JAMIA Open, 5(3), 2022, 1–9
https://doi.org/10.1093/jamiaopen/ooac057
Research and Applications

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Comorbidities and ethnic health disparities in the UK biobank

Whitney L Teagle[1], Emily T. Norris[1,2,3,4], Lavanya Rishishwar[1,2,3,4], Shashwat Deepali Nagar[3,4], I. King Jordan [2,3,4], and Leonardo Mariño-Ramírez [1,4]

[1]National Institute on Minority Health and Health Disparities, National Institutes of Health, Bethesda, Maryland, USA, [2]Applied Bioinformatics Laboratory, Atlanta, Georgia, USA, [3]School of Biological Sciences, Georgia Institute of Technology, Atlanta, Georgia, USA, and [4]PanAmerican Bioinformatics Institute, Valle del Cauca, Cali, Colombia

Whitney L. Teagle and Emily T. Norris contributed equally to this work.

Corresponding Author: Leonardo Mariño-Ramírez, PhD, National Institute on Minority Health and Health Disparities, National Institutes of Health, 9000 Rockville Pike, Building 3, Floor 5 Bethesda, MD 20892, USA; marino@nih.gov

Received 28 March 2022; Revised 15 June 2022; Editorial Decision 22 June 2022; Accepted 24 June 2022

ABSTRACT

Objective: The goal of this study was to investigate the relationship between comorbidities and ethnic health disparities in a diverse, cosmopolitan population.
Materials and Methods: We used the UK Biobank (UKB), a large progressive cohort study of the UK population. Study participants self-identified with 1 of 5 ethnic groups and participant comorbidities were characterized using the 31 disease categories captured by the Elixhauser Comorbidity Index. Ethnic disparities in comorbidities were quantified as the extent to which disease prevalence within categories varies across ethnic groups and the extent to which pairs of comorbidities co-occur within ethnic groups. Disease-risk factor comorbidity pairs were identified where one comorbidity is known to be a risk factor for a co-occurring comorbidity.
Results: The Asian ethnic group shows the greatest average number of comorbidities, followed by the Black and then White groups. The Chinese group shows the lowest average number of comorbidities. Comorbidity prevalence varies significantly among the ethnic groups for almost all disease categories, with diabetes and hypertension showing the largest differences across groups. Diabetes and hypertension both show ethnic-specific comorbidities that may contribute to the observed disease prevalence disparities.
Discussion: These results underscore the extent to which comorbidities vary among ethnic groups and reveal group-specific disease comorbidities that may underlie ethnic health disparities.
Conclusion: The study of comorbidity distributions across ethnic groups can be used to inform targeted group-specific interventions to reduce ethnic health disparities.

Key words: ethnic health disparity, comorbidity, Elixhauser Comorbidity Index, health equity, UK Biobank

LAY SUMMARY

Despite overall improvements in public health, ethnic health disparities persist. Ethnic minority groups living in cosmopolitan societies continue to bear a disproportionate burden of morbidity and mortality. Ethnic health disparities are characterized by complex patterns of comorbidities, that is, the presence of more than one disease at the same time in an individual patient. The aim of this study was to investigate the relationship between comorbidities and ethnic health disparities in the United Kingdom. Our study relied on the UK Biobank, a progressive cohort of more than half a million participants. We measured differences in disease prevalence and patterns of comorbidities across 5 UK ethnic groups: Asian, Black, Chinese, Mixed, and White. Study participants who identified as Asian showed the highest disease prevalence and largest number of comorbidities, followed by participants from the Black and then White ethnic groups; Chinese participants have the lowest overall disease prevalence and comorbidities. Patterns of comorbidities vary widely among ethnic groups in the United Kingdom, and there are a number of group-specific disease comorbidities that contribute to ethnic health disparities, for example, for diabetes and hypertension. We hope that our results on comorbidities can be used to inform targeted group-specific interventions in support of health equity.

OBJECTIVE

The goal of this study was to investigate the relationship between comorbidities and ethnic health disparities. We characterized the landscape of comorbidities among study participants from 5 ethnic groups in the diverse, cosmopolitan population of the United Kingdom.

BACKGROUND AND SIGNIFICANCE

According to the US National Institutes of Health, health disparities are "differences in the incidence, prevalence, mortality, and burden of diseases and other adverse health conditions that exist among specific population groups." Health disparities are often manifested as differences between racial or ethnic groups, such as higher rates of chronic disease and premature death among ethnic minorities in modern, cosmopolitan populations. Ethnic health disparities have been linked to disease comorbidities, the presence of more than one disease at the same time in an individual.[1,2] Comorbidities can interact with and complicate each other, leading to an increased risk of severe disease or increased risk of acquiring new diseases.

Comorbidity measures are used to evaluate the overall health of a patients and populations. These measures can be used to determine if a patient has any preexisting conditions that may affect treatment, to assist in evaluating health plans and providers, or to study the impact of healthcare policies. Comorbidity measures categorize disease into broad categories, which together represent the overall burden of illness for a patient. The first of these measures was developed by Mary Charlson in 1987, using 19 disease categories.[3] Although widely adopted, the Charlson Comorbidity Index (CCI) was criticized based on its breadth and applicability to administrative health data.[4,5] The Elixhauser Comorbidity Index (ECI) was developed in 1998 to contain more disease categories (30) and summarize more conditions than the CCI.[6] The ECI was updated in 2012 to include 31 comorbidity disease categories,[7] and it has been shown to be more versatile and statistically rigorous than the CCI.[8,9] Both comorbidity measures make use of International Classification of Disease (ICD) codes as a means to capture a patient's medical history. ICD codes link administrative codes to diagnoses, allowing for researchers to quickly quantify comorbidities by mapping codes to disease categories.

