INCIDENCE AND PREVALENCE OF FETAL ALCOHOL SPECTRUM DISORDER BY SEX AND AGE GROUP IN ALBERTA, CANADA

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ABSTRACT

Objectives
To estimate incidence and prevalence of FASD by sex and age in Alberta, Canada.

Methods
We included all patients recorded in the Alberta provincial health databases of inpatients, outpatients, and practitioner claims from 2003 to 2012. The number of people with FASD were calculated from available data on FAS (ICD-9 code 760.71; ICD-10 codes Q86.0 and P04.3) and estimated prevalence of FASD among individuals diagnosed with 21 FASD-related conditions (identified by a literature review) for which there are ICD codes, such as learning disability, mental retardation, and nervous system defects (Table 1). Fractions of FASD-related diagnoses that can be attributed to alcohol use during pregnancy were estimated by a systematic review. The incidence was measured as the number of new cases per 1000 births. The prevalence was measured as the number of cases per 1000 population in 2012.

Results
Annually, 739 to 1884 people were born with FASD in Alberta establishing an incidence of 14.2 to 43.8 per 1000 births, depending on the length of follow–up. There were about 46,000 people living with FASD in Alberta 2012, including 6,000 FAS cases and 40,000 FASD-related cases. The prevalence of FASD was 11.7 (range 8.2 to 15.1) per 1000 population. The incidence and prevalence varied greatly by sex and age group. Generally, male and younger outnumbered female and older.

Conclusion
This study suggests new incidence and prevalence of FASD, which are higher than what has been commonly used (1%), and its variations among sex and age groups.

Key Words: *FASD, incidence, prevalence, Alberta*

Fetal Alcohol Spectrum Disorder (FASD) is a term describing a range of physical, cognitive, and behavioural impairments that are precipitated by maternal alcohol consumption during pregnancy. The Institute of Medicine[1] recognizes four diagnostic categories within FASD spectrum: fetal alcohol syndrome (FAS), partial FAS (pFAS), alcohol-related neurodevelopmental disorders (ARND), and alcohol-related birth defects (ARBD). While there is conclusive scientific evidence that alcohol is teratogenic, there are no known levels of alcohol during pregnancy that is safe.[2]

Some individuals with an FASD exhibit a characteristic series of physical anomalies, including those evident in the face, bones, and major organs. However, the primary impact of prenatal alcohol exposure common to all individuals with an FASD is permanent alterations in the structure and function of the brain, which

has been increasingly recognized as both the most common and most serious consequence. As a result, especially in the absence of appropriate diagnosis and support, people with FASD are at high risk for a number of negative outcomes, such as homelessness, alcohol and drug abuse, unemployment, mental illnesses, school dropout, and conflict with the law.[3,4]

In developed countries, FASD consequently comes with significant costs to society for health, social, educational, justice, and correctional services. The total annual cost of FASD in Canada is conservatively estimated at $6.2 billion in 2009 dollars.[5]

The incidence and prevalence of FASD vary greatly by country, study population, and study method. For example, studies using an active case finding methodology have identified higher incidence rates than do those using passive surveillance. Globally, the average incidence of FASD has been estimated at 3 to 5 per 1000 births.[6] In the US, the frequently cited rates of FASD is 9.1 per 1000 births (estimated by Sampson et al. 1997).[7] For example, this rate is cited by the Centers for Disease Control and Prevention.[8] Recently, May et al. (2009)[9] re-estimated the prevalence of FASD in the US at 20 to 50 per 1000.

In Canada, the specific incidence or prevalence of FASD has not been established for the general population.[10] Drawing on estimates from the US, it is commonly cited that 9 of every 1000 newborns in Canada are affected with FASD,[11] equating to more than 3000 new cases each year.[12] In the province of Alberta, using a prevalence of 10 cases per 1000, it has been estimated that 36,000 people are living with FASD[13] and that approximately 500 babies are born with FASD each year. However, caution should always be taken when generalizing the rates of FASD to other contexts or populations.[14] Furthermore, there are no estimates of incidence or prevalence of FASD by sex and age in the literature worldwide. The absence of such data compromises abilities to effectively and efficiently identify and plan appropriate policy and service responses to meet the needs of people with FASD, and to monitor the effectiveness of FASD prevention activities at the population level.

