

Disparities of Cancer Incidence in Michigan's American Indians

Spotlight on Breast Cancer

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BACKGROUND: In American Indians (AIs), cancer is a leading cause of mortality, yet their disease burden is not fully understood due to unaddressed racial misclassification in cancer registries. This study describes cancer trends among AIs in Michigan, focusing on breast cancer, in a linked data set of Indian Health Service (IHS), tribal, and state cancer registry data adjusted for misclassification. **METHODS:** AI status was based on reported race and linkage to IHS data and tribal registries. Data with complete linkage on all incident cancer cases in Michigan from 1995 to 2004 was used to calculate age-standardized incidence estimates for invasive all-site and female breast cancers stratified by racial group. For female breast cancers, stage- and age-specific incidence and percent distributions of early- versus late-stage cancers and age of diagnosis were calculated. **RESULTS:** More than 50% of all AI cases were identified through IHS and/or tribal linkage. In the linked data, AIs had the lowest rates of all-sites and breast cancer. For breast cancers, AI women had a greater late-stage cancer burden and a younger mean age of diagnosis as compared to whites. Although the age-specific rate for whites was greater than for AI women in nearly all age groups, the difference in hazard ratio increased with increasing age. **CONCLUSIONS:** Our state-specific information will help formulate effective, tailored cancer prevention strategies to this population in Michigan. The data linkages used in our study are crucial for generating accurate rates and can be effective in addressing misclassification of the AI population and formulating cancer prevention strategies for AI nationwide. *Cancer* 2014;120:1847-53. © 2014 American Cancer Society.

KEYWORDS: cancer, American Indians, breast cancer, incidence, Michigan.

INTRODUCTION

According to the US Centers for Disease Control and Prevention (CDC), cancer is a leading cause of death within the American Indian/Alaskan Native (AI/AN) population¹ and data from the Surveillance, Epidemiology, and End Results (SEER) registries of the National Cancer Institute show little progress in lowering the cancer burden of the AI population compared to other racial groups.^{2,3} For women nationwide and in Michigan specifically, breast cancer is of concern as the leading cause of cancer and second-leading cause of cancer-related death.^{2,3} In 2008 in Michigan, 6711 women were diagnosed with an invasive breast cancer, and in 2009, 1406 died from breast cancer.^{4,5} Little is known, however, of the breast cancer burden specifically for AI women in Michigan. National data shows that whereas breast cancer mortality rates have been decreasing for all races, AI women have seen no change.^{2,6,7} In addition, a higher percentage of breast cancers diagnosed among AI/AN women are at a later stage and earlier age of diagnosis than non-Hispanic white (NHW) women.⁶ The mean age of diagnosis for AI/AN was 57.5 years as compared to 63.4 years for NHW women.⁸

Racial or ethnic minority individuals are underrepresented in cancer registries mainly due to racial misclassification, resulting from incorrect or missing racial information on medical forms. For AI/AN individuals, this misclassification is particularly high.⁹⁻¹⁶ To improve accurate classification, data linkage is a technique that matches multiple records from different sources that identify the same person. For identification of AI/AN individuals, the Indian Health Service (IHS) and CDC have arranged for annual linkage of state cancer registries to IHS participant files to address AI misclassification.

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Some states also link their registries to tribal enrollment records. These techniques have been very effective, and many cancer registries nationwide now use them as a standard tool for improving racial data.¹³

By working with the Michigan Intertribal Council and individual tribes, the Michigan registry has developed an understanding with the tribes that has permitted tribal linkages for use by tribal health planners in assessing and addressing cancer prevention and control issues for their tribe with a side benefit of improving the completeness of AI ascertainment within the state registry. Tribe-specific cancer incidence data will be shared with a tribe for their analysis while protecting the identity of individual cancer patients. The state can use the results to improve the accuracy of AI classification within the statewide registry, and data specific to an individual tribe will not be released without tribal knowledge and consent. At present, 5 tribal rolls have been linked, which represents more than 80% of the Michigan tribal population, according to Intertribal Council records.

