Comparison of the Seasonal Pattern in the Clinical Onset of IDDM in Finland and Sardinia

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OBJECTIVE — To examine the seasonal pattern for the clinical onset of IDDM in Finland and Sardinia, two areas where the incidence of IDDM is the highest in the world, and to determine the effect of climate and temperature on the clinical onset of IDDM.

RESEARCH DESIGN AND METHODS — Analysis of seasonality for the diagnosis of IDDM was based on 1,405 cases in Finland and 425 cases in Sardinia diagnosed at ≤14 years of age from 1989 to 1992. The average annual incidence of IDDM was 36.4/100,000 in Finland and 34.4/100,000 in Sardinia. Seasonal patterns were estimated presenting the data as short Fourier series up to three harmonics together with a possible linear trend. Likelihood ratio tests and Akaike's information criterion were used to determine the number of harmonics necessary to model the seasonal pattern. Seasonal patterns in both countries were compared between sexes and between the three 5-year age-groups, each controlling for the other's effect.

RESULTS — In both countries, a significant seasonal pattern during a calendar year was found for the sexes combined and for two age-groups (0–9 and 10–14 years). In Sardinia, two distinct cycles were found in the younger age-group, with a decreased incidence during May through August and an increased incidence during the autumn months. Two cycles were apparent in the older age-group, with the nadir occurring during June through September. In Finland, one cycle was found in the younger age-group, with a decreased incidence in June. In the older age-group, there were two distinct cycles, with a decreased incidence in June and in the September through December period.

CONCLUSIONS — Differences between Finland and Sardinia in the seasonal pattern for the incidence of newly diagnosed IDDM cannot be explained by differences in climate, temperature, a longer warm period in Sardinia, or other climatic phenomena. The results do not provide evidence in favor of a specific viral etiology of IDDM. It may be suggested that there are triggering events at certain times, but they are likely to be unspecific. Nevertheless, why the incidence of IDDM in these two populations is equally high despite differences in climate, environment, and genetic background remains an unsolved question.

Several epidemiological studies have described seasonal patterns in newly diagnosed cases of IDDM in children. Most studies have reported a higher occurrence of IDDM during the cold autumn and winter months than during the warmer spring and summer months (1–16). Seasonal variation in the diagnosis of IDDM has been considered as indirect evidence for environmental exposure in the development of IDDM. Recent studies have provided more indirect evidence for an association between viral infections and the pathogenesis of IDDM, but definitive evidence for viral causes of IDDM is still missing (17,18).

Worldwide variation in the incidence of IDDM, both between and within continents, is prominent. Data on incidence reported during the 1980s and 1990s suggested a correlation between the incidence and northern latitude or cooler average yearly temperature (19). A striking exception to this rule is the Mediterranean island of Sardinia (20). The highest incidence in the world is in Finland (21), but in Sardinia, the incidence is similarly high—approximately three times higher than the average incidence in Europe (22). Therefore, it is interesting to compare the seasonal patterns of newly diagnosed IDDM between these two high-risk populations.

This study compared the seasonal variation in the onset of IDDM among children aged ≤14 years in Finland and Sardinia, two areas that have different climates but an equally high incidence of IDDM, and examined the suggested association between a cool environment and an increased incidence of IDDM. Limited data exist on seasonality of the IDDM incidence in Finland. During the 1950s, the onset of IDDM seemed to be distributed rather evenly throughout the year, although the number of new cases was highest in September (23). During the period from 1968 to 1979, seasonal variation was noted in the incidence of IDDM, with peaks in April and September reported in children aged ≤14 years in northern Finland (24). The most recent report on the seasonal pattern in Finland showed a significantly decreased incidence of IDDM in June and during the period from November to December (25). In Sardinia, the high incidence was reported during 1989–1992, with peaks in the fall and winter and a lower incidence in the summer (26).

RESEARCH DESIGN AND METHODS

Finland

Population data were obtained from the National Population Registry, which is updated continuously. The Finnish population aged ≤14 years varied from 952,943 to 968,280 during 1989–1992.

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Abbreviations: AIC, Akaike's information criterion.