This study sought to fill these gaps in knowledge by estimating 1) the sex-specific incidence of FASD (measured as the number of new cases per 1000 births), and 2) the sex- and age-specific prevalence of FASD (measured as the number of cases per 1000 population).

METHODS

This study was conducted under protocol number 1208 and was ethically approved by the Community Research Ethics Board of Alberta (CREBA) on May 18, 2012.

We used three administrative health databases in Alberta.[15] The Discharge Abstract Database (DAD) is morbidity data and the Alberta version of the Canadian Institute of Health Information (www.cihi.ca) Discharge Abstract Database, which contains information on the recipient, service, diagnosis, and procedure interventions for people who have been discharged from an inpatient bed. There are 25 diagnostic code fields for each discharge abstract, and ICD-10 codes have been used since 2002. The Ambulatory Care Classification System (ACCS) contains facility-based ambulatory care information regarding recipient, service, diagnosis, and procedure interventions. An ambulatory care service is defined as any contact with a health service provider that does not require an inpatient stay. Examples are same-day surgery, day procedures, emergency room visits, and community rehabilitation services occurring in publicly-funded facilities. There are ten diagnostic code fields for each record, and ICD-10 codes have been used since 2002. The Claims Database includes fee-for-service claims by physicians and other providers for insured health services. This database contains information on the recipient, provider, and service. There are three diagnostic code fields for each claim, and ICD-9 codes have been used to date.

The current provincial standard of care with regards to diagnosis of FASD is to include medical, cognitive and behavioural assessments by a multidisciplinary team based on the Canadian

guidelines for diagnosis.[14] However, this may only be true within the Alberta FASD Cross-Ministry Committee (CMC) funded networks (http://fasd.alberta.ca/) where it is a funding criteria. For diagnosis outside of network funding, Government of Alberta has not stipulated a protocol and physicians or neuro-psychologists do not necessarily adhere to the Canadian guidelines except the academic teaching institutions, such as the Glenrose FASD Clinic in Edmonton and the Alberta Children's Hospital in Calgary which are not funded through the networks but expected to follow and teach evidence based practices and hence adhere to the Canadian guidelines. Of note, a majority of the cases is diagnosed outside of the networks. In young children, the provincial standard is to defer FASD diagnosis in the early years unless there is evidence of severe impairment (typical FAS) and in those cases a careful differential diagnosis still needs to be considered. Most young children present with delays in development that are not specific to FASD. They need assessment by community based developmental services or general developmental clinics and referral for interventions based on functional needs (personal communication with Janice Penner and Kesa Shikaze, Co-chairs of the Alberta FASD CMC, and Gail Andrew, Medical Director of FASD Clinic, Glenrose Rehabilitation Hospital).

For this study, we included all patients recorded in the Alberta provincial DAD, ACCS, or Claims Databases from 2002/3 to 2011/12 (administrative data are recorded by fiscal year from April 1 to March 31). Hereafter, 2002/3 to 2011/12 will be denoted 2003 to 2012.

As there are International Classification of Diseases (ICD) codes for FAS but not for FASD, the estimated number of FASD cases was the sum of FAS cases identified by ICD code and the FASD fractions among people diagnosed with FASD-related conditions.

People with FAS were identified by ICD-9 code 760.71 in the Claims Database and ICD-10 codes Q86.0 and P04.3 in the DAD and ACCS databases (in any of the diagnostic code fields). We used personal health numbers to avoid duplicates among the databases.

FASD-related cases were estimated through FASD-related conditions and alcohol attributable fractions of those conditions. We performed a systematic review of literature and a meta-analysis to identify FASD-related conditions and to estimate the fractions of cases that can be attributed to alcohol (details on the systematic review and meta-analysis are upon request).

Based on previous studies,[16-20] we identified 21 potentially FASD-related conditions (e.g., neurodevelopmental disorders and birth defects) for which there are ICD codes, such as attention deficit hyperactivity disorder, learning disability, developmental disability, and cleft palate (Table 1). We systematically searched electronic databases (Medline, Embase, and PsycINFO) to find publications relating to prenatal alcohol exposure as a cause/etiology/risk factor of those conditions. The search included numerous subject headings and keyword terms for the concepts of FASD, drinking during pregnancy, and those conditions. We limited the scope of the search to studies examining the rate of FASD and alcohol use during pregnancy among those conditions. We did not limit the search by country or year. Only English studies were included in our search. Reference lists of included studies were also searched in order to identify further studies.

