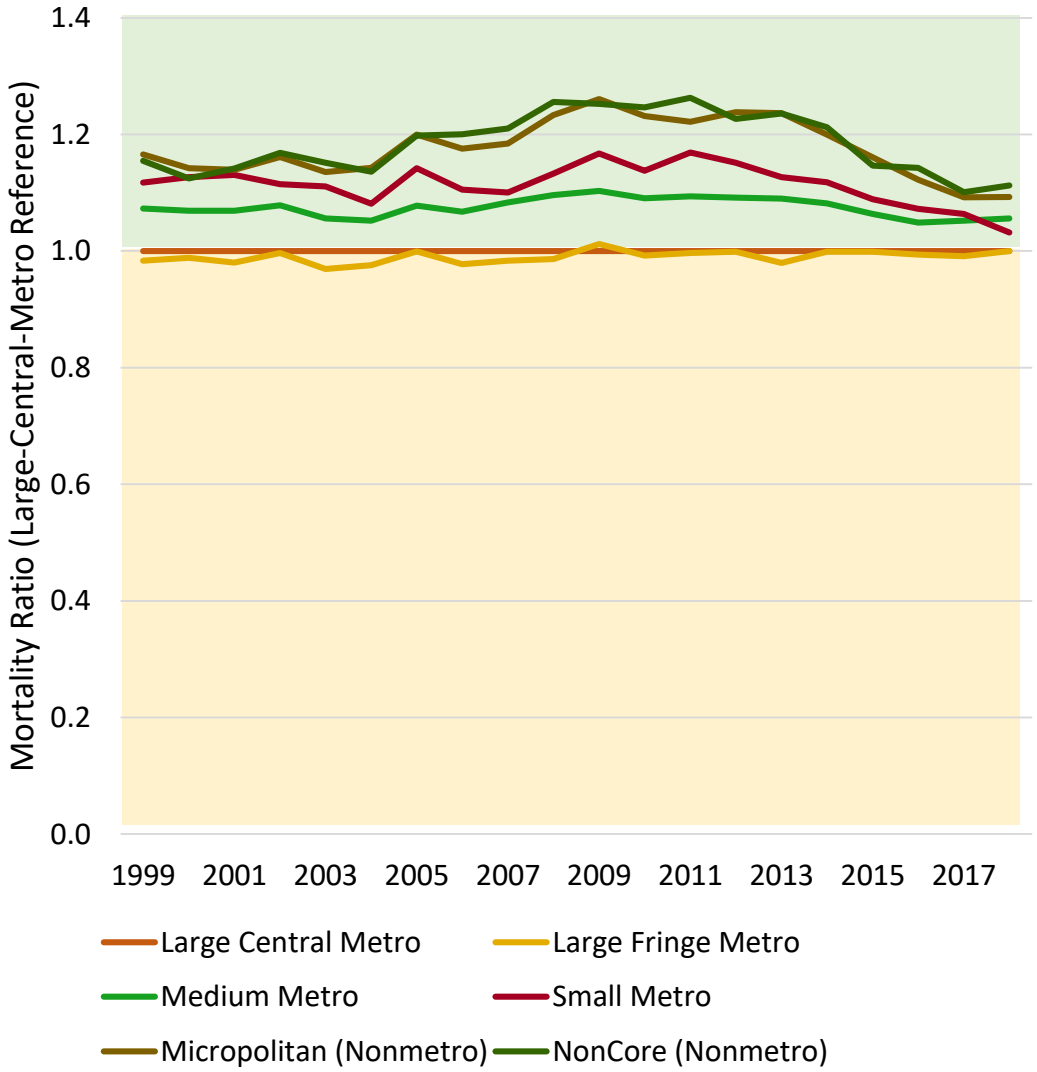
  - **Minority health research and related activities**
  - **Rural health research and related activities**
  - **Research and other activities related to the socioeconomically disadvantaged in the urban setting.**

- **… also, *Healthy Persons 2030* (the guiding document for all of HHS)**
  - **Among 7 founding principles: *Achieving health and well-being requires eliminating health disparities, achieving health equity, and attaining health literacy.***
  - **Among 5 overarching aims: *Eliminate health disparities, achieve health equity, and attain health literacy to improve the health and well-being of all.***

