The Economic and Social Imperatives of Disease Prevention: The Obesity-Diabetes-Kidney Disease Paradigm

Griffin P. Rodgers, M.D., M.A.C.P.
Director

March 8, 2019
In compliance with ACCME Guidelines, I hereby declare:

• I do not have financial or other relationships with the manufacturer(s) of any commercial services(s) discussed in this educational activity.

Griffin P. Rodgers, M.D., M.A.C.P.
Director of the National Institute of Diabetes and Digestive and Kidney Diseases
Obesity

- Approx. 2/3 of U.S. adults overweight or obese
- Nearly 40% of U.S. adults obese
- Increasing in the young
- Annual medical cost: $147B
- Approx. 30.3 million U.S. cases (9.4% of population)
  - 90-95% T2D
- Projected to ~50 million by 2050
  - Increasing in the young
  - Annual total cost: $327B

Type 2 Diabetes

- Obesity Disparities: 47% of Hispanics and 46.8% of NH Black (compared to 37.9% of Whites)
- Age-adjusted Diagnosed Diabetes:
  - 15.1% of AIAN
  - 12.1% of NH Black
  - 12.1% of Hispanic
  - 7.4% of White

Chronic Kidney Disease

- Nearly 15% of the U.S. population have CKD
- Major causes: diabetes, hypertension
- Annual Medicare cost of CKD and kidney failure: $98B
- ESRD prevalence, compared to U.S. white population:
  - 3 times higher in NH Black
  - 1.3 times higher in Hispanic

NIDDK’s Integrated Research Programs: Implications for Health Disparities
Obesity Trends* Among U.S. Adults
Behavioral Risk Factor Surveillance System (BRFSS), 1985

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1986

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1987

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1988

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1989

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1990

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1992

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1993

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1994

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1995

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1996

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1997

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1998

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 1999

*BMI ≥30 kg/m^2 or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults

BRFSS, 2000

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2001

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2002

*BMI $\geq 30$ kg/m$^2$ or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults  
BRFSS, 2003

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2004

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2005

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2006

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults  
BRFSS, 2007

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2008

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2009

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2010

*BMI $\geq 30$ kg/m$^2$ or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends* Among U.S. Adults
BRFSS, 2011

*BMI ≥30 kg/m² or ~30 pounds overweight for 5’4” woman

Source: CDC Behavioral Risk Factor Surveillance System.
Obesity Trends Continue Unabated

From: CDC NCHS Data Brief 288
The Public Health Problem of Obesity: Prevalence and Associated Health Conditions

17.0% of 2- to 19-year-old children/adolescents and 36.5% of adults are obese

Image credit: Adapted from image created by Dr. Wei Shen and Dr. Steven Heymsfield, New York Obesity Research Center, St. Luke’s-Roosevelt Hospital, Columbia University, New York.
A few examples of NIH obesity research areas

**Lifestyle**
- Environmental & behavioral interventions

**Bariatric surgery**
- Long-term risks & benefits?
- Underlying mechanisms?

**Brown & beige fat**
- Potential target for obesity treatment: fat that burns itself

**Microbiome**
- Our gut companions: Effects on weight?
- Therapeutic targets?
Age-adjusted Prevalence of Obesity and Diabetes Among U.S. Adults

**Obesity**

**1994**

**2000**

**2010**

**Diabetes (diagnosed)**

- <14%
- 14-17.9%
- 18-21.9%
- 22-25.9%
- ≥ 26%

- <4.5%
- 4.5-5.9%
- 6.0-7.4%
- 7.5-8.9%
- ≥ 9.0%

[Map showing prevalence of obesity and diabetes in the U.S. by year and state]
Type 2 Diabetes Clinical Studies

Normal ↔ Pre-diabetes ↔ Type 2 Diabetes → Complications
Complications Common to Both Type 1 and Type 2 Diabetes

**BRAIN**
People with diabetes have about twice the risk for stroke, a higher risk of dementia, and increased symptoms of depression.