TABLE 1 Diagnostic codes of FASD-related conditions

Conditions	ICD-9 codes	ICD-10 codes	Pooled RR (95%CI)	PAF% (95%CI)*
Significant RR				
Nervous system defects	740-742	Q00-Q07	2.41 (1.75, 3.31)	26.52 (15.12, 37.92)
Learning disability	315	F81, F83	1.77 (1.09, 2.86)	26.28 (4.07, 48.48)
Anomalies of eyes	743	Q10-Q15	1.65 (1.29, 2.10)	23.17 (11.90, 34.44)
Anomalies of ear, face, neck	744	Q16-Q18	2.02 (1.52, 2.70)	20.95 (12.39, 29.51)
Anomalies of circulatory system	747	P29.3, Q25-Q28	2.62 (1.57, 4.37)	17.40 (8.15, 26.65)
Mental retardation	317-319	F70-F79	1.44 (1.23, 1.68)	14.26 (8.16, 20.36)
Anomalies of heart	745-746	Q20-Q24	1.18 (1.02, 1.36)	10.89 (1.43, 20.35)
Anomalies of upper alimentary tract	750	Q38-Q40	1.31 (1.06, 1.62)	10.50 (2.25, 18.75)
Congenital musculoskeletal deformities	754-756	Q65-Q79, R29.4	1.23 (1.08, 1.41)	7.98 (2.84, 13.12)
Oppositional defiant disorder	313.81	F91.3	1.54 (1.21, 1.95)	6.61 (2.96, 10.26)
Cleft palate/Cleft lip	749.0-749.2	Q35-Q37	1.10 (1.03, 1.18)	3.24 (0.93, 5.55)
Other & unspecified anomalies	237.7, 759.0-759.6, 759.9	Q85, Q89.0-Q89.4, Q89.9	1.66 (1.11,2.48)	5.65 (1.17, 10.13)
Not significant RR				
Attention-deficit hyperactivity disorder	314	F90	2.29 (0.94, 5.55)	
Developmental disability	783.4	R62	2.00 (0.77, 5.16)	
Anomalies of respiratory system	748	Q30-Q34	1.56 (0.51, 4.79)	
Other anomalies of digestive system	751	Q41-Q45	1.58 (0.61, 4.09)	
Anomalies of genital organs	752	Q50-Q56	1.31 (0.72, 2.37)	
Anomalies of urinary system	753	Q60-Q64	1.03 (0.83, 1.28)	
Multiple anomalies	759.7-759.8	Q86.1-Q86.8, Q87, Q89.7-Q89.8	1.03 (0.58, 1.85)	
Anomalies of the integument	228, 757	D18, Q80-Q84	0.52 (0.23, 1.17)	
Chromosomal anomalies	758	Q90-Q99	0.32 (0.07, 1.52)	

*PAF(%)=P_e(RR-1)/[1+P_e (RR-1)]x100, where PAF is population attributable fraction, P_e is proportion of exposed individuals, and RR is relative risk

After scanning titles and abstracts, we selected cohort and case-control studies for review and data extraction. Papers were included in the review if they were peer-reviewed primary research articles which reported the incidence of the FASD-related conditions in both alcohol exposed and non-exposed groups from which relative risk and proportion of exposed individuals could be calculated. Case-control studies that reported raw data permitting additional calculations were also included. We applied a random effects meta-analysis to estimate the Mantel-Haenszel pooled relative risk from different relative risks extracted from reviewed studies.[21] Of note, we pooled the relative risk and the odds ratio separately and then combined them on the assumption that the odds ratio approximated relative risk. On the basis of the meta-analysis results, 12 (out of 21) conditions with a pooled relative risk significantly greater than 1 were confirmed as FASD-related (Table 1). Individuals were considered potential FASD cases if they had the code of at least one of these 12 FASD-related conditions in any of the diagnostic fields. We used personal health numbers to avoid duplicates among the databases and conditions.