Recent Pattern of Urban-Rural Disparities in Stroke Mortality

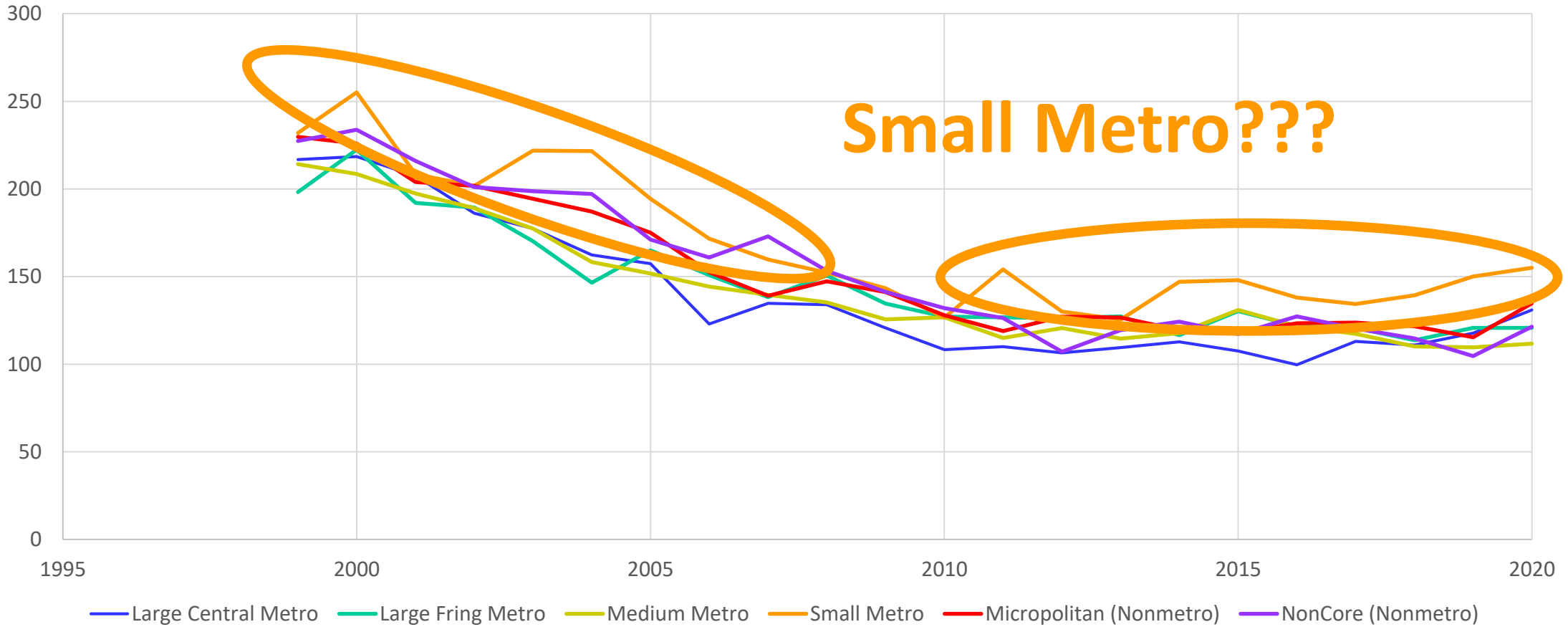
CDC WONDER: 1999 – 2018





2013 Urbanization categories

Urban-Rural Difference in Stroke Mortality North Carolina Only



Why Small Metro in NC?

