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Racial differences in the proportion of myeloma cases attributable to excess body weight and diabetes mellitus in the United States

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Conflicts of Interest

U.A.S. reports support research funding support from Celgene/BMS and Janssen to the institution; research support from Sabinsa Pharmaceuticals and M&M Labs to the institution; and consulting/advisory board from Janssen Biotech, Sanofi, and i3Health outside the submitted work.

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Author Contributions

A.A., D.R. collected data, performed the analysis, wrote the manuscript with support from U.A.S. A.D. contributed to data and analysis tools, performed the analysis. S.Z.U. contributed to manuscript review and revision. U.A.S. conceived the study concept, designed the analysis. All authors reviewed and revised the final manuscript.

Multiple myeloma (MM) is a hematologic malignancy that disproportionately affects Black populations. In the US, Black individuals are twice as likely to be diagnosed with MM compared to their White counterparts[1]. This disparity can be attributed to a combination of genetic, socio-environmental and lifestyle factors. Notably, modifiable risk factors such as elevated body mass index (BMI) and diabetes mellitus (DM) have been identified as risk factors for MM[2-4]. MM is one of 13 cancers associated with obesity[5]. The prevalence of obesity and DM is also higher in non-Hispanic Black (NHB) and Hispanic adults than in non-Hispanic White (NHW) adults[6].

Recent studies have highlighted concerning trends in MM incidence. For instance, the incidence of MM has risen among young adults in the United States[7]. Globally, MM incidence has shown an increasing trend over the past several decades[8], with this rise paralleling an increase in obesity prevalence. This pattern is consistent with research indicating that obesity is a risk factor for MM, and maybe driven by multiple mechanisms such as chronic inflammation where stressed adipocytes and fat-infiltrating immune cells secrete adipokines and inflammatory cytokines which facilitate MM expansion[9]. Similarly, DM is also considered as a risk factor for MM with possible mechanisms including hyperinsulinemia, hyperglycemia, inflammation, immune suppression, and increased insulin-like growth factor[3, 10].

As obesity and DM rates continue to rise in the US and worldwide, its effect on incidence of obesity-related neoplasms such as MM, make it important to estimate the percentage of MM cases attributed to elevated BMI and DM. Additionally given the differences in MM risk by race, we further evaluated the contribution of these modifiable risk factors by racial groups. Therefore, our study aims to quantify the proportion of MM cases attributable to these modifiable risk factors among adults aged 18 and older. We calculated the population attributable fraction (PAF) which is an estimate of the proportion of cases attributable to elevated BMI or DM overall and for NHWs, NHBs and Hispanics[11].

This study was conducted using de-identified, publicly available data and did not require institutional review board approval or patient written consent. It respects the ethical research guidelines and considerations set in the United States. The number of MM cancer cases from 2016 to 2021 in the United States (US), including stratification by age, race, and ethnicity, was obtained from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program[1].

Data on prevalence of overweight (BMI: 25-30 kg/m^2) and obese (BMI: ≥30 kg/m^2) BMI and DM per race for age groups 18-44, 45-64, 65-74 and 75+ years from 2006-11 was obtained from the Integrated Public Use Microdata Series (IPUMS) Health Surveys database which harmonizes the National Health Interview Survey (NHIS) data provided by the National Center for Health Statistics (Table S1)[6, 12]. NHIS is a survey collecting information on the health, health care access, and health behaviors of the civilian, non-institutionalized U.S. population, with digital data files available from 1963 to present. We used the 2006-to-2011-time frame to allow for an approximate 10-year lag period between BMI and DM prevalence and MM occurrence based on prior literature[11] given similar rate of progression from MGUS to MM by race/ethnicity[13].

We calculated the PAF of incident MM cases attributable to BMI and DM based on hazard ratios (HR) estimates from two large epidemiologic studies evaluating MM risk with elevated BMI in the NIH AARP Diet and Health Study and DM using healthcare databases from Ontario, Canada[2, 3]. The estimate of MM risk for overweight HR 1.09 (95% confidence interval (CI): 0.82 - 1.47) was used. For obesity the lower range estimates HR 1.26 (95% CI: 1.01 - 1.64) based on BMI 30-34.9 kg/m^2 and upper range estimates HR 1.55 (95% CI: 1.01 - 2.39) based on BMI ≥35 kg/m^2 for MM risk were used. CIs were set to have the same p-value as reported for BMI ≥35 kg/m^2 patients[2]. For elevated BMI we utilized two estimates - BMI PAF_{BMI30} (overweight and

lower range obesity HR estimates) and BMI PAF_{BMI35} (overweight and upper range obesity HR estimates). The estimate of MM risk for DM HR 1.15 (95% CI: 1.09 - 1.23) was used. The race and age-specific PAFs with corresponding 95% CIs were estimated using 10,000 parametric bootstrap replications based on above hazard ratios, BMI or DM prevalence, and corresponding standard errors estimated from NHIS data.

Across all age groups, NHB and Hispanic populations have higher obesity rates compared to NHW populations (Table S1). For example, in the 45-64 age group, obesity affected 44% of NHB, 37.5% of Hispanics and 34% of NHW whereas for ages 65-74, rates were 41.9% in NHB, 36.3% in Hispanics and 32.3% in NHW (Table S1). The PAF_{BMI30} for MM cases attributable to elevated BMI is 10.8% (95% CI: -1.0-22.0%) overall, 12.7% (95% CI: 0.0-24.7%) in NHB, 11.7% (95% CI: -1.0-23.7%) in Hispanics and 10.5% (95% CI: -1.0-21.8%) in NHW (Tables 1 and S2, Figure 1A). Whereas the PAF_{BMI35} is 17.1% (95% CI: 0.3-31.7%) overall, 20.0% (95% CI: 1.5-37.3%) in NHB, 18.1% (95% CI: 0.8-34.2%) in Hispanics and 16.3% (95% CI: 0.8-31.3%) in NHW (Tables 1 and S2, Figure 1B). Therefore, an additional 2.3-3.7% of MM cases in NHBs and an additional 1.2-1.8% of MM cases in Hispanics may be attributable to elevated BMI when compared to NHW.

