The prevalence of concurrently raised blood glucose and blood pressure in India

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The prevalence of concurrently raised blood glucose and blood pressure in India: a cross-sectional study of 2,035,662 adults

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Abstract:	Objective: In order to inform integrated, person-centered interventions, this study aimed to determine the prevalence of having both a raised blood glucose (BG) and blood pressure (BP) in India, and its variation among states and population groups. Methods: We pooled data from three large household surveys (the AHS, DLHS-4, and NFHS-4), which were carried out between 2012 and 2016 and included adults aged ≥15 years. Raised BG was defined as having a plasma glucose reading ≥126 mg/dl if fasted and ≥200 mg/dl if not fasted, and raised BP as a systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg. The prevalence of having a concurrently raised BG and BP ('co-morbid') was age-standardized to India's national population structure, and disaggregated by sex, age group, BMI group, rural-urban residency, household wealth quintile, education, state, and region. Results: The age-standardized prevalence of the co-morbidity was 1.5% (95% CI, 1.5-1.5), varying by a factor of 8.3 between states. Among those aged ≥50 years, 4.5% (95% CI, 4.3-4.7) with a BMI<23.0kg/m2 and 16.1% (95% CI, 15.0-17.4) with a BMI ≥30kg/m2 were co-morbid. Age, BMI, household wealth quintile, male sex, and urban location were all positively associated with the co-morbidity. Conclusions: A substantial proportion of India's population had both a raised BG and BP, calling for integrated interventions to reduce CVD risk. We identified large variation among states, age groups, and by rural-urban residency, which can inform health system planning and the targeting of interventions, such as appropriate screening programs, to those most in need.

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
Department of Global Health and Population

February 26th 2019

Dear *Journal of Hypertension* editorial team,

Thank you very much for considering our manuscript for publication in *Journal of Hypertension*.

In the enclosed study, we leverage a huge dataset of two million adults in India to examine the co-morbidity of three major cardiovascular disease (CVD) risk factors: diabetes, hypertension, and overweight and obesity. In our view, this study is of great interest to the general medical and cardiovascular health reader because i) CVD is the number one cause of death in low- and middle-income countries (LMICs),[1] including in India, ii) India accounts for over 20% of the population in LMICs and is projected to add the most people to global population growth until at least 2050,[2] iii) due to its large sample size, coverage of all states and Union Territories in India, and assessment of diabetes, hypertension, and Body Mass Index using physical measurements rather than self-report, this is by far the most representative and rigorous study of the co-morbidity of these important CVD risk factors in India to date, and iv) the findings are of relevance not just to Indian policy makers but to those in South Asia in general, as well as policy makers and clinicians in settings with a large Indian diaspora.

Our study has several important policy implications:

1. We found a high prevalence of having both a raised blood glucose and blood pressure, especially among older age groups (e.g., 7.9% and 6.1% among women and men aged ≥50 years, respectively), which demonstrates the urgency of moving towards more integrated primary healthcare for CVD risk factors in India – a setting in which separate diabetes and hypertension specialty clinics are common and increasing in number.
2. 4.5% of those aged ≥50 years and with a BMI≤23.0kg/m^2 had both raised blood glucose and blood pressure. This high prevalence among those with a low or normal BMI should be appreciated in conjunction with the fact that only 4.3% of adults in our sample were obese. Combined, these two observations make BMI potentially far less useful for risk stratification and targeting of appropriate interventions than in many other populations, such as the United States.
3. We identified (and visualized in maps and heatmaps for easy 'digestion' by policy makers) important variation in concurrently raised blood glucose and blood pressure among states and population groups in India. Evidence on this variation is invaluable for health system planning and to inform the targeting of relevant interventions

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Please let us know any time if there is further information we can provide in support of this analysis.

Yours sincerely,

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References:

1. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390(10100): 1151-210.
2. United Nations Population Division. World Population Prospects: The 2017 Revision, Key Findings and Advance Tables. New York, NY: United Nations, 2017.

Abbreviations:

AHS	Annual Health Survey
CVD	Cardiovascular Disease
DLHS-4	District Level Household and Facility Survey
LMICs	Low- and Middle-income Countries
NCD	Non-communicable diseases
NFHS	National Family Health Survey
PSU	Primary Sampling Unit
SSU	Secondary Sampling Unit
WHO	World Health Organization

Point-by-point reply to the reviewer comments

Reviewer #1:

Comment: *"1. The authors argue that stratification of risk according to BMI may not be useful. I do not fully understand this. Clearly the best form of screening is BP measurement and blood sugar or HbA1c measurement. Where this is not possible one has to focus on those at highest risk. Even if there are still a considerable number of people with low BMI and diabetes the prevalence is higher in those with higher BMI. As always in epidemiology, the absolute number of people at risk in the highest risk group may be lower than the absolute number in the lower risk groups. But one has to start somewhere, especially if resources are limited. I would like to encourage the authors to provide a positive message in the discussion, i.e. a clear message that is informed by the present data on how screening should be conducted in the future - not just a "negative" message that BMI screening may not work."*

Response: Thank you very much for this thoughtful comment. We have now reworded the discussion in both the abstract and the manuscript. The relevant sections now read:

- "We identified large variation among states, age groups, and by rural-urban residency, which can inform health system planning and the targeting of interventions, such as appropriate screening programs, to those most in need." (Abstract, Discussion)
- "A second key finding of this study is that in older age groups, having both a high BG and BP measurement was also common among those with a low or normal BMI (e.g., 4.5% among those aged ≥50 years and with a BMI≤23.0kg/m^2). In fact, our regression results show that a higher BMI category was associated with a higher probability of having a concurrently raised BG and BP even within the normal and low BMI range. This finding – combined with the fact that only 6.3% of adults in India (according to our sample) had a BMI ≥27.5kg/m^2 and 2.8% had a BMI ≥30.0kg/m^2 – implies that screening for diabetes and hypertension based on BMI will likely miss many individuals with these conditions. Nonetheless, BMI likely is useful as one criterion for risk stratification in the targeting of relevant programs for diabetes and hypertension in India to those most in need. Other variables that our analysis identified as being predictive of a concurrently raised BG and BP – and thus as potentially useful for the targeting of diabetes and hypertension interventions – were older age, living in an urban area, and state, with the prevalence of having both a raised BG and BP varying by a factor of 8.3 between states and being particularly high in South India and in Goa." (Discussion, para 2)

Comment: "*2. My other issue relates to the definition of "uncontrolled hypertension" and "uncontrolled diabetes". I agree that for epidemiological purposes the approach that the authors undertook is acceptable. In fact, data quality is pretty good as BP and blood glucose have actually been measured in these cohorts. However, in order to produce accurate data on prevalence of each condition alone and in combination one would like to see data also on people with diabetes and hypertension whose blood glucose and blood pressure are controlled. Are there any data on diagnosis of diabetes or hypertension in the study participants? The authors say that people with such diagnoses in the past "were not classified as having the condition in this study", so I assume the data must be available. Is there an opportunity to perform further sensitivity analyses using "diagnosis of…" rather than "uncontrolled…"?"*

Response: We agree with this comment. While the DLHS-4 and AHS did not ask participants about a prior diagnosis or current treatment for diabetes and hypertension, the NFHS-4 did ask such questions. We have undertaken the following changes in the manuscript to address this comment:

- Because of the limitation in our definition of diabetes and hypertension, we now refer to these conditions as 'raised blood glucose' and 'raised blood pressure' throughout the manuscript.
- In the appendix, we now show the results of all analyses when restricting the sample to the NFHS-4 and defining diabetes and hypertension based on a high blood glucose/pressure measurement or being aware of one's condition or reporting to be on treatment. The relevant files in the appendix are Table S13, Table S14, Figure S7, Figure S8, Figure S9, and Figure S10. Apart from referring to these files in the results section, we now also detail this approach in the methods: "In contrast to the DLHS-4 and AHS, the NFHS-4 asked participants about a previous diagnosis of, and treatment for diabetes and hypertension. Specifically, the relevant questions in the NFHS-4 were "Do you currently have diabetes?", "Have you sought treatment for this issue [diabetes]?" (this question was only asked to those who responded with "yes" to currently having diabetes), "Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?", and "To lower your blood pressure, are you now taking a prescribed medicine". In the appendix, we show the results of all analyses when restricting the sample to the NFHS-4 and defining raised BG as a high BG measurement (as above) or reporting to currently have diabetes, and raised BP as a high BP measurement (as above) or reporting to have been told to have hypertension or to be a taking BP-lowering medication." (Methods, Outcome variables, para 2)

Comment: *"3. In the introduction the authors comment on the healthcare system with a strong prevalence of diabetes clinics. But in light of the present data, isn't this the right strategy? People with diabetes seem to be particularly affected by hypertension (and possibly other comorbidities) and as long as such conditions are also looked after and treated in the diabetes clinics these seem to be the best place, rather than a hypertension clinic that tries to deal with diabetes. Needless to say that a fully functional primary care system would be best."*
Response: Thank you for this thoughtful comment. We have reworded this section in the introduction, which now reads: "A key characteristic of the country's healthcare system is the prominent role of private providers, which account for a much larger proportion (58-79%) of healthcare visits in India than in most other LMICs.[6] This is one reason for the high out-of-pocket healthcare expenditures incurred by India's population,[7] particularly for non-communicable disease (NCD) care.[8] It is common for these fee-paying patients, especially in urban areas, to seek out specialists for their care based on the type of condition from which they perceive to suffer,[9] which contributes to the fragmentation of India's health system. Studying the degree to which CVD risk factors in India co-occur may not only inform the integration of NCD care services, but could also provide a sense of urgency, and thus an impetus for policy, to rapidly move towards more integrated, person-centered primary healthcare for NCDs in which only those with complicated cases of a condition are cared for by specialists." (Introduction, para 2)

Comment: *"4. It is indeed unfortunate that only data on hypertension and diabetes (and BMI) are available. These are important but as stated above I am not overly surprised by the data, as much as the present paper has the potential to inform local and national strategies. In an era of multimorbidity it would be really interesting to see other conditions also featuring here: cancer, automimmune diseases and chronic kidney disease to name a few. Such data are probably not available and the authors comment on it in the limitations section. But maybe call for action in the discussion and say how important such data are - that hypertension and diabetes are somewhat connected is not particularly novel but we really need to learn more about other conditions."*
Response: This is an excellent suggestion and we have now added such a section to the discussion, which reads: "As the Indian population continues to age,[1] the prevalence of chronic disease multimorbidity will likely increase. However, evidence from population-based studies on the patterns of multimorbidity in India is sparse.[2] We would, therefore, encourage policy makers and researchers to increase the array of chronic conditions that are assessed in future waves of the NFHS and similar surveys. This could, for instance, include chronic kidney disease, chronic obstructive pulmonary disease, asthma, mental health (e.g., depression and anxiety), and cognition." (Discussion, para 4)

Comment: *"5. Thanks for mentioning the ethics vote. This applies to the present analysis of the datasets. Could you please remind the reviewer and other readers of the original ethical approvals for the three surveys?"*
Response: We have now added this information in the methods section: This analysis of de-identified data in the public domain received a determination of "not human subjects research" by the institutional review board (IRB) of the Harvard T. H. Chan School of Public Health on 9 May 2018. The AHS and DLHS-4 obtained ethical clearance by the IRB of the National Institute of Health & Family Welfare and the International Institute for Population Sciences. As part of the Demographic and Health Survey series, the NFHS-4 was reviewed and approved by the ICF IRB." (Methods, Ethical approval, para 1)

Reviewer #2:

Comment: *"1. The majority of papers focus on prevalence of hypertension and diabetes and the co-occurrence rather than the prevalence of only the uncontrolled subset. While the stated rationale is in part to determine the need for integrated primary care services, this need can also be determined by more standard awareness, treatment, prevalence and control analysis on the total population of adults with hypertension and diabetes. The focus only on uncontrolled renders comparisons with prior reports more challenging. Differences between regions in uncontrolled patients would also reflect variations in the percentage of individuals receiving effective treatment, which were not acknowledged as a limitation."*
Response: Thank you for this important comment. Unfortunately, the DLHS-4 and AHS did not ask participants about a prior diagnosis or current treatment for diabetes and hypertension.

However, the NFHS-4 did ask such questions. We have thus undertaken the following changes in the manuscript to address this comment:

- Because of the limitation in our definition of diabetes and hypertension, we now refer to these conditions as ‘raised blood glucose’ and ‘raised blood pressure’ throughout the manuscript.
- In the appendix, we now show the results of all analyses when restricting the sample to the NFHS-4 and defining diabetes and hypertension based on a high blood glucose/pressure measurement or being aware of one’s condition or reporting to be on treatment. The relevant files in the appendix are Table S13, Table S14, Figure S7, Figure S8, Figure S9, and Figure S10. Apart from referring to these files in the results section, we now also detail this approach in the methods: “In contrast to the DLHS-4 and AHS, the NFHS-4 asked participants about a previous diagnosis of, and treatment for diabetes and hypertension. Specifically, the relevant questions in the NFHS-4 were “Do you currently have diabetes?”, “Have you sought treatment for this issue [diabetes]?” (this question was only asked to those who responded with “yes” to currently having diabetes), “Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?”, and “To lower your blood pressure, are you now taking a prescribed medicine”. In the appendix, we show the results of all analyses when restricting the sample to the NFHS-4 and defining raised BG as a high BG measurement (as above) or reporting to currently have diabetes, and raised BP as a high BP measurement (as above) or reporting to have been told to have hypertension or to be a taking BP-lowering medication.” (Methods, Outcome variables, para 2)

Comment: *“2. In comparing of differences across regions, it is unclear to this reviewer how much of the differences can be explained by variations in age and body mass index, two major drivers of hypertension, diabetes, and their concurrence. Data available to the authors should also permit an estimate of how much of the differences between regions may be attributed to effective treatment of these chronic conditions or non-communicable diseases. It would be instructive if the authors could determine the contribution of region or state that is independent of factors that were predictive of diabetes, hypertension and their co-occurrence.”*
Response: Thank you very much for this thoughtful comment. We have tried to address this comment in three ways:

1. We have added multivariable regression results in the appendix (Table S6) with an indicator variable for each state. The regression coefficient for each state indicates the difference in probability (in percentage points) of the co-morbidity in a given state (compared to the reference state, which was Jammu and Kashmir) after adjusting for all other variables included in the regression (BMI group, age group, education, and household wealth quintile).
2. We have added a map (Figure S5) that plots the regression coefficient for each state (from Table S6) so that readers can more easily compare the results to the map of the unadjusted prevalence of the co-morbidity in the main manuscript. The pattern is very similar and we now state this in the results section: “This pattern remained similar when adjusting for differences in the age, sex, BMI, education, and household wealth quintile distribution between states (Table S6 and Figure S5).

3. We have added multivariable regression results in the appendix (Table S7) with an indicator variable for each region. As for the indicator variables for state, the regression coefficient for each region indicates the difference in probability (in percentage points) of the co-morbidity in a given region (compared to the reference region, which was West India) after adjusting for all other variables included in the regression.

Comment: *"Minor comments:*
1. Men were older than women. It would be instructive to provide the mean and standard deviation of age for both men and women (Table 1). It would be helpful to understand the sampling issues that led to oversampling of younger women."
Response: We have now added mean age along with the standard deviation in Table 1 (for the entire sample and separately for men and women). The reason that women are on average somewhat younger than men is that a larger proportion of female participants in our study were from the NFHS-4, which only sampled women aged 15 to 49 years. We would like to note that our sampling weights weight both men and women to the age distribution of the entire population of India. However, we have now added this explanation in the description of Table 1: "46.6% of participants were aged between 15 and 34 years, whereby men were on average older than women because a higher share of women were participants of the NFHS-4, which sampled only those aged 15 to 49 years." (Results, Sample characteristics, para 1)

Comment: *"2. The normal BMI category spans 4.4 kg/m2, roughly double the other categories. It would be of interest to assess the relationship of diabetes, hypertension and their co-occurrence over the wide range of normal BMI."*
Response: As suggested, we have now used a finer categorization of BMI for our analyses, namely <18.5kg/m^2, 18.5-19.9 kg/m^2, 20.0-22.9 kg/m^2, 23.0-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2, and ≥ 30.0 kg/m^2.

