SHORT COMMUNICATION

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Incidence of thyroid cancer in England by ethnic group, 2001–2007

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Background: Thyroid cancer incidence is increasing worldwide, but with large variations in incidence that may reflect either diagnostic bias or true ethnic differences. We sought to determine the effect of ethnicity on the incidence of thyroid cancer in England, a multiethnic population with a single health-care system.

Methods: We analysed 11 263 thyroid cancer registrations with ethnicity obtained by linkage to the Hospital Episodes Statistics database. Incidence rate ratios (RRs) adjusted for age, sex and income were calculated for the six main non-White ethnic groups in England compared with Whites and to each other.

Results: Thyroid cancer incidence was higher in all ethnic groups, except Indians, compared with Whites: in Pakistanis (RR 1.79, 99% floating confidence interval (FCI) 1.47–2.19); Bangladeshis (RR 1.99, 99% FCI 1.46–2.71); Black Africans (RR 1.69, 99% FCI 1.34–2.13); Black Caribbeans (RR 1.56, 99% FCI 1.25–1.93); and Chinese (RR 2.14, 99% FCI 1.63–2.80).

Conclusion: The risk of thyroid cancer in England varies significantly by ethnicity. The elevated incidence in most ethnic minorities is unlikely to be due to diagnostic bias and warrants further investigation.

The worldwide incidence of thyroid cancer is increasing (Ferlay *et al*, 2010) with considerable international variation in incidence (Woodruff *et al*, 2010). Thyroid cancer is an indolent disease often detected by ultrasound of incidentally discovered nodules and this may be due to diagnostic bias rooted in differential access to health care. (Davies and Welch, 2006). However, other studies suggest changes in risk factors such as iodine supplementation, obesity and the frequency of use of medical diagnostic radiation may be partly responsible (Blomberg *et al*, 2012; Zhao *et al*, 2012).

Studying incidence in different ethnic groups in a single country can help to understand this variation (and offer insights into aetiology) as similar diagnostic, reporting and registration procedures are used regardless of ethnic group (Parkin and Khlat, 1996). In England, there were 2208 new cases of thyroid cancer in 2010 with incidence rates having increased by more than 150% since 1975 (Office For National Statistics, 2011). As a multiethnic nation (14% of England's population were 'non-White' in 2011 (Office For National Statistics, 2012) with a unified health-care system, England provides an ideal setting in which to do this. Since 1995, self-assigned ethnicity has also been recorded in the National Health System's Hospital Episodes Statistics (HES) database (using the same classification system as used in the census) and HES records can now be linked to cancer registrations, providing more reliable information on ethnicity (The Health And Social Care Information Centre, 2011) and allowing individual ethnic groups to be analysed separately for the first time (Jack *et al*, 2006).

In this paper, we compare the incidence of thyroid cancer among the six largest 'non-White' ethnic groups in England with each other and with Whites using self-assigned ethnicity.

MATERIALS AND METHODS

We obtained data from the National Cancer Intelligence Network for all cancer registrations from 2001 to 2007 in England with the following information: cancer site coded to the International Classifications of Diseases, 10th Revision (ICD-10; World Health

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Organisation, 1992); morphology coded to the ICD of Oncology, 2nd and 3rd Revisions (ICD-O-2 and ICD-O-3; World Health Organisation, 1990; World Health Organisation, 2000); deprivation assessed from the income domain of the Index of Multiple Deprivation 2007 (IMD 2007; Noble *et al*, 2008); age at diagnosis of cancer; sex; ethnicity and regional cancer registry. To determine population incidence data, we used mid-year population estimates produced by the Office of National Statistics from 2001 to 2007 stratified by age, sex and ethnicity.

We used ICD-10 code C73 to identify all thyroid cancers and morphology codes to identify follicular and papillary subtypes. NCRS obtained the self-assigned ethnicity for each cancer registration by record linkage to the HES database. We classified ethnicity as White, Indian, Pakistani and Bangladeshi, with the three groups combined to form the category 'South Asian', Black African, Black Caribbean (again both combined to form the category 'Black') and Chinese.

We estimated age-standardised rates of cancer per 100 000 person-years for all ethnic groups using direct standardisation to the 1960 Segi world population (Segi, 1960) with age divided into six categories: (<40, 40–49, 50–59, 60–69, 70–79, $80+$). We used Poisson regression to estimate incidence rate ratios (RRs) comparing each ethnic group (and 'South Asians' and 'Blacks') with Whites adjusting for sex, age and deprivation. We performed pre-specified subgroup analyses by sex (male *vs* female), age (<50 *vs* $\geqslant 50$ years), deprivation (quintile 1 *vs* quintiles 2–4 of the income domain of the index of IMD 2007) and by tumour type (follicular *vs* papillary).