As the number of individuals identified as AI/AN increases after linkage, the cancer incidence estimates are expected to increase for that population as well,¹³⁻¹⁶ which was previously demonstrated after conducting a linkage with one tribe in Michigan. Linkage with IHS records from 1995 to 2004 revealed 643 racially misclassified cancer cases, with an additional 190 misclassified cases found through tribal linkage. These corresponded to a 97% and 15% increase in number of AI cases, respectively. After both linkages, the all-sites age-adjusted incidence rate estimates increased dramatically.¹³ These findings support the importance of using both IHS and tribal records for linkage despite previous evidence suggesting little added benefit of using tribal links.¹⁷ Similarly, dramatic increases in individuals identified and cancer rates were observed in 2 linkage studies conducted in Wisconsin and Minnesota.^{14,15}

There are 12 federally recognized tribes in Michigan and a total AI population of 82,565 (0.8% of the total Michigan population) in 2010.^{18,19} The number of AI individuals has been increasing by approximately 44% over the past 20 years and is experiencing the same demographic shift as the rest of the United States with an increasing presence of middle-aged and older populations. Between 1990 and 2010, the AI population aged 65 years and older increased by more than 100%.¹⁹

Because of the previous underreporting of AI cancer cases and the current demographic shift, the cancer burden in the AI population is only partially understood, but is likely much larger than currently estimated, indicating

the need for more targeted cancer prevention and control programs. Now that the quality of racial data has improved, the objective of this study was to investigate the all-sites and breast cancer trends that affect Michigan's AI population as compared to other racial groups. This will provide new insights into the corrected incidence estimates allowing for future epidemiologic and cancer prevention studies in this population.

MATERIALS AND METHODS

Data on all incident cancer cases in Michigan from 1985 to 2009 was obtained from the Michigan Department of Community Health (MDCH). The variables used for analysis included self-reported race, an IHS link variable, a tribal link variable, year of diagnosis, primary cancer site code, tumor behavior, summary stage, sex, and age at diagnosis. IHS linkage for all cancer cases in Michigan is conducted annually in coordination with the CDC Division of Epidemiology in Albuquerque, NM, assigned to the IHS. Tribal linkages using tribal enrollment records are done sporadically at the convenience and with the permission and cooperation of individual tribes.¹³ For this analysis, a case's racial identity was determined based on the reported race, IHS, and tribal linkage variables. A case that had any mention of AI as a reported race, a positive IHS link, or a positive tribal link was classified as AI. Cases of white or black race were also classified as such based on reported race and the absence of a positive IHS or tribal link.

Incidence estimates were calculated for all-sites and female breast cancers stratified by sex, race (all races, white, black, AI), and year of diagnosis. Rate calculations were restricted to the years 1995-2004. This restriction was necessary to address the combined effects of tribal enrollment file completeness and the cancer diagnosis years linked to all 5 participating tribes. At the time of the study, 5 tribes had completed one tribal linkage conducted between 2006 and 2012. Matching over these 6 years resulted in tribal enrollment being matched against varying cancer incidence time periods from through 2004 to through 2009. The years selected restrict the analysis to diagnosis years for which all 5 tribal linkages are complete.

For the all-sites and breast cancer incidence rates, only invasive cancers (behavior code of 3 and all bladder cancers) were included, and only females were included for breast cancer calculations. Stage-specific breast cancer rates were also calculated for those ages 50 years and older. Early-stage was defined as all in situ and localized cancers, whereas late-stage included all regional and distant

cancers. The 95% confidence intervals (CIs) were generated using a binominal approximation.²⁰ All rates used the corresponding population from census data as the denominator, were age-standardized to the United States standard population for 2000 and were calculated using SAS 9.3 and Microsoft Excel 2010.

Differences in age of diagnosis and late-stage breast cancer for whites compared to AIs were also analyzed. Early and late-stage cases of breast cancer were classified as premenopausal (age of diagnosis <50 years) and postmenopausal (age of diagnosis ≥50 years), and the percentage of AI and white women within each group was calculated and compared. In addition, the percentage of cases within each 5-year age group (from age 30-34 years through ≥80 years) for AI as compared to white women was calculated and plotted as a line graph. Of all early- and late-stage breast cancers, the percentage of AI and white individuals with a corresponding late-stage cancer was calculated. The chi-square test was used to determine the presence of a statistically significant difference in percentages, and these statistics were also restricted to cases diagnosed between 1995 and 2004. In addition, the age-specific breast cancer incidence rates and corresponding hazard ratios comparing AI rate to white rate were calculated for all years combined in 5-year age groups.