Comment: *"3. On a related note, the authors noted that BMI was not especially useful, especially with aging as a substantial proportion of older subjects with normal had uncontrolled hypertension and diabetes. Since lean body mass falls as a function of age, a 'normal' BMI may occur in the presence of excess adiposity. While the authors do not appear to have data to address this issue, they may have sufficient data to determine if there is a 'healthy' BMI or a level at which hypertension and diabetes are less likely to occur."*
Response: Thank you for this thoughtful suggestion. While we think it would be ideal to investigate this question in a longitudinal dataset, we now comment on this in the discussion: "In fact, our regression results show that a higher BMI category was associated with a higher probability of having a concurrently raised BG and BP even within the normal and low BMI range." (Discussion, para 2)

References

[1] United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, Key Findings and Advance Tables. Working Paper No. ESA/P/WP/248

[2] Pati S, Swain S, Hussain MA, et al. (2015) Prevalence and outcomes of multimorbidity in South Asia: a systematic review. BMJ open 5: e007235

Condensed abstract

This nationally representative study from India found that the prevalence of having both a raised blood glucose and blood pressure was high in older age groups, even among those with a normal Body Mass Index (BMI). We identified wide variation in the prevalence of this co-morbidity among states. Those with a higher age, BMI, and household wealth, as well men and those in urban areas had a higher probability of having the co-morbidity. The findings of this study highlight the need for integrated cardiovascular disease interventions and can inform the targeting of such interventions to those most in need.

The prevalence of concurrently raised blood glucose and blood pressure in India: a cross-sectional study of 2,035,662 adults

Short title: Blood glucose and pressure in India

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Abstract

Objective: In order to inform integrated, person-centered interventions, this study aimed to determine the prevalence of having both a raised blood glucose (BG) and blood pressure (BP) in India, and its variation among states and population groups.

Methods: We pooled data from three large household surveys (the AHS, DLHS-4, and NFHS-4), which were carried out between 2012 and 2016 and included adults aged ≥15 years. Raised BG was defined as having a plasma glucose reading ≥126 mg/dl if fasted and ≥200 mg/dl if not fasted, and raised BP as a systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg. The prevalence of having a concurrently raised BG and BP ('co-morbid') was age-standardized to India's national population structure, and disaggregated by sex, age group, BMI group, rural-urban residency, household wealth quintile, education, state, and region.

Results: The age-standardized prevalence of the co-morbidity was 1.5% (95% CI, 1.5-1.5), varying by a factor of 8.3 between states. Among those aged ≥50 years, 4.5% (95% CI, 4.3-4.7) with a BMI<23.0kg/m^2 and 16.1% (95% CI, 15.0-17.4) with a BMI ≥30kg/m^2 were co-morbid. Age, BMI, household wealth quintile, male sex, and urban location were all positively associated with the co-morbidity.

Conclusions: A substantial proportion of India's population had both a raised BG and BP, calling for integrated interventions to reduce CVD risk. We identified large variation among states, age groups, and by rural-urban residency, which can inform health system planning and the targeting of interventions, such as appropriate screening programs, to those most in need.

Condensed abstract

This nationally representative study from India found that the prevalence of having both a raised blood glucose and blood pressure was high in older age groups, even among those with a normal Body Mass Index (BMI). We identified wide variation in the prevalence of this co-morbidity among states. Those with a higher age, BMI, and household wealth, as well men and those in urban areas had a higher probability of having the co-morbidity. The findings of this study highlight the need for integrated cardiovascular disease interventions and can inform the targeting of such interventions to those most in need.

Keywords:

cardiovascular disease, co-morbidity, diabetes, hypertension, blood pressure, blood glucose, India

Introduction

The cardiovascular disease (CVD) burden in low and middle-income countries (LMICs) is increasing.[1] In India, CVD accounted for 14.1% of the country's total disability-adjusted life years (DALYs) in 2016, up from 6.9% in 1990.[2] Raised blood glucose (BG) and blood pressure (BP) are both important – yet treatable – risk factors for CVD.[1, 3] While we know that the prevalence of raised BG and BP among adults in India is high at 7.5% and 25.3%, respectively,[4] little is known about the degree to which these conditions overlap, and how this co-morbidity is related to other CVD risk factors – such as obesity – and socio-demographic characteristics.

This knowledge of concurrently raised BG and BP, however, is essential to build an effective public health and health services response to the rise of CVD in India. A key characteristic of the country's healthcare system is the prominent role of private providers, which account for a much larger proportion of healthcare provision (more than 70% of illness episodes and 58-79% of healthcare visits) in India than in most other LMICs.[5, 6] This is one reason for the high out-of-pocket healthcare expenditures incurred by India's population,[7] particularly for non-communicable disease (NCD) care.[8] It is common for these fee-paying patients, especially in urban areas, to seek out specialists for their care based on the type of condition from which they perceive to suffer,[9] which contributes to the fragmentation of India's health system. Studying the degree to which CVD risk factors in India co-occur may not only inform the integration of healthcare services for NCD care, but could also create a sense of urgency, and thus an impetus for policy, to rapidly move towards more integrated, person-centered primary healthcare for NCDs in which only those with complicated cases of a condition are cared for by specialists.

Thus far, evidence on the co-morbidity of raised BG and BP in India has been largely restricted to relatively small cohorts or healthcare facility-based studies in specific states. To our knowledge, this is the first study to use nationally representative data to examine this co-morbidity of two major CVD risk factors. Specifically, analyzing data from two million adults, this study aims to determine the prevalence of concurrently raised BG and BP in India, and how the prevalence of this co-morbidity varies by BMI, state, region, rural versus urban residence, and individual-level socio-demographic characteristics.

Methods

Data sources:

We pooled data from three large population-based household surveys in India: the second update of the Annual Health Survey (AHS), the fourth round of the District-Level-Household Survey (DLHS-4), and the fourth National Family Health Survey (NFHS-4). The NFHS-4, conducted from 2015-2016, is the most recent of these three surveys, and the only one that covered all states and Union Territories. However, it only included men aged 15-54 and women aged 15-49 years. The AHS and DLHS-4, on the other hand, included adults aged ≥18 years. These two surveys were carried out simultaneously between 2012 and 2014 using a similar questionnaire, and jointly covered 34 of 36 states (all except for Jammu and Kashmir, and Gujarat) and five of seven Union Territories (all except for Dadra and Nagar Haveli, and Lakshadweep). No areas in India were covered by both the AHS and the DLHS-4. We thus pooled the AHS and DLHS-4 data with the NFHS-4 data to obtain a dataset that is representative for all adults in India aged 15 years and older, and that covered all states and Union Territories in the country. The only population groups not represented in this dataset are women ≥50 years and men ≥54 years in two of 36 states (Jammu and Kashmir, and Gujarat) and two of seven Union Territories (Dadra and Nagar Haveli, and Lakshadweep).

All three surveys covered all districts in the states covered by the survey and used two-stage cluster random sampling, stratified by rural versus urban areas, within each district. Primary sampling units (PSU) were defined as villages in rural areas, and census enumeration blocks (AHS, NFHS-4) or urban frame survey blocks (DLHS-4) in urban areas. Secondary sampling units (SSU) were households. PSUs were selected using random sampling with equal weighting (DLHS-4) or probability proportional to population size (AHS, NFHS-4). SSUs were selected through systematic random sampling.

In the AHS and DLHS-4, interviewers administered a questionnaire to the household head on socio-demographic information of all household members (regardless of whether the household members were present at the interviewer's visit). Except in the AHS – where these physical measurements were only administered in a sub-sample of, on average, 12 PSUs per district - all non-pregnant household members aged ≥18 years then underwent a height, weight, BG, and BP measurement. Households were not revisited in cases where an eligible adult was absent at the time of the interviewer's visit. The AHS participants' socio-demographic information was merged with the participants' BG and BP data as described in the appendix (see Methods S1, Supplemental Digital Content). In the NFHS-4, the household head questionnaire was used to identify eligible women and men for an additional women's / men's questionnaire. The interviewers then administered the women's questionnaire as well as weight, height, BG, and BP measurements to all women aged 15-49 who resided in the household. The questionnaire and physical measurements for men aged 15-54 years (height, weight, BG, and BP measurements) were only administered in a random subsample of 15 percent of households (every alternate household in 30 percent of the selected PSUs). The sections of the questionnaire used to derive the variables for this analysis were identical between the women's and men's questionnaire. Households in the NFHS-4 were revisited at least two times (on separate times of the day) if not all eligible household members were present at the time of the interviewer's visit. No revisits were conducted in the AHS and DLHS-4.

BG was measured once using a capillary blood sample (finger prick) and a hand-held blood glucometer (SD CodeFree (SD Biosensor) in the AHS and DLHS-4; FreeStyle Optium H (Abbott) in the NFHS-4). The capillary measurements were then multiplied by 1.11 to display the plasma equivalent.[10] Participants of the AHS and DLHS-4 were instructed to fast overnight until the blood glucose was measured in the morning. In the DLHS-4, fasting status was assessed through self-report (58.4% reported to have fasted), while fasting status was not recorded in the AHS. The prevalence and regression analyses in this paper assume that all AHS participants were fasted. However, in the appendix, we present prevalence estimates assuming all AHS participants were non-fasted, as well as regression results for DLHS-4 and NFHS-4 participants only (see Table S8/Table S10/Table S14, Supplemental Digital Content). In the NFHS-4, blood glucose was measured at a random time point

(without instruction to fast prior to the measurement), and participants were asked about the time of last food and drink intake. We defined fasting status as the last food or drink intake (except plain water) being at least eight hours prior to the blood glucose measurement.
In the AHS and DLHS-4, BP was measured twice using an electronic upper arm monitor (Rossmax AW150 (Rossmax Swiss GmbH)) in the left upper arm with an interval of at least three minutes in between measurements. In the NFHS-4, BP was measured three times (using the Omron HEM-8712 (Omron Corporation)) in the left upper arm with at least five minutes between each measurement as well as five minutes of quiet sitting prior to the first measurement.

Weight was measured using a digital scale, and height using a Seca 213 stadiometer (NFHS-4) or wall-mounted statute meter (AHS/DLHS-4).

Outcome variables

The main outcome variables of this analysis were i) concurrently raised BG and BP, ii) raised BP conditional on having a raised BG (i.e., having a raised BP among only those with a raised BG), and iii) raised BG conditional on having a raised BP (i.e., having a raised BG among only those with a raised BP). We defined raised BG as having a high plasma glucose reading (≥126 mg/dl if an AHS participant or reporting to be fasted, or ≥200 mg/dl if reporting to be non-fasted [11]). Raised BP was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg based on the mean of the two (or, in the case of the NFHS-4, three) BP measurements taken.[12]

In contrast to the DLHS-4 and AHS, the NFHS-4 asked participants about a previous diagnosis of, and treatment for diabetes and hypertension. Specifically, the relevant questions in the NFHS-4 were “Do you currently have diabetes?”, “Have you sought treatment for this issue [diabetes]?” (this question was only asked to those who responded with “yes” to currently having diabetes), “Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?”, and “To lower your blood pressure, are you now taking a prescribed medicine”. In the appendix, we show the results of all analyses when restricting the sample to the NFHS-4 and defining raised BG as a high BG measurement (as above) or reporting to currently have diabetes, and raised BP as a high BP measurement (as above) or reporting to have been told to have hypertension or to be a taking BP-lowering medication.

Predictor variables:

Predictor variables of interest were state, region, sex, age, BMI, household wealth quintile, education, marital status, and rural versus urban residency. Given that the World Health Organization considers the BMI cut-offs of ≥23.0 kg/m^2 and ≥27.5kg/m^2 to be additional thresholds (to the traditional ≥25.0 kg/m^2 and ≥30.0 kg/m^2 cut-offs for overweight and obesity) of public health significance in South Asian populations,[13-15] we classified BMI into the following categories: <18.5kg/m^2, 18.5-19.9 kg/m^2, 20.0-22.9 kg/m^2, 23.0-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2, ≥30.0 kg/m^2.

Household wealth quintile was based on a household wealth index, which was computed separately for rural and urban areas using a principal component analysis as per the methodology developed by Filmer and Pritchett. [16, 17] The index was then categorized into quintiles, again separately for rural and urban areas. A more detailed description of the computation of the household wealth quintiles can be found in the appendix (see Methods S2, Supplemental Digital Content).

Statistical analysis:

The prevalence of each outcome variable was disaggregated by age, sex, BMI, state, household wealth quintile, education, and rural-urban residency. All prevalence estimates account for the complex survey design (and pooling of the surveys) using sampling weights. These weights also account for the lower sampling probability of men in the NFHS-4 by assigning a higher weight to men than women in this survey. Prevalence estimates were age-standardized using the age distribution of the 2015 Global Burden of Disease population estimates for India. [18] Age-standardization was done for India as a whole (not separately for each state). To further investigate the association of each outcome variable with individual-level socio-demographic characteristics, we ran linear probability models separately for rural and urban locations with age, BMI, sex, household wealth quintile, education, and marital status as explanatory variables. To filter out area-level effects on the outcomes, these models also included a fixed effect (i.e., a binary indicator variable) for each PSU, which was the lowest identifiable geographic unit in the data. Standard errors were adjusted for clustering at the PSU level. The regression coefficients of these models can be interpreted as the absolute differences in the probability of the outcome (expressed in percentage points). We chose to use a linear probability model rather than a logistic model to avoid the incidental parameter problem.[19] All analyses presented in this manuscript are complete case analyses. R version 3.4.2 was used for statistical analyses,[20] and figures were created with the ggplot2 package and Adobe Illustrator CC 2019.[21, 22]

Ethical approval:

This analysis of de-identified data in the public domain received a determination of “not human subjects research” by the institutional review board (IRB) of the Harvard T.H. Chan School of Public Health on 9 May 2018. The AHS and DLHS-4 obtained ethical clearance by the IRB of the National Institute of Health & Family Welfare and the International Institute for Population Sciences. As part of the Demographic and Health Survey series, the NFHS-4 was reviewed and approved by the ICF IRB.

Data availability:

The datasets supporting the conclusions of this article are publically available via https://www.dhsprogram.com/Data/, https://nrhm-mis.nic.in/hmisreports/AHSReports.aspx, and http://www.iipsindia.ac.in. The merged dataset and statistical code will be made available on the Harvard Dataverse once the manuscript is accepted for publication.

Results

Sample characteristics:

2,035,662 (87.7%) of all 2,320,551 participants had non-missing measurements of BG and BP. Table 1 shows the unweighted (age-unstandardized) sample characteristics. 22.1% had a raised BP, 6.4% had a raised BG, and 4.3% had a BMI≥30.0 kg/m^2. 46.6% of participants were aged between 15 and 34 years, whereby men were on average older than women because a higher share of women were participants of the NFHS-4, which sampled only those aged 15 to 49 years. 63.7% of participants were women, and more than a third (30.5%) had no formal education. Approximately two thirds (68.8%) of participants lived in a rural area. The sample characteristics of those with a missing BG or BP are shown in the appendix (see Table S1, Supplemental Digital Content).

National prevalence of concurrently raised blood glucose and blood pressure:

The (age-standardized) prevalence of having both a raised BG and BP was 1.5% (95% CI, 1.5 - 1.5%) among non-pregnant adults. The prevalence of this co-morbidity was higher in older age groups (Table 2). Those aged ≥50 years had a prevalence of 7.9% (95% CI, 7.6-8.1) and 6.1% (95% CI, 5.8-6.3%) among women and men, respectively. While there was a higher overall prevalence among men (1.6% [95% CI, 1.6 - 1.7%]) than women (1.3% [95% CI, 1.3 - 1.4%]), women had a higher prevalence in the age groups 55-64 and ≥65 years. The prevalence of having both a raised BG and BP was greater in higher BMI groups. Among those who were normal weight (18.5kg/m^2 ≤ BMI < 23.0kg/m^2), the prevalence of this co-morbidity was 0.8% (95% CI, 0.8-0.8%) and 1.0% (95% CI, 1.0-1.1%) in women and men, respectively. 9.6% (95% CI, 9.4 - 9.9%) of participants with a raised BP and 36.7% (95% CI, 36.0 - 37.5%) of participants with a raised BG were co-morbid. Figure 1 depicts the weighted and age-standardized prevalence of raised BG and BP in a Venn diagram. The prevalence of raised BG and BP in the NFHS-4 when also using diabetes and hypertension diagnosis and treatment in the definition of raised BG and BP is shown in Table S14 and Figure S6.

State-level prevalence of concurrently raised blood glucose and blood pressure:

The age-standardized prevalence of concurrently raised BG and BP by state ranged from 0.6% (95% CI, 0.4%-0.8%) in Jammu and Kashmir to 3.3% (95% CI, 2.3% - 4.6%) in Daman and Diu (Figure 2). Except for Daman and Diu, the West Indian state of Goa (3.2% [95% CI,2.5-4.1]) and the Northern Union Territory of Chandigarh (3.0% [95% CI, 2.2%-4.3%]), the highest prevalence tended to be in South India, especially in Kerala (3.0% [95% CI, 2.7-3.4]), Andaman and Nicobar (2.9 % [95% CI, 2.2-3.6]), Puducherry (2.8% [95% CI, 2.2-3.5]) and Tamil Nadu (2.6% [95% CI, 2.5-2.8]). This pattern remained similar when adjusting for differences in the age, sex, BMI, education, and household wealth quintile distribution between states (Table S6 and Figure S5).