The alcohol-attributable (FASD) fraction of each of the 12 FASD-related conditions was estimated by using the formula $PAF(\%)=P_e(RR-1)/[1+P_e(RR-1)]x100$, in which PAF is population attributable fraction, P_e is proportion of exposed individuals, and RR is relative risk.[22] P_e was calculated as the total number of exposed to alcohol divided by the total number of both exposed and not exposed to alcohol.

The incidence of FASD was defined as the number of new cases of FASD per 1000 births. We estimated the incidence by sex and year. For the 2003 birth cohort, new cases included zero-year-old cases diagnosed in 2003, 1-year-old cases diagnosed in 2004, 2-year-old cases diagnosed in 2005, 3-year-old cases diagnosed in 2006, 4-year-old cases diagnosed in 2007, 5-year-old cases diagnosed in 2008, 6-year-old cases diagnosed in 2009, 7-year-old cases diagnosed in 2010, 8-year-old cases diagnosed in 2011, and 9-year-old cases diagnosed in 2012. Similar estimates were made for later years; however, the later the year the shorter the follow-up time, so that in 2012 the incidence included only the zero-year-old new cases. The numbers of births in Alberta by year were retrieved from Statistics Canada.[23] For estimating the sex-specific incidence of FASD, we assumed an equal number of boys and girls among the births.

The prevalence of FASD was defined as the number of people with FASD who were alive in 2012 per 1000 population in the same year. People with FASD who died during the years were identified by linking personal health numbers to the Vital Statistics Death Registry[24] and the Alberta Health Care Insurance Plan Central Stakeholder Registry. [25] Mid-year population data were retrieved from the Alberta Health Interactive Health Data Application.[26] We estimated the prevalence of FASD by sex and 10-year-interval age group.

A one-way sensitivity analysis was performed for all FASD fractions among FASD-related conditions. The variations were between the lower and the upper values of 95% confidence intervals. For each FASD-related condition, the same range of FASD fraction was applied to both sexes and to all age groups and years. Stata MP 11.2 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA) was used for analysis.

RESULTS

The number of new cases and the incidence rate of FASD by sex and birth cohort are shown in Table 2. With the shortest time of follow-up, the cohort born in 2012 had the smallest number of people diagnosed with FASD (739). However, those with the longest time of follow-up, the cohort born in 2003, did not have the highest number of people diagnosed with the conditions. The 2008 birth cohort had the highest number of people with FASD (1884). Males outnumbered females in all birth cohorts.

TABLE 2 Incidence of FASD by sex and birth cohort (year)

Birth cohort		Number of new cases (% of both sexes)			Incidence per 1000 births (95% confidence interval)		
		Female	Male	Both	Female	Male	Both
2003	#	708	1028	1736	35.2	51.0	43.1
	%	41%	59%	100%	(22.6-47.7)	(26.7-75.3)	(24.6-61.5)
2004	#	722	1062	1784	35.4	52.1	43.8
	%	40%	60%	100%	(22.0-48.8)	(27.2-76.9)	(24.6-62.9)
2005	#	741	1025	1766	35.2	48.7	41.9
	%	42%	58%	100%	(22.0-48.4)	(24.5-72.8)	(23.3-60.6)
2006	#	732	1095	1826	32.4	48.4	40.4
	%	40%	60%	100%	(19.6-45.1)	(25.2-71.6)	(22.4-58.5)
2007	#	809	1063	1872	33.0	43.4	38.2
	%	43%	57%	100%	(21.3-44.7)	(24.2-62.5)	(22.8-53.6)
2008	#	827	1057	1884	32.5	41.6	37.0
	%	44%	56%	100%	(17.7-43.6)	(23.5-59.6)	(22.5-51.6)
2009	#	716	930	1646	27.7	36.0	31.8
	%	43%	57%	100%	(17.1-37.6)	(20.3-51.6)	(19.0-44.6)
2010	#	636	790	1426	25.0	31.1	28.1
	%	45%	55%	100%	(16.6-32.9)	(19.6-42.6)	(18.4-37.7)
2011	#	555	647	1202	21.7	25.3	23.5
	%	46%	54%	100%	(11.0-26.7)	(19.0-31.6)	(17.8-29.1)
2012	#	327	413	739	12.5	15.8	14.2
	%	44%	56%	100%	(11.0-14.0)	(14.1-17.5)	(12.6-15.7)

Estimates of the sex-specific incidence rates of FASD per 1000 births (Table 2) were based on the number of births in each year of the study period from 2003 to 2012: 40,287 (2003); 40,779 (2004); 42,110 (2005); 45,229 (2006); 49,028 (2007); 50,856 (2008); 51,722 (2009); 50,846 (2010); 51,175 (2011); and 52,243 (2012).[21] The numbers of boys and girls were assumed to be equal at birth.