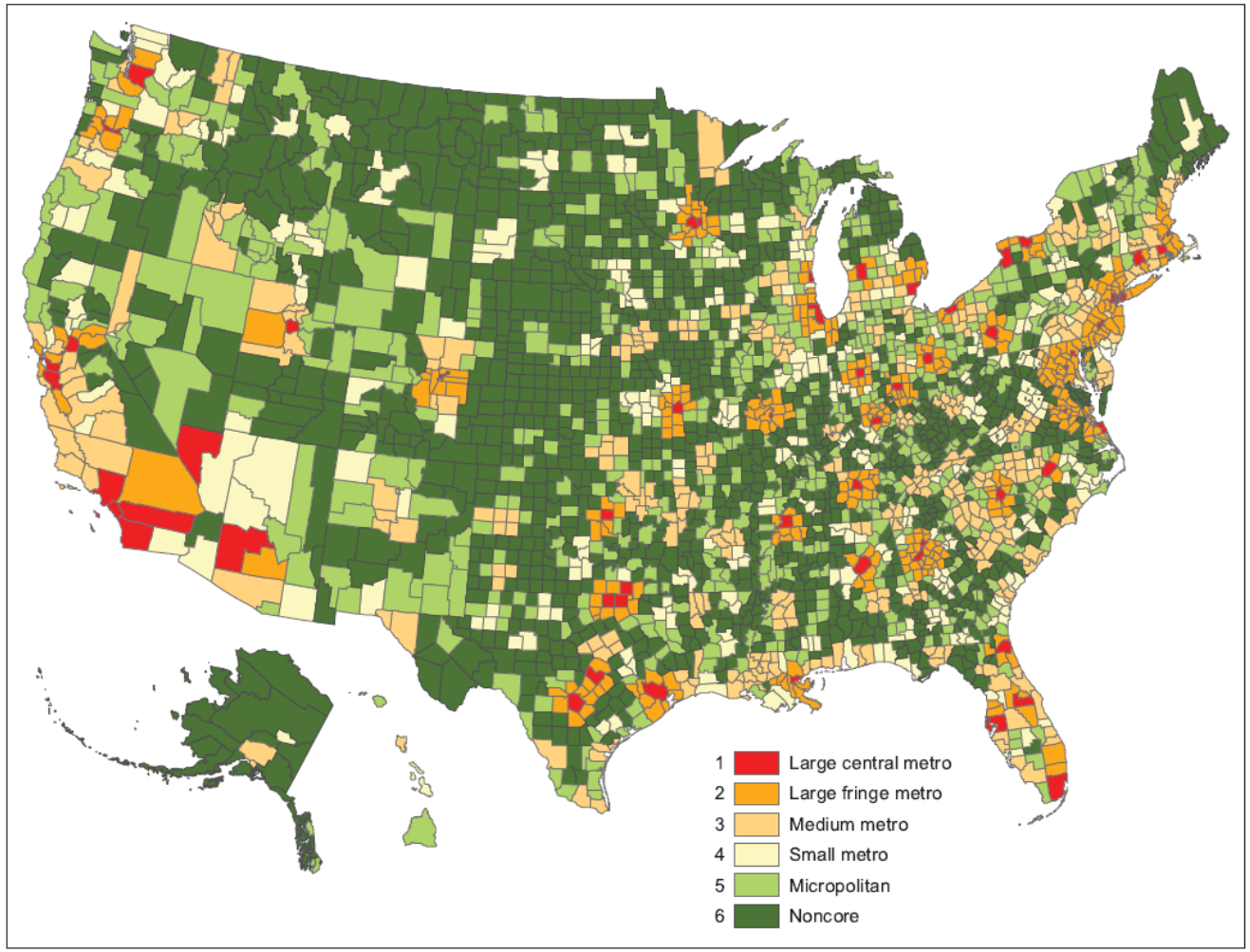
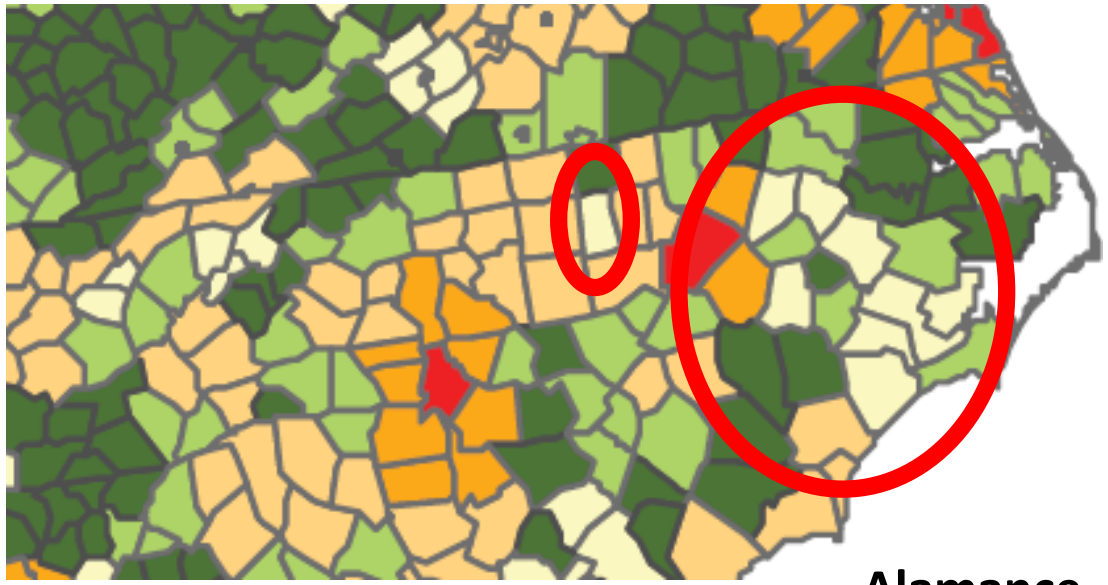