The prevalence of having a raised BG conditional on having a raised BP ranged from 4.5% (95% CI, 3.3-6.1) in Jammu and Kashmir to 19.6% (95% CI, 15.3-24.8) in Goa, and was again particularly high in South India (especially Kerala at 15.8% [95% CI,14.3-17.4] and Lakshadweep at 16.7% [95% CI, 9.9-26.8]) and in Goa (19.6% [95% CI, 15.3-24.8]). The prevalence of raised BP conditional on having a raised BG varied from 26.0% (95% CI, 20.9-31.8-34.43) in Odisha to 51.4% (95% CI, 44.3-58.4) in Himachal Pradesh, and was generally highest in North India - particularly in Punjab (51.2% [95% CI, 48.7-53.8]) and Chandigarh (48.7% [95% CI, 38.4-59.1]) - and in the Northeastern states of Sikkim (50.6% [95% CI, 44.9 -56.4]) and Nagaland (50.4% [95% CI, 44.9-56.4]). Detailed age-standardized prevalence estimates by state, sex, and rural versus urban location are shown in the appendix (see Table S2-S4, Supplemental Digital Content).

Prevalence by individual-level characteristics:

The prevalence of each outcome variable tended to be higher in older age groups, richer household wealth quintiles, and in urban areas (Figure 3). The relative differences between household wealth quintiles were higher in rural than in urban areas for all three outcome variables. Stratifying by BMI group shows that the prevalence of all three outcome variables is strongly positively associated with increasing BMI in both rural and urban areas and in all age groups (Figure 4). However, in older age groups, there was a substantial prevalence of concurrently raised BG and BP even among those with a low or normal BMI. For instance, those aged ≥50 years with a BMI <23.0kg/m^2 had a prevalence of 4.5% (95% CI, 4.3-4.7).

In regressions with PSU-level fixed effects, age and BMI group were both strong predictors of having both a raised BG and BP (Table 3). Household wealth quintile was also positively associated with the co-morbidity, although the association was small in magnitude (less than 0.8 percentage points in both rural and urban areas in the fully adjusted model). Similarly, being a man was associated with the co-morbidity but the coefficients were small (0.49 [95% CI, 0.36 to 0.61] and 0.12 [95% CI, 0.05 to 0.19]).

There was no clear trend in the association of the co-morbidity with education. The regression results for raised BG conditional on having a raised BP, and raised BP conditional on having a raised BG (see Table S5, Supplemental Digital Content) show similar trends, except that household wealth quintile was not significantly associated with a raised BP conditional on having a raised BG.

Discussion

This nationally representative study found that 1.5% (95% CI, 1.5-1.5%) of adults in India had both a high BG and BP. This overall prevalence estimate was weighted to the population structure of India, in which 26.7% of those aged 15 years and older are younger than 30 years.[23] The overall relatively low prevalence estimate thus obscures a high prevalence of this co-morbidity among older adults in India. For instance, among those aged ≥50 years, the prevalence of having a concurrently raised BG and BP was 6.8.% (95% CI, 6.6-7.0), and increased to 9.0% (95% CI, 8.8-9.3) among those ≥65 years. Similarly, we found a high prevalence of raised BG among those with raised BP (9.6% [95% CI, 9.4-9.9] overall, and 18.1% [95% CI,17.6-18.6] in those ≥50 years), and an even higher prevalence of raised BP among those with raised BG (36.7% [95% CI, 36.0-37.5] overall, and 49.8% [95% CI, 48.8-50.8] in those ≥50 years). Apart from highlighting a large unmet need for CVD care in India, these co-morbidity estimates clearly show the urgency of transitioning the Indian health system towards more integrated primary healthcare for effectively managing CVD and CVD risk factors.

A second key finding of this study is that in older age groups, having both a high BG and BP measurement was also common among those with a low or normal BMI (e.g., 4.5% among those aged ≥50 years and with a BMI≤23.0kg/m^2). In fact, our regression results show that a higher BMI category was associated with a higher probability of having a concurrently raised BG and BP even within the normal and low BMI range. This finding – combined with the fact that only 6.3% of adults in India (according to our sample) had a BMI ≥27.5kg/m^2 and 2.8% had a BMI ≥30.0kg/m^2 – implies that screening for diabetes and hypertension based on BMI will likely miss many individuals with these conditions. Nonetheless, BMI likely is useful as one criterion for risk stratification in the targeting of relevant programs for diabetes and hypertension in India to those most in need. Other variables that our analysis identified as being predictive of a concurrently raised BG and BP – and thus as potentially useful for the targeting of diabetes and hypertension interventions – were older age, living in an urban area, and state, with the prevalence of having both a raised BG and BP varying by a factor of 8.3 between states and being particularly high in South India and in Goa.

To date, studies on co-morbid diabetes and hypertension in India have been largely restricted to smaller community-based cohorts or healthcare facility-based samples in specific states. To our knowledge, the only published multi-state population-based assessment of diabetes and hypertension co-morbidity in India is the first phase of the ICMR-INDIAB study (carried out between 2008 and 2010), which was conducted among 14,059 adults in three of 29 states and one of seven Union Territories in India.[24] The only co-morbidity reported in this study was the prevalence of diabetes among hypertensive adults. ICMR-INDIAB reported a prevalence of diabetes conditional on having hypertension of 17.5% in Tamil Nadu, 14.3% in Maharashtra, 13.3% in Jharkhand, and 20.7% in Chandigarh. The corresponding results in our study were 15.7% (95% CI, 14.7-16.6) in Tamil Nadu, 6.2% (95% CI, 5.6-6.9) in Maharashtra, 5.2% (95% CI, 3.9-6.9) in Jharkhand, and 12.2% (9.2 - 16.0) in Chandigarh. The likely reason for which our state-level estimates for this outcome were generally lower than those by ICMR-INDIAB is that we used only BG and BP measurements, while ICMR-INDIAB also used data on a self-reported diagnosis of, or current treatment for diabetes and hypertension. Punjab had a relatively large (2,499 fasted adults) assessment of diabetes and hypertension co-morbidity in 2014-2015,[25] which reported a prevalence of 4.5% for the co-existence of both diseases compared to 1.8% (95% CI, 1.7-2.0) in this study. Again, the somewhat lower prevalence in our study may be explained by our narrower definition of diabetes and hypertension.

This study has several limitations. First, 12.3% of adults in this population-based survey had a missing value for the BG or BP measurement. Second, our diabetes definition based on a one-time capillary BG measurement, especially if non-fasted, is not recommended for a clinical diagnosis of diabetes.[26] We thus chose to refer to this variable as ‘raised BG’ rather than ‘diabetes’. Third, our definition of raised BP was based on a one-off (rather than on two occasions) measurement of BP whereby BP was measured only twice (rather than three times) in the AHS and DLHS-4. Third, the AHS did not verify fasting status before the BG measurement. In addition to having led to a higher overall prevalence of having both a high BG and BP, assuming all participants were fasted at the time of measurement may in particular have led us to overestimate prevalence among poorer participants, because the AHS focusses on India's poorest states. We therefore also provide prevalence estimates assuming all AHS participants were non-fasted and regression results among participants for whom fasting status was verified by self-report (i.e., DLHS-4 and NFHS-4 only) in the appendix. Finally, we were only able to evaluate the co-morbidities between raised BG, raised BP, and obesity, but it is likely that other co-morbidities are common in this population, such as depression and dyslipidemia. Unfortunately, these chronic conditions were not assessed in these surveys. As the Indian population continues to age,[23] the prevalence of chronic disease multimorbidity will likely increase. However, evidence from population-based studies on the patterns of multimorbidity in India is sparse.[27] We would, therefore, encourage policy makers and researchers to increase the array of chronic conditions that are assessed in future waves of the NFHS and similar surveys. This could, for instance, include chronic kidney disease, chronic obstructive pulmonary disease, asthma, mental health (e.g., depression and anxiety), and cognition.

Conclusion

We identified a substantial prevalence, especially among older age groups, of having both a raised BG and BP in India. Apart from highlighting a large need for care for these conditions, this finding provides new evidence for public health interventions and health system design, and underscores the urgency for transitioning the Indian health system towards integrated primary healthcare for cardiometabolic disease and NCDs more generally. Such integration of primary healthcare service delivery is particularly needed in urban areas and in South India, Goa, and Chandigarh, where the prevalence of this co-morbidity was the highest. Targeting diabetes and hypertension programs, such as screening activities, at those with a high BMI may be less effective in India than in many other populations given i) that we found the prevalence of having both a raised BG and BP to be high among those with a low or normal BMI, and ii) the fact that only a minority of Indians are overweight or obese. More generally, with India accounting for over 20% of the population in LMICs, [23] this study is an important contribution to addressing the dearth of national-level evidence on NCD co-morbidities in LMICs.

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Figure Legends

Figure 1. Venn diagram of raised blood glucose and blood pressure prevalence for three 10-year age groups[*, †]

[*] Numbers account for sampling weights, including age-standardization to India's population structure.

[†] Venn diagrams for all 10-year age groups and for the total sample are shown in the appendix (see Figure S1-4, Supplemental Digital Content).

Figure 2. Age-standardized prevalence (in percent) of each outcome variable, by state*

* AP indicates AN, Andaman and Nicobar Islands; AP, Andhra Pradesh; AR, Arunachal Pradesh; AS, Assam; BR, Bihar; CG, Chhattisgarh; CH, Chandigarh; DD, Daman and Diu; DL, Delhi; DN, Dadra and Nagar Haveli; GA, Goa; GJ, Gujarat; HR, Haryana; HP, Himachal Pradesh; JH, Jharkhand; JK, Jammu and Kashmir; KA, Karnataka; KL, Kerala; LD, Lakshadweep; MP, Madhya Pradesh; MH, Maharashtra; MN, Manipur; ML, Meghalaya; MZ, Mizoram; NL, Nagaland; OD, Odisha (Orissa); PB, Punjab; PY, Puducherry; RJ, Rajasthan; SK, Sikkim; TN, Tamil Nadu; TS, Telangana State; TR, Tripura; UP, Uttar Pradesh; UK, Uttarakhand (Uttaranchal); WB, West Bengal.

Figure 3. Age-standardized prevalence (in percent) of each outcome variable by rural versus urban residence, sex, age group, and household wealth quintile

Figure 4. Age-standardized prevalence (in percent) of each outcome variable by rural versus urban residence, sex, age group, and BMI group

Tables

*Table 1: Sample characteristics**

	Total (%)	**Women (%)**	**Men (%)**
n	2,035,662	1,297,084 (63.7)	738,578 (36.3)
Raised blood pressure, n (%)	449,703 (22.1)	240,781 (18.6)	208,922 (28.3)
Mean systolic blood pressure, mmHg (SD)	125.7 (20.2)	124.3 (21.1)	127.1 (19.1)
Mean diastolic blood pressure, mmHg (SD)	80.3 (12.9)	79.4 (13.0)	81.2 (12.7)
Raised blood glucose, n (%)	130,176 (6.4)	69,697 (5.4)	60,479 (8.2)
Mean blood glucose, mg/dl (SD)	114.8 (33.3)	114.8 (33.2)	114.8 (33.5)
BMI group, n (%)			
<18.5kg/m^2	398,658 (19.8)	268,822 (20.9)	129,836 (17.8)
18.5-19.9 kg/m^2	303,195 (15.1)	194,723 (15.1)	108,472 (14.9)
20.0-22.9 kg/m^2	642,570 (31.9)	396,046 (30.8)	246,524 (33.8)
23.0-24.9 kg/m^2	288,639 (14.3)	172,381 (13.4)	116,258 (16.0)
25.0-27.4 kg/m^2	197,210 (9.8)	124,698 (9.7)	72,512 (10.0)
27.5-29.9 kg/m^2	97,072 (4.8)	65,998 (5.1)	31,074 (4.3)
≥ 30.0 kg/m^2	86,420 (4.3)	62,694 (4.9)	23,726 (3.3)
Missing (%)	*1.1*	*0.9*	*1.4*
Age (mean (SD))	37.7 (15.0)	36.3 (14.1)	40.3 (16.0)
Age group (years), n (%)			

15-24	428,808 (21.1)	289,299 (22.3)	139,509 (18.9)
25-34	519,538 (25.5)	352,070 (27.1)	167,468 (22.7)
35-44	472,082 (23.2)	317,465 (24.5)	154,617 (20.9)
45-54	318,993 (15.7)	192,017 (14.8)	126,976 (17.2)
55-64	160,318 (7.9)	81,132 (6.3)	79,186 (10.7)
≥65	135,923 (6.7)	65,101 (5.0)	70,822 (9.6)
Missing (%)	*0*	*0*	*0*
Urban residency, n (%)	635,080 (31.2)	396,066 (30.5)	239,014 (32.4)
Missing (%)	*0*	*0*	*0*
Household wealth quintile, n (%)			
1	391,109 (19.8)	251,670 (19.9)	139,439 (19.6)
2	391,804 (19.8)	251,794 (19.9)	140,010 (19.7)
3	392,469 (19.9)	252,717 (20.0)	139,752 (19.7)
4	396,925 (20.1)	252,737 (20.0)	144,188 (20.3)
5	404,084 (20.4)	257,275 (20.3)	146,809 (20.7)
Missing (%)	*2.9*	*2.4*	*3.8*
Education, n (%)			
No formal education	619,506 (30.5)	469,436 (36.3)	150,070 (20.4)
< Primary School	131,945 (6.5)	80,248 (6.2)	51,697 (7.0)
Primary School	213,147 (10.5)	124,174 (9.6)	88,973 (12.1)
Middle School	497,734 (24.5)	339,349 (26.2)	158,385 (21.5)
Secondary School	243,616 (12.0)	128,079 (9.9)	115,537 (15.7)

>Secondary School	324,321 (16.0)	153,337 (11.8)	170,984 (23.2)
Missing (%)	*0.3*	*0.2*	*0.4*
Currently married, n (%)	1,514,172 (74.4)	980,686 (75.6)	533,486 (72.4)
Missing (%)	*0.1*	*0*	*0.2*

Abbreviations: n=number, %=percentage
* All numbers and percentages shown do not account for sampling weights (and are not age-standardized)

Table 2. National-level prevalence by age group, BMI group, and sex *, †

	Concurrently raised blood glucose and blood pressure		Raised blood glucose conditional on having a raised blood pressure		Raised blood pressure conditional on having a raised blood glucose	
	Women Percent (95% CI)	**Men** Percent (95 % CI)	**Women** Percent (95% CI)	**Men** Percent (95 % CI)	**Women** Percent (95% CI)	**Men** Percent (95 % CI)
Age group (years)						
15-24	0.1 (0.1-0.1)	0.2 (0.2-0.2)	3.0 (2.6-3.4)	2.6 (2.3-3.1)	11.5 (10.1-13.0)	16.2 (14.0-18.6)
25-34	0.5 (0.5-0.5)	0.9 (0.8-1.0)	5.1 (4.8-5.4)	5.4 (4.9-5.9)	20.3 (19.2-21.5)	30.3 (28.1-32.6)
35-44	1.6 (1.6-1.7)	2.4 (2.3-2.6)	8.8 (8.5-9.2)	9.9 (9.2-10.7)	32.9 (31.8-33.9)	39.5 (37.1-41.9)
45-54	4.0 (3.8-4.1)	4.2 (3.9-4.5)	14.1 (13.7-14.6)	13.9 (13.1-14.8)	43.1 (41.9-44.2)	44.8 (42.7-46.9)
55-64	8.3 (8.0-8.6)	7.8 (7.5-8.1)	20.3 (19.7-21.0)	19.6 (18.9-20.3)	53.9 (52.7-55.1)	49.4 (47.8-51.1)
≥65	9.4 (9.1-9.8)	8.6 (8.3-9.0)	19.3 (18.7-20.0)	19.8 (19.1-20.5)	57.9 (56.5-59.2)	51.7 (50.3-53.2)
BMI group						
<18.5kg/m^2	0.4 (0.4 to 0.4)	0.5 (0.5 to 0.6)	5.6 (5.2 to 5.9)	6.1 (5.5 to 6.8)	18.4 (17.2 to 19.5)	21.2 (19.3 to 23.3)
18.5-19.9 kg/m^2	0.5 (0.5 to 0.5)	0.7 (0.6 to 0.8)	6.0 (5.5 to 6.4)	6.2 (5.5 to 6.9)	22.3 (20.8 to 23.8)	26.4 (23.8 to 29.2)

20.0-22.9 kg/m^2	1.0 (0.9 to 1.0)	1.2 (1.1 to 1.3)	8.0 (7.7 to 8.4)	7.4 (6.9 to 7.9)	30.9 (29.7 to 32.0)	33.3 (31.5 to 35.3)
23.0-24.9 kg/m^2	1.7 (1.6 to 1.8)	2.0 (1.9 to 2.2)	10.1 (9.6 to 10.6)	8.9 (8.3 to 9.6)	37.5 (36.0 to 39.0)	40.1 (37.7 to 42.4)
25.0-27.4 kg/m^2	2.6 (2.4 to 2.7)	3.4 (3.1 to 3.7)	11.9 (11.4 to 12.5)	11.6 (10.7 to 12.6)	40.9 (39.4 to 42.4)	48.5 (45.6 to 51.4)
27.5-29.9 kg/m^2	3.7 (3.5 to 4.0)	5.3 (4.8 to 5.9)	14.7 (13.9 to 15.5)	14.7 (13.3 to 16.3)	45.9 (44.1 to 47.8)	54.3 (50.2 to 58.3)
≥30.0 kg/m^2	5.2 (5.0 to 5.4)	6.7 (5.9 to 7.5)	17.3 (16.6 to 18.0)	17.1 (15.2 to 19.1)	46.8 (45.1 to 48.6)	49.3 (43.9 to 54.8)
Total	1.3 (1.3-1.4)	1.6 (1.6-1.7)	10.0 (9.8-10.2)	9.4 (9.0-9.7)	34.6 (34.0-35.2)	38.4 (37.2-39.6)

* These prevalence estimates assume all AHS participants were fasted at the time of the blood glucose measurement. In the appendix (see Table S8, Supplemental Digital Content), we show the corresponding prevalences assuming all AHS participants were non-fasted.