We chose the age division so that cancer rates in first *vs* later generations of South Asians could be examined – the percentage of South Asians born outside the United Kingdom is 97% for those aged $\geqslant 50$ years, whereas for those aged <50 years the majority (58%) were born in the United Kingdom (Office For National Statistics, 2001). Subgroup analysis by age for Blacks and Chinese was also done for completeness but it does not allow the same discrimination by generation.

When comparing 'South Asians' and 'Blacks' with Whites, we present results as RRs with 99% confidence intervals (owing to multiple tests performed across subgroups.) When comparing the individual ethnic groups, we use 99% floating confidence intervals (FCIs), calculated using the method of floating absolute risks, which enable valid comparisons between any two groups, even if neither one is the baseline (Easton *et al*, 1991; Plummer, 2004).

As ethnicity information was not complete for all registered cancers, we did a sensitivity analysis using multiple imputations of the missing ethnicity values age, sex, income domain of IMD 2007, site of cancer and region.

Analyses were performed using Stata (version 12; StataCorp, College Station, TX, USA) and R statistical software packages (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Table 1 shows socio-demographic information from the 2001 census by ethnic group. All non-White groups are younger than Whites and all except Chinese are also more deprived, with Pakistanis, Bangladeshis and Black Africans being the most deprived. About half of the South Asian and Black Caribbean populations were born in the United Kingdom compared with only about 30% of Black Africans and Chinese.

Table 2 shows the total number of thyroid cancer registrations with missing ethnicity values for each subtype.

For all thyroid cancers (Figure 1), there was a statistically significantly higher incidence in all ethnic groups (except Indians) compared with Whites, with significant heterogeneity between the groups ($P<0.001$). Among South Asians, the rates were statistically significantly higher in both British Pakistanis (RR 1.79, 99% FCI 1.47–2.19) and British Bangladeshis (RR 1.99, 99% FCI 1.46–2.71), but not in British Indians (RR 1.09, 99% FCI 0.90 to 1.32), demonstrating heterogeneity between these groups ($P<0.001$). In Blacks, the incidence of thyroid cancer was also statistically

Table 1. Comparison of demographic characteristics by ethnic group in England in 2001

	White		Indian		Pakistani		Bangladeshi		Black African		Black Caribbean		Chinese	
	N	**(%)**	***N***	**(%)**	***N***	**(%)**	***N***	**(%)**	***N***	**(%)**	***N***	**(%)**	***N***	**(%)**
Census data for 2001														
Total population	42 747 136	(100.0)	1 028 546	(100.0)	706 539	(100.0)	275 394	(100.0)	475 938	(100.0)	561 246	(100.0)	220 681	(100.0)
Sex														
Male	20 828 644	(48.7)	511 204	(49.7)	358 043	(50.7)	138 972	(50.5)	229 103	(48.1)	259 881	(46.3)	105 913	(48.0)
Age														
<50	27 665 393	64.7	828 200	80.5	625 118	88.5	248 841	90.4	432 985	91.0	426 424	76.0	184 675	83.7
$50+$	15 081 743	35.3	200 346	19.5	81 421	11.5	26 553	9.6	42 953	9.0	134 822	24.0	36 006	16.3
Deprivation														
Low income (quintile 1)	7 305 527	(17.1)	347 098	(33.7)	455 710	(64.5)	198 884	(72.2)	277 858	(58.4)	292 537	(52.1)	49 427	(22.4)
Middle income (quintiles 2,3 and 4)	26 315 786	(61.6)	563 939	(54.8)	222 038	(31.4)	69 325	(25.2)	177 234	(37.2)	245 103	(43.7)	123 994	(56.2)
High income (quintile 5)	9 125 823	(21.3)	117 509	(11.4)	28 791	(4.1)	7185	(2.6)	20 846	(4.4)	23 606	(4.2)	47 260	(21.4)
Country of birth														
United Kingdom	41 911 150	(98.0)	472 545	(45.9)	387 198	(54.8)	127 902	(46.4)	161 050	(33.8)	324 764	(57.9)	62 209	(28.2)
Other	835 986	(2.0)	556 001	(54.1)	319 341	(45.2)	147 492	(53.6)	314 888	(66.2)	236 482	(42.1)	158 472	(71.8)