Similarly, DM prevalence was significantly higher in NHB populations compared to NHW populations across all age groups, with a greater increase observed in NHBs as age advanced. For example, in the 45-64 age group, rates were 17.0% in NHB, 17.1% in Hispanics versus 9.9% in NHW and for ages 65-74, it was 31.1% in NHB, 29.3% in Hispanics and 16.5% in NHW (Table S1). These findings highlight a significantly higher proportion of DM in NHB and Hispanics. The PAF_{DM} of MM cases being attributable to DM is 1.2% (95% CI: 1.0-1.8%) overall, 1.7% (95% CI: 1.0-2.2%) in NHB, 1.2% (95% CI: 1.0-2.0%) in Hispanics and 1.1% (95% CI: 1.0-

1.8%) in NHW (Tables 1 and S3, Figure 1C). Thus, an additional 0.6% of MM cases in NHBs and an additional 0.1% of MM cases in Hispanics may be attributable to DM compared to NHW.

We applied these findings to estimate the annual number of MM cases that were attributable to elevated BMI and DM. We estimate there were 31,780[14] average newly diagnosed MM cases annually in the US between 2016-2021 of which 29,320 cases were in NHWs, NHBs and Hispanics. Of these MM cases, at least 3178 (PAF_{BMI30} = 10.84%) and up to 5026 (PAF_{BMI35} = 17.14%) cases were attributable to an elevated BMI. In NHW there were between 1963-3063 cases out of 18,765 cases (PAF_{BMI30} = 10.46%; PAF_{BMI35} = 16.32%), in NHB there were between 800-1261 cases out of 6298 cases (PAF_{BMI30} = 12.7%; PAF_{BMI35} = 20.0%), and in Hispanics there were between 496-769 cases out of 4257 (PAF_{BMI30} = 11.66%, PAF_{BMI35} = 18.06%) attributable to an elevated BMI (Table 1). Similarly, up to 345 (PAF_{DM} = 1.18%) cases were attributable to DM. In NHW, there were 207 cases out of 18,765 cases (PAF_{DM} = 1.1%), in NHB, there were 106 cases out of 6298 cases (PAF_{DM} =1.7%), and in Hispanics, there were about 52 cases out of 4257 cases (PAF_{DM} = 1.2%) attributable to DM (Table 1). These findings suggest that preventive methods could be successful in decreasing the incidence of MM.

Strengths of this analysis include utilizing risk estimates from large epidemiologic studies and data from national publicly available datasets and a 5-year period over which we assessed risk with an estimated 10-year lag time to account for time from metabolic disorder to MM diagnosis. Some limitations include the estimates utilized being limited by available research with wide confidence intervals, elevated BMI and DM status are self-reported so they may be underreported, and prediabetes may also increase risk and was not included in the estimates. BMI and DM have been analyzed as separate conditions, as it was not possible to conduct an interaction analysis for those with a concomitant diagnosis of elevated BMI and DM with the

available data. All races were also not included and therefore the absolute number of cases attributable to these risk factors is likely an underestimate. While elevated BMI and DM contribute to a substantial proportion of the increased risk of MM overall, it does not fully account for the two times higher incidence in NHB compared to NHW.

These findings suggest a need for researching comprehensive lifestyle intervention strategies to lower BMI and reduce DM incidence among the general population. Dietary trials such as NUTRIVENTION (NCT04920084, NCT05640843) are evaluating whether strategies such as high fiber plant based diets that reduce weight, insulin resistance and improve microbiome composition and inflammation may delay progression from monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) to MM and early evidence suggests this may be possible in certain cases[15]. Drug strategies such as the glucagon-like peptide 1 receptor agonists (GLP-1RAs) are being used widely for weight and DM management. They have been associated with reduced risk of obesity-related cancers such as MM when compared with insulin or metformin in patients with type 2 DM[16] although interventional trials for cancer risk reduction are lacking. Thus, drugs such as GLP-1RAs and lifestyle strategies such as fiber rich diets highlight potential strategies for MM risk reduction to reduce the significant financial, emotional, and social burden of this diagnosis.

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Table 1: Estimated Number of Multiple Myeloma (MM) cases Attributable to Elevated Body Mass Index (BMI) and Diabetes Mellitus (DM) in Adults 18 Years or Older, 2016-2021

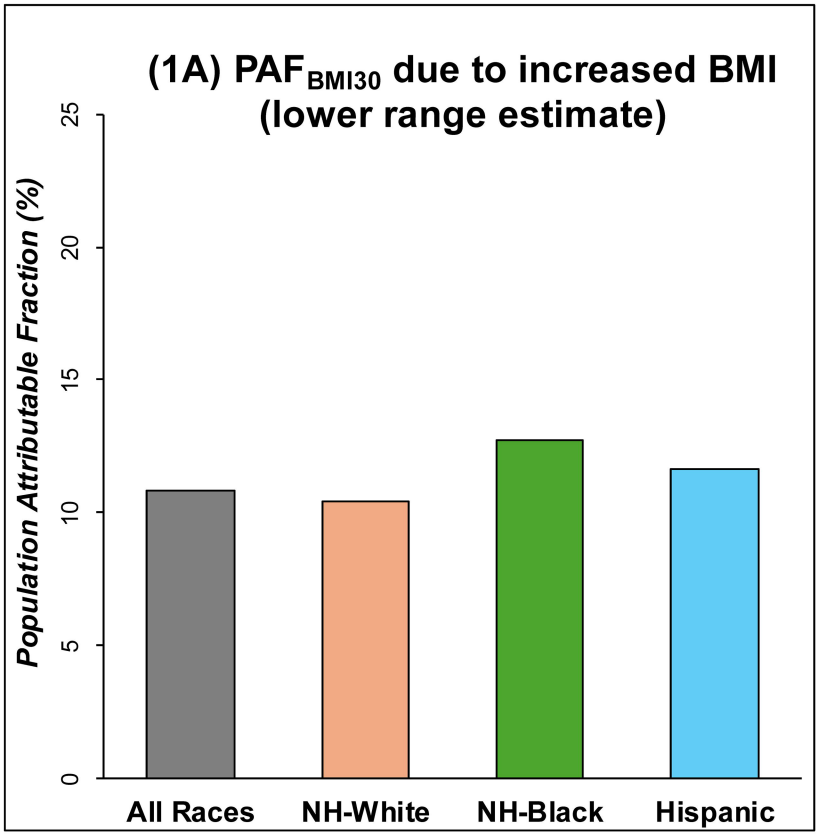
The estimated proportion and average number of multiple myeloma cases attributable to elevated body mass index (BMI) and diabetes mellitus across different racial and ethnic groups. The population attributable fraction (PAF) and corresponding 95% confidence intervals (CIs) are reported for BMI-related risk estimates based on hazard ratios corresponding to the lower and upper ranges of obesity (PAF_{BMI30} and PAF_{BMI35}, respectively), as well as for diabetes mellitus-related risk estimates (PAF_{DM}). The number of attributable cases is calculated for each category, and total cases are provided for all racial and ethnic groups, including Non-Hispanic White (NHW), Non-Hispanic Black (NHB), and Hispanic populations.