† All prevalence estimates are weighted (using sampling weights) and age-standardized to India's population structure.

Table 3. Partially and fully adjusted linear regressions of having both a raised blood glucose and blood pressure on socio-demographic characteristics[*, †, ‡]

	Partially adjusted				**Fully adjusted**			
	Urban		***Rural***		***Urban***		***Rural***	
	Diff. in probability (95% CI)	*P*	*Diff. in probability (95% CI)*	*P*	*Diff. in probability (95% CI)*	*P*	*Diff. in probability (95% CI)*	*P*
Men	0.36 (0.24 to 0.48)	<0.001	0.19 (0.12 to 0.25)	<0.001	0.49 (0.36 to 0.61)	<0.001	0.12 (0.05 to 0.19)	<0.001
BMI group								
<18.5 kg/m^2	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
18.5-19.9 kg/m^2	0.43 (0.30 to 0.56)	<0.001	0.36 (0.30 to 0.42)	<0.001	0.40 (0.26 to 0.53)	<0.001	0.33 (0.27 to 0.39)	<0.001
20.0-22.9 kg/m^2	1.12 (1.00 to 1.24)	<0.001	0.78 (0.72 to 0.84)	<0.001	1.07 (0.95 to 1.19)	<0.001	0.73 (0.67 to 0.79)	<0.001
23.0-24.9 kg/m^2	1.93 (1.77 to 2.09)	<0.001	1.61 (1.52 to 1.71)	<0.001	1.84 (1.68 to 2.01)	<0.001	1.52 (1.42 to 1.62)	<0.001
25.0-27.4 kg/m^2	3.36 (3.16 to 3.56)	<0.001	2.88 (2.74 to 3.02)	<0.001	3.28 (3.08 to 3.48)	<0.001	2.73 (2.59 to 2.87)	<0.001
27.5-29.9 kg/m^2	4.76 (4.50 to 5.03)	<0.001	4.30 (4.07 to 4.53)	<0.001	4.67 (4.40 to 4.94)	<0.001	4.12 (3.90 to 4.35)	<0.001
≥ 30.0 kg/m^2	6.39 (6.09 to 6.69)	<0.001	5.63 (5.35 to 5.91)	<0.001	6.31 (6.01 to 6.61)	<0.001	5.43 (5.15 to 5.72)	<0.001
Age group (years)								
15-19	-	-	-	-	0.00 (Reference)		0.00 (Reference)	
20-24	-	-	-	-	-0.47 (-0.57 to -0.38)	<0.001	-0.17 (-0.22 to -0.11)	<0.001

25-29	-	-	-	-	-0.56 (-0.70 to -0.43)	<0.001	-0.15 (-0.23 to -0.08)	<0.001
30-34	-	-	-	-	-0.17 (-0.33 to -0.01)	0.043	0.09 (0.00 to 0.17)	0.057
35-39	-	-	-	-	0.59 (0.41 to 0.77)	<0.001	0.51 (0.42 to 0.61)	<0.001
40-44	-	-	-	-	1.86 (1.65 to 1.06)	<0.001	1.06 (1.95 to 1.17)	<0.001
45-49	-	-	-	-	3.43 (3.19 to 3.66)	<0.001	1.87 (1.75 to 1.99)	<0.001
50-54	-	-	-	-	6.34 (5.99 to 6.68)	<0.001	3.43 (3.25 to 3.62)	<0.001
55-59	-	-	-	-	8.07 (7.64 to 8.50)	<0.001	4.60 (4.37 to 4.84)	<0.001
60-64	-	-	-	-	10.06 (9.58 to 10.55)	<0.001	5.70 (5.44 to 5.97)	<0.001
≥65	-	-	-	-	11.21 (10.78 to 11.64)	<0.001	6.92 (6.68 to 6.16)	<0.001
Education								
No formal education	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
< Primary School	0.51 (0 0.80)	0.001	0.39 (0.28 to 0.49)	<0.001	0.26 (-0.03 to 0.55)	0.078	0.24 (0.13 to 0.359	<0.001
Primary School	0.71 (0 0.94)	<0.001	0.67 (0.57 to 0.77)	<0.001	0.35 (0.12 to 0.58)	0.003	0.42 (0.32 to 0.52)	<0.001
Middle School	0.95 (0 1.12)	<0.001	0.74 (0.66 to 0.81)	<0.001	0.43 (0.25 to 0.62)	0.326	0.37 (0.29 to 0.45)	<0.001
Secondary School	1.17 (0 1.37)	0.985	0.95 (0.84 to 1.06)	<0.001	0.51 (0.30 to 0.72)	<0.001	0.45 (0.33 to 0.56)	<0.001
> Secondary School	0.89 (0 1.08)	<0.001	0.86 (0.75 to 0.97)	<0.001	0.07 (-0.14 to 0.28)	0.5066	0.20 (0.08 to 0.31)	<0.001
Household wealth quintile								

1 (Poorest)	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
2	0.68 (0.52 to 0.83)	<0.001	0.21 (0.13 to 0.28)	<0.001	0.38 (0.22 to 0.53)	<0.001	0.08 (0.00 to 0.16)	0.047
3	1.03 (0.86 to 1.21)	<0.001	0.38 (0.29 to 0.48)	<0.001	0.51 (0.33 to 0.69)	<0.001	0.12 (0.02 to 0.21)	0.014
4	1.44 (1.25 to 1.63)	<0.001	0.70 (0.60 to 0.81)	<0.001	0.74 (0.54 to 0.94)	<0.001	0.25 (0.15 to 0.36)	<0.001
5 (Richest)	1.63 (1.41 to 1.84)	<0.001	1.57 (1.44 to 1.69)	<0.001	0.77 (0.55 to 0.00)	<0.001	0.78 (0.65 to 0.91)	<0.001
Currently married	-0.12 (-0.27 to 0.02)	0.102	-0.14 (-0.22 to -0.06)	<0.001	-0.33 (-0.48 to -0.18)	<0.001	-0.26 (-0.34 to -0.18)	<0.001

* All models included PSU-level fixed effects (i.e., a binary indicator for each PSU), and standard errors were adjusted for clustering at the PSU level. Partially adjusted models were additionally adjusted for age group only, while the fully adjusted model was adjusted for all variables shown in the table.

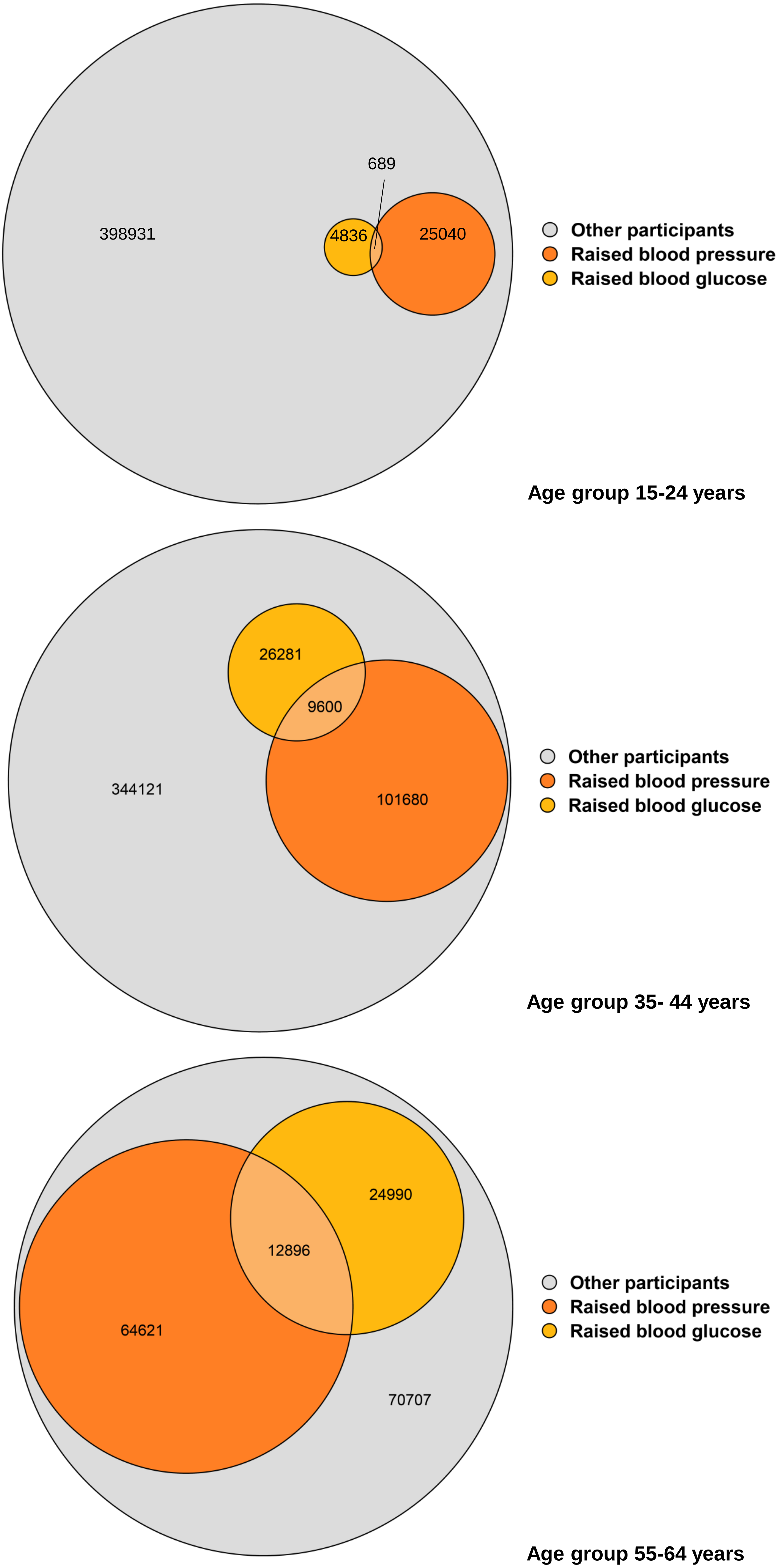
† Coefficients should be interpreted as the absolute change in the probability of the outcome (compared to the reference category) in percentage points.

‡ For these regression models, AHS participants were assumed to be fasted at the time of the blood glucose measurement. Regression results among only those in whom fasting status was verified through self-report (i.e., DLHS-4 and NFHS-4) are shown in the appendix (see Table S10/Table S14, Supplemental Digital Content)

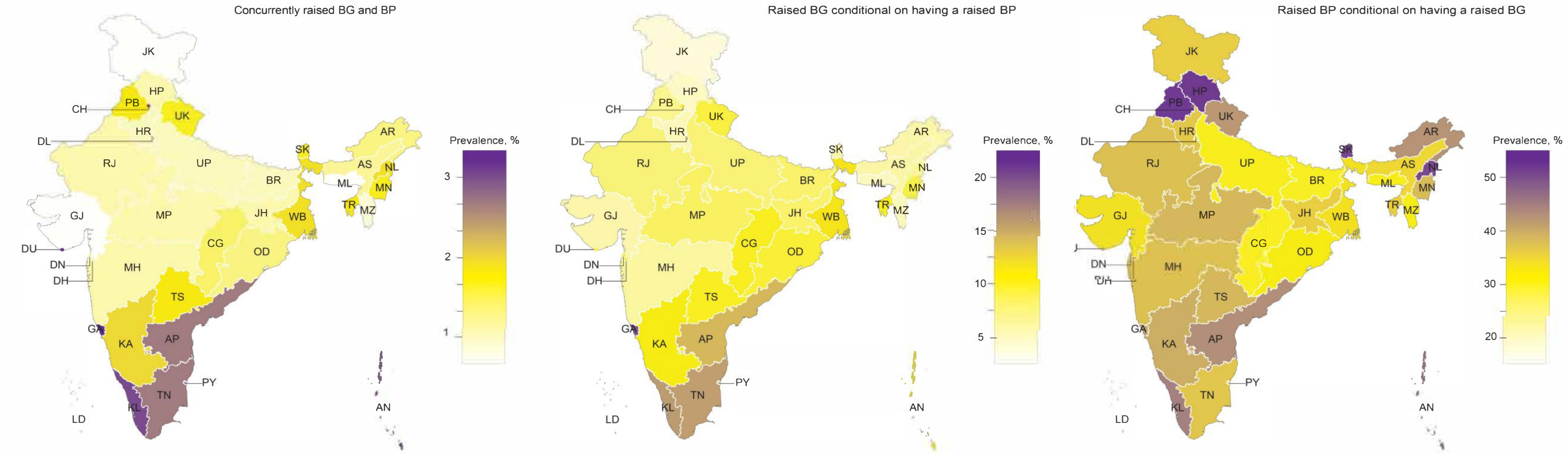
Supplemental Digital Content

Supplementary Appendix.pdf

Figure 1



398931
4836
689
25040
Other participants
Raised blood pressure
Raised blood glucose
Age group 15-24 years
26281
9600
344121
101680
Other participants
Raised blood pressure
Raised blood glucose
Age group 35- 44 years
24990
12896
64621
70707
Other participants
Raised blood pressure
Raised blood glucose
Age group 55-64 years



Concurrently raised BG and BP
Raised BG conditional on having a raised BP
Raised BP conditional on having a raised BG
JK
HP
PB
CH
UK
HR
DL
RJ
UP
BR
SK
AR
AS
NL
ML
MN
TR
MZ
GJ
MP
JH
WB
DU
CG
OD
DN
MH
DH
TS
GA
KA
AP
PY
TN
KL
LD
AN
Prevalence, %
1
2
3
5
10
15
20
20
30
40
50