Table 2. Distribution of registered cancers from 2001–2007 in England by ethnic group (percentages in brackets)

	White	Indian	Pakistani	Bangladeshi	Black African	Black Caribbean	Chinese	All other ethnicities	No ethnicity recorded	Total
All cancers	7396 (65.7)	178 (1.6)	170 (1.5)	70 (0.6)	124 (1.1)	142 (1.3)	90 (0.8)	1216 (10.8)	1877 (16.7)	11 263
Follicular cancer	1762 (70.7)	20 (0.8)	39 (1.6)	23 (0.9)	32 (1.3)	43 (1.7)	13 (0.5)	203 (8.2)	357 (14.3)	2492
Papillary cancer	4195 (63.8)	128 (2.0)	115 (1.8)	38 (0.6)	67 (1.0)	73 (1.1)	72 (1.1)	808 (12.3)	1076 (16.4)	6572
Other cancer	1439 (65.4)	30 (1.4)	16 (0.7)	9 (0.4)	223 (1.1)	26 (1.2)	5 (0.2)	205 (9.3)	444 (20.2)	2199

significantly higher in both Africans (RR 1.69, 99% FCI 1.34–2.13) and Caribbeans (RR 1.56, 99% FCI 1.25–1.93) but with no heterogeneity between these groups ($P = 0.5$). The risk for thyroid cancer was highest in Chinese (RR 2.14, 99% FCI 1.63–2.80).

The increased risk in the non-White ethnic groups was evident in men and women, in those aged <50 and $\geqslant 50$ years and in those who were most deprived (quintile 1), as well as those in quintiles 2–5.

However, as also shown in Figure 1, in South Asians the rate of follicular thyroid cancer was not statistically significantly higher than in British Whites, whereas the RR for papillary thyroid cancer was statistically significantly higher (RR 1.47, 99% CI 1.25–1.73). This difference is mainly because of the statistically significantly lower incidence of follicular thyroid cancer in Indians (RR 0.55, 99% FCI 0.31–0.98), whereas the incidence of both follicular and papillary thyroid cancers were statistically significantly higher in both the Pakistanis (follicular: RR 1.95, 99% FCI 1.29–2.96, papillary: RR 1.85, 99% FCI 1.46–2.36) and Bangladeshis (follicular: RR 3.15, 99% FCI 1.84–5.41, papillary: RR 1.63, 99% FCI 1.07–2.07).

In Blacks, the incidence of both follicular and papillary thyroid cancers was statistically significantly higher than in Whites. However, the incidence rate ratios were statistically significantly higher in follicular (RR 2.09, 99% CI 1.53–2.86) than in papillary (RR 1.34, 99% CI 1.07–1.68), with significant heterogeneity between the two ($P = 0.003$).

The opposite pattern was seen in Chinese, with incidence rate ratios being statistically significantly higher for papillary cancer (RR 2.64, 99% FCI 1.94–3.58) than follicular cancer (RR 1.38, 99% FCI 0.68–2.83), again with significant heterogeneity between the two ($P = 0.03$).

In the sensitivity analysis, which assigned missing values using multiple imputation, results similar to those shown in Figure 1 were obtained as shown in Supplementary Figure 2 (online).

DISCUSSION

In this study, we compared, for the first time, incidence rates for thyroid cancers in the main 'non-White' ethnic groups in England-South Asian (Indian, Pakistani and Bangladeshi), Black (African and Caribbean) and Chinese with Whites and with each other. There was considerable variation by ethnic group, even when gender, age and socio-economic factors are taken into account. Overall, the risk of thyroid cancer was significantly higher in all 'non-White' ethnic groups except Indians, with the increased risk also seen in the subgroupings by gender, age, deprivation and histology. There were significant differences in the incidence of thyroid cancer among South Asians with the risk of both follicular and papillary cancer being higher in Pakistanis and Bangladeshis but not in Indians. The higher rate of thyroid cancer in Blacks was driven principally by an increased risk of follicular cancer, whereas in Chinese, the higher rate was due to an increased risk of papillary cancer.

There is only one previous report of thyroid cancer incidence by ethnicity in England (using name analysis), which showed a higher thyroid cancer incidence in South Asians compared with non-South Asians, but only in females (Winter *et al*, 1999). Studies from the United States have shown a lower incidence in African Americans compared with Whites (Ries *et al*, 2008), in contrast to our findings, but also found the highest incidence in South East Asians and Chinese, consistent with our results (Spitz *et al*, 1988).