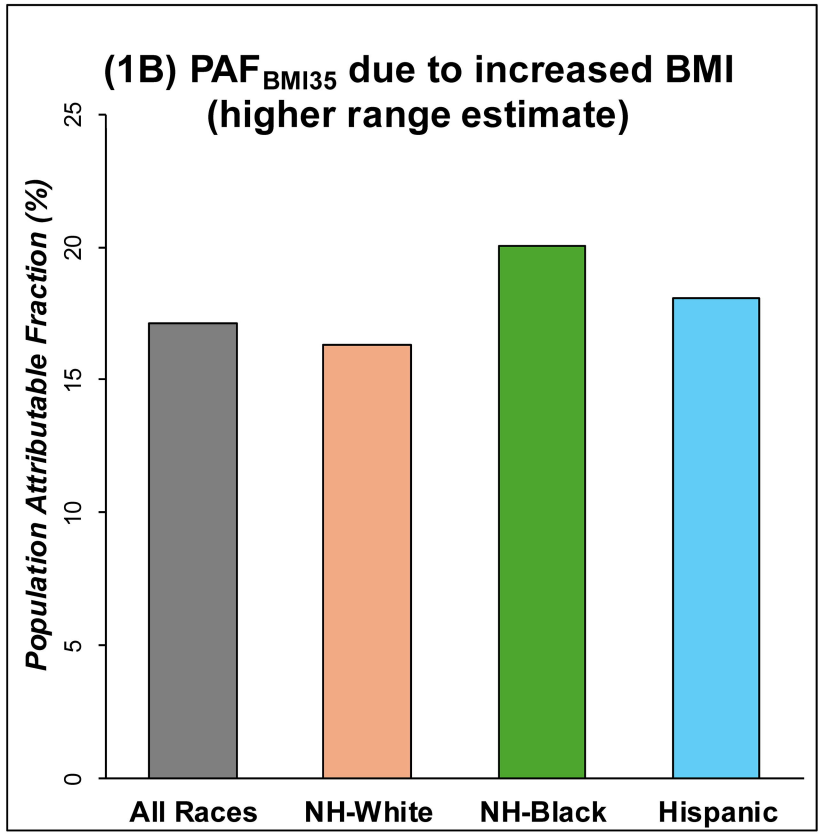
Annual MM cases	Cases PAF 95% CI	All Races	NHW	NHB	Hispanic
Overall estimate	Cases - N	29,320	18,765	6,298	4,257
Elevated BMI (lower range) estimate	PAF_{BMI30}%	10.8%	10.5%	12.7%	11.7%
	95% CI	(-1.0%-22.0%)	(-1.0%-21.8%)	(0.0%-24.7%)	(-1.0%-23.7%)
	Cases - N	3,178	1,963	800	496
Elevated BMI (upper range) estimate	PAF_{BMI35}%	17.1%	16.3%	20.0%	18.1%
	95% CI	(0.3%-31.7%)	(0.8%-31.3%)	(1.5%-37.3%)	(0.8%-34.2%)
	Cases - N	5,026	3,063	1,261	769
Diabetes mellitus estimate	PAF_{DM}%	1.2%	1.1%	1.7%	1.2%
	95% CI	(1.0%-1.8%)	(1.0%-1.8%)	(1.0%-2.2%)	(1.0%-2.0%)
	Cases - N	345	207	106	52