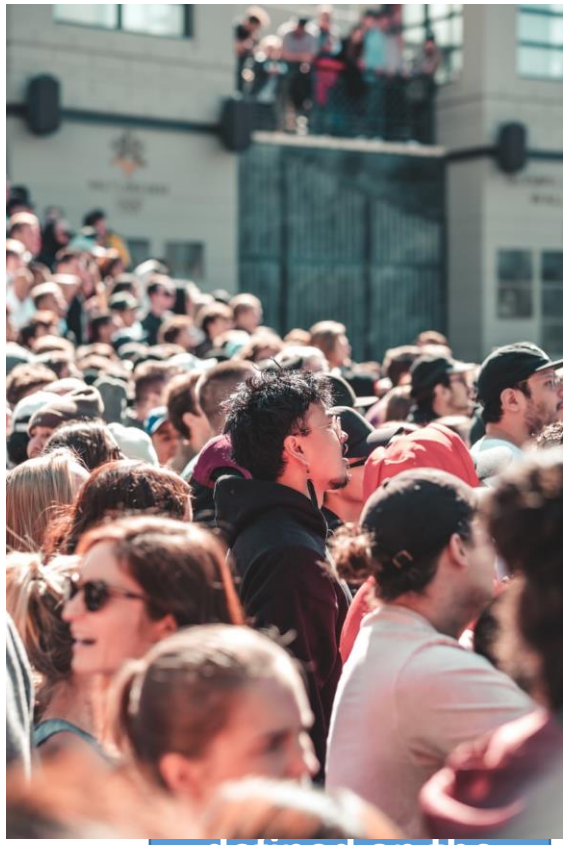
Figure 2. Distribution of counties according to the 2013 NCHS Urban–Rural Classification Scheme for Counties



Alamance
Craven
Edgecombe
Jones
Nash
Onslow
Pamlico
Pitt
Wayne

Ingram DD, Franco SJ. 2013 NCHS urban–rural classification scheme for counties. National Center for Health Statistics. Vital Health Stat 2(166). 2014.

What we know
… and what we need to know



defined on the basis of Vital Statistics data

= Stroke Incidence x Case Fatality after Stroke

If stroke incidence is driving disparity …

then need to focus on prestroke prevention in the general population

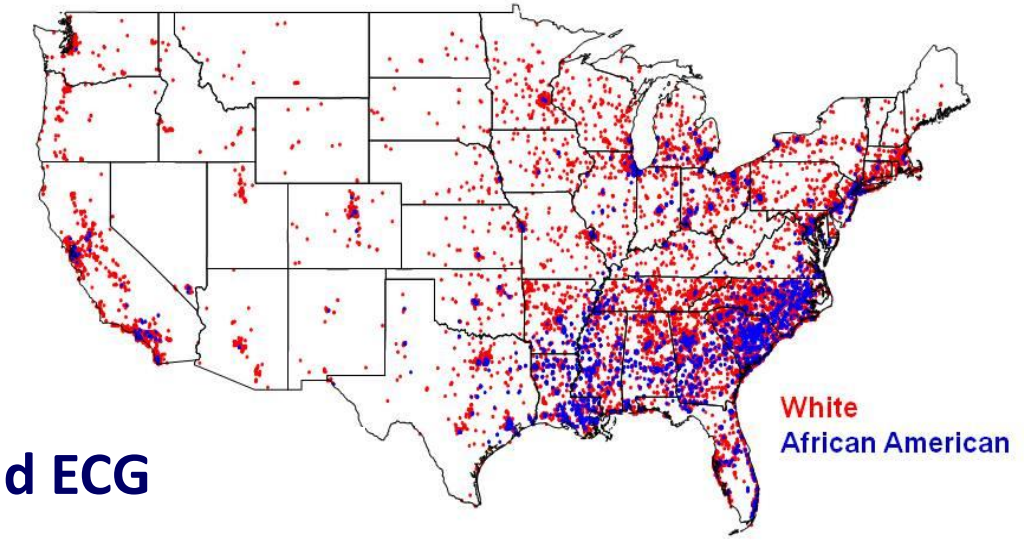
If case fatality is driving disparity …

then need to focus on
1. severity disparities, and
2. improved care in the hospital

The rest of the data for this talk are from the:

REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

- General population study with diverse aims … but for today …
- Central participant recruitment and telephone interview
  - 30,239 white and black participants aged 45+
  - 56% from the Stroke Belt
  - 42% black



- In-home evaluation for physical, venipuncture and ECG
- Central follow-up at 6-month intervals for detection of suspected stroke events (and other outcomes)
- Physician adjudication of new stroke events
- Provides both measures of stroke incidence and case fatality
- One of the very few cohort studies with data from rural areas

… and using these data, let's focus on two questions

1. **Is it that rural people are having more strokes, or is it that a person living in rural area is more likely to die after having a stroke?**
2. **… and cheating and looking ahead, what is it that makes rural people more likely to have a stroke?**

Statistical Methods for Question 1

(Incidence versus Case-Fatality as the Contributor to Rural Excess)

- **Two separate analyses**
  - **Incidence**
    - **Outcome: Incidence of stroke**
    - **Proportional hazards analysis, adjusting for age, race, sex and region**
  - **Case fatality**
    - **Outcome: Death within 30-day among those with a stroke**
    - **Logistic regression analysis, adjusting for age, race, sex and region**
- **Adjustment for region allows contrasting rural-urban differences while removing confounding with larger Southern rural population**
- **In both cases – assess interactions between age, race and sex, and include significant terms ($p < 0.10$)**

Howard G, et al. Stroke 2016;47:1893-1898

Question #1: Incidence vs Case Fatality as the Contributor to Urban-Rural Differences in Mortality

			Age-Race-Sex and Region
Hazard Ratio for Incident Stroke	County Urban / Rural Status	Urban	1.00 (ref)
		Large Rural	1.23 (1.01 – 1.51)
		Small Rural City/Town or Isolated Area	1.30 (1.03 – 1.62)
	P-value for trend		0.0073

- Urban-rural disparities seem driven by higher incidence, with case fatality playing minor role
- Again … this implies that reduction of the disparities needs to focus on reduction of stroke risk in rural areas *(more than improved stroke care in rural areas)*
- But what seem to be the contributors to the higher incidence (a.k.a., question #2)?