The different patterns of cancer risk seen across each of the different ethnic groups as well as differences by sex, age, deprivation and tumour subtype suggest that our findings are unlikely to be due to systematic over-reporting of thyroid cancer in the ethnic minority groups. Our previous work using the same data set also showed reduced risks of gastrointestinal cancers in the same ethnic groups that further supports the absence of an over-reporting bias (Ali *et al*, 2013). The differences we found are also between populations with equal access to health care (Nazroo *et al*, 2009) and there is evidence that non-White ethnic groups are less likely to access services such as cancer screening (Szczepura *et al*, 2008). It is, therefore, very unlikely that increased access (diagnostic bias) could explain the increased incidence in the non-White groups, although of course there may be other confounding factors, and studies with individual-level exposure are needed to address this.

The environmental and genetic factors that lead to thyroid cancer are not fully known, but there are some established risk factors – pre-existing thyroid disease, iodine status and exposure to radiation (Navarro Silvera *et al*, 2005). Insufficient iodine in the diet is associated with an increase in the risk of follicular thyroid cancer and it is therefore less prevalent in areas where fortification of salt with iodine is the norm. By contrast, a diet high in iodine, such as one rich in sea food, has been associated with an increased risk in papillary thyroid cancer (Delange, 1998). In the United Kingdom, salt iodisation is long standing and there is no evidence of difference in iodine status by ethnic group and this is therefore unlikely to explain the ethnic variation. The reduced incidence of follicular thyroid cancer in Indians and increased risk of papillary thyroid cancer is striking (a similar pattern is also seen for Chinese) and would be consistent with increased iodine levels but there is no evidence of this. However, some groups – Pakistanis, Bangladeshis and Blacks – have an increased risk of both follicular and papillary cancers, and this cannot be explained by their iodine status.

Other risk factors that are more contentious include an association between increased BMI and thyroid cancer, diabetes, female reproductive factors and exposure to endocrine-disrupting agents (Meinhold *et al*, 2010; Peterson *et al*, 2012; Zhao *et al*, 2012). Although there are some differences in these risk factors (for example, obesity) by ethnic group (Sproston and Mindell, 2006), it is unlikely that this could explain the significant differences in risk we have observed.

Our finding of an increased risk in Blacks is in contrast to studies in the United States but this is likely to be mainly due to a reduction in the recording of thyroid cancer cases in African Americans owing to their inferior access to health care