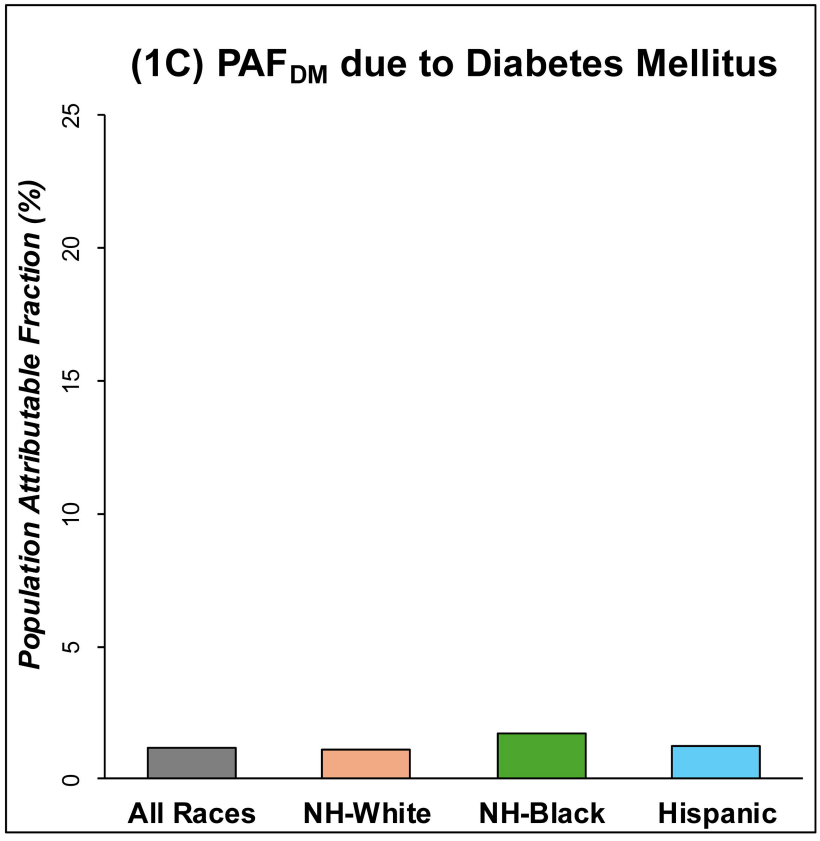
Abbreviations: MM, multiple myeloma; PAF, Population Attributable Fraction; N, number of attributable cases; NHW, Non-Hispanic White; NHB, Non-Hispanic Black. All Races: Aggregate of Non-Hispanic White + Non-Hispanic Black + Hispanic; CI, confidence interval.

Figure 1: Population Attributable Fraction (PAF) values due to Elevated Body Mass Index and Diabetes Mellitus, 2016-21

(1A): Population Attributable Fraction (PAF_{BMI30}) of multiple myeloma cases attributable to elevated body mass index, calculated using hazard ratios corresponding to the lower range of obesity estimates (BMI 30-34.9 kg/m^2).
(1B): Population Attributable Fraction (PAF_{BMI35}) of multiple myeloma cases attributable to elevated body mass index, calculated using hazard ratios corresponding to the upper range of obesity estimates (BMI ≥35 kg/m^2).
(1C): Population Attributable Fraction (PAF_{DM}) of multiple myeloma cases attributable to diabetes mellitus, calculated using hazard ratio estimates for diabetes mellitus.







Abbreviations: PAF, Population Attributable Fraction; NHW, Non-Hispanic White; NHB, Non-Hispanic Black. All Races: Aggregate of Non-Hispanic White + Non-Hispanic Black + Hispanic.

Table S1: Prevalence

Overweight Prevalence												
Year	Non-Hispanic White				Non-Hispanic Black				Hispanic			
	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+
2006	30.50%	35.00%	37.80%	33.80%	32.70%	30.90%	36.70%	27.90%	35.60%	41.70%	39.50%	33.80%
2007	29.60%	36.30%	36.30%	34.70%	31.30%	33.00%	33.00%	39.40%	34.50%	43.60%	43.60%	35.20%
2008	31.20%	33.10%	37.20%	36.80%	29.60%	35.00%	32.30%	31.90%	36.00%	37.70%	41.70%	39.30%
2009	30.70%	37.00%	37.40%	36.30%	30.40%	34.50%	32.70%	36.00%	38.10%	41.30%	37.70%	34.20%
2010	29.80%	35.10%	38.40%	34.80%	30.90%	33.90%	36.80%	29.80%	37.80%	39.90%	37.40%	32.10%
2011	30.10%	36.20%	37.10%	35.30%	30.20%	36.00%	33.00%	36.60%	33.90%	40.60%	42.00%	36.00%
Overweight Total	**30.32%**	**35.45%**	**37.37%**	**35.28%**	**30.85%**	**33.88%**	**34.08%**	**33.60%**	**35.98%**	**40.80%**	**40.32%**	**35.10%**
Obesity Prevalence												
Year	Non-Hispanic White				Non-Hispanic Black				Hispanic			
	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+
2006	25.90%	33.90%	30.90%	20.70%	35.10%	43.10%	42.10%	36.90%	28.70%	34.10%	35.50%	30.50%
2007	26.60%	33.40%	31.80%	21.30%	38.50%	43.20%	39.20%	28.70%	31.70%	34.80%	27.50%	23.20%
2008	25.40%	35.30%	32.80%	18.90%	37.00%	42.50%	41.00%	34.80%	32.80%	38.70%	36.20%	26.30%
2009	25.30%	33.60%	31.10%	19.80%	38.50%	43.60%	41.30%	31.00%	31.80%	39.00%	41.90%	25.30%
2010	25.70%	34.20%	33.70%	20.10%	35.80%	46.10%	40.50%	31.00%	30.60%	40.20%	39.20%	31.70%
2011	25.70%	33.40%	33.40%	20.70%	38.80%	45.50%	46.80%	32.10%	32.20%	37.90%	37.50%	28.40%
Obesity Total	**25.77%**	**33.97%**	**32.28%**	**20.25%**	**37.28%**	**44.00%**	**41.82%**	**32.42%**	**31.30%**	**37.45%**	**36.30%**	**27.57%**
Diabetes Mellitus Prevalence												
Year	Non-Hispanic White				Non-Hispanic Black				Hispanic			
	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+	18-44	45-64	65-74	75+
2006	2.30%	9.00%	15.60%	16.40%	4.80%	14.90%	31.00%	24.80%	2.30%	15.90%	25.10%	25.60%
2007	2.00%	8.50%	17.40%	14.80%	3.10%	17.30%	28.80%	35.80%	2.00%	16.00%	30.10%	29.00%
2008	2.10%	10.20%	17.50%	15.70%	3.00%	16.40%	29.70%	25.00%	2.50%	17.70%	27.80%	21.10%
2009	2.60%	11.10%	16.90%	16.80%	3.50%	19.00%	35.30%	28.60%	3.10%	17.30%	29.30%	33.70%
2010	2.40%	10.10%	19.00%	18.70%	3.90%	17.60%	30.20%	32.20%	3.10%	18.40%	31.70%	37.40%
2011	1.90%	10.40%	19.50%	16.60%	4.30%	16.90%	31.80%	28.20%	3.10%	17.40%	32.00%	26.70%
Diabetes Mellitus Total	**2.22%**	**9.88%**	**17.65%**	**16.50%**	**3.77%**	**17.02%**	**31.13%**	**29.10%**	**2.68%**	**17.12%**	**29.33%**	**28.92%**