Howard G, et al. Stroke 2017;48:1773-1778

Statistical Methods for Question 2:

(What are the apparent contributors to the excess stroke incidence in rural areas?)

- **General approach:**
  1. **We start by considering risk factors and socio-economic status factors that we <u>know</u> are associated with stroke**

     and then

  2. **See if these same**

  If so, we then we can a magnitude of the estir analysis)

- **Factors considered include:**
  - **Risk factors: hypertension, diabetes, smoking, atrial fibrillation, le icular hypertrophy, and heart disease**
  - **SES: household income ≤$35K, education ≤ high school, and neighborhood SES**

"Traditional" index calculated at the Census tract level, including:

- **median household income**
- **median value of housing units**
- **proportion of households receiving interest-dividend-rental income**
- **proportion of adults with a high-school diploma**
- **proportion of adults with college degree**
- **proportion of people used in executive-managerial-professional occupations**

Step 1: Are Stroke Risk Factors and SES more Adverse in Rural Areas?

Risk factors	Hypertension, %
	Diabetes mellitus, %
	Smoking, %
	Atrial fibrillation, %
	Left ventricular hypertrophy, %
	Heart disease, %

We already know that these risk factors and SES measures are related to stroke … so now let's see how much of the *rurality → stroke-risk* relationship is mediated by adjustment for them?

Calculate the odds of prevalent condition after adjustment for age, sex, race and geographic region … looking for a "dose response" relationship with rurality

2. See … even <u>more</u> promising for SES measures

Why is the incidence of stroke higher in rural areas?

			Age-Race-Sex and Region
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		Large Rural	1.23 (1.01 – 1.51)
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So here is that relationship we had with incidence

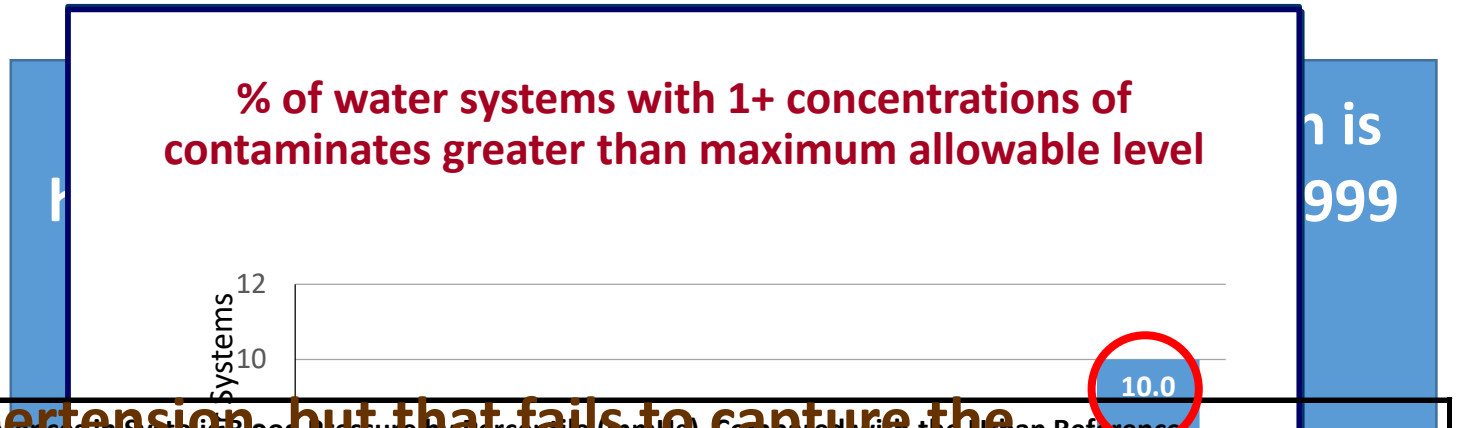
→ 18% = 22% attenuation

→ 19% = 37% attenuation

- What does adjustment for risk factors and SES do to this relationship?
- Adjustment for risk factors and SES partially mediates association … it even becomes non-significant
- Most of this attenuation seems tied to SES measures
- Suggests that risk factors and SES are contributors to excess rural stroke mortality … and are targets for intervention
- However, (while no longer significant), over half the association remains
- Gee … we need to understand what else is contributing

What else could be going on?
Well … lots!