Previous studies on comorbidities and health disparities have focused largely on Black, White, and to a lesser extent Hispanic, groups in the United States and have considered a limited number of primary conditions, including psychiatric disorders and substance abuse,[10–13] cardiometabolic disease,[14,15] cancer,[16,17] HIV,[18] and COVID-19.[19] More recent studies have used large-scale analysis of electronic health records to reveal race- and ethnic-specific disease comorbidity networks for US populations.[2,20] This data-driven approach has the potential to reveal unexpected comorbidity patterns within and between groups. We took a similar large-scale approach here, analyzing disease diagnosis data gleaned from electronic health records for more than 1500 diseases and hundreds-of-thousands of participants. Our study is distinguished by our focus on ethnic groups in the United Kingdom, for which comorbidity networks have not yet been characterized, and our novel approach to defining comorbid disease pairs and networks.

We utilized the UK Biobank (UKBB), a progressive cohort study of the UK population,[21] to study the relationship between comorbidities and ethnic health disparities. The UKBB provides researchers with access to clinical data from more than 500 000 volunteer participants, including ICD-10 codes, as well as information on participants' ethnicity. We quantified ethnic health disparities in the UKBB using the ECI disease categories and participants' self-identified ethnicity. We explored differences in the connectedness of comorbidities among ethnic groups and identified if any the comorbidity measures were themselves risk factors for other measures. We found evidence for ethnic health disparities for diabetes and hypertension as well as group-specific comorbidities contributing to the prevalence of both measures.

MATERIALS AND METHODS

Study cohort

The study cohort for this work was collected from the UKBB, a large-scale biomedical database and research resource providing researchers with access to clinical data from more than 500 000 participants.[21] For each UKBB participant, we extracted their ethnicity (Field 21000: Ethnic background) and ICD-10 codes (Field 41202: Diagnoses—main ICD10). We included participants in our study if they belonged to 1 of the 5 main self-identified ethnic groups in the UKBB: Asian, Black, Chinese, Mixed, or White. These ethnic group labels are based on the UK National Health Service's ethnicity categories.[22] For this ethnic grouping, Asian refers to individuals of South Asian descent, such as those from India, Pakistan, or Bangladesh. Individuals who are Asian and do not identify as South Asian, could identify as either Chinese or "Other ethnic group." The ICD-10 codes capture the participants' medical history via diagnoses they received across all of their inpatient hospital records. The final cohort contained 502 520 individuals across 5 ethnic groups as shown in Table 1.

Table 1. Comorbidity study cohort

Demographic characteristics[a]	Total cohort								UK Biobank ethnic group			
			Asian		Black		Chinese		Mixed		White	
	($n = 491\,587$)		($n = 9839$)		($n = 8034$)		($n = 1574$)		($n = 2909$)		($n = 472\,140$)	
Age, years (mean [SD])	57	(8)	53	(8)	52	(8)	53	(8)	52	(8)	57	(8)
Age, years												
<45	49 668	(10%)	1897	(19%)	1698	(21%)	283	(18%)	673	(23%)	45 790	(10%)
45–54	138 177	(28%)	3596	(37%)	3568	(44%)	644	(41%)	1208	(42%)	130 369	(28%)
55–64	208 557	(42%)	3081	(31%)	1929	(24%)	509	(32%)	772	(27%)	203 038	(43%)
65+	94 583	(19%)	1249	(13%)	819	(10%)	133	(8%)	255	(9%)	92 382	(20%)
Not Reported	602	(0%)	16	(0%)	20	(0%)	5	(0%)	1	(0%)	561	(0%)
Sex												
Female	267 078	(54%)	4558	(46%)	4631	(58%)	987	(63%)	1822	(63%)	256 902	(54%)
Male	223 907	(46%)	5265	(54%)	3383	(42%)	582	(37%)	1086	(37%)	214 677	(46%)
Not Reported	602	(0%)	16	(0%)	20	(0%)	5	(0%)	1	(0%)	561	(0%)

Note: Demographic characteristics and ethnic groups for the UKBB cohort studied here.

[a]Numbers of participants (n) and percentages (%) are shown for each demographic category.

Comorbidity measures

For each individual, comorbidities were categorized and quantified using the Elixhauser Comorbidity Index (ECI).[6,7] The ECI is a means of categorizing comorbidities in patients based on the ICD-10 diagnosis codes; the first version was developed with 30 disease categories,[6] and the most recent version has 31 categories.[7] ICD-10 diagnosis codes of the study participants were mapped to ECI disease categories using the R package comorbidity.[23] For each participant, ECI categories were scored as 0 or 1 according to the absence (0) or presence (1) of corresponding ICD-10 codes. Participants are given an ECI score that is the summation of all of their individual ECI disease category scores; the larger the score, the greater number of comorbidities a given individual has.

The variation in ECI scores for each disease category were compared across ethnic groups using the Relative Comorbidity Index (RCI), a measure of the mean normalized morbidity frequency for a given category:

$$\mathrm{RCI} = \log_2\left(\frac{\bar{x}}{\frac{1}{n}\sum_1^n \bar{x}}\right)$$

where $\bar{x}$ is the mean ECI frequency across all individuals for a given disease category for each ethnic group ($n = 5$). Statistical significance of the variation of RCI values across ethnic groups was calculated using the Kruskal–Wallis test by ranks,[24] and P values were corrected for multiple tests using the Benjamini–Hochberg false discovery rate (FDR) correction, with a significance threshold of $q < 0.05$.[25]

Comorbidity disparities

For each ethnic group, for each pair of comorbidities (c_1 *and* c_2), we compared the frequency of the observation of the pair co-occurrence ($\mathrm{Obs}_{1,2} = f(c_1c_2)$) to the frequency of the expected co-occurrence ($\mathrm{Exp}_{1,2} = f(c_1)f(c_2)$) by $\mathrm{CM}_{1,2} = \mathrm{Obs}_{1,2} - \mathrm{Exp}_{1,2}$. Due to the majority of the study cohort being comprised individuals belonging the White ethnic group (93.95%), any signal of significant pairs of comorbidities in any other ethnic group is diluted. To account for this, we scaled each ethnic group to 1000 individuals when calculating the expected frequency of any pair of comorbidities. Following this, the significance of each pair of comorbidities was calculated using a G-test, an extension of Fisher's exact test to handle larger study sizes, implemented in R. As before, correction for multiple tests was performed using the Benjamini-Hochberg FDR correction. Significant ($q < 0.05$) comorbidity pairs were retained for further analysis, resulting in only the Asian, Black, and White ethnic groups remaining in the study cohort.