Figure 3

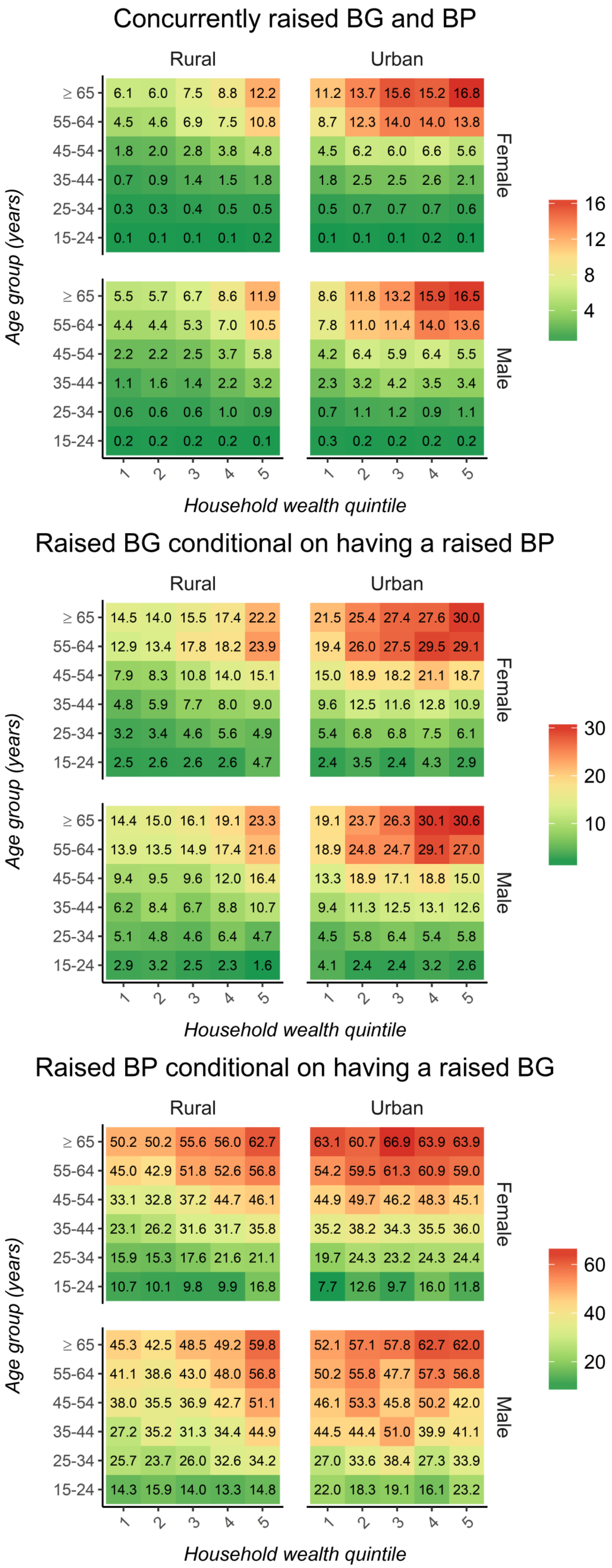
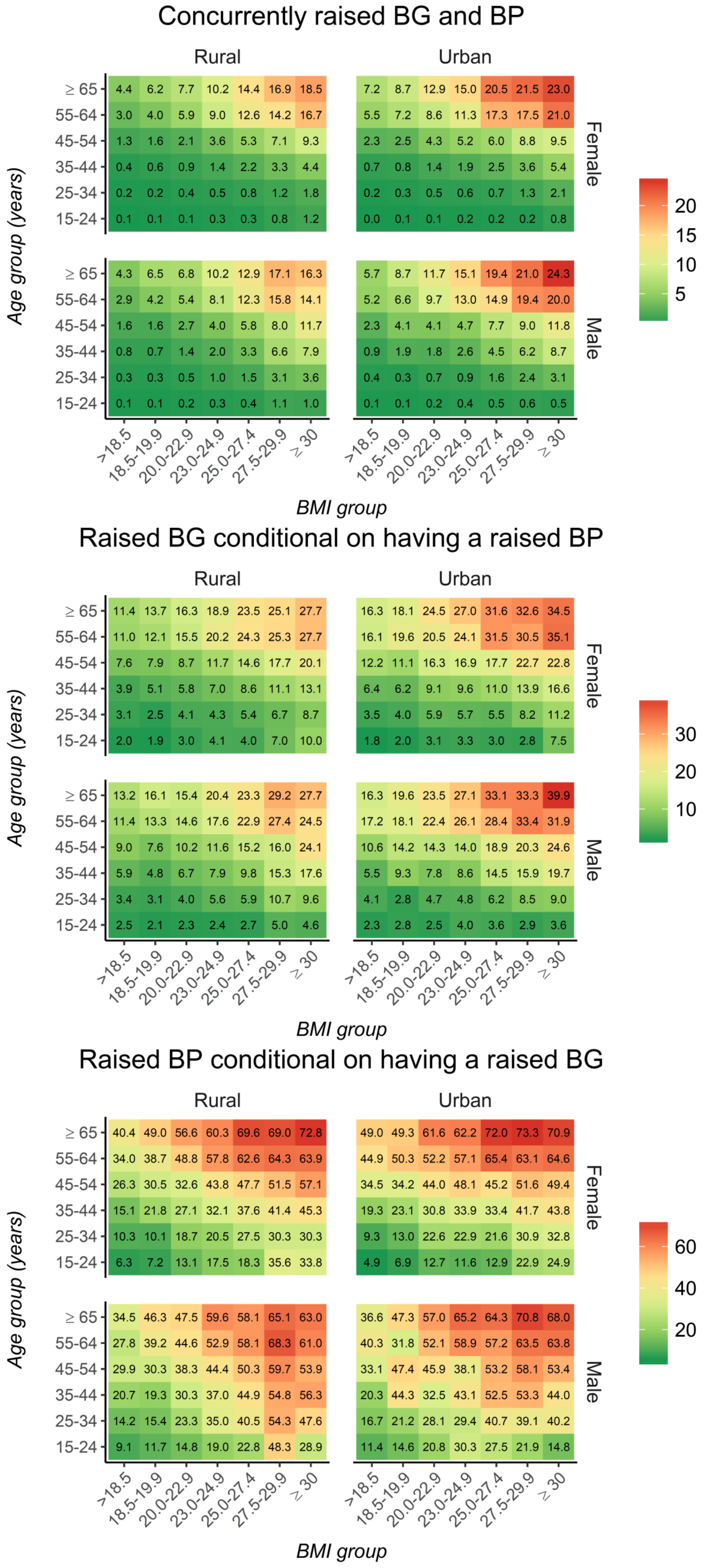

Concurrently raised BG and BP
Rural
Urban
≥ 65 6.1 6.0 7.5 8.8 12.2 11.2 13.7 15.6 15.2 16.8
55-64 4.5 4.6 6.9 7.5 10.8 8.7 12.3 14.0 14.0 13.8
45-54 1.8 2.0 2.8 3.8 4.8 4.5 6.2 6.0 6.6 5.6
35-44 0.7 0.9 1.4 1.5 1.8 1.8 2.5 2.5 2.6 2.1
25-34 0.3 0.3 0.4 0.5 0.5 0.5 0.7 0.7 0.7 0.6
15-24 0.1 0.1 0.1 0.1 0.2 0.1 0.1 0.1 0.2 0.1
Female
≥ 65 5.5 5.7 6.7 8.6 11.9 8.6 11.8 13.2 15.9 16.5
55-64 4.4 4.4 5.3 7.0 10.5 7.8 11.0 11.4 14.0 13.6
45-54 2.2 2.2 2.5 3.7 5.8 4.2 6.4 5.9 6.4 5.5
35-44 1.1 1.6 1.4 2.2 3.2 2.3 3.2 4.2 3.5 3.4
25-34 0.6 0.6 0.6 1.0 0.9 0.7 1.1 1.2 0.9 1.1
15-24 0.2 0.2 0.2 0.2 0.1 0.3 0.2 0.2 0.2 0.2
Male
Age group (years)
1 2 3 4 5 1 2 3 4 5
Household wealth quintile
16
12
8
4
Raised BG conditional on having a raised BP
Rural
Urban
≥ 65 14.5 14.0 15.5 17.4 22.2 21.5 25.4 27.4 27.6 30.0
55-64 12.9 13.4 17.8 18.2 23.9 19.4 26.0 27.5 29.5 29.1
45-54 7.9 8.3 10.8 14.0 15.1 15.0 18.9 18.2 21.1 18.7
35-44 4.8 5.9 7.7 8.0 9.0 9.6 12.5 11.6 12.8 10.9
25-34 3.2 3.4 4.6 5.6 4.9 5.4 6.8 6.8 7.5 6.1
15-24 2.5 2.6 2.6 2.6 4.7 2.4 3.5 2.4 4.3 2.9
Female
≥ 65 14.4 15.0 16.1 19.1 23.3 19.1 23.7 26.3 30.1 30.6
55-64 13.9 13.5 14.9 17.4 21.6 18.9 24.8 24.7 29.1 27.0
45-54 9.4 9.5 9.6 12.0 16.4 13.3 18.9 17.1 18.8 15.0
35-44 6.2 8.4 6.7 8.8 10.7 9.4 11.3 12.5 13.1 12.6
25-34 5.1 4.8 4.6 6.4 4.7 4.5 5.8 6.4 5.4 5.8
15-24 2.9 3.2 2.5 2.3 1.6 4.1 2.4 2.4 3.2 2.6
Male
Age group (years)
1 2 3 4 5 1 2 3 4 5
Household wealth quintile
30
20
10
Raised BP conditional on having a raised BG
Rural
Urban
≥ 65 50.2 50.2 55.6 56.0 62.7 63.1 60.7 66.9 63.9 63.9
55-64 45.0 42.9 51.8 52.6 56.8 54.2 59.5 61.3 60.9 59.0
45-54 33.1 32.8 37.2 44.7 46.1 44.9 49.7 46.2 48.3 45.1
35-44 23.1 26.2 31.6 31.7 35.8 35.2 38.2 34.3 35.5 36.0
25-34 15.9 15.3 17.6 21.6 21.1 19.7 24.3 23.2 24.3 24.4
15-24 10.7 10.1 9.8 9.9 16.8 7.7 12.6 9.7 16.0 11.8
Female
≥ 65 45.3 42.5 48.5 49.2 59.8 52.1 57.1 57.8 62.7 62.0
55-64 41.1 38.6 43.0 48.0 56.8 50.2 55.8 47.7 57.3 56.8
45-54 38.0 35.5 36.9 42.7 51.1 46.1 53.3 45.8 50.2 42.0
35-44 27.2 35.2 31.3 34.4 44.9 44.5 44.4 51.0 39.9 41.1
25-34 25.7 23.7 26.0 32.6 34.2 27.0 33.6 38.4 27.3 33.9
15-24 14.3 15.9 14.0 13.3 14.8 22.0 18.3 19.1 16.1 23.2
Male
Age group (years)
1 2 3 4 5 1 2 3 4 5
Household wealth quintile
60
40
20

Figure 4



Concurrently raised BG and BP
Rural
Urban
Female
Male
Age group (years)
BMI group
≥ 65 4.4 6.2 7.7 10.2 14.4 16.9 18.5 7.2 8.7 12.9 15.0 20.5 21.5 23.0
55-64 3.0 4.0 5.9 9.0 12.6 14.2 16.7 5.5 7.2 8.6 11.3 17.3 17.5 21.0
45-54 1.3 1.6 2.1 3.6 5.3 7.1 9.3 2.3 2.5 4.3 5.2 6.0 8.8 9.5
35-44 0.4 0.6 0.9 1.4 2.2 3.3 4.4 0.7 0.8 1.4 1.9 2.5 3.6 5.4
25-34 0.2 0.2 0.4 0.5 0.8 1.2 1.8 0.2 0.3 0.5 0.6 0.7 1.3 2.1
15-24 0.1 0.1 0.1 0.3 0.3 0.8 1.2 0.0 0.1 0.1 0.2 0.2 0.2 0.8
≥ 65 4.3 6.5 6.8 10.2 12.9 17.1 16.3 5.7 8.7 11.7 15.1 19.4 21.0 24.3
55-64 2.9 4.2 5.4 8.1 12.3 15.8 14.1 5.2 6.6 9.7 13.0 14.9 19.4 20.0
45-54 1.6 1.6 2.7 4.0 5.8 8.0 11.7 2.3 4.1 4.1 4.7 7.7 9.0 11.8
35-44 0.8 0.7 1.4 2.0 3.3 6.6 7.9 0.9 1.9 1.8 2.6 4.5 6.2 8.7
25-34 0.3 0.3 0.5 1.0 1.5 3.1 3.6 0.4 0.3 0.7 0.9 1.6 2.4 3.1
15-24 0.1 0.1 0.2 0.3 0.4 1.1 1.0 0.1 0.1 0.2 0.4 0.5 0.6 0.5
>18.5 18.5-19.9 20.0-22.9 23.0-24.9 25.0-27.4 27.5-29.9 ≥ 30
20 15 10 5
Raised BG conditional on having a raised BP
≥ 65 11.4 13.7 16.3 18.9 23.5 25.1 27.7 16.3 18.1 24.5 27.0 31.6 32.6 34.5
55-64 11.0 12.1 15.5 20.2 24.3 25.3 27.7 16.1 19.6 20.5 24.1 31.5 30.5 35.1
45-54 7.6 7.9 8.7 11.7 14.6 17.7 20.1 12.2 11.1 16.3 16.9 17.7 22.7 22.8
35-44 3.9 5.1 5.8 7.0 8.6 11.1 13.1 6.4 6.2 9.1 9.6 11.0 13.9 16.6
25-34 3.1 2.5 4.1 4.3 5.4 6.7 8.7 3.5 4.0 5.9 5.7 5.5 8.2 11.2
15-24 2.0 1.9 3.0 4.1 4.0 7.0 10.0 1.8 2.0 3.1 3.3 3.0 2.8 7.5
≥ 65 13.2 16.1 15.4 20.4 23.3 29.2 27.7 16.3 19.6 23.5 27.1 33.1 33.3 39.9
55-64 11.4 13.3 14.6 17.6 22.9 27.4 24.5 17.2 18.1 22.4 26.1 28.4 33.4 31.9
45-54 9.0 7.6 10.2 11.6 15.2 16.0 24.1 10.6 14.2 14.3 14.0 18.9 20.3 24.6
35-44 5.9 4.8 6.7 7.9 9.8 15.3 17.6 5.5 9.3 7.8 8.6 14.5 15.9 19.7
25-34 3.4 3.1 4.0 5.6 5.9 10.7 9.6 4.1 2.8 4.7 4.8 6.2 8.5 9.0
15-24 2.5 2.1 2.3 2.4 2.7 5.0 4.6 2.3 2.8 2.5 4.0 3.6 2.9 3.6
30 20 10
Raised BP conditional on having a raised BG
≥ 65 40.4 49.0 56.6 60.3 69.6 69.0 72.8 49.0 49.3 61.6 62.2 72.0 73.3 70.9
55-64 34.0 38.7 48.8 57.8 62.6 64.3 63.9 44.9 50.3 52.2 57.1 65.4 63.1 64.6
45-54 26.3 30.5 32.6 43.8 47.7 51.5 57.1 34.5 34.2 44.0 48.1 45.2 51.6 49.4
35-44 15.1 21.8 27.1 32.1 37.6 41.4 45.3 19.3 23.1 30.8 33.9 33.4 41.7 43.8
25-34 10.3 10.1 18.7 20.5 27.5 30.3 30.3 9.3 13.0 22.6 22.9 21.6 30.9 32.8
15-24 6.3 7.2 13.1 17.5 18.3 35.6 33.8 4.9 6.9 12.7 11.6 12.9 22.9 24.9
≥ 65 34.5 46.3 47.5 59.6 58.1 65.1 63.0 36.6 47.3 57.0 65.2 64.3 70.8 68.0
55-64 27.8 39.2 44.6 52.9 58.1 68.3 61.0 40.3 31.8 52.1 58.9 57.2 63.5 63.8
45-54 29.9 30.3 38.3 44.4 50.3 59.7 53.9 33.1 47.4 45.9 38.1 53.2 58.1 53.4
35-44 20.7 19.3 30.3 37.0 44.9 54.8 56.3 20.3 44.3 32.5 43.1 52.5 53.3 44.0
25-34 14.2 15.4 23.3 35.0 40.5 54.3 47.6 16.7 21.2 28.1 29.4 40.7 39.1 40.2
15-24 9.1 11.7 14.8 19.0 22.8 48.3 28.9 11.4 14.6 20.8 30.3 27.5 21.9 14.8
60 40 20

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The ~~co-morbidity of uncontrolled diabetes and hypertension~~prevalence of concurrently raised blood glucose and blood pressure in India: a cross-sectional ~~nationally representative~~ study of 2,035,662~~two million~~ adults

Short title: Blood glucose and pressure in India~~Co-morbid diabetes&hypertension in India~~

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Abstract

Objective:

In order to inform integrated, person-centered interventions, this study aimed to determine the prevalence of ~~co-morbid uncontrolled diabetes and hypertension~~having both a raised blood glucose (BG) and blood pressure (BP) in India, and its variation among states and population groups.

Methods:

We pooled data from three large household surveys (the AHS, DLHS-4, and NFHS-4), which were carried out between 2012 and 2016 and included adults aged ≥15 years. ~~Uncontrolled diabetes~~Raised BG was defined as having a ~~high~~ plasma glucose reading ~~(~~≥126 mg/dl if fasted and~~, or~~ ≥200 mg/dl if not fasted~~)~~, and ~~uncontrolled hypertension~~raised BP as a systolic ~~blood pressure (~~BP~~)~~ ≥140 mmHg or diastolic BP ≥90 mmHg. The prevalence of having a ~~both uncontrolled diabetes and hypertension~~ concurrently raised BG and BP (‘co-morbid’) was age-standardized to India’s national population structure, and disaggregated by sex, age group, BMI group, rural-urban residency, household wealth quintile, education, ~~and~~ state, and region.

