High Prevalence of Compensatory Hyperinsulinemia in U.S. Teenagers: The 2015-2018 National Health and Nutrition Examination Survey (NHANES)

India C. Bradley, B.S.[1], Alok K. Dwivedi, Ph.D[2] and David P. Cistola, M.D., Ph.D[1,*]
[1]Center of Emphasis in Diabetes & Metabolism and [2]Division of Biostatistics and Epidemiology,
Paul L. Foster School of Medicine and GSBS, Texas Tech Univ. Health Sciences Center El Paso, Texas USA

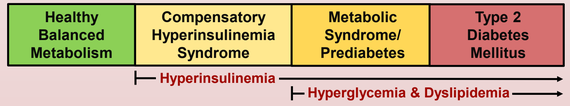
TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER™ EL PASO
Paul L. Foster School *of* Medicine

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER™ EL PASO
Graduate School *of* Biomedical Sciences

Introduction

Compensatory Hyperinsulinemia (CH):
the pancreatic response to early insulin resistance (IR)

- beta-cell insulin secretion is intact and adaptive
- glucose and lipids remain *within normal limits*
- does not meet criteria for prediabetes or metabolic syndrome; *eludes screening for diabetes risk*
- **hidden risk factor for type 2 diabetes (see Cistola and Dwivedi, Abstract 106)**
- part of a syndrome that also includes inflammation, pro-coagulation and hypoxia



Research Question

How prevalent is CH in the U.S. and its subpopulations?

Hypothesis:
Compensatory hyperinsulinemia is prevalent in the U.S., especially in younger individuals.

Specific Aim:
Estimate the prevalence of CH in the U.S. population as a whole, and by subpopulations, for 2015-2018.

Experimental Approach

- analyzed fasting subsample (n=6,227) of National Health and Nutrition Examination Survey (NHANES); combined 2015-2016 and 2017-2018 cycles
- weighted subsample represents non-institutionalized U.S. population, ages 12 and up: 270,185,908 people
- categorized subjects into four groups by metabolic status
- fasting insulin cutpoint calibrated with time-ROC analysis
- estimated unadjusted prevalence of CH using population-weighted survey analysis in Stata v. 17.0
- adjusted for confounding using multinomial logistic regression; prevalence is mean of predicted probability

Participants Grouped by Metabolic Status

Reference Group (RG)
normal fasting insulin (<9.0 microIU/mL)
normal fasting glucose and A1C (no prediabetes)
normal fasting TG and HDL (no metabolic syndrome)
no diabetes mellitus

Compensatory Hyperinsulinemia (CH)
hyperinsulinemia (fasting insulin >=9.0 microIU/mL)
normal fasting glucose and A1C (no prediabetes)
normal fasting TG and HDL (no metabolic syndrome)
no diabetes mellitus

Hyperglycemia/Dyslipidemia (HD)
elevated fasting glucose or elevated A1C or
elevated fasting TG or low HDL
no diabetes mellitus

Diabetes Mellitus (DM)
ADA diagnostic criteria or participant-reported provider diagnosis plus taking diabetes meds

Results

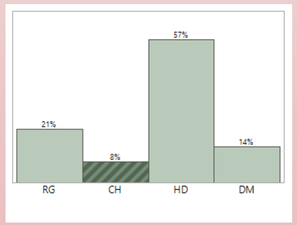


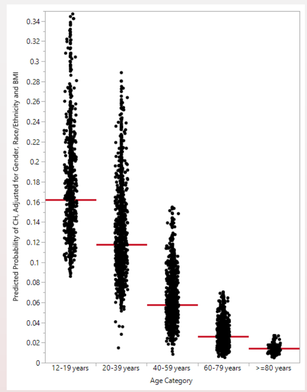
Fig. 1 U.S. prevalence by metabolic status, 2015-2018, ages 12 and up.