Counting only the cases diagnosed within the first year of life (e.g., the 2012 birth cohort), the incidence rates of FASD was estimated at 14.2 per 1000 births. The sensitivity analysis showed that the incidence rate of FASD varied between 12.6 and 15.7 per 1000 births. The incidence rate of FASD among females in this cohort was 12.5 (range 11.0 to 14.0) per 1000 births. The incidence rate among males was 1.3 times higher than that among females.

If cases diagnosed in later years of life were included, the estimated incidence rate of FASD was much higher. For example, counting new cases diagnosed from age 0 to 9 in the 2003 birth cohort - the longest time of follow-up - resulted in an FASD incidence rate of 43.1 (range 24.6 to 61.5) per 1000 births (both sexes).

It is difficult to compare the incidence rate for different years because of the difference in the follow-up times. However, the highest incidence rate of FASD (43.8; range 24.6 to 62.9) was found in the 2004 birth cohort. In an average year, the incidence rate FASD among males was 1.4 times higher than those among females.

Approximately 46,000 people with FASD were living in Alberta in 2012 (Table 3). Those in the age group 0 to 9 accounted for the largest percentage of FASD cases (36%), followed by ages 10 to 19 (29%), 50+ (13%), 20 to 29 (12%),

30 to 39 (6%), and 40 to 49 (5%). For all ages in general, males outnumbered females. However, specifically, males outnumbered females in age groups younger than 30 years and females outnumbered males in older age groups.

The prevalence rate of FASD per 1000 population were calculated based on the mid-2012 population[24] by sex and age group and are shown in Table 3.

For both sexes and all age groups, the prevalence rate of FASD was 11.7 (range 8.2 to 15.1) per 1000 population. The prevalence rate of FASD among females was 10.4 (range 7.9 to 12.8) per 1000 population. The prevalence rate of FASD among males was 1.2 times higher than that among females.

The prevalence rate of FASD was the highest in the youngest group (32.7, range 21.5 to 43.8, per 1000 population). The lowest prevalence of FASD (3.9, range 3.6 to 4.2, per 1000 population) was found in age group 40 to 49.

TABLE 3 Prevalence of FASD by sex and age group in 2012

	Number of FASD cases (% of total)			**Prevalence of FASD per 1000 population (95% confidence interval)**		
Age group	**Female**	**Male**	**Both**	**Female**	**Male**	**Both**
0 to 9	7071	9595	16,666	28.5	36.6	32.7
	35%	37%	36%	(19.9-37.0)	(23.1-50.2)	(21.5-43.8)
10 to 19	5053	8374	13,427	21.7	34.1	28.1
	25%	33%	29%	(13.5-29.9)	(18.1-50.1)	(15.9-40.3)
20 to 29	2318	2978	5296	7.7	9.8	8.8
	11%	12%	12%	(6.2-9.2)	(7.0-12.7)	(6.6-11.0)
30 to 39	1410	1124	2534	4.7	3.7	4.2
	7%	4%	6%	(4.4-5.1)	(3.3-4.1)	(3.8-4.6)
40 to 49	1221	986	2207	4.4	3.4	3.9
	6%	4%	5%	(4.1-4.7)	(3.1-3.7)	(3.6-4.2)
50+	3274	2578	5852	5.4	4.4	4.9
	16%	10%	13%	(5.2-5.7)	(4.2-4.6)	(4.7-5.2)
Total	**20,348**	**25,635**	**45,984**	**10.4**	**12.9**	**11.7**
	100%	**100%**	**100%**	**(7.9-12.8)**	**(8.5-17.3)**	**(8.2-15.1)**

DISCUSSION

Annually from 2003 to 2012, 739 to 1884 people were born with FASD in Alberta. These numbers establish the incidence of FASD at 14.2 to 43.8 per 1000 births, depending on year and the length of follow-up. This is much higher than the most frequently cited rate of 9.1 per 1000 births, an estimate that was based on follow-up to age 7 by Sampson et al. in Seattle, USA.[7] The difference may be due to differences between the two studies in year, geographic area, population, and methodology, among other factors. For example, the Seattle study included FAS and ARND but did not include ARBD, while our study included all categories of FASD.