Table S2: Total Number of Incident MM Cases Attributable to Elevated Body Mass Index (BMI) in Adults 18 Years or Older, 2016-2021

Year	Age	NHW							NHB							Hispanic							All races						
		PAF 1	95% CI	Attributable	PAF 2	95% CI	Attributable	Total	PAF 1	95% CI	Attributable	PAF 2	95% CI	Attributable	Total	PAF 1	95% CI	Attributable	PAF 2	95% CI	Attributable	Total	PAF 1	95% CI	Attributable	PAF 2	95% CI	Attributable	Total
2016	18-44	9.47%	(-1.0%-22.0%)	29	14.95%	(1.0%-32.0%)	45	302	11.69%	(-1.0%-23.0%)	33	18.48%	(1.0%-35.0%)	53	285	10.49%	(-1.0%-22.0%)	27	16.37%	(1.0%-32.0%)	42	254	10.53%	(-1.0%-22.7%)	89	16.57%	(1.0%-33.0%)	139	841
	45-64	11.60%	(-1.0%-23.0%)	623	18.22%	(1.0%-34.0%)	979	5,372	13.29%	(0.0%-25.0%)	289	21.08%	(2.0%-39.0%)	458	2,172	12.09%	(-2.0%-25.0%)	202	18.67%	(1.0%-35.0%)	312	1,673	12.09%	(-1.0%-24.3%)	1,114	18.98%	(1.3%-36.0%)	1,749	9,217
	65-74	11.13%	(-2.0%-23.0%)	677	17.33%	(1.0%-33.0%)	1,054	6,082	13.47%	(-1.0%-26.0%)	248	21.08%	(2.0%-39.0%)	389	1,843	11.60%	(-1.0%-25.0%)	116	18.22%	(1.0%-36.0%)	182	998	11.67%	(-1.3%-24.7%)	1,041	18.21%	(1.3%-36.0%)	1,625	8,923
	75+	8.49%	(-2.0%-19.0%)	562	13.07%	(0.0%-26.0%)	865	6,620	11.75%	(0.0%-23.0%)	184	18.82%	(2.0%-36.0%)	294	1,563	10.74%	(-1.0%-22.0%)	107	16.88%	(1.0%-33.0%)	168	994	9.29%	(-1.0%-21.3%)	852	14.46%	(1.0%-31.7%)	1,327	9,177
	All age groups	**10.33%**	**(-1.0%-21.0%)**	**1,899**	**16.25%**	**(1.0%-31.0%)**	**2,986**	**18,377**	**12.34%**	**(0.0-24%)**	**724**	**19.55%**	**(2.0%-37.0%)**	**1,146**	**5,863**	**10.98%**	**(-1.0%-23.0%)**	**430**	**17.09%**	**(1.0%-33.0%)**	**670**	**3,919**	**10.99%**	**(-1.0%-22.0%)**	**3,094**	**17.38%**	**(1.0%-32.0%)**	**4,894**	**28,158**
2017	18-44	9.66%	(-1.0%-23.0%)	36	15.17%	1.0%-33.0%)	56	371	12.43%	(0.0%-24.0%)	33	19.62%	(1.0%-37.0%)	52	266	11.18%	(-1.0%-23.0%)	28	17.41%	(1.0%-33.0%)	44	253	10.92%	(-0.7%-23.3%)	97	17.14%	(1.0%-35.3%)	153	891
	45-64	11.70%	(-1.0%-24.0%)	614	18.15%	(1.0%-35.0%)	953	5,248	13.54%	(0.0%-26.0%)	319	21.26%	(1.0%-39.0%)	501	2,358	12.48%	(-2.0%-26.0%)	214	19.04%	(0.0%-36.0%)	326	1,712	12.31%	(-1.0%-25.3%)	1,147	19.10%	(0.7%-36.7%)	1,780	9,318
	65-74	11.44%	(-1.0%-23.0%)	685	17.66%	(1.0%-34.0%)	1,057	5,986	12.97%	(-1.0%-25.0%)	234	20.15%	(1.0%-38.0%)	364	1,808	11.70%	(-3.0%-24.0%)	141	18.15%	(0.0%-32.0%)	220	1,209	11.78%	(-1.7%-24.0%)	1,060	18.22%	(0.7%-34.7%)	1,641	9,003
	75+	8.81%	(-2.0%-20.0%)	566	13.42%	(0.0%-27.0%)	861	6,418	10.85%	(-2.0%-23.0%)	159	16.56%	(0.0%-32.0%)	243	1,467	9.28%	(-2.0%-21.0%)	88	14.19%	(0.0%-29.0%)	135	952	9.20%	(-2.0%-21.3%)	813	14.02%	(0.0%-29.3%)	1,239	8,837