- Other factors could be playing a role, including:
  - Psychosocial
  - Structural
  - Environmental
  - Of course, others!
- Residual confounding
- Effect modification
  - We have adjusted for hypertension, but that fails to capture the distribution of blood pressure
  - Don't have a good example … but there could be factors more "potent" in rural areas
- Measurement error
- No good talk neglects to state that a lot more work is needed to understand these effects!



Differences in Systolic Blood Pressure by Percentile (mm Hg), Compared With the Urban Reference (95% Confidence Interval)							
RUCA Classification	5	10	25	50	75	90	95
Urban	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Large Rural	2.00 (1.11 to 2.89) *P* < .0001	1.88 (1.20 to 2.57) *P* < .0001	1.25 (0.68 to 1.81) *P* < .0001	0.92 (0.33 to 1.52) *P* = .002	1.73 (0.97 to 2.49) *P* < .0001	1.92 (0.63 to 3.20) *P* = .004	3.23 (1.39 to 5.06) *P* = .0006
Small-Isolated Rural	0.50 (-0.66 to 1.66) *P* = .39	0.07 (-0.81 to 0.95) *P* = .88	0.06 (-0.62 to 0.74) *P* = .86	0.23 (-0.51 to 0.97) *P* = .54	1.45 (0.44 to 2.46) *P* = .005	3.08 (1.43 to 4.73) *P* = .0002	3.23 (1.41 to 5.05) *P* = .0005