This study was approved by the University of Michigan and MDCH Institutional Review Boards and the Intertribal Council of Michigan and deemed no more than minimal risk.

RESULTS

A total of 579,332 cancer cases were diagnosed in Michigan between 1995 and 2004. Out of these 84.9% were white, 12.1% black, 0.3% AI and 2.7% of another racial group. Females comprised 51.9% and males 48.1% of all cancer cases. The mean age at diagnosis among males was 65.9 years (standard deviation = 14.1) compared to 60.6 years (standard deviation = 18.4) for females.

In total, 1981 cancer cases were identified as AI between 1995 and 2004 (Fig. 1). The most cases were classified as AI based on reported race alone (508 cases, 25.6%). After IHS and tribal linkage, the number of cases identified as AI increased by more than 100%, adding 1056 cases. Tribal link-only uncovered 299 (15.1%) cases and IHS link-only uncovered 262 (13.2%) cases. Only 246 cases (12.4%) were identified as AI by all 3 methods.

From 1995-2004, there was an increase in all-sites rate for AIs, from 382.4 cases per 100,000 persons (95% CI = 313.0, 451.8) in 1995 to 405.5 cases per 100,000 persons (95% CI = 343.3, 467.6) in 2004 (Table 1). Sim-

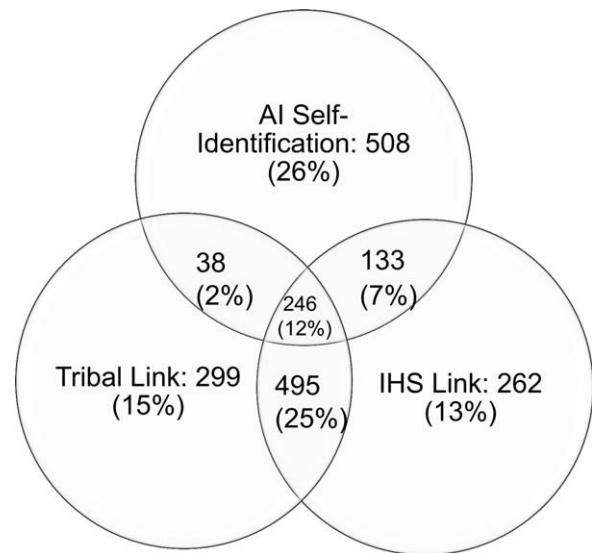


Figure 1. Number and Percentage of Cases by Reported Race and Linkage Status.

ilar increases were observed for males and females individually (data not shown). Rates for both sexes combined were lower for AIs than any other race. The number of all-sites cases for all races ranged from 47,440 cases in 1995 to 54,514 in 2003 and from 140 cases in 1995 to 211 cases in 2003 for AIs.

Table 1 shows that breast cancer rates were highest for white women and lowest for AI women. Both racial groups experienced a peak in 2000 at 141.4 cases per 100,000 women (95% CI = 137.9, 144.8) for whites and 118.2 cases per 100,000 women (95% CI = 70.8, 165.7) for AIs with a subsequent decline in rate (Table 1). Among AI women there were 236 breast cancer cases seen between 1995 and 2004 versus 71,747 among all races.

For all races, the early-stage breast cancer rates were greater than those for late-stage breast cancers. From 1995-2004 AI women had a 60% decrease in early-stage breast cancer rate with the lowest rate of all racial groups. However, late-stage rates steadily increased for AI women and, while still lower than that of other groups, approached the rate for white women. A greater percentage of AIs were diagnosed with a late-stage cancer (31.0%) as compared to white women (26.3%); however, this result was not statistically significant ($\chi^2 = 2.8$, $P = .1$).