	All age groups	**10.52%**	**(-1.0%-22.0%)**	**1,896**	**16.38%**	**(0.0%-31.0%)**	**2,952**	**18,024**	**12.77%**	**(0.0%-25.0%)**	**753**	**20.07%**	**(1.0%-38.0%)**	**1,184**	**5,899**	**11.44%**	**(-1.0%-23.0%)**	**472**	**17.68%**	**(0.0%-34.0%)**	**729**	**4,126**	**10.91%**	**(-1.0%-22.0%)**	**3,061**	**17.20%**	**(0.0%-31.0%)**	**4,825**	**28,049**
2018	18-44	9.47%	(-1.0%-24.0%)	41	14.80%	(1.0%-32.0%)	64	433	11.96%	(0.0%-23.0%)	34	18.96%	(1.0%-35.0%)	54	287	11.51%	(-1.0%-24.0%)	27	17.90%	(1.0%-32.0%)	43	238	10.73%	(-0.7%-23.7%)	103	16.82%	(1.0%-33.0%)	161	958
	45-64	11.84%	(0.0%-24.0%)	577	18.59%	(1.0%-34.0%)	906	4,874	13.52%	(0.0%-26.0%)	328	21.12%	(2.0%-39.0%)	513	2,428	12.92%	(-1.0%-26.0%)	242	20.04%	(1.0%-35.0%)	376	1,876	12.50%	(-0.3%-25.3%)	1,148	19.55%	(1.3%-36.0%)	1,795	9,178
	65-74	11.59%	(-1.0%-24.0%)	696	17.95%	(1.0%-33.0%)	1,078	6,004	13.00%	(0.0%-25.0%)	257	20.42%	(2.0%-39.0%)	403	1,973	11.84%	(-1.0%-26.0%)	134	18.59%	(1.0%-36.0%)	210	1,130	11.92%	(-0.7%-25.0%)	1,086	18.56%	(1.3%-36.0%)	1,690	9,107
	75+	8.38%	(-3.0%-20.0%)	564	12.56%	(0.0%-26.0%)	845	6,728	11.65%	(-1.0%-23.0%)	177	18.32%	(2.0%-36.0%)	279	1,523	10.28%	(-2.0%-23.0%)	116	15.68%	(1.0%-33.0%)	176	1,126	9.14%	(-2.0%-22.0%)	857	13.87%	(1.0%-31.7%)	1,300	9,377
	All age groups	**10.48%**	**(-1.0%-22.0%)**	**1,890**	**16.36%**	**(1.0%-31.0%)**	**2,952**	**18,038**	**12.53%**	**(0.0%-24.0%)**	**779**	**19.76%**	**(2.0%-37.0%)**	**1,227**	**6,211**	**11.90%**	**(-1.0%-24.0%)**	**520**	**18.45%**	**(1.0%-33.0%)**	**807**	**4,370**	**10.92%**	**(-1.0%-22.0%)**	**3,127**	**17.13%**	**(0.0%-32.0%)**	**4,904**	**28,620**
2019	18-44	9.39%	(-1.0%-23.0%)	37	14.78%	(1.0%-34.0%)	58	393	12.32%	(0.0%-24.0%)	27	19.60%	(1.0%-37.0%)	44	223	11.40%	(-1.0%-23.0%)	25	17.69%	(1.0%-34.0%)	39	218	10.70%	(-0.7%-23.3%)	89	16.83%	(1.0%-35.0%)	140	834
	45-64	11.71%	(-1.0%-24.0%)	610	18.26%	(1.0%-35.0%)	951	5,205	13.67%	(0.0%-26.0%)	343	21.51%	(1.0%-40.0%)	539	2,507	13.18%	(-1.0%-26.0%)	216	20.40%	(1.0%-38.0%)	335	1,642	12.49%	(-0.7%-25.3%)	1,169	19.51%	(1.0%-37.7%)	1,825	9,354
	65-74	11.21%	(-1.0%-23.0%)	707	17.40%	(1.0%-33.0%)	1,098	6,310	13.07%	(0.0%-25.0%)	267	20.63%	(1.0%-39.0%)	421	2,039	11.71%	(0.0%-26.0%)	132	18.26%	(1.0%-39.0%)	207	1,131	11.67%	(-0.3%-24.7%)	1,106	18.20%	(1.0%-37.0%)	1,725	9,481
	75+	8.52%	(-3.0%-20.0%)	614	12.91%	(1.0%-26.0%)	930	7,210	11.08%	(-1.0%-23.0%)	167	17.26%	(1.0%-33.0%)	261	1,511	9.63%	(-2.0%-21.0%)	111	14.94%	(0.0%-30.0%)	173	1,157	9.04%	(-2.0%-21.3%)	893	13.81%	(0.7%-29.7%)	1,364	9,878
	All age groups	**10.38%**	**(-1.0%-22.0%)**	**1,985**	**16.23%**	**(1.0%-31.0%)**	**3,102**	**19,118**	**12.76%**	**(0.0%-25.0%)**	**801**	**20.21%**	**(1.0%-38.0%)**	**1,269**	**6,280**	**11.95%**	**(-1.0%-24.0%)**	**496**	**18.54%**	**(1.0%-35.0%)**	**769**	**4,149**	**10.78%**	**(-1.0%-22.0%)**	**3,186**	**17.18%**	**(1.0%-31.0%)**	**5,076**	**29,547**