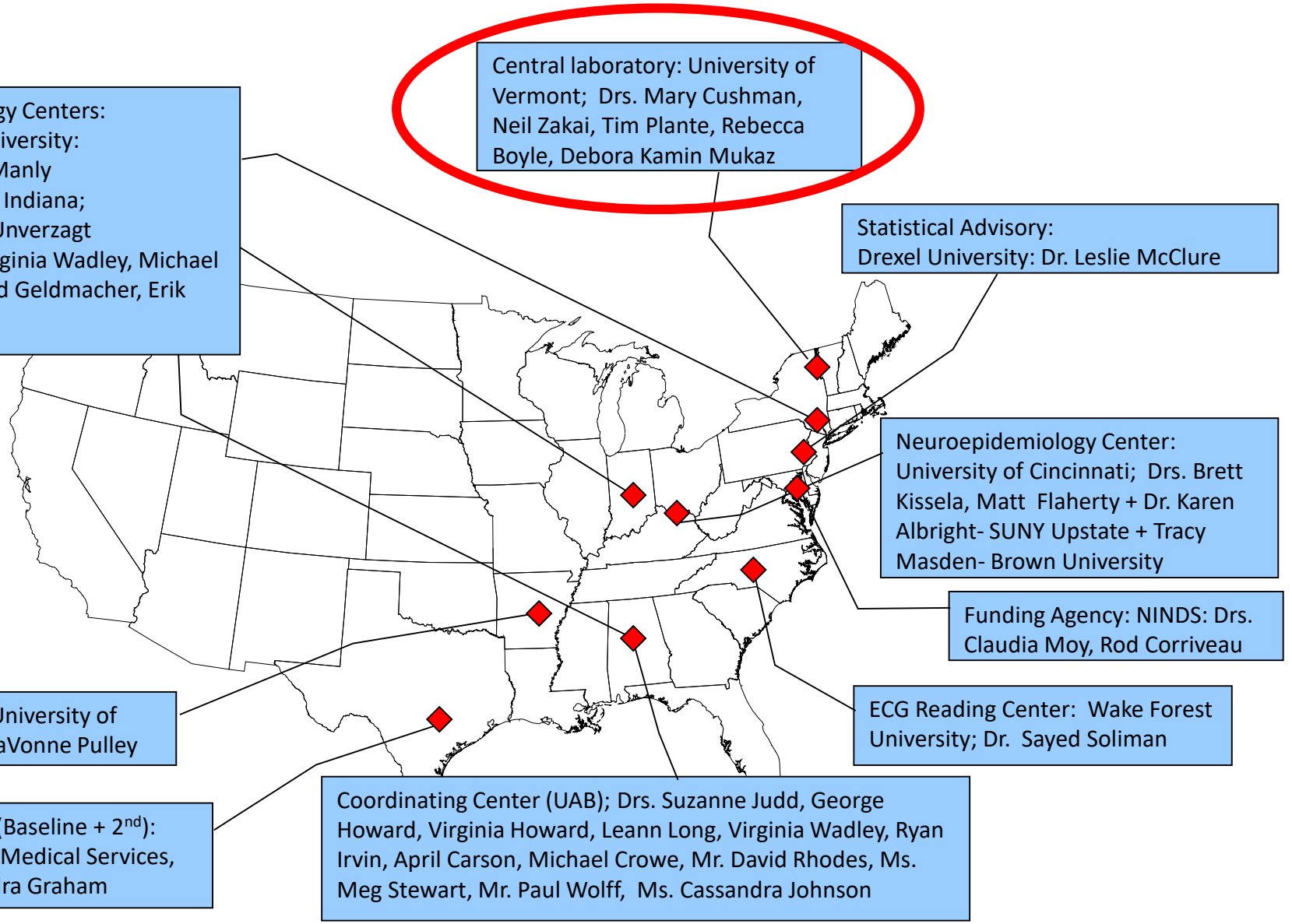
Conclusions

- **Data from Vital Statistics shows a nearly monotonically higher risk of stroke death with increasing rurality**
  - **This disparity increased from ≈16% in 1999 → ≈25% in 2009**
  - **Has been fairly rapidly decreasing to ≈11% in 2018**
- **Data from REGARDS shows:**
  - **The higher risk in rural areas appears to be nearly completely related to higher stroke incidence in rural areas (with higher case-fatality playing a minor role)**
  - **This suggests the focus of interventions needs to be community-based efforts to reduce risk of incident stroke in rural areas**
  - **A heavier risk factor burden and poorer SES profile contribute about 25% to 35% of this excess, and are clearly targets for intervention**
  - **This implies that the factors driving 65% to 75% of the excess are not understood (… yes … the more work is needed statement)**
- **We welcome others to join in analysis of REGARDS data to better understand this disparity**

Acknowledgments

- REGARDS is supported by cooperative agreement U01 NS041588 from NINDS/NIH-NIA
- We thank the investigators, staff, and participants of the REGARDS study for their valuable contributions. A full list of participating investigators and institutions can be found at http://www.regardsstudy.org

REGARDS Functional Units



Questions?

REGARDS

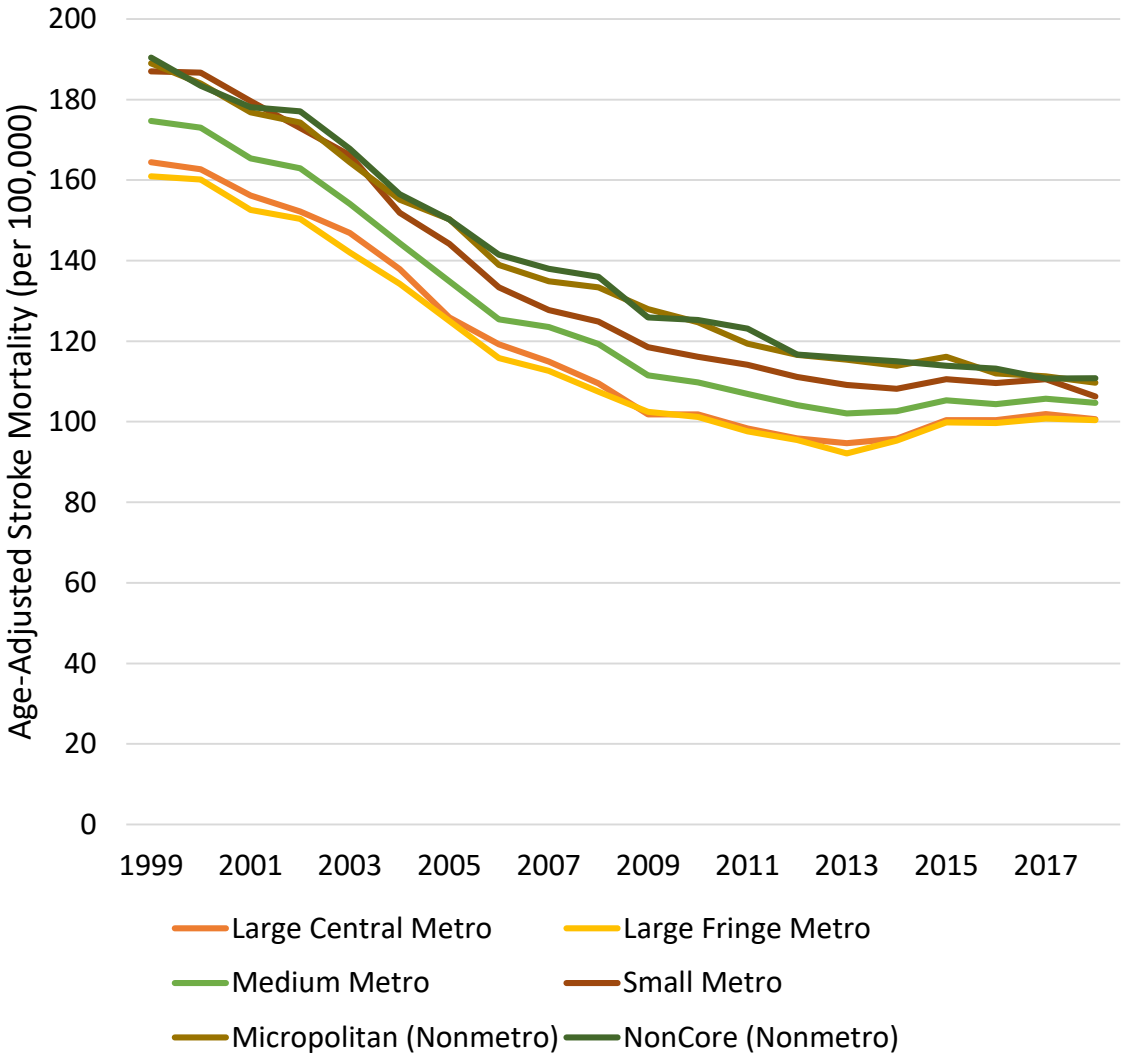
Reasons for Geographic and Racial Differences in Stroke