The mean age at diagnosis for women with early- or late-stage breast cancer was 55.4 years (standard deviation = 14.3) for AI women and 61.7 years (standard deviation = 13.9) for white women. 36.5% of breast cancers in AI women were diagnosed before age 50 as

TABLE 1. Age-Adjusted Invasive All-Sites and Breast Cancer Case Counts and Incidence Rates^a (Per 100,000 Persons) by Race

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
All Sites	513.9 (509.3, 518.5)	513.4 (508.8, 518.0)	520.5 (515.9, 525.1)	524.8 (520.3, 529.4)	533.9 (529.4, 538.5)	534.4 (529.9, 538.9)	529.6 (525.1, 534.0)	529.9 (525.4, 534.3)	526.8 (522.4, 531.2)	503.9 (499.7, 508.2)
# Cases	47,440	48,058	49,297	50,264	51,705	52,550	52,906	53,874	54,514	53,343
White Rate	501.1 (496.3, 505.9)	501.8 (497.0, 506.7)	511.3 (506.4, 516.1)	516.5 (511.7, 521.3)	525.9 (521.1, 530.8)	527.4 (522.6, 532.3)	525.1 (520.4, 529.9)	519.1 (514.4, 523.9)	514.8 (510.1, 519.4)	492.7 (488.1, 497.2)
# Cases	40,661	41,234	42,462	43,322	44,547	45,308	45,720	45,931	46,297	45,156
AI Rate	382.4 (313.0, 451.8)	370.5 (306.3, 434.7)	381.2 (319.1, 443.2)	389.8 (325.3, 454.2)	385.4 (323.1, 447.8)	420.5 (352.4, 488.6)	407.7 (341.4, 474.1)	468.0 (396.7, 539.3)	469.4 (399.6, 539.3)	405.5 (343.3, 467.6)
# Cases	140	148	161	157	164	173	176	197	211	196
Black Rate	581.0 (566.0, 595.9)	582.8 (568.0, 597.6)	581.7 (567.1, 596.4)	577.9 (563.4, 592.4)	583.3 (568.9, 597.7)	574.6 (560.4, 588.8)	566.0 (542.2, 569.9)	575.1 (561.2, 589.1)	563.6 (550.0, 577.2)	522.3 (509.4, 535.1)
# Cases	5,868	6,007	6,082	6,125	6,296	6,298	6,214	6,581	6,638	6,411
Breast	136.6 (133.4, 139.9)	132.2 (129.0, 135.3)	136.5 (133.3, 139.7)	137.2 (134.0, 140.4)	138.2 (135.1, 141.4)	139.2 (136.0, 142.4)	136.1 (133.0, 139.2)	133.6 (130.6, 136.7)	128.0 (125.0, 131.0)	124.5 (121.6, 127.4)
# Cases	6,872	6,749	7,066	7,186	7,332	7,467	7,408	7,393	7,171	7,103
White Rate	136.9 (133.4, 140.4)	133.1 (129.7, 136.5)	137.5 (134.0, 141.0)	138.8 (135.3, 142.2)	139.9 (136.5, 143.4)	141.4 (137.9, 144.8)	138.7 (135.4, 142.1)	134.3 (131.0, 137.6)	128.9 (125.7, 132.1)	124.9 (121.8, 128.1)
# Cases	5,997	5,900	6,166	6,292	6,411	6,556	6,506	6,399	6,199	6,106
AI Rate	86.0 (43.4, 128.5)	112.5 (66.2, 158.9)	89.2 (51.8, 126.6)	78.9 (43.9, 113.8)	88.4 (50.1, 126.7)	118.2 (70.8, 165.7)	75.2 (40.3, 110.2)	110.0 (70.3, 149.6)	96.4 (57.1, 135.7)	64.8 (33.6, 96.0)
# Cases	18	26	23	21	23	27	21	32	26	19
Black Rate	130.3 (121.1, 139.6)	120.5 (111.8, 129.3)	129.8 (120.8, 138.8)	124.3 (115.6, 133.0)	126.5 (117.8, 135.2)	125.7 (117.0, 134.4)	119.5 (111.1, 127.9)	123.6 (115.2, 132.0)	117.3 (109.2, 125.4)	118.3 (110.3, 126.3)
# Cases	773	733	808	792	817	811	785	833	811	841

Abbreviations: AI, American Indian; CI, confidence interval.
^a Age-adjusted rate per 100,000 persons age standardized to the 2000 United States standard population.