Results:

The age-standardized prevalence of the co-morbidity was 1.5% (95% CI, 1.5-1.5), varying by a factor of 8.3 between states. Among those aged ≥50 years, 4.5% (95% CI, 4.3-4.7) with a BMI<23.0kg/m^2 and 16.1% (95% CI, 15.0-17.4) with a BMI ≥30kg/m^2 were co-morbid. Age, BMI, household wealth quintile, male sex, and urban location were all positively associated with the co-morbidity.

Conclusions:

A substantial proportion of India’s population had~~s~~ ~~concurrent~~both a raised BG and BP ~~uncontrolled diabetes and hypertension~~, calling for integrated interventions to reduce CVD risk.

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~~While the co-morbidity's high prevalence among those with a BMI<23.0kg/m^2 limits the usefulness of BMI in targeting screening efforts,~~ W~~w~~e identified large variation among states, age groups, and by rural-urban residency, which can inform health system planning and the targeting of interventions, such as appropriate screening programs, to those most in need.

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Condensed a~~A~~bstract

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~~Until today, there have been no large-scale population-based studies from India on the degree to which diabetes and hypertension overlap, and how the prevalence of this co-morbidity varies with BMI and among different socio-demographic groups.~~ This ~~large~~ nationally representative study from India ~~-~~found that the prevalence of having both a raised blood glucose and blood pressure ~~co-morbid uncontrolled diabetes and hypertension in India~~ was ~~is~~ high in~~, particularly in~~ older age groups, even among those with a normal Body Mass Index (BMI). ~~Among these older age groups, there is a high prevalence of this co-morbidity among those with a low or normal BMI, which limits the usefulness of BMI for risk stratification.~~ We identified ~~a large degree of~~wide variation ~~among states, age groups, and rural-urban location~~in the prevalence of this co-morbidity among states. Those with a higher age, BMI, and household wealth, as well men and those in urban areas had a higher probability of having the co-morbidity. The findings of this study highlight the need for integrated cardiovascular disease interventions and can inform the targeting of such interventions to those most in need.~~, which can be used to inform health system planning and the targeting of relevant interventions.~~

Keywords:

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cardiovascular disease, co-morbidity, diabetes, hypertension, blood pressure, blood glucose, India~~, multimorbidity~~

Introduction

The cardiovascular disease (CVD) burden in low and middle-income countries (LMICs) is increasing.(1) In India, CVD accounted for 14.1% of the country's total disability-adjusted life years (DALYs) in 2016, up from 6.9% in 1990.[2] ~~Diabetes and hypertension~~Raised blood glucose (BG) and blood pressure (BP) are both important – yet ~~imminently~~ treatable ~~–~~ – risk factors for CVD.[1, 4] While we know that the prevalence of ~~uncontrolled diabetes and hypertension~~raised BG and BP among adults in India is high at 7.5% and 25.3%, respectively,[5] little is known about the degree to which these conditions overlap, and how this co-morbidity is related to other CVD risk factors ~~–~~, such as obesity ~~–~~, and socio-demographic characteristics.

This knowledge of ~~co-morbid uncontrolled diabetes and hypertension~~concurrently raised BG and BP, however, is essential to build an effective public health and health services response to the rise of CVD in India. A key characteristic of the country's healthcare system is the prominent role of private providers, which account for a much larger proportion of healthcare provision (~~58-79~~more than 70% of illness episodes and 58-79% of healthcare visits~~%~~) ~~of healthcare visits~~ in India than in most other LMICs.[6][ref] This is one reason for the high out-of-pocket healthcare expenditures incurred by India's population,[7] particularly for non-communicable disease (NCD) care.[8] It is common for these fee-paying patients, especially in urban areas, to seek out specialists for their care based on the type of condition from which they perceive to suffer~~.~~,[9] which contributes to the fragmentation of India's health system. ~~As such, specialist diabetes care clinics – and thus siloed rather than integrated primary care – are common in India.[10]~~ Studying the degree to which CVD risk factors in India co-occur ~~– particularly if focusing on the co-morbidity of *uncontrolled* CVD risk factors as these depict unmet need for care –~~ may not only inform the integration of healthcare services for NCD care ~~services~~, but

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could also ~~provide~~ create a sense of urgency, and thus an impetus for policy, to rapidly move towards more integrated, person-centered primary healthcare for NCDs in which only those with complicated cases of a condition are cared for by specialists.

Thus far, evidence on the co-morbidity of ~~diabetes and hypertension~~ raised BG and BP in India has been largely restricted to relatively small cohorts or healthcare facility-based studies in specific states. To our knowledge, this is the first study to use nationally representative data to examine this co-morbidity of two major CVD risk factors. Specifically, analyzing data from two million adults, this study aims to determine the prevalence of ~~co-morbid uncontrolled diabetes and hypertension~~concurrently raised BG and BP in India, and how the prevalence of this co-morbidity varies by BMI, state, region, rural versus urban residence, and individual-level socio-demographic characteristics.

Methods

Data sources:

We pooled data from three large population-based household surveys in India: the second update of the Annual Health Survey (AHS), the fourth round of the District-Level-Household Survey (DLHS-4), and the fourth National Family Health Survey (NFHS-4). The NFHS-4, conducted from 2015-2016, is the most recent of these three surveys, and the only one that covered all states and Union Territories. However, it only included men aged 15-54 and women aged 15-49 years. The AHS and DLHS-4, on the other hand, included adults aged ≥18 years. These two surveys were carried out simultaneously between 2012 and 2014 using a similar questionnaire, and jointly covered 34 of 36 states (all except for Jammu and Kashmir, and Gujarat) and five of seven Union Territories (all except for Dadra and Nagar Haveli, and Lakshadweep). No areas in

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India were covered by both the AHS and the DLHS-4. We thus pooled the AHS and DLHS-4 data with the NFHS-4 data to obtain a dataset that is representative for all adults in India aged 15 years and older, and that covered all states and Union Territories in the country. The only population groups not represented in this dataset ~~for whom this pooled dataset is not representative~~ are women ≥50 years and men ≥54 years in two of 36 states (Jammu and Kashmir, and Gujarat) and two of seven Union Territories (Dadra and Nagar Haveli, and Lakshadweep). ~~Union Territories are henceforth also referred to as 'states'.~~

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All three surveys covered all districts in the states covered by the survey and used two-stage cluster random sampling, stratified by rural versus urban areas, within each district. Primary sampling units (PSU) were defined as villages in rural areas, and census enumeration blocks (AHS, NFHS-4) or urban frame survey blocks (DLHS-4) in urban areas. Secondary sampling units (SSU) were households. PSUs were selected using random sampling with equal weighting (DLHS-4) or probability proportional to population size (AHS, NFHS-4). SSUs were selected through systematic random sampling.

In the AHS and DLHS-4, interviewers administered a questionnaire to the household head on socio-demographic information of all household members (regardless of whether the household members were present at the interviewer's visit). Except in the AHS – where these physical measurements were only administered in a sub-sample of, on average, 12 PSUs per district - all non-pregnant household members aged ≥18 years then underwent a height, weight, ~~blood glucose~~BG, and ~~blood pressure (BP~~BP~~)~~ measurement. Households were not revisited in cases where an eligible adult was ~~not present~~absent at the time of the interviewer's visit. The AHS

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participants' socio-demographic information was merged with the participants' ~~blood glucose~~BG and BP data as described in the appendix (see Methods S1, Supplemental Digital Content~~pp 2-7~~). In the NFHS-4, the household head questionnaire was used to identify eligible women and men for an additional women's / men's questionnaire. The interviewers then administered the women's questionnaire as well as weight, height, ~~blood glucose~~BG, and BP measurements to all women aged 15-49 who resided in the household. The questionnaire and physical measurements for men aged 15-54 years (height, weight, ~~blood glucose~~BG, and BP measurements) were only administered in a random subsample of 15 percent of households (every alternate household in 30 percent of the selected PSUs). The sections of the questionnaire used to derive the ~~predictor~~ variables for ~~in~~ this ~~study~~ analysis were identical between the women's and men's questionnaire. Households in the NFHS-4 were revisited at least two times (on separate times of the day) if not all eligible household members were present at the time of the interviewer's visit. No revisits were conducted in the AHS and DLHS-4.

~~Blood glucose~~BG was measured once using a capillary blood sample (finger prick) and a hand-held blood glucometer (SD CodeFree (SD Biosensor) in the AHS and DLHS-4; FreeStyle Optium H (Abbott) in the NFHS-4). The capillary measurements were then multiplied by 1.11 to display the plasma equivalent.[11] Participants of the AHS and DLHS-4 were instructed to fast overnight until the blood glucose was measured in the morning. In the DLHS-4, fasting status was assessed through self-report (58.4% reported to have fasted), while fasting status was not recorded in the AHS. The prevalence and regression analyses in this paper assume that all AHS participants were fasted. However, in the appendix, we present prevalence estimates assuming all AHS participants were non-fasted, as well as regression results for DLHS-4 and NFHS-4

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participants only (see Table S8/Table S10/Table S14, Supplemental Digital Content~~pp 18-20 and 26f~~). In the NFHS-4, blood glucose was measured at a random time point (without instruction to fast prior to the measurement), and participants were asked about the time of last food and drink intake. We defined f~~F~~asting status ~~was defined~~ as the last food or drink intake (except plain water) being at least~~≥ 8~~eight hours ~~ago~~prior to the blood glucose measurement.

In the AHS and DLHS-4, BP was measured twice using an electronic upper arm monitor (Rossmax AW150 (Rossmax Swiss GmbH)) in the left upper arm with an interval of at least three minutes in between measurements. In the NFHS-4, BP was measured three times (using the Omron HEM-8712 (Omron Corporation)) in the left upper arm with at least five minutes between each measurement as well as five minutes of quiet sitting prior to the first measurement.

Weight was measured using a digital scale, and height using a Seca 213 stadiometer (NFHS-4) or wall~~-~~-mounted statute meter (AHS/DLHS-4).

~~Due to data limitations, we cannot provide data on the diagnosis of diabetes and hypertension, however we provide these analyses for the NFHS-4 in the appendix. In addition to the biodata based definitions, hypertension and diabetes status was further investigated with the questions:" Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?", "To lower your blood pressure, are you now taking a prescribed medicine " and " Do you currently have diabetes?".~~

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Outcome variables

The main outcome variables of this analysis were i) ~~co-morbid diabetes and hypertension~~concurrently raised BG and BP ~~(having both diabetes and hypertension among all participants)~~, ii) ~~hypertension~~ raised BP conditional on having ~~diabetes~~ a raised BG (i.e., having ~~both hypertension~~ a raised BP ~~and diabetes~~ among only those with ~~diabetes~~a raised BG), and iii) ~~diabetes~~ raised BG conditional on having ~~hypertension~~ a raised BP (i.e., having ~~both diabetes~~ a raised BG ~~and hypertension~~ among only those with ~~hypertension~~a raised BP). We defined ~~diabetes~~ raised BG as having a high plasma glucose reading (≥126 mg/dl if an AHS participant or reporting to be fasted, or ≥200 mg/dl if reporting to be non-fasted [12]). ~~Hypertension~~ Raised BP was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg based on the mean of the two (or, in the case of the NFHS-4, three) BP measurements taken~~with systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg being considered hypertension~~.[13]

~~The terms 'diabetes' and 'hypertension' in this analysis refer to *uncontrolled* diabetes and hypertension because participants who were diagnosed with the condition in the past, but successfully controlled their blood glucose or BP (through lifestyle modification or medication), are not classified as having the condition in this study.~~

In contrast to the DLHS-4 and AHS, the NFHS-4 asked participants about a previous diagnosis of, and treatment for diabetes and hypertension. Specifically, the relevant questions in the NFHS-4 were "Do you currently have diabetes?", "Have you sought treatment for this issue [diabetes]?" (this question was only asked to those who responded with "yes" to currently having diabetes), "Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?", and "To lower your blood pressure, are you now taking a prescribed medicine". In the appendix, we show the results of all analyses when

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restricting the sample to the NFHS-4 and defining raised BG as a high BG measurement (as above) or reporting to currently have diabetes, and raised BP as a high BP measurement (as above) or reporting to have been told to have hypertension or to be a taking BP-lowering medication.

~~Due to data limitations, we cannot provide data on the diagnosis of diabetes and hypertension, however we provide these analyses for the NFHS-4 in the appendix. In addition to the biodata based definitions, hypertension and diabetes status was further investigated with the questions:" Were you told on two or more different occasions by a doctor or other health professional that you had hypertension or high blood pressure?", "To lower your blood pressure, are you now taking a prescribed medicine " and " Do you currently have diabetes?".~~

Predictor variables:

Predictor variables of interest were state, region, sex, age, BMI, household wealth quintile, education, marital status, and rural versus urban residency. Given that the ~~WHO~~ World Health Organization considers the BMI cut-offs of ≥23.0 kg/m^2 and ≥27.5kg/m^2 to be additional thresholds (to the traditional ≥25.0 kg/m^2 and ≥30.0 kg/m^2 cut-offs for overweight and obesity) of public health significance in South Asian populations,[14-16] we classified BMI into the following categories: <18.5kg/m^2, 18.5-19.9 kg/m^2, 20.0~~18.5~~-22.9 kg/m^2, 23.0-24.9 kg/m^2, 25.0-27.4 kg/m^2, 27.5-29.9 kg/m^2, ≥30.0 kg/m^2.

Household wealth quintile was based on a household wealth index, which was computed separately for rural and urban areas using a principal component analysis as per the methodology developed by Filmer and Pritchett. [17, 18] The index was then categorized into quintiles, again separately for rural and urban areas. A more detailed description of the computation of the household wealth quintiles can be found in the appendix (see Methods S2, Supplemental Digital Content~~p.8~~).

Statistical analysis:

The prevalence of each outcome variable was disaggregated by age, sex, BMI, ~~sex,~~ state, household wealth quintile, education, and rural-urban residency. All prevalence estimates account for the complex survey design (and pooling of the surveys) using sampling weights. These weights also account for the lower sampling probability of men in the NFHS-4 by assigning a higher weight to men than women in this survey. Prevalence estimates were age-standardized using the age distribution of the 2015 Global Burden of Disease population estimates for India. [19] Age-standardization was done for India as a whole (not separately for each state). To further investigate the association of each outcome variable with individual-level socio-demographic characteristics, we ran linear probability models separately for rural and urban locations with age, BMI, sex, household wealth quintile, education, and marital status as explanatory variables. To filter out area-level effects on the outcomes, these models also included a fixed effect (i.e., a binary indicator variable) for each PSU, which was the lowest identifiable geographic unit in the data. Standard errors were adjusted for clustering at the PSU level. The regression coefficients of these models can be interpreted as the absolute differences in the probability of the outcome (expressed in percentage points). We chose to use a linear probability model rather than a logistic model to avoid the incidental parameter problem.[20] All analyses presented in this manuscript are complete case analyses. R version 3.4.2 was used for statistical analyses,[21] and figures were created with the ggplot2 package.[22]

Ethical~~s~~ approval:

This analysis of de-identified data in the public domain received a determination of "not human subjects research" by the institutional review board (IRB) of the Harvard T.~~-~~H. Chan School of Public Health on 9 May 2018. The AHS and DLHS-4 obtained ethical clearance by the IRB of the National Institute of Health & Family Welfare and the International Institute for Population Sciences. As part of the Demographic and Health Survey series, the NFHS-4 was reviewed and approved by the ICF IRB.

~~AHS/DLHS4: A centralized ethical clearance was provided by NIHFW/IIPS. Dr. Shiv Lal took responsibility for the adherence to proper ethical guidelines for the implementation of the CAB tests (AHS).~~

~~NFHS4: DHS surveys have been reviewed and approved by ICF Institutional Review Board (IRB), which also guarantees that the survey complies with the U.S. Department of Health and Human Services regulations for the protection of human subjects (45 CFR 46). The Indian IRB guarantees that the NFHS4 survey adheres to the Indian laws and norms.~~

Data availability:

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The datasets supporting the conclusions of this article are publically available via https://www.dhsprogram.com/Data/, https://nrhm-mis.nic.in/hmisreports/AHSReports.aspx, and http://www.iipsindia.ac.in. The merged dataset and statistical code will be made available on the Harvard Dataverse once the manuscript is accepted for publication.