Network analysis

Significant comorbidity pairs, as discussed in the previous section, were used to generate ethnic group-specific comorbidity networks. Network nodes correspond to ECI disease categories and pairs of comorbid disease categories with significant G-test values are connected by edges; node sizes are scaled to the prevalence of the disease category in the specific ethnic group. Edge lengths were calculated based on the difference between the observed and expected co-occurrence, as described above. Edge weights represent the fold-change of the comorbid disease pair across the 3 ethnic groups in this portion of the study: Asian, Black, and White. All networks were generated using Cytoscape 3.8.2[26] using the Edge-weighted Spring Embedded Layout. Network topological parameters were computed using the NetworkAnalyzer application within Cytoscape.[27]

Comorbidity risk factors

Knowledge of which ECI disease categories were risk factors for others was mined from the scientific literature and online medical resources. We performed a literature search for disease-risk factor relationships by searching PubMed using the keywords "[EC1 disease category 1] risk factor [EC1 disease category 2]." PubMed searches were limited to papers and review articles using human subjects from the last 10 years. The same keywords were used to search online medical resources, such as the Cleveland Clinic (https://my.clevelandclinic.org/), Healthline (https://www.healthline.com/), and the Mayo Clinic (https://www.mayoclinic.org/). ECI disease categories were characterized as disease risk factors if they were listed as either a risk factor or cause for diseases categorized in any of the other ECI disease categories. For disease-risk factor pairs for which we found a significant ethnic health disparity, we conducted an additional search in PubMed to confirm that the relationships found

were statistically significant or otherwise well-established in the biomedical community. We overlaid this information on the significant comorbid disease pairs in order to identify disease risk factors that could impact the observed ethnic disparities in disease outcomes (Figure 5).

RESULTS

Morbidity disparities between ethnic groups

We characterized comorbidities using the ECI[6,7] for a diverse, multiethnic cohort of 502 520 UKBB participants (Table 1). ECI scores were computed as the sum of individual ECI disease category scores, to capture the overall burden of comorbidities for all cohort participants. The majority of the study cohort participants (53.96%) show an ECI score of 0 (ie, no comorbidities); 20.08% of the cohort show an ECI score of 1, and less than 26% have ECI ≥ 2, that is, 2 or more comorbidities (Figure 1). When the ~100k individuals with 1 or more comorbidities are stratified by ethnic group, Asian ethnic group has the greatest average number of comorbidities, followed by the Black, White, Mixed, and Chinese ethnic groups, respectively (Figure 2A). Similar trends can be seen for ethnic group-specific frequencies of participants with multiple comorbidities (3–4 and 5+ categories in Figure 2B).

For each ECI disease category, we quantified the variation in prevalence across ethnic groups using the Relative Comorbidity Index (RCI) (Figure 3). The RCI metric captures the relative number of comorbidities seen in each ethnic group, compared to all 5 ethnic groups, for any given disease category. RCI values show significant variation ($q < 0.05$) for the vast majority of disease categories (93.55%), underscoring the extent of ethnic health disparities in the UKBB cohort. Diabetes and hypertension show the highest RCI variation across ethnic groups, with the Asian and Black groups showing the highest relative prevalence values. Solid tumor metastasis shows the next highest RCI variation, with the White ethnic group showing the highest relative prevalence. Other ECI disease categories that show high RCI variation across ethnic groups include deficiency anemia (highest prevalence in the Asian group), psychoses (highest in prevalence in the Mixed group), AIDS/HIV (highest prevalence in the Black group), alcohol abuse, and cardiac arrhythmias (highest prevalence the in White group).

Comorbidity disparities between ethnic groups

We evaluated whether any comorbid pairs of ECI disease categories (hereafter referred to as comorbidities) co-occur more often than expected, based on the ethnic group-specific frequencies of each disease category in the pair. Using a G-test and FDR correction for multiple tests, we identified pairs of disease categories that significantly co-occur in each ethnic group (Supplementary Table S1). Significantly co-occurring disease categories were only found in the Asian, Black, and White ethnic groups, and thus no further results are shown for the Chinese or Mixed ethnic groups. This may be due to smaller numbers of participants in these groups, more ethnic het-

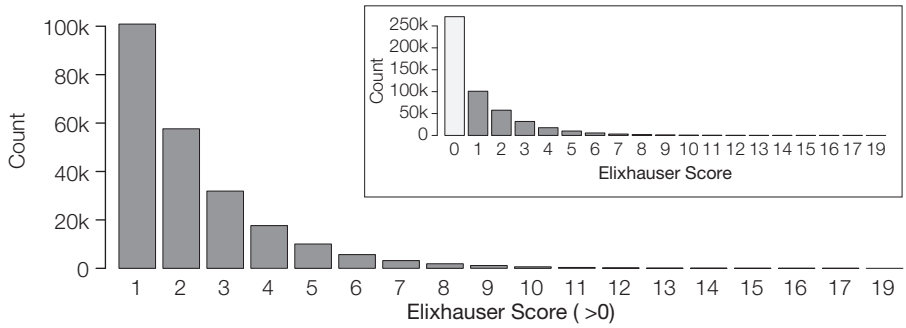

Figure 1. Distribution of Elixhauser Comorbidity Index (ECI) scores in the UKBB. Main panel: Distribution of ECI scores for ECI ≥ 1. Inset: Distribution of all ECI scores.