Our study indicates that the incidence of FASD is higher among males than among females. The incidence of FASD among males is 15.8 to 52.1 per 1000 births compared to 12.5 to 35.4 per 1000 births among females, depending on year and the length of follow-up. There are no previously published studies on the sex-specific incidence of FASD with which to compare or

explain our findings. This suggests that further investigations on sex differences in the incidence of FASD are needed.

Since incidence rates depend in part on the length of follow-up, the incidence of FASD found in this study may be underestimated due to the relatively short time of follow-up (10 years). If the follow-up had been longer, the rates would have been found to be higher. Therefore, we can conclude that the incidence of FASD in Alberta is at least 44 (range 25 to 63) per 1000 births.

About 46,000 people were living with FASD in Alberta at the end of March 2012, including 6000 FAS cases and 40,000 FASD-related cases. Our estimate of the number of people with FASD is approximately 30% higher than the previous estimate of 36,000.[13]

The overall prevalence of FASD was estimated at 11.7 (range 8.2 to 15.1) per 1000 population. This is slightly higher than the most-cited estimate, which is 1% of the population.[13] However, our results show that prevalence varies greatly by age group. Sixty percent of people with FASD were younger than 20 years old. This was also reflected in the age-specific prevalence rates FASD, which were 32.7, 28.1, 8.8, 4.2, 3.9, and 4.9 per 1000 population, for age groups 0 to 9, 10 to 19, 20 to 29, 30 to 39, 40 to 49, and 50+, respectively. These findings suggest that caution should be taken in generalizing the results of studies of one particular age group (e.g., schoolchildren) to the whole population.

Prevalence rates of FASD of 14.1 to 24.8 per 1000 have recently been estimated among first grade children in the US.[9] The rates among school children in Italy have been estimated at 20 to 55 per 1000.[9,27] These rates are comparable to our estimates of prevalence among children aged 0 to 9 (32.7 per 1000) and 10 to 19 (28.1 per 1000). Of note, since FASD is lifelong disabilities, our findings on incidence and prevalence (the incidence being higher than the prevalence, and the prevalence being lower in older groups) may suggest that people with FASD are unlikely to live as long as people without these conditions. A study on the survival and life expectancy of people with FASD is therefore desirable. Another explanation can be that better FASD diagnostic process in recent years may be partially responsible for the increased prevalence in younger age groups. This deserves further investigations as well.

The sex-specific prevalence of FASD among males is 12.9 (range 8.5 to 17.3) per 1000 population compared to 10.4 (range 7.9 to 12.8) per 1000 population among females. These differences were found only in younger age groups (0 to 29 years). In older age groups, the prevalence was similar among males and females. This may reflect the fact that males have a higher incidence of FASD (as was found in this study), but a shorter life expectancy than females. However, since there are no published studies on the differences in the sex-specific prevalence of FASD, further investigations are needed in this area.

There are some limitations to be acknowledged. First, due to a lack of data, migration was not considered. This may have resulted in an overestimation of the number of new cases diagnosed in later years within birth cohorts. However, the impact of migration is likely small since the net number of migrants to Alberta (both interprovincial and international) as a percentage of the population is small (~1.8% of the population in 2012).[28]

Second, the number of FAS cases was likely overestimated because in the Claims Database the ICD-9 code for FAS, 760.71, is truncated to 760.7, a code that indicates fetal exposure to a variety of noxious substances, only one of which is alcohol. However, this bias was likely small because most FAS patients (~80%) also used inpatient and outpatient services, where they were identified by the more specific ICD-10 code for FAS and because FAS accounts for a small proportion (~13%) of FASD. Similarly, the code for oppositional defiant disorder (ODD), 313.81, is truncated to 313.8 in the Claims Database. The effect of this is negligible, however, as only 0.17% of FASD cases were identified by a diagnosis of ODD.

Finally, as based on administrative health databases, people with FASD who did not use health services during the study period (2003 to 2012) were not included. However, it is likely that the number of people who did not use any health services over 10 consecutive years is small.

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