Results

Sample ~~C~~characteristics:

2,035,662 (87.7%) of all 2,320,551 participants had non-missing measurements of B~~P~~G and ~~blood glucose~~BP. Table 1 shows the unweighted (age-unstandardized) sample characteristics. 22.1% had ~~hypertension~~a raised BP, 6.4% had ~~diabetes~~a raised BG, and 4.3% had a BMI≥30.0 kg/m^2. 46.6% of participants were aged between 15 and 34 years, whereby men were on average older than women because a higher share of women were participants of the NFHS-4, which sampled only those aged 15 to 49 years.~~.~~ 63.7% of participants were women, and more than a third (30.5%) had no formal education. Approximately two thirds (68.8%) of participants lived in a rural area. The sample characteristics of those with a missing ~~blood glucose~~BG or BP ~~were similar to the characteristics of those who were included in the analysis~~are shown in the appendix (see Table S1, Supplemental Digital Content~~appendix pp. 9-10~~)~~, except that the former were more likely to be male, less likely to have a BMI<18.5kg/m^2, and more likely to have a BMI between 23.0 and 24.9kg/m^2~~.

National prevalence of ~~comorbid diabetes and hypertension~~concurrently raised blood glucose and blood pressure:

The (age-standardized) prevalence of ~~co-morbid diabetes and hypertension~~having both a raised BG and BP was 1.5% (95% CI, 1.5 - 1.5%) among ~~Indian~~ non-pregnant adults. The prevalence of this co-morbidity was higher in older age groups (Table 2). Those aged ≥50 years had a prevalence of 7.9% (95% CI, 7.6-8.1) and 6.1% (95% CI, 5.8-6.3%) among women and men, respectively. While there was a higher overall prevalence among men (1.6% [95% CI, 1.6 - 1.7%]) than women (1.3% [95% CI, 1.3 - 1.4%]), women had a higher prevalence in the age groups 55-64 and ≥65 years. The prevalence of ~~co-morbid diabetes and hypertension~~having both

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a raised BG and BP was greater in higher BMI groups. Among those who were normal weight ($18.5kg/m^2 \leq BMI < 23.0kg/m^2$), the prevalence of ~~co-morbid diabetes and hypertension~~this co-morbidity was 0.8% (95% CI, 0.8-0.8%) and 1.0% (95% CI, 1.0-1.1%) in women and men, respectively. 9.6% (95% CI, 9.4 - 9.9%) of ~~hypertensive~~ participants with a raised BP and 36.7% (95% CI, 36.0 - 37.5%) of ~~diabetic participants~~participants with a raised BG were co-morbid. Figure 1 depicts the weighted and age-standardized prevalence of raised BG and BP~~diabetes and hypertension co-morbidity~~ in a Venn diagram. The prevalence of raised BG and BP in the NFHS-4 when also using diabetes and hypertension diagnosis and treatment in the definition of raised BG and BP is shown in Table S14 and Figure S6~~Table S13 and Figure S7~~.

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State-level prevalence of ~~co-morbid diabetes and hypertension~~concurrently raised blood glucose and blood pressure:

The age-standardized prevalence of ~~co-morbid diabetes and hypertension~~concurrently raised BG and BP by state ranged from 0.6% (95% CI, 0.4%-0.8%) in Jammu and Kashmir to 3.3% (95% CI, 2.3% - 4.6%) in Daman and Diu (Figure 2). Except for Daman and Diu, the West Indian state of Goa (3.2% [95% CI,2.5-4.1]) and the Northern Union Territory of Chandigarh (3.0% [95% CI, 2.2%-4.3%]), the highest prevalence tended to be in South India, especially in Kerala (3.0% [95% CI, 2.7-3.4]), Andaman and Nicobar (2.9 % [95% CI, 2.2-3.6]), Puducherry (2.8% [95% CI, 2.2-3.5]) and Tamil Nadu (2.6% [95% CI, 2.5-2.8]). This pattern remained similar when adjusting for differences in the age, sex, BMI, education, and household wealth quintile distribution between states (Table S6 and Figure S5~~Table S6 and Figure Sx~~).

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The prevalence of having ~~diabetes~~ a raised BG conditional on having ~~hypertension~~ a raised BP ranged from 4.5% (95% CI, 3.3-6.1) in Jammu and Kashmir to 19.6% (95% CI, 15.3-24.8) in Goa, and was again particularly high in South India (especially Kerala at 15.8% [95% CI,14.3-17.4] and Lakshadweep at 16.7% [95% CI, 9.9-26.8]) and in Goa (19.6% [95% CI, 15.3-24.8]). The prevalence of ~~hypertension~~ raised BP conditional on having ~~diabetes~~ a raised BG varied from 26.0% (95% CI, 20.9-31.8-34.43) in Odisha to 51.4% (95% CI, 44.3-58.4) in Himachal Pradesh, and was generally highest in North India - particularly in Punjab (51.2% [95% CI, 48.7-53.8]) and Chandigarh (48.7% [95% CI, 38.4-59.1]) - and in the Northeastern states of Sikkim (50.6% [95% CI, 44.9 -56.4]) and Nagaland (50.4% [95% CI, 44.9-56.4]). Detailed age-standardized prevalence estimates by state, sex, and rural versus urban location are shown in the appendix (see Table S2-S4, Supplemental Digital Content~~pp 11-15~~).

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Prevalence ~~of co-morbid diabetes and hypertension~~ by individual-level characteristics:

The prevalence of each outcome variable tended to be higher in older age groups, richer household wealth quintiles, and in urban areas (Figure 3). The relative differences between household wealth quintiles were higher in rural than in urban areas for all three outcome variables. Stratifying by BMI group shows that the prevalence of all three outcome variables is strongly positively associated with increasing BMI in both rural and urban areas~~,~~ and in all age groups (Figure 4). However, in older age groups, there was a substantial prevalence of ~~co-morbid diabetes and hypertension~~concurrently raised BG and BP even among those with a low or normal BMI. For instance, those aged ≥50 years with a BMI <23.0kg/m^2 had a prevalence of 4.5% (95% CI, 4.3-4.7).

In ~~multivariable~~ regressions with PSU-level fixed effects, age and BMI group were both strong predictors ~~group was the strongest predictor~~ of ~~co-morbid diabetes and hypertension~~having both a raised BG and BP (Table 3). ~~The second strongest predictor was BMI group with those with a BMI ≥30.0kg/m² having, compared to those with a BMI <18.5kg/m², a 6.31 (6.01 to 6.615.87 to 6.46) percentage point higher probability of co-morbid diabetes and hypertension in urban areas and 5.4332 (5.15 to 5.725.04 to 5.60) percentage points in rural areas.~~ Household wealth quintile was also positively associated with the co-morbidity, although the association was small in magnitude (less than 0.8~~6~~ percentage points in both rural and urban areas in the ~~multivariable~~ fully adjusted ~~regressions~~model). Similarly, being a man was associated with the co-morbidity but the coefficients were small (0.49 [95% CI, 0.36 to 0.61] and 0.12 [95% CI, 0.05 to 0.19]). There was no clear trend in the association of the co-morbidity with education. The regression results for ~~diabetes~~ raised BG conditional on having ~~hypertension~~a raised BP, and ~~hypertension~~ raised BP conditional on having ~~diabetes~~ a raised BG (see Table S5, Supplemental Digital Content ~~appendix (pp. 16-17))~~ show similar trends, except that household wealth quintile was not significantly associated with ~~hypertension~~ a raised BP conditional on having a ~~diabetes~~raised BG.

Discussion

This ~~first~~ nationally representative study ~~of co-morbid diabetes and hypertension in India~~ found that ~~in~~ 1.5% (95% CI, 1.5-1.5%) of adults in India had both a high ~~conditions were uncontrolled~~BG and BP. This overall prevalence estimate was weighted to the population

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structure of India, in which 26.7% of those aged 15 years and older are younger than 30 years.[23] The overall relatively low prevalence estimate thus obscures a high prevalence of this co-morbidity among older adults in India. For instance, among those aged ≥50 years, the prevalence of having a ~~co-morbid uncontrolled diabetes and hypertension~~concurrently raised BG and BP was 6.8.% (95% CI, 6.6-7.0), and increased to 9.0% (95% CI, 8.8-9.3) among those ≥65 years. Similarly, we found a high prevalence of ~~uncontrolled diabetes~~raised BG among those with ~~uncontrolled hypertension~~raised BP (9.6% [95% CI, 9.4-9.9] overall, and 18.1% [95% CI,17.6-18.6] in those ≥50 years), and an even higher prevalence of ~~uncontrolled hypertension~~raised BP among those with raised BG~~uncontrolled diabetes~~ (36.7% [95% CI, 36.0-37.5] overall, and 49.8% [95% CI, 48.8-50.8] in those ≥50 years). Apart from highlighting a large unmet need for CVD care in India, these co-morbidity estimates clearly show the urgency of transitioning the Indian health system ~~moving~~ towards more integrated primary healthcare for effectively managing CVD and CVD risk factors. ~~CVD risk factors in India~~.

A second key finding of this study is that in ~~these~~ older age groups, ~~co-morbid uncontrolled diabetes and hypertension~~having both a high BG and BP measurement was also common ~~even~~ among those with a low or normal BMI (e.g., 4.5% among those aged ≥50 years and with a BMI≤23.0kg/m^2). In fact, our regression results show that a higher BMI category was associated with a higher probability of having a concurrently raised BG and BP even within the normal and low BMI range. This finding – combined with the fact that only 6.3% of adults in India (according to our sample) had a BMI ≥27.5kg/m^2 and 2.8% had a BMI ≥30.0kg/m^2 ~~–~~– implies that screening for diabetes and hypertension based on BMI will likely miss many individuals with these conditions. Nonetheless, BMI likely is useful as one criterion for risk stratification in

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the targeting of relevant programs for diabetes and hypertension in India to those most in need. Other variables that our analysis identified as being predictive of a concurrently raised BG and BP – and thus as potentially useful for the targeting of diabetes and hypertension interventions – ~~calls into question the usefulness of BMI in stratifying risk for diabetes and hypertension (e.g., to guide the targeting of screening programs) among older Indian adults. However, we did identify important variation among population groups in India, which can be used to inform the targeting of relevant interventions. Specifically, other than the strong association with~~ were ~~age group~~older age, ~~urban areas~~living in an urban area, and state, ~~those living in certain states had a substantially higher prevalence of the co-morbidity. In fact,~~with the prevalence of ~~co-morbid uncontrolled diabetes and hypertension~~ having both a raised BG and BP varyin~~gied~~ by a factor of 8.3 between states~~,~~ and ~~was~~ being particularly high in South India and in Goa.

To date, s~~S~~tudies on co-morbid diabetes and hypertension in India have been ~~so far~~largely ~~been~~ restricted to smaller community-based cohorts or healthcare facility-based samples in specific states. To our knowledge, the only published multi-state population-based assessment of diabetes and hypertension co-morbidity in India is the first phase of the ICMR-INDIAB study (carried out between 2008 and 2010), which was conducted among 14,059 adults in three of 29 states and one of seven Union Territories in India.[24] The only co-morbidity reported in this study was the prevalence of diabetes among hypertensive adults. ~~Our state-level estimates for this outcome are not directly comparable to those of ICMR-INDIAB because we defined diabetes and hypertension based only on blood glucose and BP measurements, while ICMR-INDIAB also considered those who self-reported the diagnosis or treatment for the condition as being diabetic/hypertensive.~~ ICMR-INDIAB reported a prevalence of diabetes conditional on having

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hypertension of 17.5% in Tamil Nadu, 14.3% in Maharashtra, 13.3% in Jharkhand, and 20.7% in Chandigarh. The corresponding results in our study were 15.7% (95% CI, 14.7-16.6) in Tamil Nadu, 6.2% (95% CI, 5.6-6.9) in Maharashtra, 5.2% (95% CI, 3.9-6.9) in Jharkhand, and 12.2% (9.2 - 16.0) in Chandigarh. The likely reason for which our state-level estimates for this outcome were generally lower than those by ICMR-INDIAB is that we used only BG and BP measurements, while ICMR-INDIAB also used data on a self-reported diagnosis of, or current treatment for diabetes and hypertension. ~~Except for Tamil Nadu, the most likely reason for our estimates being lower than those by ICMR-INDIAB is that we only examined uncontrolled diabetes and hypertension.~~ Punjab had a relatively large (2,499 fasted adults) assessment of diabetes and hypertension co-morbidity in 2014-2015,[25] which reported a prevalence of 4.5% for the co-existence of both diseases compared to 1.8% (95% CI, 1.7-2.0) in this study. Again, the somewhat lower prevalence in our study may be explained by our narrower definition of diabetes and hypertension.

This study has several limitations. First, 12.3% of adults in this population-based survey had a missing value for the ~~blood glucose~~BG or BP measurement. ~~While we cannot exclude the possibility that those with a missing measurement were systematically different compared to those included in the analysis, the sample characteristics between the two groups (missing and non-missing) were similar.~~ Second, our diabetes definition based on a one-time capillary ~~blood glucose~~BG measurement, especially if non-fasted, is not recommended for a clinical diagnosis of diabetes.[26] We thus chose to refer to this variable as ‘raised BG’ rather than ‘diabetes’. Third, our definition of raised BP was based on a one-off (rather than on two occasions) measurement of BP whereby BP was measured only twice (rather than three times) in the AHS and DLHS-4. ~~Nonetheless, this definition is a standard in population-based surveys, including the WHO~~

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~~STEPwise Approach to NCD Risk Factor Surveillance.[27-28]~~ Third, the AHS did not verify fasting status before the ~~blood glucose~~BG measurement. In addition to having led to a higher overall prevalence of ~~co-morbid uncontrolled diabetes and hypertension~~having both a high BG and BP, assuming all participants were fasted at the time of measurement may in particular have led us to overestimate prevalence among poorer participants, because the AHS focusses on India's poorest states. We therefore also provide prevalence estimates assuming all AHS participants were non-fasted and regression results among participants for whom fasting status was verified by self-report (i.e., DLHS-4 and NFHS-4 only) in the appendix. ~~Fourthly, this study could not distinguish between type 1 and type 2 diabetes. Yet, the International Diabetes Federation estimates that merely 0.02% of the country's population aged zero to 14 years had type 1 diabetes in 2015.[29,30] Extrapolating this percentage to adults would suggest that our sample likely contains only a very small proportion of adults with type 1 diabetes.~~ Finally, we were only able to evaluate the co-morbidities between ~~hypertension, diabetes~~raised BG, raised BP, and obesity, but it is likely that other co-morbidities are common in this population, such as depression and dyslipidemia. Unfortunately, these chronic conditions were not assessed in these surveys. As the Indian population continues to age,[ref] the prevalence of chronic disease multimorbidity will likely increase. However, evidence from population-based studies on the patterns of multimorbidity in India is sparse.[ref] ~~{Pati, 2015 #3687}~~We would, therefore, encourage policy makers and researchers to increase the array of chronic conditions that are assessed in future waves of the NFHS and similar surveys. This could, for instance, include chronic kidney disease, chronic obstructive pulmonary disease, asthma, mental health (e.g., depression and anxiety), and cognition.

Commented [GP3]: Please add the UN Population Revision 2017 here as reference

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Conclusion

We identified a substantial prevalence, especially among older age groups, of ~~concurrent uncontrolled diabetes and hypertensio~~having both a raised BG and BP ~~n~~ in India. Apart from highlighting a large ~~unmet~~ need for care for these conditions, this finding provides new evidence for public health interventions and health system design, and underscores the urgency for transitioning the Indian health system towards integrated primary healthcare for cardiometabolic disease and NCDs more generally. ~~underscores the urgency for India to move towards integrated primary healthcare for cardiometabolic disease and NCDs more generally.~~ Such integration of primary healthcare service delivery is particularly needed in urban areas and in South India, Goa, and Chandigarh, where the prevalence of this co-morbidity was the highest. Targeting diabetes and hypertension programs, such as screening activities, at those with a high BMI may be less effective in India than in many other populations given i) that we found the prevalence of ~~co-morbid uncontrolled diabetes and hypertension~~having both a raised BG and BP ~~to also be~~to be high among those with a low or normal BMI, and ii) the fact that only a minority of Indians are overweight or obese. More generally, with India accounting for over 20% of the population in LMICs, [23] this study ~~represents an important step in~~is an important contribution to addressing the dearth of national-level evidence on NCD co-morbidities in LMICs.

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Figure Legends

Figure 1. Venn diagram of ~~diabetes and hypertension co-morbidity~~raised blood glucose and blood pressure prevalence~~at the national level~~ for three 10-year age groups*, †

* Numbers account for sampling weights, including age-standardization to India's population structure.

† ~~Further~~ Venn diagrams ~~of diabetes and hypertension co-morbidity~~ for all 10-year age groups and for the total sample are shown in the appendix see Figure S1-4, Supplemental Digital Content~~(pp. 28-31~~).