**TEETH & GUMS**
People with diabetes, especially those with poorly controlled diabetes, have a greater risk for gum disease, a major cause of tooth loss.

**HEART & BLOOD VESSELS**
People with diabetes are twice as likely to have heart disease and have an increased risk of peripheral artery disease.

**LIVER**
People with diabetes are more than twice as likely to have nonalcoholic fatty liver disease, which can lead to cirrhosis and liver cancer.

**FEET**
Diabetic foot ulcers are common in people with diabetes. Healing of foot ulcers may take months to years, and ulcers can lead to amputation.

**EYES**
Diabetes increases the risk for eye diseases such as retinopathy, cataracts, and glaucoma, contributing to an overall increased risk of vision loss.

**EARS**
Diabetes approximately doubles the risk of hearing loss, especially in the speaking range.

**AIRWAYS**
Two in three people with diabetes have obstructive sleep apnea, which can lead to fatigue, irritability, and deficits in attention and memory.

**KIDNEYS & LOWER URINARY TRACT**
Diabetes is the leading cause of kidney failure and can also lead to complications of the lower urinary tract, such as urinary incontinence and erectile dysfunction.

**BONE**
Bone fractures, osteoarthritis, and rheumatoid arthritis are more common in people with diabetes.

The Financial Costs of Diabetes

Diabetes: The Tip of the Iceberg

**U.S. Diabetes**
30.3 million*
23.1 million diagnosed;
7.2 million undiagnosed

**U.S. Prediabetes**
84.1 million†
9.8 million aware of their prediabetes
74.3 million unaware

*All ages, 2015
† Age 18 and older with IFG +/or A1c between 5.7 and 6.4 (2015)
The DPP Study

- 3234 participants (45% minority) with IGT who were overweight or obese
- Compared 3 approaches to diabetes prevention for 3 years:
  - Placebo
  - Metformin
  - Lifestyle
Lifestyle Intervention

- Intensive behavioral modification program with the following goals
  - 7% weight loss
  - 150 minutes/week physical activity

- Intervention delivery
  - 16 session core curriculum delivered one-on-one over 24 weeks
  - Monthly visits post core
DPP Results

Cases/100 person-yr

- **Placebo**
- **Metformin**
- **Lifestyle**

- Caucasian (n=1768)
- African American (n=645)
- Hispanic (n=508)
- American Indian (n=171)
- Asian (n=142)
Effect of Age on Intervention Response

DPP Interventions by Age Group

- Metformin especially effective for younger adults
- Lifestyle especially effective among older adults
- 71% reduction

Cases/100 person-yr

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Lifestyle</th>
<th>Metformin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-44 (n=1000)</td>
<td>6</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>45-59 (n=1586)</td>
<td>6</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>&gt; 60 (n=648)</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
</tbody>
</table>
Cumulative Incidence of Diabetes in DPP
Women without and with a History of GDM

**without GDM**

- **Risk reduction vs. placebo**
  - 14% by metformin ($p=0.280$)
  - 49% by lifestyle ($p<0.001$)

- **Risk reduction vs. metformin**
  - 41% by lifestyle ($p=0.001$)

**with GDM**

- **Risk reduction vs. placebo**
  - 51% by metformin ($p=0.006$)
  - 55% by lifestyle ($p=0.002$)

- **Risk reduction vs. metformin**
  - 8% by lifestyle ($p=0.781$)

*Adjusted for age*
The Diabetes Prevention Program: Collaborative and Transformative

Diabetes Prevention Program (DPP)
3,234 individuals at risk for type 2 diabetes

- Lifestyle modification lowered risk by 58% (modest weight loss, from exercise and reduced fat and caloric intake)
- Metformin medication lowered risk by 31%