TABLE 2. Invasive Breast Cancer Age-Specific Incidence by Race and Age Group

Age Group	AI			White			Hazard Ratio (AI:White)	95% CI
	% of Cases	Rate (Per 100,000 Persons)	95% CI	% of Cases	Rate (Per 100,000 Persons)	95% CI		
30-34	4.0	32.2	(11.2, 53.2)	1.3	28.3	(26.4, 30.2)	1.1	(0.6, 2.3)
35-39	5.7	45.1	(20.6, 69.7)	3.2	61.3	(58.6, 63.9)	0.7	(0.5, 1.2)
40-44	9.7	78.2	(45.5, 110.9)	6.5	120.5	(116.8, 124.2)	0.7	(0.5, 0.9)
45-49	13.2	116.8	(75.0, 158.5)	9.6	192.6	(187.7, 197.5)	0.6	(0.5, 0.8)
50-54	12.8	143.1	(91.1, 195.2)	10.9	258.4	(252.2, 264.5)	0.6	(0.4, 0.7)
55-59	9.7	158.3	(92.2, 224.4)	11.0	322.0	(314.4, 329.6)	0.5	(0.4, 0.7)
60-64	14.1	325.2	(212.7, 437.7)	10.7	385.2	(376.0, 394.4)	0.8	(0.6, 1.2)
65-69	9.3	278.9	(159.8, 398.0)	11.1	431.3	(421.1, 441.5)	0.7	(0.5, 0.9)
70-74	8.8	331.9	(186.7, 477.1)	11.5	463.2	(452.5, 474.0)	0.7	(0.5, 1.0)
75-79	7.0	369.1	(188.6, 549.6)	10.6	485.1	(473.4, 496.8)	0.8	(0.5, 1.2)
80+	5.7	278.0	(127.1, 428.9)	13.7	436.1	(426.9, 445.3)	0.6	(0.4, 1.0)

Abbreviations: AI, American Indian; CI, confidence interval.

compared to 22.2% for white women ($\chi^2 = 29.9$, $P < .0001$). A greater percentage of AI women with breast cancer were diagnosed at younger ages than white women. The age group with the greatest percentage of breast cancer cases for AI women was 60-64 years (14.1%), after which there was a drop-off with lower percentages of women affected at older ages. Conversely for white women, there was a large plateau in percentage of women from the 50-54 through the 70-74 age groups and subsequently a decline (Table 2). In terms of age-specific invasive breast cancer rates both racial groups had the highest rate in the 75-79 age group, but white women had greater age-specific rates than AI women in each age group except 30-34 years. The age-specific hazard ratio (AI: white) steadily decreased between ages groups from 30-34 to 55-59 (from 1.1 to 0.5) before increasing slightly to 0.8 at ages 60-64 years, and then continuing to decrease (Table 2). Comparisons of the age-specific incidence of invasive breast cancer rates between black and AI women are shown in the supporting information.

DISCUSSION

Because of the small number of AI individuals relative to other racial groups, it can be difficult to generate accurate data on cancer incidence in the AI population. Widespread misclassification of this group makes assessment of cancer burden in this population group suspect without adjustment. As a result, cancer incidence in this population is understudied and not well understood. Other studies have focused on comparing groupings of AIs, often by IHS or CHSDA areas, to understand relative disease burden,²¹⁻²³ but these fail to take into account the heteroge-

neity of tribes in terms of culture and associated risk factors.²³ To our knowledge, this study was the first to focus on the all-sites and breast cancer burden for AIs in Michigan specifically after conducting IHS and tribal linkages.

These results were similar compared to those seen in other studies and the SEER cancer database. SEER 13 data revealed the AI/AN all-sites rate for both sexes to be lower than that of all other racial groups with a slight increase over time. Equivalent trends were seen in Michigan, although the incidence estimates for some years were slightly higher than those for SEER. Breast cancer rates for AI/AN females in SEER were lower than those for whites; however, no decrease in rate was seen in the SEER data as compared to the slight decrease in Michigan.² SEER is meant to give representative data based on specified catchment areas, and the SEER 13 database was expanded to include the Alaskan Native Tumor Registry. Therefore, trends in SEER may be skewed toward the AI/AN populations represented.²⁴ Similar statewide linkage studies have also found AI all-sites and breast cancer rates to be lower than that of all-races or NHWs, although the degree of difference varied widely and temporal relationships were not taken into account.¹⁴⁻¹⁶