2020	18-44	9.46%	(-2.0%-23.0%)	29	14.83%	(0.0%-33.0%)	46	311	11.84%	(0.0%-23.0%)	29	18.67%	(1.0%-35.0%)	46	246	11.19%	(-2.0%-23.0%)	26	17.22%	(0.0%-33.0%)	40	232	10.71%	(-1.3%-23.0%)	85	16.73%	(0.3%-33.7%)	132	790
	45-64	11.79%	(-1.0%-24.0%)	601	18.37%	(1.0%-35.0%)	935	5,093	14.22%	(0.0%-27.0%)	375	22.27%	(2.0%-41.0%)	588	2,639	13.40%	(-1.0%-26.0%)	238	20.68%	(1.0%-39.0%)	367	1,775	12.77%	(-0.7%-25.7%)	1,214	19.88%	(1.3%-38.3%)	1,890	9,507
	65-74	11.91%	(-1.0%-24.0%)	745	18.37%	(1.0%-35.0%)	1,150	6,259	13.25%	(-1.0%-26.0%)	262	20.60%	(1.0%-39.0%)	408	1,979	11.79%	(-1.0%-26.0%)	154	18.37%	(1.0%-38.0%)	240	1,306	12.17%	(-1.0%-25.3%)	1,161	18.83%	(1.0%-37.3%)	1,797	9,544
	75+	8.53%	(-2.0%-19.0%)	612	12.91%	(1.0%-26.0%)	927	7,179	10.67%	(-1.0%-22.0%)	171	16.84%	(1.0%-33.0%)	270	1,603	11.00%	(-1.0%-22.0%)	114	17.24%	(1.0%-33.0%)	179	1,036	9.14%	(-1.3%-21.0%)	897	14.01%	(1.0%-30.7%)	1,375	9,818
	All age groups	**10.52%**	**(-1.0%-22.0%)**	**1,983**	**16.40%**	**(1.0%-32.0%)**	**3,091**	**18,842**	**12.71%**	**(0.0%-25.0%)**	**822**	**19.99%**	**(1.0%-38.0%)**	**1,293**	**6,468**	**11.88%**	**(-1.0%-24.0%)**	**517**	**18.35%**	**(1.0%-35.0%)**	**798**	**4,349**	**10.80%**	**(-1.0%-22.0%)**	**3,202**	**16.99%**	**(0.0%-32.0%)**	**5,040**	**29,659**
2021	18-44	9.50%	(-1.0%-23.0%)	42	14.83%	(1.0%-34.0%)	65	437	12.44%	(0.0%-24.0%)	38	19.59%	(1.0%-37.0%)	60	309	11.28%	(-1.0%-23.0%)	29	17.53%	(1.0%-34.0%)	45	256	10.86%	(-0.7%-23.3%)	109	16.99%	(1.0%-35.0%)	170	1,002
	45-64	11.70%	(-1.0%-24.0%)	612	18.08%	(1.0%-35.0%)	945	5,226	14.27%	(0.0%-27.0%)	391	22.13%	(2.0%-41.0%)	606	2,739	12.97%	(-1.0%-26.0%)	227	19.89%	(1.0%-38.0%)	347	1,747	12.65%	(-0.7%-25.7%)	1,229	19.55%	(1.3%-38.0%)	1,899	9,711
	65-74	11.78%	(-1.0%-24.0%)	836	18.14%	(1.0%-35.0%)	1,288	7,096	14.31%	(0.0%-27.0%)	315	22.36%	(2.0%-41.0%)	492	2,202	11.70%	(-1.0%-26.0%)	173	18.08%	(1.0%-37.0%)	267	1,476	12.28%	(-0.7%-25.7%)	1,324	19.00%	(1.3%-37.7%)	2,047	10,775
	75+	8.72%	(-2.0%-20.0%)	648	13.14%	(1.0%-27.0%)	977	7,433	11.45%	(-1.0%-23.0%)	208	17.64%	(1.0%-34.0%)	321	1,818	10.57%	(-2.0%-22.0%)	121	16.24%	(0.0%-32.0%)	187	1,149	9.40%	(-1.7%-21.7%)	978	14.27%	(0.7%-31.0%)	1,484	10,400
	All age groups	**10.52%**	**(-1.0%-22.0%)**	**2,124**	**16.30%**	**(1.0%-32.0%)**	**3,291**	**20,192**	**13.15%**	**(0.0%-25.0%)**	**929**	**20.59%**	**(2.0%-39.0%)**	**1,455**	**7,068**	**11.81%**	**(-1.0%-24.0%)**	**547**	**18.26%**	**(1.0%-35.0%)**	**845**	**4,628**	**10.63%**	**(-1.0%-22.0%)**	**3,389**	**16.96%**	**(0.0%-32.0%)**	**5,407**	**31,887**
2016-21 Weighted Average		**10.46%**	**~**	**3,062**	**16.32%**	**~**	**3,062**	**18,765**	**12.72%**	**~**	**1,262**	**20.04%**	**~**	**1,262**	**6,298**	**11.67%**	**~**	**770**	**18.08%**	**~**	**770**	**4,257**	**10.83%**	**~**	**5,024**	**17.14%**	**~**	**5,024**	**29,320**