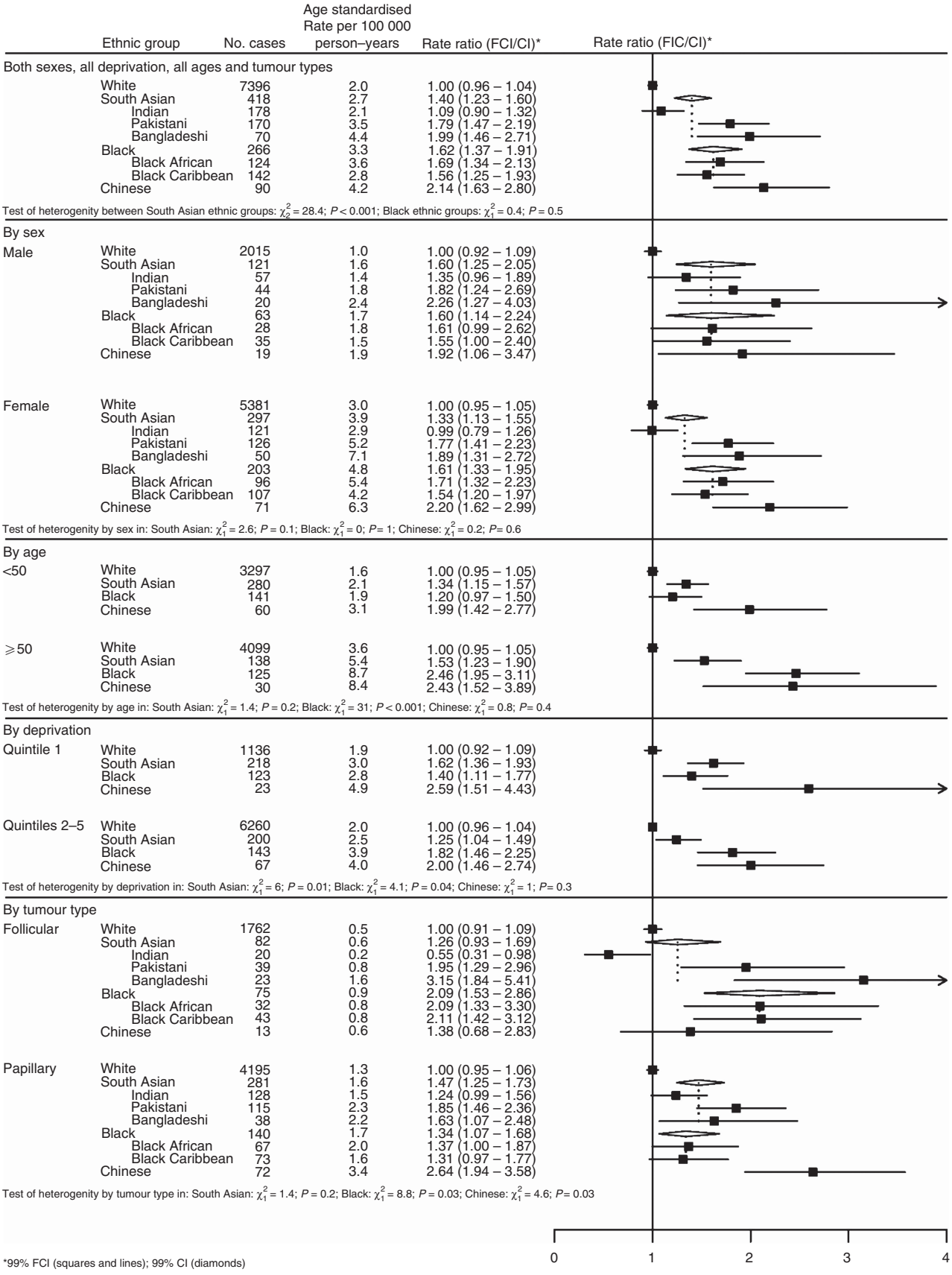

Figure 1. Age-standardised incidence rates and rate ratios (adjusted by age, sex and deprivation) for all thyroid cancer by individual ethnic group compared with Whites. Bangladeshis compared with British Whites. Subgroups show rates and rate ratios subdivided by sex, age, deprivation and by histology (follicular and papillary).

(Morris *et al*, 2008) compared with US Whites. It could also reflect differences in the ancestry of the US and UK Black populations, with UK Blacks having migrated relatively recently and coming from the Caribbean and East Africa, whereas US Black immigration is more historic and largely from West Africa (Nazroo *et al*, 2007).

The increased risk we found in Chinese is consistent with studies in the United States where a higher frequency of thyroid nodules and goitre and reduced consumption of carotenoids explained more than half the increased risk (Haselkorn *et al*, 2003). Furthermore, the incidence of thyroid cancer in Hong Kong, where the majority of British Chinese originate, is even higher than that in British Chinese (Ferlay *et al*, 2010). In contrast, rates in the countries of origin for all other ethnic groups in our study is much lower (Ferlay *et al*, 2010).

The main strength of our study is the use of a reliable and self-assigned measure of ethnicity. We also adjusted for socio-economic status, which is of particular importance for comparisons involving Pakistanis, Bangladeshis and Blacks owing to their higher levels of deprivation. The main limitation of this type of descriptive study is the lack of individual-level information available on exposures. Ethnicity information was also missing for 16.7% of cancer registrations but the similar results found in the sensitivity analyses suggest that this did not affect our results.

In conclusion, the higher incidence of thyroid cancer in most ethnic minority groups compared with Whites, and the differences by subtype cannot be explained by known risk factors and requires further investigation. Establishing the determinants of this variation with individual-level data of exposures and prevalence of known thyroid cancer genetic risk factors could offer new insights into its aetiology. Our findings also have important public health implications; clinicians serving those areas with large non-White populations need to be aware of the increased risk and commissioners need to consider the implications of the increased thyroid cancer incidence for these areas.

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CONFLICT OF INTEREST

RA, IB, AF, SS and VB are employed by the Cancer Epidemiology Unit at the University of Oxford, which is supported by Cancer Research UK. BM is employed by the Mayo Clinic in Rochester, MN, USA.

AUTHOR CONTRIBUTIONS

RA and IB conceived and designed the study. RA, IB, AF and SS contributed to the analysis and interpretation of the data. AF drafted the report, which was critically revised for important intellectual content by RA, IB and SS. All authors approved the report. RA is the guarantor.

DISCLAIMER

The sponsor of the study had no role in design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript.

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