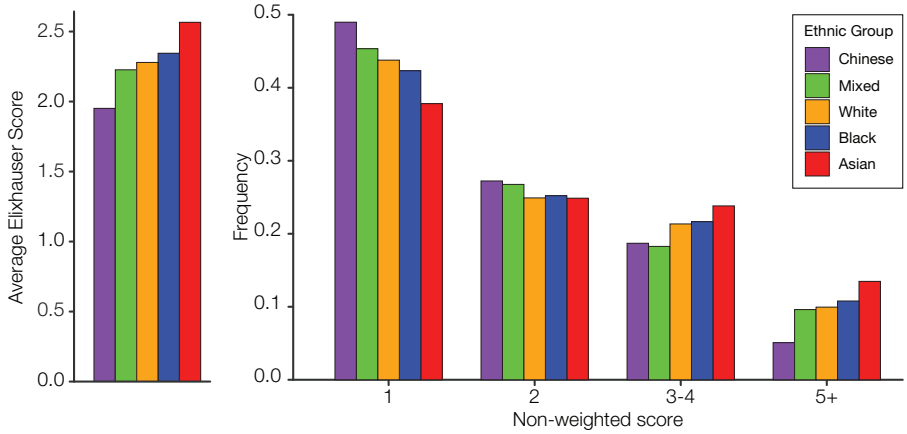

Figure 2. Distribution of Elixhauser Comorbidity Index (ECI) scores for UKBB ethnic groups. (A) Average ECI score for each of the ethnic groups. (B) Frequency (*y* axis) of each ECI scores ≥ 1 (*x* axis) for each ethnic group.

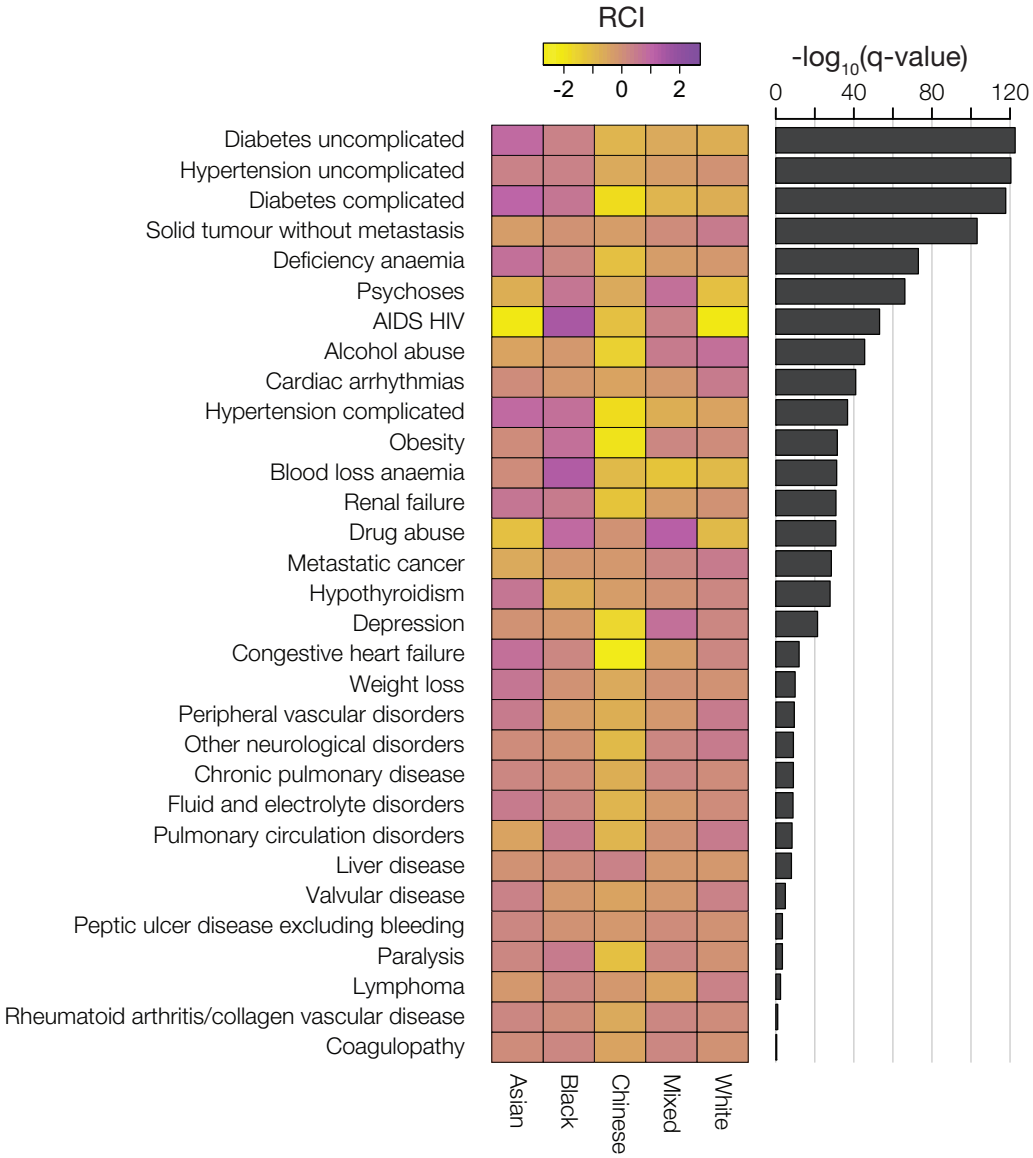

Figure 3. Relative Comorbidity Index (RCI) for ECI disease categories across the ethnic groups in the UKBB. RCI values for each ECI disease category are shown across ethnic groups (color coded as shown in the RCI key). Statistical significance values for the variation of RCI (FDR *q* value) are shown on the right.

erogeneity in the Mixed group, and/or fewer comorbidities in the Chinese group, which has the lowest overall disease prevalence for any group.