Percent Reduction in Diabetes Incidence Compared to Placebo

• Metformin cost-saving

DPPOS 15-year follow-up:
Translating from Efficacy Research to Public Health

On July 7, 2016, the Centers for Medicare & Medicaid Services proposed changes to the Physician Fee Schedule to begin coverage of certain DPP adaptations in April, 2018.
Proportion of Type 1 and Type 2 DM by Race/Ethnicity in Youth Aged 10-19 Years

NHW: non-Hispanic white; NHB: non-Hispanic black; API: Asian or Pacific Islander; AIAN: American Indian or Alaska Native

Hamman et al. ADA 2012
**Treatment Options for type 2 Diabetes in Adolescents and Youth**

**Rationale:**
- Increased youth T2D
- Adult drugs not tested/approved in youth
- Adolescent effects on glycemia/metabolism

**Cohort:**
- Age 10-17 years (avg 14)
- BMI >85th p’tile (avg 35.7)
- T2D <2 yr (avg 8 months)
- 35% male
- 20% White
- 32% NHB
- 41% Hispanic
- 6% AI

**Treatment groups:**
- Metformin
- Metformin + rosiglitazone*
- Metformin + intensive lifestyle

*Use of rosiglitazone was investigational under FDA IND
Time-to-outcome Analyses

Cohort Overall

Treatment failure rates:
- M: 51.7%
- M+R: 38.6%
- M+L: 46.6%

Pairwise Tests:
- M+L vs. M+R: p=0.15
- M vs. M+R: p=0.006
- M vs. M+L: p=0.17

Number at Risk:
- Time from randomization in months

NH Black

Treatment failure rates:
- M: 66.2%
- M+R: 43.8%
- M+L: 47.7%

Pairwise Tests:
- M+L vs. M+R: p=0.64
- M vs. M+R: p=0.003
- M vs. M+L: p=0.008

Number at Risk:
- Time from randomization in months

National Institute of Diabetes and Digestive and Kidney Diseases
RISE Pediatric Medication Study

Though uncommon in young people, pediatric T2D is occurring more often, especially in minority groups.

• T2D occurs when long-term insulin resistance leads to eventual loss of proper insulin secretion from pancreas

• Restoring Insulin Secretion (RISE) studies ask if glucose-lowering treatment can reduce loss of insulin response in those with prediabetes, or restore some function in those with recent onset T2D

• RISE Pediatric Medication Study in 91 10-19 y.o. participants compared treatment with long-acting insulin followed by metformin with metformin alone.

• Neither treatment either preserved or restored insulin secretion. Insulin and metformin are the only drugs FDA-approved for treating pediatric T2D.

• Substudies found that participants in this study had better insulin secretion, but more profound insulin resistance than do adults at a similar stage of T2D progression.
NIDDK’s Integrated Research Programs: Implications for Health Disparities

Obesity → Type 2 Diabetes → Chronic Kidney Disease
Increased Kidney Disease Risk Among African Americans Mostly Explained by APOL1 Gene Mutation

- **African Americans**: 42% (0 copies), 46% (1 copy), 12% (2 copies)
- **FSGS risk (lifetime)**: 0.2% (0 copies), 0.3% (1 copy), 4% (25-fold increase)
- **Hypertensive kidney disease risk**:
  - 0 copies: --
  - 1 copy: --
  - 2 copies: ~5-10% (5-fold increase)
(Re)Building a Kidney Consortium seeks to optimize approaches for the isolation, expansion, and differentiation of appropriate kidney cell types and their integration into complex structures that replicate human kidney function.