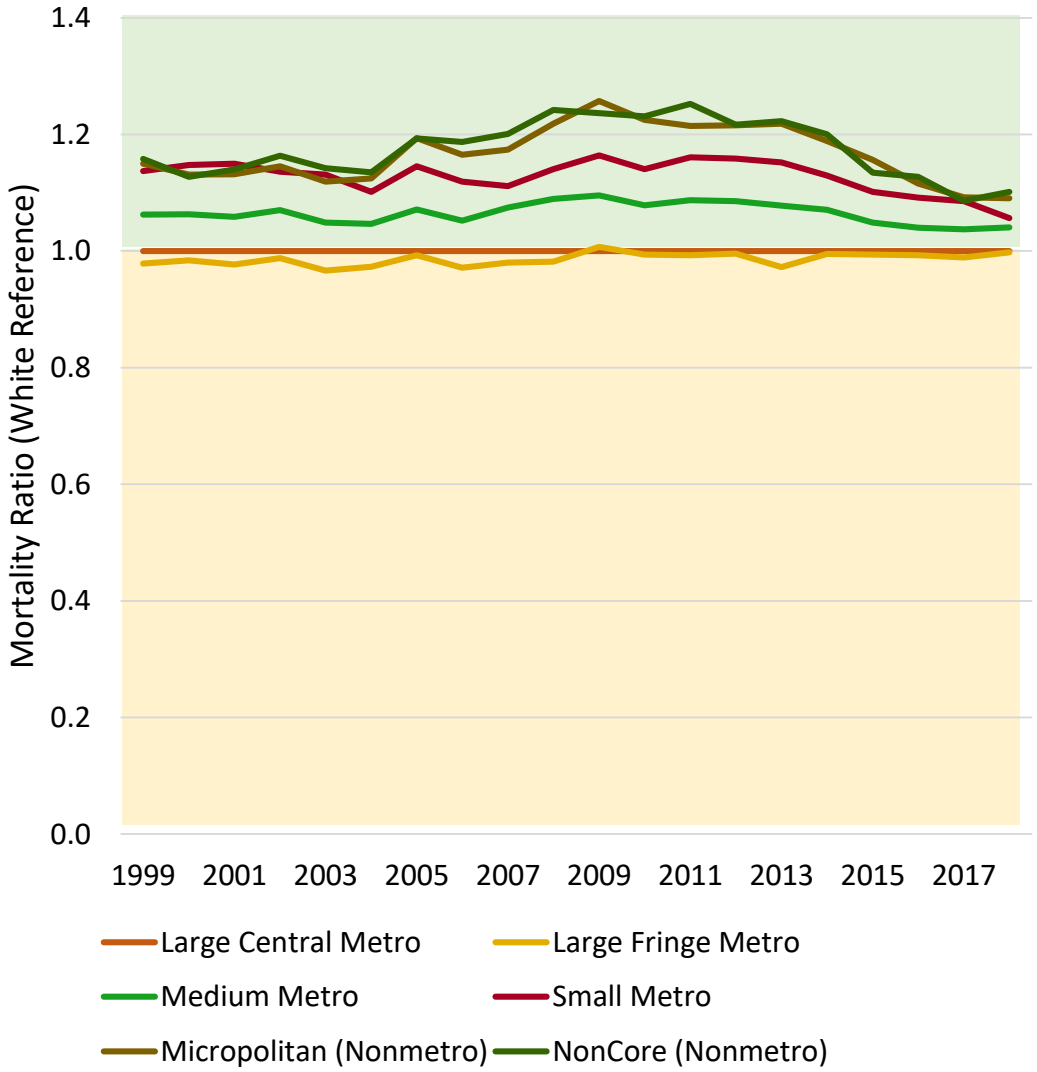
REGARDS

NIH/NINDS U01 NS41588

Recent Pattern of Urban-Rural Disparities in Stroke Mortality

(1999 – 2018)





2006 Urbanization categories