We generated comorbidity networks for the Asian, Black, and White ethnic groups, by connecting significantly co-occurring disease pairs for each group, to visualize the landscape of ethnic group-specific comorbidities (Figure 4). For each network, nodes are scaled by the prevalence of the ECI disease category in the group, edges represent the difference between the observed and expected pair co-occurrence (shorter length corresponds to greater difference), and the edge weights represent the fold-change of the pair when compared to the average difference of observed and expected of the 3 ethnic groups (Asian, Black, and White). The networks were evaluated using a number of parameters to describe their global topological properties (Supplementary Figure S1). While the 3 networks have a comparable number of nodes, the Asian network has more edges (Supplementary Figure S1A). In addition, the Asian network has a greater node degree (Supplementary Figure S1B) and average number of neighbors for each node (Supplementary Figure S1C). The Asian network has a smaller diameter than either the Black or White networks, indicating larger differences between the observed and expected comorbidity co-occurrences. In all 3 networks, diabetes and hypertension are central nodes, with both the greatest prevalence and largest number of connections. When the networks are filtered to only those nodes and edges connected to diabetes, both complicated and uncomplicated, we see that they are highly connected within all 3 ethnic group networks (Supplementary Figure 2A). However, the Asian diabetes network has a greater number of nodes than either the Black or White. Filtering the networks to links to hypertension shows similar patterns as with diabetes, however both the Asian and Black networks are much denser than the White network (Supplementary Figure 3A).

Comorbidities and disease risk factors

While the disease categories in the ECI allow for characterization of large numbers of patient diagnoses, these broad categories do not

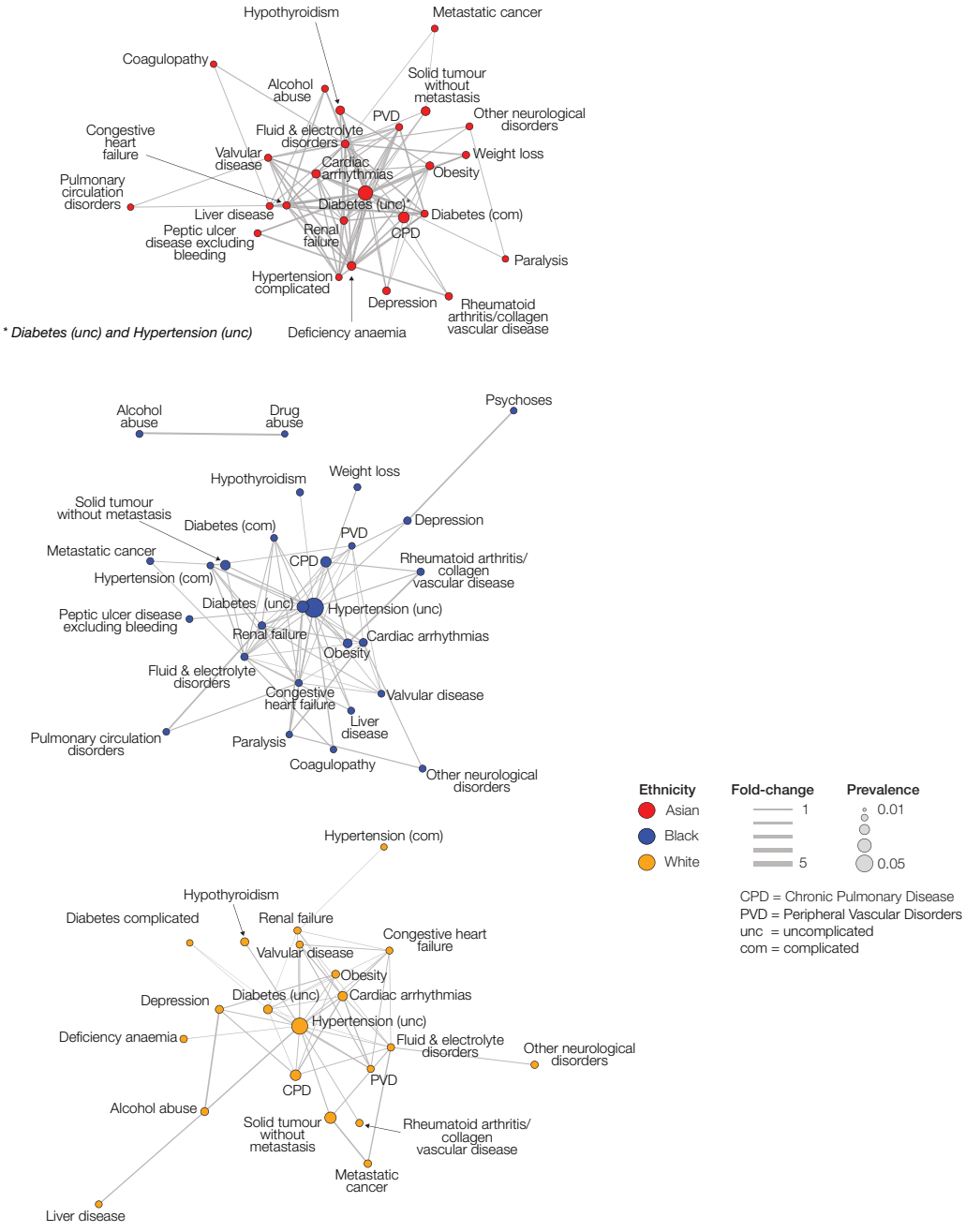

Figure 4. Ethnic group-specific networks for comorbid disease pairs. For each ethnicity (Asian-red, top network, Black-blue, middle network, and White-orange, bottom network), a network of significantly co-occurring pairs of comorbidities is shown. Each comorbid disease is represented as a node in the network; nodes are scaled based on the prevalence of the comorbid disease in the ethnic group. Nodes are connected if they have a significant G-test FDR *q* value; edge lengths represent the differences in observed and expected comorbidity pairs; edge weight represent the fold-change value of the comorbidity pair when compared across the 3 ethnicities.