The longer term goal is to stabilize, reverse, or restore lost kidney function.
Human Kidney Precision Medicine Project

- Human CKD is mixture of multiple diseases (CKDs)
- Molecular mechanisms of human CKDs not well known → relative paucity of CKD therapeutics
- Recent genetics, epidemiology, and animal models have validated only two CKD targets (ApoL1 and FGF23)
- Nephrologists have performed few kidney biopsies for 40 years, as unlikely to change care. Self-fulfilling prophecy
- Need human biopsy tissue
- New methods to understand each cell types contribution to disease are now available
  - Kidney is anatomically complex; many cell types
  - Can now work at individual cell level
- Goal: Understand subgroups, mechanisms of disease, and lead to new therapeutics, earlier treatment and patient-specific prevention
Kidney Precision Medicine Project

Goals of 10-15 year project

Understand and treat human kidney disease

- Ethically obtain kidney biopsies from participants with AKI or CKD
- Find disease subgroups to stratify patients
- Find disease pathways in key cells
- Devise individualized treatments
- Improve scientific knowledge base
- Improve pipeline
Training and Outreach Programs
NIDDK and Our Partners Invest Heavily in Workforce Development

$144.1 Million – FY18
(7.3% of total DK budget)

Intramural

Professional Societies/Foundations

$61.4 M
T35, T32, F30, F31, F32

$6.1 M
R03

$4.4 M
K24

$4.3 M
R25

$144.1 Million – FY18
(7.3% of total DK budget)

HS/Undergraduate
Graduate/ Medical School
Postdoctoral
Transition/Jr. Faculty
Faculty/Tenured

F/T to K
K to R
R renewal

NIH
National Institute of Diabetes and Digestive and Kidney Diseases
NIDDK Works To Preserve this Investment

ASPIRNAUT™
STEP-UP & DSRTP

HS Undergraduate
Graduate Medical School
Postdoctoral
R25 T35, T32, F30, F31, F32

“Life after K” Workshop
LRP
K01, K08, K23, K12, K99
R03

“New PI” Workshop
Independent Faculty
ESI renew bonus
Maximize payline

www.niddk.nih.gov

NIH National Institute of Diabetes and Digestive and Kidney Diseases
STEP-UP in the Pacific
HS STEP-UP Puerto Rico

Primary Research Sites

Hometown of 2018 STEP-UP Participant
109 Aspirnaut™ Undergraduates from 25 universities: 2009-2018

83% in advanced STEM degree/STEM workforce:

- Dual M.D./Ph.D.: 2
- Medical School: 19
- Grad School – Ph.D.: 12
- Masters (6 were M.P.H.): 7
- STEM Workforce: 15
- Gap Year: 7
- Dental School: 3
- Pharm.D.: 1
- Other Workforce: 5
NIDDK Medical Student Research Program in Diabetes

• Tenth summer (2009-2018)
• 4-10 students/Diabetes Center
• Over 1000 students from >120 medical schools
• Funding
  – Supplement to T32s at Diabetes Centers
  – Diabetic Complications Consortium
Goals:

• Encourage underrepresented minority investigators to choose a career in NIDDK mission areas

• Facilitate mentoring of junior investigators by experienced and accomplished researchers

http://nmri.niddk.nih.gov/
NIDDK’s Network of Minority Health Research Investigators

- Current Membership ~ 200, 20% are senior members (Associate Professor or higher)
- Over 700 have attended the annual meetings in the past 10 years
- Numerous Grants, publications and poster presentations at national and international conferences.

http://nmri.niddk.nih.gov/
NDEP Resources: Prevention

Available to download at www.ndep.nih.gov
National Kidney Disease Education Program

Community

Health Care Professionals

nkdep.nih.gov
• Healthy Moments radio program reaches over 60 million listeners.

• Airs weekly in
  - WMMJ Majic 102.3 FM  Washington, DC
  - WWIN Magic 95.9 FM  Baltimore, MD
  - KMJQ Majic 102.1 FM  Houston, TX
  - WAMJ Majic 107.5 FM  Atlanta, GA
  - WHHL Hot 104.1 FM  St. Louis, MO
  - WENZ Z 107.9 FM  Cleveland, OH
  - Get Up! Mornings with Erica Campbell Network (38 stations)

• Airs nationally 10 times a year in 10 additional cities on a celebrity morning radio show.

Follow @NIDDKgov on Twitter