Metabolic Status	Prevalence (95% CI)
RG	21.1% (19.1, 23.2)
CH	**8.2% (7.2, 9.3)**
HD	56.8% (54.6, 58.9)
DM	14.0% (12.6, 15.5)

Table 1 U.S. prevalence by metabolic status

Overall, 8.2% of U.S. population has CH: 22.1M people, ages 12 and above

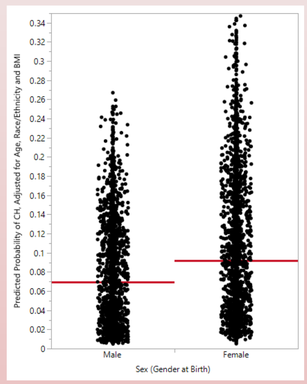
Results (continued)



CH prevalence is high in teenagers and decreases with age:

18.9% (CI: 15.8, 22.5), unadjusted
16.2% (CI: 15.7, 16.8), adjusted

Fig. 2 Prevalence of CH by age category, adjusted for sex, race/ethnicity and BMI.

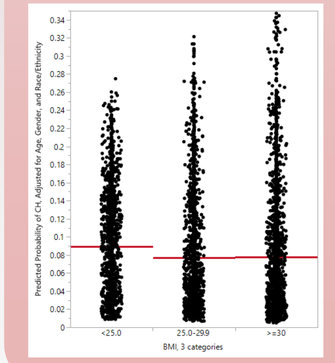


CH prevalence is higher in females:

9.2% (CI: 8.8, 9.6), female
7.0% (CI: 6.7, 7.2), male

Fig. 3 Prevalence of CH by sex, adjusted for age, race/ethnicity and BMI

Unadjusted prevalence:
9.6% (8.1, 11.3), female
6.7% (5.8, 7.7), male



CH is prevalent across all BMI categories:

9.0% (CI: 8.6,9.3), BMI <25
7.7% (CI: 7.4, 8.1), BMI 25.0-29.9
7.8% (CI: 7.3, 8.2), BMI >=30

Fig. 4 Prevalence of CH by BMI category, adjusted for age, gender and race/ ethnicity

Unadjusted prevalence:
8.6% (6.5, 11.3), BMI <25
6.5% (5.1, 8.2), BMI 25.0-29.9
9.3% (7.6, 11.2), BMI >=30

Results (continued)

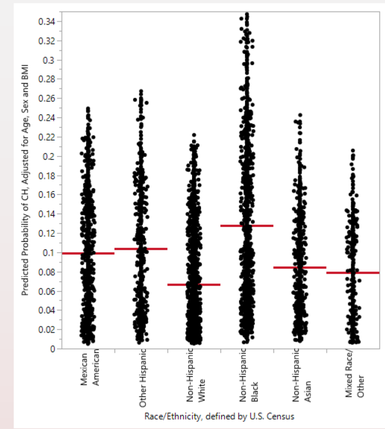


Fig. 5 Prevalence of CH by race/ethnicity, adjusted for age, gender and BMI.

CH prevalence varies by race/ethnicity:

9.9% (CI: 9.3, 10.5) Mexican American
10.4 % (CI: 9.8, 11.1) Other Hispanic
6.7% (CI: 6.4, 7.0) Non-Hispanic White
12.8% (CI: 12.3, 13.3) Non-Hispanic Black
8.5% (CI: 7.9, 9.0) Non-Hispanic Asian
7.9 % (CI: 7.2, 8.6) Other/Mixed Race

22.8% (CI: 21.9, 23.6) Black Teens
19.1% (CI: 18.2, 20.1) Other Hispanic Teens

Summary & Conclusions

Compensatory hyperinsulinemia is prevalent in the U.S. and its subpopulations:

- **U.S. prevalence: 8.2% overall**
- **teenagers have a high prevalence of CH: double the national average**
- **nearly 1 in 4 Black and Hispanic teens have CH, a hidden risk factor for diabetes**
- **teenagers with CH: target population for early screening and intervention to prevent prediabetes**

This study was funded by NIH/NHLBI R21 HL143030 and Texas Tech University Health Sciences Center El Paso. We gratefully acknowledge the heroic efforts of the many human volunteers who contributed to NHANES and the investigators/staff of the U.S. Centers for Disease Control & Prevention.