exist independently of one another. Rather, it has been demonstrated in the medical field that one or more of the comorbidity categories could be a risk factor for another, for example, hypertension is a known risk factor for diabetes.[28,29] Using the 31 ECI disease categories, we identified pairs of comorbidities in which one disease category was a known risk factor for the other (Supplementary Figure S4). The references in support of these disease-risk factor pairs are provided in Supplementary Table S2. By overlaying this information on the network of significant co-occurrences of comorbidities for the 3 ethnic groups (Figure 4), we were able to characterize ethnic group-specific comorbidities that included risk factors for the most significant disease category disparities (Figure 5). Overall, the Asian ethnic group contains the greatest number of risk factor-comorbidity pairs, followed by the Black and White ethnic groups. While the 3 ethnic groups have many of the same risk factor-comorbidity pairs, there are some that are specific to 1 or 2 of the groups, for example, obesity as a risk factor for cardia arrhythmias in the Asian group, pulmonary circulation disorders as a risk factor for renal failure in the Black group, and depression as a risk factor for alcohol abuse in the White group. Several of the observed ethnic

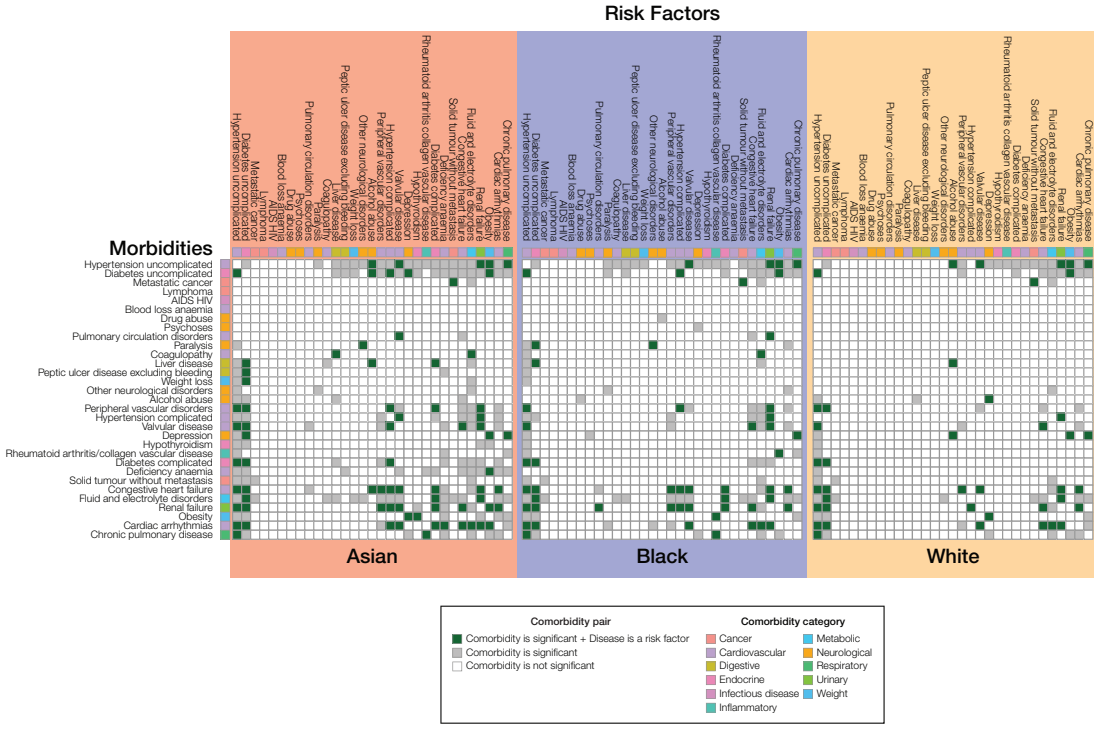

Figure 5. Ethnic group-specific risk factors for comorbid disease pairs. The relationship between comorbidities as risk factors (green boxes) is shown overlaid on the presence/absence of significant comorbid disease pairs (gray boxes) for each ethnic group (Asian, Black, and White). Risk factors are indicated on the *x* axis and the disease categories that they affect are indicated on the *y* axis. Comorbidities are categorized into categories as shown.

disease category disparities show a combination of both shared and unique risk factors. For diabetes (uncomplicated), all 3 ethnic groups share the risk factors of hypertension (uncomplicated) and obesity; however, the Black ethnic group additionally has hypertension (complicated) as a risk factor, and the Asian group has depression and alcohol abuse as additional risk factors (Supplementary Figure 2B). For hypertension (complicated), all 3 groups share renal failure as a risk factor, whereas the Asian group has valvular disease as an additional comorbid risk factor (Supplementary Figure 3B).

DISCUSSION

Ethnic disease disparities and comorbidities in UKBB

Diabetes and hypertension are the most pronounced ethnic disease disparities in the UKBB cohort, with both showing relatively high prevalence in the Asian and Black ethnic groups (Figure 3). Diabetes, both complicated and uncomplicated, is most prevalent in the Asian ethnic group followed by the Black group. Diabetes in the Asian population has more comorbidity pairs than either the Black or White ethnic groups, indicating a greater burden of diabetes-related comorbidities (Supplementary Figure 2A). These results align with what is known about the prevalence of diabetes in South Asians in the United Kingdom. South Asians have higher prevalence of diabetes than their Black or White counterparts.[30] The likelihood of developing type 2 diabetes is reported to be as much as 6 times higher in South Asians than Europeans, and even though South Asian people make up just 4% of the total UK population, they account for an estimated 8% of all diagnosed cases of diabetes.[31] South Asians without diabetes are also 3 times more likely to develop cardiovascular disease, but combined with type 2 diabetes, this risk for cardiovascular disease rises even further, particularly for adults with type 2 diabetes aged 20 to 60. In addition, survival rates in young South Asian patients with diabetes are significantly lower compared to the White population.[32]

For uncomplicated diabetes, we found several ethnic group-specific comorbidities that could impact ethnic disease prevalence disparities (Supplementary Figure 2A). All 3 ethnicities shared obesity and uncomplicated hypertension as comorbidities for uncomplicated diabetes, however complicated hypertension does not appear as a comorbidity for the White ethnic group. Furthermore, the Asian ethnic group has both depression and alcohol abuse risk factors as group-specific comorbidities for uncomplicated diabetes.