Abbreviations: PAF, Population Attributable Fraction; CI, Confidence Interval; NHW, Non-Hispanic White; NHB, Non-Hispanic Black
All races: Non-Hispanic White + Non-Hispanic Black + Hispanic

Table S3: Total Number of Incident MM Cases Attributable to Diabetes Mellitus (DM) in Adults 18 Years or Older, 2016-21

Year	Age	NHW				NHB				Hispanic				All races			
		PAF	95% CI	Attributable	Total	PAF	95% CI	Attributable	Total	PAF	95% CI	Attributable	Total	PAF	95% CI	Attributable	Total
2016	18-44	0.03%	0.0%-1.0%	0	302	0.90%	0.0%-1.0%	3	285	0.04%	0.0%-1.0	0	254	0.33%	0.0%-1.0%	3	841
	45-64	1.27%	1.0%-2.0%	68	5,372	2.18%	1.0%-3.0%	47	2,172	2.32%	1.0%-3.0%	39	1,673	1.68%	1.0%-2.7%	154	9,217
	65-74	2.29%	1.0%-3.0%	139	6,082	4.44%	3.0%-6.0%	82	1,843	1.27%	2.0%-5.0%	13	998	2.62%	2.0%-4.7%	234	8,923
	75+	2.41%	1.0%-3.0%	159	6,620	3.59%	2.0%-5.0%	56	1,563	3.68%	2.0%-6.0%	37	994	2.75%	1.7%-4.7%	252	9,177
	All age groups	**1.03%**	**1.0%-2.0%**	**189**	**18,377**	**1.62%**	**1.0%-2.0%**	**95**	**5,863**	**1.05%**	**1.0%-2.0%**	**41**	**3,919**	**1.25%**	**1.0%-2.0%**	**352**	**28,158**
2017	18-44	0.01%	0.0%-0.0%	0	371	0.35%	0.0%-1.0%	1	266	0.01%	0.0%-0.0%	0	253	0.11%	0.0%-0.3%	1	891
	45-64	1.16%	1.0%-2.0%	61	5,248	2.51%	1.0%-4.0%	59	2,358	2.34%	1.0%-3.0%	40	1,712	1.72%	1.0%-3.0%	160	9,318
	65-74	2.53%	2.0%-4.0%	152	5,986	4.13%	2.0%-6.0%	75	1,808	1.16%	2.0%-6.0%	14	1,209	2.67%	2.0%-5.3%	240	9,003
	75+	2.16%	1.0%-3.0%	138	6,418	5.09%	3.0%-7.0%	75	1,467	4.16%	2.0%-6.0%	40	952	2.86%	2.0%-5.3%	253	8,837
	All age groups	**1.01%**	**1.0%-1.0%**	**182**	**18,024**	**1.65%**	**1.0%-2.0%**	**97**	**5,899**	**1.07%**	**1.0%-2.0%**	**44**	**4,126**	**1.29%**	**1.0%-1.0%**	**361**	**28,049**
2018	18-44	0.01%	0.0%-1.0%	0	433	0.30%	0.0%-1.0%	1	287	0.10%	0.0%-1.0%	0	238	0.12%	0.0%-1.0%	1	958
	45-64	1.50%	1.0%-2.0%	73	4,874	2.39%	1.0%-3.0%	58	2,428	2.58%	2.0%-4.0%	48	1,876	1.96%	1.3%-3.0%	180	9,178
	65-74	2.55%	2.0%-4.0%	153	6,004	4.27%	2.0%-6.0%	84	1,973	1.50%	2.0%-6.0%	17	1,130	2.80%	2.0%-5.3%	255	9,107
	75+	2.30%	1.0%-3.0%	155	6,728	3.61%	2.0%-5.0%	55	1,523	3.06%	2.0%-5.0%	34	1,126	2.60%	1.7%-4.3%	244	9,377
	All age groups	**1.08%**	**1.0%-2.0%**	**195**	**18,038**	**1.52%**	**1.0%-2.0%**	**95**	**6,211**	**1.14%**	**1.0%-2.0%**	**50**	**4,370**	**1.28%**	**1.0%-2.0%**	**365**	**28,620**
2019	18-44	0.10%	0.0%-1.0%	0	393	0.54%	0.0%-1.0%	1	223	0.33%	0.0%-1.0%	1	218	0.28%	0.0%-1.0%	2	834
	45-64	1.65%	1.0%-2.0%	86	5,205	2.76%	2.0%-4.0%	69	2,507	2.52%	1.0%-4.0%	41	1,642	2.10%	1.3%-3.3%	197	9,354
	65-74	2.46%	1.0%-3.0%	155	6,310	5.00%	3.0%-7.0%	102	2,039	1.65%	2.0%-6.0%	19	1,131	2.91%	2.0%-5.3%	276	9,481
	75+	2.44%	1.0%-3.0%	176	7,210	4.08%	2.0%-6.0%	62	1,511	4.78%	3.0%-7.0%	55	1,157	2.97%	2.0%-5.3%	293	9,878
	All age groups	**1.17%**	**1.0%-2.0%**	**224**	**19,118**	**1.81%**	**1.0%-3.0%**	**113**	**6,280**	**1.30%**	**1.0%-2.0%**	**54**	**4,149**	**1.13%**	**1.0%-2.0%**	**334**	**29,547**
2020	18-44	0.04%	0.0%-1.0%	0	311	0.68%	0.0%-1.0%	2	246	0.34%	0.0%-1.0%	1	232	0.33%	0.0%-1.0%	3	790
	45-64	1.48%	1.0%-2.0%	75	5,093	2.57%	2.0%-4.0%	68	2,639	2.68%	2.0%-4.0%	48	1,775	2.01%	1.7%-3.3%	191	9,507
	65-74	2.76%	2.0%-4.0%	173	6,259	4.32%	3.0%-6.0%	86	1,979	1.48%	3.0%-6.0%	19	1,306	2.91%	2.7%-5.3%	278	9,544
	75+	2.73%	2.0%-4.0%	196	7,179	4.60%	3.0%-7.0%	74	1,603	5.30%	3.0%-8.0%	55	1,036	3.31%	2.7%-6.3%	325	9,818
	All age groups	**1.17%**	**1.0%-2.0%**	**221**	**18,842**	**1.76%**	**1.0%-2.0%**	**114**	**6,468**	**1.44%**	**1.0%-2.0%**	**63**	**4,349**	**1.06%**	**1.0%-2.0%**	**313**	**29,659**
2021	18-44	0.00%	0.0%-1.0%	0	437	0.84%	0.0%-1.0%	3	309	0.36%	0.0%-1.0%	1	256	0.35%	0.0%-1.0%	4	1,002
	45-64	1.55%	1.0%-2.0%	81	5,226	2.48%	1.0%-4.0%	68	2,739	2.54%	2.0%-4.0%	44	1,747	1.99%	1.3%-3.3%	193	9,711
	65-74	2.85%	2.0%-4.0%	202	7,096	4.55%	3.0%-6.0%	100	2,202	1.55%	3.0%-6.0%	23	1,476	3.02%	2.7%-5.3%	325	10,775
	75+	2.43%	1.0%-3.0%	181	7,433	4.06%	2.0%-6.0%	74	1,818	3.85%	2.0%-6.0%	44	1,149	2.87%	1.7%-5.0%	299	10,400
	All age groups	**1.17%**	**1.0%-2.0%**	**237**	**20,192**	**1.76%**	**1.0%-2.0%**	**124**	**7,068**	**1.44%**	**1.0%-2.0%**	**67**	**4,628**	**1.07%**	**1.0%-2.0%**	**341**	**31,887**
2016-21 Weighted Average		**1.11%**	**~**	**208**	**18,765**	**1.69%**	**~**	**106**	**6,298**	**1.25%**	**~**	**53**	**4,257**	**1.17%**	**~**	**344**	**29,320**

Abbreviations: PAF, Population Attributable Fraction; CI, Confidence Interval; NHW, Non-Hispanic White; NHB, Non-Hispanic Black
All Races: Non-Hispanic White + Non-Hispanic Black + Hispanic