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Figure 2. Age-standardized prevalence (in percent) of each outcome variable, by state

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Figure 3. Age-standardized prevalence (in percent) of each outcome variable by rural versus urban residence, sex, age group, and household wealth quintile

Commented [GP5]: Could you change the labelling to:
i) Concurrently raised BG and BP
ii) Raised BG conditional on having a raised BP
iii) Raised BP conditional on having a raised BG

Figure 4. Age-standardized prevalence (in percent) of each outcome variable by rural versus urban residence, sex, age group, and BMI group

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Commented [GP6]: Could you change the titles of the figures as for figure 3. In addition, the BMI group labelling seems to be out of whack – I think you forgot to adjust the labelling in your code to the new more finely-categorized BMI variable.

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Tables

*Table 1: Sample characteristics**

	Total (%)	Women (%)	Men (%)
n	2,035,662	1,297,084 (63.7)	738,578 (36.3)
~~Hypertension~~Raised blood pressure, n (%)	449,703 (22.1)	240,781 (18.6)	208,922 (28.3)
Mean systolic blood pressure, mmHg (SD)	125.7~~66~~ (20.2~~1~~)	124.3~~28~~ (21.1~~1~~)	127.1~~2~~ (19.1~~0~~)
Mean diastolic blood pressure, mmHg (SD)	80.3~~2~~ (12.9~~88~~)	79.4~~4~~ (13.0~~12.96~~)	81.2~~4~~ (12.7~~4~~)
~~Diabetes~~Raised blood glucose, n (%)	130,176 (6.4)	69,697 (5.4)	60,479 (8.2)
Mean blood glucose, mg/dl (SD)	114.8~~0~~ (33.3~~27~~)	114.8~~3~~ (33.2~~15~~)	114.8~~77~~ (33.5~~48~~)
BMI group, n (%)			
<18.5kg/m^2	398,658 (19.8)	268,822 (20.9)	129,836 (17.8)
18.5-19.9 kg/m^2	303,195 (15.1)	194,723 (15.1)	108,472 (14.9)
20.0-22.9 kg/m^2	642,570 (31.9)	396,046 (30.8)	246,524 (33.8)
23.0-24.9 kg/m^2	288,639 (14.3)	172,381 (13.4)	116,258 (16.0)
25.0-27.4 kg/m^2	197,210 (9.8)	124,698 (9.7)	72,512 (10.0)
27.5-29.9 kg/m^2	97,072 (4.8)	65,998 (5.1)	31,074 (4.3)
≥ 30.0 kg/m^2	86,420 (4.3)	62,694 (4.9)	23,726 (3.3)
Missing (%)	*1.1*	*0.9*	*1.4*

Commented [AB7]: New BMI category

Age (mean (SD))	37.7~~3~~ (15~~4~~.0~~98~~)	36.3~~28~~ (14.1~~4~~)	40.3~~28~~ (16.0~~3~~)
Age group (years), n (%)			
15-24	428,808 (21.1)	289,299 (22.3)	139,509 (18.9)
25-34	519,538 (25.5)	352,070 (27.1)	167,468 (22.7)
35-44	472,082 (23.2)	317,465 (24.5)	154,617 (20.9)
45-54	318,993 (15.7)	192,017 (14.8)	126,976 (17.2)
55-64	160,318 (7.9)	81,132 (6.3)	79,186 (10.7)
≥65	135,923 (6.7)	65,101 (5.0)	70,822 (9.6)
Missing (%)	*0*	*0*	*0*
Urban residency, n (%)	635,080 (31.2)	396,066 (30.5)	239,014 (32.4)
Missing (%)	*0*	*0*	*0*
Household wealth quintile, n (%)			
1	391,109 (19.8)	251,670 (19.9)	139,439 (19.6)
2	391,804 (19.8)	251,794 (19.9)	140,010 (19.7)
3	392,469 (19.9)	252,717 (20.0)	139,752 (19.7)
4	396,925 (20.1)	252,737 (20.0)	144,188 (20.3)
5	404,084 (20.4)	257,275 (20.3)	146,809 (20.7)
Missing (%)	*2.9*	*2.4*	*3.8*
Education, n (%)			
No formal education	619,506 (30.5)	469,436 (36.3)	150,070 (20.4)
< Primary School	131,945 (6.5)	80,248 (6.2)	51,697 (7.0)
Primary School	213,147 (10.5)	124,174 (9.6)	88,973 (12.1)
Middle School	497,734 (24.5)	339,349 (26.2)	158,385 (21.5)

Secondary School	243,616 (12.0)	128,079 (9.9)	115,537 (15.7)
>Secondary School	324,321 (16.0)	153,337 (11.8)	170,984 (23.2)
Missing (%)	*0.3*	*0.2*	*0.4*
Currently married, n (%)	1,514,172 (74.4)	980,686 (75.6)	533,486 (72.4)
Missing (%)	*0.1*	*0*	*0.2*

Abbreviations: n=number, %=percentage
* All numbers and percentages shown do not account for sampling weights (and are not age-~~un~~standardized)

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Table 2. National-level prevalence by age group, BMI group, and sex *, †

	~~Co-morbid diabetes and hypertension~~Concurrently raised blood glucose and blood pressure		~~Diabetes~~ Raised blood glucose conditional on having ~~hypertension~~a raised blood pressure		~~Hypertension~~ Raised blood pressure conditional on having ~~diabetes~~a raised blood glucose	
	Women Percent (95% CI)	**Men** Percent (95 % CI)	**Women** Percent (95% CI)	**Men** Percent (95 % CI)	**Women** Percent (95% CI)	**Men** Percent (95 % CI)
Age group (years)						
15-24	0.1 (0.1-0.1)	0.2 (0.2-0.2)	3.0 (2.6-3.4)	2.6 (2.3-3.1)	11.5 (10.1-13.0)	16.2 (14.0-18.6)
25-34	0.5 (0.5-0.5)	0.9 (0.8-1.0)	5.1 (4.8-5.4)	5.4 (4.9-5.9)	20.3 (19.2-21.5)	30.3 (28.1-32.6)
35-44	1.6 (1.6-1.7)	2.4 (2.3-2.6)	8.8 (8.5-9.2)	9.9 (9.2-10.7)	32.9 (31.8-33.9)	39.5 (37.1-41.9)
45-54	4.0 (3.8-4.1)	4.2 (3.9-4.5)	14.1 (13.7-14.6)	13.9 (13.1-14.8)	43.1 (41.9-44.2)	44.8 (42.7-46.9)
55-64	8.3 (8.0-8.6)	7.8 (7.5-8.1)	20.3 (19.7-21.0)	19.6 (18.9-20.3)	53.9 (52.7-55.1)	49.4 (47.8-51.1)
≥65	9.4 (9.1-9.8)	8.6 (8.3-9.0)	19.3 (18.7-20.0)	19.8 (19.1-20.5)	57.9 (56.5-59.2)	51.7 (50.3-53.2)
BMI group						

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<18.5kg/m^2	0.4 (0.4 to 0.4)	0.5 (0.5 to 0.6)	5.6 (5.2 to 5.9)	6.1 (5.5 to 6.8)	18.4 (17.2 to 19.5)	21.2 (19.3 to 23.3)
18.5-19.9 kg/m^2	0.5 (0.5 to 0.5)	0.7 (0.6 to 0.8)	6.0 (5.5 to 6.4)	6.2 (5.5 to 6.9)	22.3 (20.8 to 23.8)	26.4 (23.8 to 29.2)
20.0-22.9 kg/m^2	1.0 (0.9 to 1.0)	1.2 (1.1 to 1.3)	8.0 (7.7 to 8.4)	7.4 (6.9 to 7.9)	30.9 (29.7 to 32.0)	33.3 (31.5 to 35.3)
23.0-24.9 kg/m^2	1.7 (1.6 to 1.8)	2.0 (1.9 to 2.2)	10.1 (9.6 to 10.6)	8.9 (8.3 to 9.6)	37.5 (36.0 to 39.0)	40.1 (37.7 to 42.4)
25.0-27.4 kg/m^2	2.6 (2.4 to 2.7)	3.4 (3.1 to 3.7)	11.9 (11.4 to 12.5)	11.6 (10.7 to 12.6)	40.9 (39.4 to 42.4)	48.5 (45.6 to 51.4)
27.5-29.9 kg/m^2	3.7 (3.5 to 4.0)	5.3 (4.8 to 5.9)	14.7 (13.9 to 15.5)	14.7 (13.3 to 16.3)	45.9 (44.1 to 47.8)	54.3 (50.2 to 58.3)
≥30.0 kg/m^2	5.2 (5.0 to 5.4)	6.7 (5.9 to 7.5)	17.3 (16.6 to 18.0)	17.1 (15.2 to 19.1)	46.8 (45.1 to 48.6)	49.3 (43.9 to 54.8)
Total	1.3 (1.3-1.4)	1.6 (1.6-1.7)	10.0 (9.8-10.2)	9.4 (9.0-9.7)	34.6 (34.0-35.2)	38.4 (37.2-39.6)

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* These prevalence estimates assume all AHS participants were fasted at the time of the blood glucose measurement. In the appendix (see Table S8, Supplemental Digital Content ~~p. 18~~), we show the corresponding prevalences assuming all AHS participants were non-fasted.
† All prevalence estimates are weighted (using sampling weights) and age-standardized to India's population structure.

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Table 3. ~~Uni- and multivariable~~Partially and fully adjusted linear regressions of having both a ~~co-morbid diabetes and hypertension~~raised blood glucose and blood pressure on socio-demographic characteristics, †, ‡*

	~~**Univariable**~~**Partially adjusted**				~~**Multivariable**~~**Fully adjusted**			
	Urban		***Rural***		***Urban***		***Rural***	
	Diff. in probability (95% CI)	*P*	*Diff. in probability (95% CI)*	*P*	*Diff. in probability (95% CI)*	*P*	*Diff. in probability (95% CI)*	*P*
Men	0.36 (0.24 to 0.48)	<0.001	0.19 (0.12 to 0.25)	<0.001	0.49 (0.36 to 0.61)	<0.001	0.12 (0.05 to 0.19)	<0.001
BMI group								
<18.5 kg/m^2	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
18.5-19.9 kg/m^2	0.43 (0.30 to 0.56)	<0.001	0.36 (0.30 to 0.42)	<0.001	0.40 (0.26 to 0.53)	<0.001	0.33 (0.27 to 0.39)	<0.001
20.0-22.9 kg/m^2	1.12 (1.00 to 1.24)	<0.001	0.78 (0.72 to 0.84)	<0.001	1.07 (0.95 to 1.19)	<0.001	0.73 (0.67 to 0.79)	<0.001
23.0-24.9 kg/m^2	1.93 (1.77 to 2.09)	<0.001	1.61 (1.52 to 1.71)	<0.001	1.84 (1.68 to 2.01)	<0.001	1.52 (1.42 to 1.62)	<0.001
25.0-27.4 kg/m^2	3.36 (3.16 to 3.56)	<0.001	2.88 (2.74 to 3.02)	<0.001	3.28 (3.08 to 3.48)	<0.001	2.73 (2.59 to 2.87)	<0.001
27.5-29.9 kg/m^2	4.76 (4.50 to 5.03)	<0.001	4.30 (4.07 to 4.53)	<0.001	4.67 (4.40 to 4.94)	<0.001	4.12 (3.90 to 4.35)	<0.001
≥ 30.0 kg/m^2	6.39 (6.09 to 6.69)	<0.001	5.63 (5.35 to 5.91)	<0.001	6.31 (6.01 to 6.61)	<0.001	5.43 (5.15 to 5.72)	<0.001
Age group (years)								
15-19	-	-	-	-	0.00 (Reference)		0.00 (Reference)	
20-24	-	-	-	-	-0.47 (-0.57 to -0.38)	<0.001	-0.17 (-0.22 to -0.11)	<0.001

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25-29	-	-	-	-	-0.56 (-0.70 to -0.43)	<0.001	-0.15 (-0.23 to -0.08)	<0.001
30-34	-	-	-	-	-0.17 (-0.33 to -0.01)	0.043	0.09 (0.00 to 0.17)	0.057
35-39	-	-	-	-	0.59 (0.41 to 0.77)	<0.001	0.51 (0.42 to 0.61)	<0.001
40-44	-	-	-	-	1.86 (1.65 to 1.06)	<0.001	1.06 (1.95 to 1.17)	<0.001
45-49	-	-	-	-	3.43 (3.19 to 3.66)	<0.001	1.87 (1.75 to 1.99)	<0.001
50-54	-	-	-	-	6.34 (5.99 to 6.68)	<0.001	3.43 (3.25 to 3.62)	<0.001
55-59	-	-	-	-	8.07 (7.64 to 8.50)	<0.001	4.60 (4.37 to 4.84)	<0.001
60-64	-	-	-	-	10.06 (9.58 to 10.55)	<0.001	5.70 (5.44 to 5.97)	<0.001
≥65	-	-	-	-	11.21 (10.78 to 11.64)	<0.001	6.92 (6.68 to 6.16)	<0.001
Education								
No formal education	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
< Primary School	0.51 (0 0.80)	0.001	0.39 (0.28 to 0.49)	<0.001	0.26 (-0.03 to 0.55)	0.078	0.24 (0.13 to 0.359	<0.001
Primary School	0.71 (0 0.94)	<0.001	0.67 (0.57 to 0.77)	<0.001	0.35 (0.12 to 0.58)	0.003	0.42 (0.32 to 0.52)	<0.001
Middle School	0.95 (0 1.12)	<0.001	0.74 (0.66 to 0.81)	<0.001	0.43 (0.25 to 0.62)	0.326	0.37 (0.29 to 0.45)	<0.001
Secondary School	1.17 (0 1.37)	0.985	0.95 (0.84 to 1.06)	<0.001	0.51 (0.30 to 0.72)	<0.001	0.45 (0.33 to 0.56)	<0.001
> Secondary School	0.89 (0 1.08)	<0.001	0.86 (0.75 to 0.97)	<0.001	0.07 (-0.14 to 0.28)	0.5066	0.20 (0.08 to 0.31)	<0.001
Household wealth quintile								
1 (Poorest)	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	

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2	0.68 (0.52 to 0.83)	<0.001	0.21 (0.13 to 0.28)	<0.001	0.38 (0.22 to 0.53)	<0.001	0.08 (0.00 to 0.16)	0.047
3	1.03 (0.86 to 1.21)	<0.001	0.38 (0.29 to 0.48)	<0.001	0.51 (0.33 to 0.69)	<0.001	0.12 (0.02 to 0.21)	0.014
4	1.44 (1.25 to 1.63)	<0.001	0.70 (0.60 to 0.81)	<0.001	0.74 (0.54 to 0.94)	<0.001	0.25 (0.15 to 0.36)	<0.001
5 (Richest)	1.63 (1.41 to 1.84)	<0.001	1.57 (1.44 to 1.69)	<0.001	0.77 (0.55 to 0.00)	<0.001	0.78 (0.65 to 0.91)	<0.001
Currently married	-0.12 (-0.27 to 0.02)	0.102	-0.14 (-0.22 to -0.06)	<0.001	-0.33 (-0.48 to -0.18)	<0.001	-0.26 (-0.34 to -0.18)	<0.001

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* All models included PSU-level fixed effects (i.e., a binary indicator for each PSU), and standard errors were adjusted for clustering at the PSU level. ~~Univariable~~ Partially adjusted ~~regression~~ models were additionally adjusted for age group only, while the fully adjusted model was adjusted for all variables shown in the table. ~~.~~

† Coefficients should be interpreted as the absolute change in the probability of the outcome (compared to the reference category) in percentage points.

‡ For these regression models, AHS participants were assumed to be fasted at the time of the blood glucose measurement. Regression results among only those in whom fasting status was verified through self-report (i.e., DLHS-4 and NFHS-4) are shown in the appendix (see Table S10/Table S14, Supplemental Digital Content~~pp 20-21 and 26-27~~).

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Supplemental Digital Content

Supplementary Appendix.pdf

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~~Supplementary Appendix (PDF) :~~

- ~~Supplementary information on methodology~~
- ~~Sample characteristics of participants stratified by whether the blood glucose or blood pressure measurements were missing~~
- ~~State-level age-standardized prevalence estimates~~
- ~~Multivariable linear regressions of “diabetes conditional on having hypertension” and “hypertension conditional on having diabetes” on sociodemographic characteristics~~
- ~~Prevalence estimates assuming all AHS participants were non-fasted~~
- ~~Prevalence estimates among only DLHS-4 participants~~
- ~~Prevalence estimates among only DLHS-4 and AHS participants~~
- ~~Prevalence estimates among only NFHS-4 participants~~
- ~~Weighted and age standardized Venn diagrams~~