Hypertension, both complicated and uncomplicated, shows a similar pattern of ethnic disparities as seen for diabetes, with higher prevalence in the Asian and Black ethnic groups compared to the White group and other groups. Hypertension-specific network analysis shows that the Asian and Black networks are both more highly connected and larger than the White network, indicating the presence of more significant comorbidity pairs for these groups (Supplementary Figure 3A). These results are consistent with a number of previous studies showing higher prevalence of hypertension in South Asians and Blacks compared with the White ethnic group in the United Kingdom.[33–36]

In addition to hypertension being an ethnic disparity, it also shows several known risk factors as ethnic-specific comorbidities (Supplementary Figure 3B). All 3 ethnic groups share renal failure as a common comorbid risk factor for hypertension, but the Asian group also has valvular disease as a comorbid risk factor. Hypertension itself is also a major risk factor for cardiovascular and cerebrovascular disease, which are major causes of death in the United Kingdom and other western countries. Recent studies indicate sub-

stantial ethnic differences in cardiovascular mortality.[37] For example, compared to Whites, Afro-Caribbean and people of African descent have a higher incidence of stroke and end stage renal failure, whereas coronary artery disease is less common. Conversely, South Asians have a higher incidence of coronary heart disease.

Study limitations

There are several limitations to our observational study of comorbidity and ethnic health disparities. We did not take into consideration cultural factors such as diet and lifestyle, which may contribute to the observed ethnic health disparities. We also did not take into consideration immigration status, generation of immigration, and socioeconomic status, all which may affect or contribute to the relationships we see here. For example, second generation Asians in the United Kingdom are more likely to be obese than first generation immigrants.[38] Thus, the observed relationships between ethnicity and comorbid disease pairs could be complicated by unmeasured confounders.

Finally, Elixhauser Comorbidity Index values are derived from ICD-10 patient billing codes. This means that medical conditions that were not charged to insurance were not included in the analysis. Likewise, health conditions that were not evaluated by a medical provider were not included in our analysis. This means that there may be a higher prevalence of morbidity than what is reflected in our study, and some comorbidity pairs may go underreported. Some ethnic groups may be more affected by this than others, especially if there are disparities in health access or hesitancy to seek medical care.[39] Other barriers such as health literacy, language, and cultural differences can also play a role in limiting healthcare utilization.[40,41] For our analysis, this could result in underrepresentation of comorbid disease pairs, particularly for ethnic minority and immigrant groups.

CONCLUSION

Comorbidities have ethnicity-specific effects on health and are, themselves, health disparities. Using disease diagnoses and self-reported ethnicity collected from participants in the UKBB, we show that there are a number of disease categories that have different prevalence across the ethnic groups. Further, there are comorbidity disparities between the ethnic groups, and comorbidities influence health disparities by increasing disease risk in specific ethnic groups. Diabetes and hypertension were shown to be the most impactful morbidities in that they are ethnic health disparities in the UKBB and have differential comorbidity patterns, including known risk factors risk factors for disease prevalence and progression that appear as ethnic group-specific comorbidities. This study underscores the importance of understanding the impact of comorbidities and how they may serve as risk factors for ethnic health disparities. This knowledge could allow for targeted public health interventions to be implemented for comorbidities that contribute to ethnic health disparities in the United Kingdom.

FUNDING

This work was supported by the National Institutes of Health (NIH) Distinguished Scholars Program (DSP) to LMR and the Division of Intramural Research (DIR) of the National Institute on Minority Health and Health Disparities (NIMHD) at NIH. ETN, LR, SDN, and IKJ were supported by the IHRC-Georgia Tech Applied Bioinformatics Laboratory.

AUTHOR CONTRIBUTIONS

WT, ETN, and LR: data curation, methodology, analysis, visualization, and writing. SN: Data curation and analysis. IKJ and LMR: Conceptualization, funding acquisition, methodology, project administration, visualization, and writing.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *JAMIA Open* online.

ACKNOWLEDGMENTS

This study was made possible by the UKBB project ID 65206 to LMR.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY

UKBB data are made publicly available via agreements with individual researchers. This study was conducted under the UKBB project ID 65206 to LMR.

REFERENCES

1. Daw J. Contribution of four comorbid conditions to racial/ethnic disparities in mortality risk. *Am J Prev Med* 2017; 52 (1S1): S95–102.
2. Kalgotra P, Sharda R, Croff JM. Examining multimorbidity differences across racial groups: a network analysis of electronic medical records. *Sci Rep* 2020; 10 (1): 13538.
3. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40 (5): 373–83.
4. Romano PS, Roost LL, Jollis JG. Further evidence concerning the use of a clinical comorbidity index with ICD-9-CM administrative data. *J Clin Epidemiol* 1993; 46 (10): 1085–90.
5. Romano PS, Roos LL, Jollis JG. Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epidemiol* 1993; 46 (10): 1075–9; discussion 81–90.
6. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; 36 (1): 8–27.
7. Garland A, Fransoo R, Olafson K, *et al. The Epidemiology and Outcomes of Critical Illness in Manitoba*. Winnipeg, MB: Manitoba Centre for Health Policy; 2012.
8. Fortin Y, Crispo JA, Cohen D, McNair DS, Mattison DR, Krewski D. External validation and comparison of two variants of the Elixhauser comorbidity measures for all-cause mortality. *PLoS One* 2017; 12 (3): e0174379.
9. Menendez ME, Neuhaus V, van Dijk CN, Ring D. The Elixhauser comorbidity method outperforms the Charlson index in predicting inpatient death after orthopaedic surgery. *Clin Orthop Relat Res* 2014; 472 (9): 2878–86.
10. Erving CL. Physical-psychiatric comorbidity: patterns and explanations for ethnic group differences. *Ethn Health* 2018; 23 (6): 583–610.
11. Lankarani MM, Assari S. Association between number of comorbid medical conditions and depression among individuals with diabetes; race and ethnic variations. *J Diabetes Metab Disord* 2015; 14: 56.