Previously, nationwide studies have suggested that there is a greater burden of late-stage and early-onset breast cancer in this population as compared to whites.^{8,25} The results support this finding but are still inconclusive; a variety of risk factors may contribute to these patterns, and further research is needed on this point. A greater percentage of AI women were diagnosed with a late-stage breast cancer as compared to white women, and there was

an increasing trend in incidence rate from 1995 through 2004 of late-stage breast cancer in AI females as compared to decreasing rates for white females. The mean age of breast cancer diagnosis for AIs was younger than that of whites, a greater percentage of AIs diagnosed were under 50 years and the percentage distribution of individuals diagnosed within each age group was shifted toward younger age groups for AIs as compared to whites. These results parallel trends that have been observed by tribal clinic managers in Michigan as reported to the Intertribal Council. However, a potential bias may exist because the percentage of individuals within each age strata inherently depends on the total population distribution. During the study period, the population structure for AI females was shifted toward younger ages as compared to whites. 62% of all AI females ages 30 and older were in the 30-49 age group as compared to 49% of white females. Comparisons based on age-specific incidence rates may therefore be more reliable. AI women had lower age-specific rates than white women, but the gap between the 2 rates appears to become wider as age increases, which is also reflected in the hazard ratio trend up to age 60. Thus, the relative burden of invasive breast cancer for AI women compared to white women decreases with increasing age. This trend may be due to differential screening between groups, although this would not affect younger women due to screening guidelines. Because previous studies have shown that a younger age of breast cancer diagnosis confers a lower chance of survival, possibly due to later stage, larger and higher grade cancers, these results support the importance of improved, targeted screening practices for specific subgroups.^{26,27}

There were many strengths to these analyses. Cancer registry data that had previously been linked to IHS and tribal records was used, which is crucial in improving the incidence estimates for the AI population. Similar to other states, significant increases in the number of individuals defined as AI after conducting data linkage was found. More than 50% of all final cases identified as AI would not have been discovered without either IHS and/or tribal linkage. Although many states have begun to use IHS linkage in cancer registries,¹⁴⁻¹⁶ Michigan used tribal linkage as a supplement to catch those members of a tribe that may not use IHS services.¹³ When studying populations with small numbers, such as AIs, it is imperative to identify as many cases as possible for accurate estimates. This focus on Michigan AIs will better uncover the true cancer burden in their communities. Because of the diversity of individual tribes, findings from studies based on large geographic areas are likely an overgeneralization. With this updated racial data

these results will be applied to improve cancer treatment and prevention programs in Michigan specifically.

These results should be interpreted with caution. During the study years (1995-2004), AIs comprised between 0.7% and 0.8% of the Michigan population¹⁹ and only 0.3% of all cancer cases in the state. Although data linkage was completed prior to analysis, the racial data is still not completely up to date. IHS linkage is run yearly, but not all AIs in Michigan are eligible for or use IHS services and therefore are not captured by this link. Only those belonging to a federally recognized tribe are eligible, and nationwide only approximately 57% of AIs use IHS services.²⁸ Tribal linkage helps to fill in this gap. At the time of the study, however, only 5 of the 12 federally recognized tribes in Michigan had participated, missing approximately 20% of all Michigan tribal members. Tribal linkage is unique from IHS linkage in that it can be conducted only with permission and cooperation of the tribe. In addition, the completeness of available tribal enrollment information may not be complete going back in time, making assessment of cancer incidence in prior years difficult. This limitation became apparent after calculating the all-sites incidence rate estimates back through 1985 (data not shown).

An additional important limitation of our results is that the incidence estimates may also be affected by inaccuracies in census data, which was used as the denominator for analysis. Racial information within the census is based on self-report. Starting in 2000, individuals could select multiple races and were categorized separately whereas previously only one race could be marked.²⁹ Similar to racial misclassification seen in cancer registries, these categorizations may inaccurately reflect an individual's true racial identity.

In conclusion, the results of this study further our knowledge of cancer disparities, particularly breast cancer, that affect AI communities in Michigan. This work highlights the benefits of conducting regular data linkage for cancer registries against IHS and tribal records. This information will allow local health workers in Michigan to formulate the best treatment and prevention strategies possible tailored to this population to ultimately lower the cancer burden.

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CONFLICT OF INTEREST DISCLOSURES

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