12. Sanchez K, Chartier KG, Greer TL, *et al.* Comorbidities and race/ethnicity among adults with stimulant use disorders in residential treatment. *J Ethn Subst Abuse* 2015; 14 (1): 79–95.
13. Watkins DC, Assari S, Johnson-Lawrence V. Race and ethnic group differences in comorbid major depressive disorder, generalized anxiety disorder, and chronic medical conditions. *J Racial Ethn Health Disparities* 2015; 2 (3): 385–94.
14. Lee H, Shin SH, Gu S, *et al.* Racial differences in comorbidity profile among patients with chronic obstructive pulmonary disease. *BMC Med* 2018; 16 (1): 178.
15. Opara F, Hawkins K, Sundaram A, Merchant M, Rasmussen S, Holmes L. Impact of comorbidities on racial/ethnic disparities in hypertension in the United States. *Int Sch Res Notices* 2013; 2013: 1–8.
16. Tammemagi CM, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and survival disparities among black and white patients with breast cancer. *JAMA* 2005; 294 (14): 1765–72.
17. Williams CD, Stechuchak KM, Zullig LL, Provenzale D, Kelley MJ. Influence of comorbidity on racial differences in receipt of surgery among US veterans with early-stage non-small-cell lung cancer. *J Clin Oncol* 2013; 31 (4): 475–81.
18. Richardson KK, Bokhour B, McInnes DK, *et al.* Racial disparities in HIV care extend to common comorbidities: implications for implementation of interventions to reduce disparities in HIV care. *J Natl Med Assoc* 2016; 108 (4): 201–10.e3.
19. Golestaneh L, Neugarten J, Fisher M, *et al.* The association of race and COVID-19 mortality. *EClinicalMedicine* 2020; 25: 100455.
20. Glicksberg BS, Li L, Badgeley MA, *et al.* Comparative analyses of population-scale phenomic data in electronic medical records reveal race-specific disease networks. *Bioinformatics* 2016; 32 (12): i101–10.
21. Bycroft C, Freeman C, Petkova D, *et al.* The UK Biobank resource with deep phenotyping and genomic data. *Nature* 2018; 562 (7726): 203–9.
22. Gov.uk. Ethnicity facts and figures. Secondary ethnicity facts and figures 2020. https://www.ethnicity-facts-figures.service.gov.uk/style-guide/ethnic-groups. Accessed December 27, 2021.
23. Gutierrez-Sacristan A, Bravo A, Giannoula A, Mayer MA, Sanz F, Furlong LI. comoRbidity: an R package for the systematic analysis of disease comorbidities. *Bioinformatics* 2018; 34 (18): 3228–30.
24. Kruskal WH, Wallis WA. Use of ranks in one-criterion variance analysis. *J Am Stat Assoc* 1952; 47 (260): 583–621.
25. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B Methodol* 1995; 57 (1): 289–300.
26. Shannon P, Markiel A, Ozier O, *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res* 2003; 13 (11): 2498–504.
27. Assenov Y, Ramirez F, Schelhorn SE, Lengauer T, Albrecht M. Computing topological parameters of biological networks. *Bioinformatics* 2008; 24 (2): 282–4.
28. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. *Can J Cardiol* 2018; 34 (5): 575–84.
29. Gress TW, Nieto FJ, Shahar E, Wofford MR, Brancati FL. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis risk in communities study. *N Engl J Med* 2000; 342 (13): 905–12.
30. Gujral UP, Pradeepa R, Weber MB, Narayan KM, Mohan V. Type 2 diabetes in South Asians: similarities and differences with white Caucasian and other populations. *Ann N Y Acad Sci* 2013; 1281: 51–63.
31. Goff LM. Ethnicity and Type 2 diabetes in the UK. *Diabet Med* 2019; 36 (8): 927–38.
32. Palaniappan L, Garg A, Enas E, *et al.* South Asian cardiovascular disease & cancer risk: genetics & pathophysiology. *J Community Health* 2018; 43 (6): 1100–14.
33. Schofield P, Saka O, Ashworth M. Ethnic differences in blood pressure monitoring and control in south east London. *Br J Gen Pract* 2011; 61 (585): 190–6.
34. Agyemang C, Bhopal RS. Is the blood pressure of South Asian adults in the UK higher or lower than that in European white adults? A review of cross-sectional data. *J Hum Hypertens* 2002; 16 (11): 739–51.
35. Lane D, Beevers DG, Lip GY. Ethnic differences in blood pressure and the prevalence of hypertension in England. *J Hum Hypertens* 2002; 16 (4): 267–73.
36. Cappuccio FP, Cook DG, Atkinson RW, Strazzullo P. Prevalence, detection, and management of cardiovascular risk factors in different ethnic groups in south London. *Heart* 1997; 78 (6): 555–63.
37. Khan JM, Beevers DG. Management of hypertension in ethnic minorities. *Heart* 2005; 91 (8): 1105–9.
38. Smith NR, Kelly YJ, Nazroo JY. The effects of acculturation on obesity rates in ethnic minorities in England: evidence from the Health Survey for England. *Eur J Public Health* 2012; 22 (4): 508–13.
39. Szczepura A. Access to health care for ethnic minority populations. *Postgrad Med J* 2005; 81 (953): 141–7.
40. Rhodes P, Nocon A, Wright J. Access to diabetes services: the experiences of Bangladeshi people in Bradford, UK. *Ethn Health* 2003; 8 (3): 171–88.
41. Williams ED, Whitaker KL, Piano M, Marlow LAV. Ethnic differences in barriers to symptomatic presentation in primary care: a survey of women in England. *Psychooncology* 2019; 28 (12): 2336–43.