Table 1—*Number of newly diagnosed cases and the incidence of IDDM in children <15 years of age in Finland during 1987–1992 according to age, sex, and year*

	Boys (age in years)				Girls (age in years)				
	0–4	5–9	10–14	All	0–4	5–9	10–14	All	All
Year									
1989									
Incidence	28.4	44.3	54.2	42.3 (36.6–48.1)	27.0	27.0	37.8	30.6 (26.4–34.8)	36.5 (32.9–40.0)
Number	45	74	90	209	41	43	60	144	353
1990									
Incidence	28.9	34.7	36.7	33.4 (28.3–38.5)	34.2	38.2	37.1	36.5 (32.1–40.1)	35.0 (31.6–38.3)
Number	46	58	61	165	52	51	59	172	337
1991									
Incidence	32.2	41.5	52.6	42.1 (36.4–47.8)	27.2	41.5	44.8	37.8 (33.4–42.3)	40.0 (36.3–43.6)
Number	52	69	87	208	42	66	71	179	387
1992									
Incidence	23.8	37.2	45.9	35.6 (30.3–40.8)	27.3	39.5	29.6	32.1 (28.2–36.1)	33.9 (30.6–37.1)
Number	39	61	76	176	43	62	47	152	328
All years									
Incidence	28.3	39.4	47.4	38.4 (35.6–41.1)	28.9	36.6	37.3	34.3 (31.6–36.9)	36.4 (34.4–38.3)
Number	182	262	314	758	178	232	237	647	1,405

Age-adjusted 95% CI is given in parentheses.

Since 1987, all hospitals in Finland treating diabetic children have participated in the prospective nationwide registration of childhood IDDM (27). The case ascertainment is virtually 100% complete. Details of the procedures in case-ascertainment have previously been described elsewhere (27). During 1989–1992, IDDM was diagnosed in 1,405 Finnish children aged ≤14 years.

Finland is one of the northernmost countries in the world. Although other countries extend further north, the focus of their regional structure and distribution of population lies further south. Finland is in an area with a snowy forest climate and damp cold winters. The mean temperature in the warmest month of the year is >10°C and in the coldest month it is below −3°C. Precipitation occurs in all months, and the area has at least a short period of distinct summer and winter (28). However, due to the Gulf Stream, Finland's climate is more favorable than that of most other areas at the same latitude. The basic features of the Finnish climate and its regional variations are mainly products of location in the middle latitudes, with the Gulf Stream in the West and the vast continent of Eurasia in the East. Finland's location means that it

Table 2—*Number of newly diagnosed cases and the incidence of IDDM in children <15 years of age in Sardinia during 1987–1992 according to age, sex and year*

	Boys (age in years)				Girls (age in years)				
	0–4	5–9	10–14	All	0–4	5–9	10–14	All	All
Year									
1989									
Incidence	22.7	42.4	56.9	40.7 (30.9–50.4)	24.0	43.5	35.3	34.3 (27.2–41.3)	37.5 (31.4–43.5)
Number	10	22	36	68	10	21	21	52	120
1990									
Incidence	27.2	50.1	28.4	35.2 (25.9–44.6)	24.0	29.0	33.6	28.9 (21.9–35.9)	32.1 (26.2–37.9)
Number	12	26	18	56	10	14	20	44	100
1991									
Incidence	24.9	44.3	42.7	37.3 (33.0–53.4)	21.6	37.3	16.8	25.2 (19.4–31.1)	31.3 (25.7–36.8)
Number	11	23	27	61	9	18	10	37	98
1992									
Incidence	31.8	52.0	45.8	43.2 (33.0–54.3)	24.0	27.0	23.5	24.8 (18.2–31.3)	34.0 (28.0–40.0)
Number	14	27	29	70	10	13	14	37	107
All years									
Incidence	26.7	47.2	43.5	39.1 (34.3–43.9)	23.4	34.2	27.3	28.3 (24.0–32.6)	34.4 (30.6–37.1)
Number	47	98	110	255	39	66	65	170	425

Age-adjusted 95% CI is given in parentheses.

lies at the polar front, at the boundary separating the cold air masses of the arctic area from the warmer subtropical masses.

Sardinia

The population denominator was obtained from the 1991 population census for the relevant age-groups (29). The Sardinian population aged ≤14 years in 1991 was 303,958. The Sardinian IDDM Incidence Registry was established in 1993. The criteria for the diagnosis of IDDM were those adopted by the EURODIAB ACE Study (22). Since 1 January 1989, all newly diagnosed cases aged ≤29 years as notified by all Sardinian hospitals, outpatient clinics, family doctors and pediatricians have been registered and reported in the newsletter issued by the Epidemiological Observatory (30), which served as a primary data source. The secondary, independent source was the local IDDM patient association, Associazione Diabete Infantile Giovanile Sardegna. The case ascertainment was 91%. During 1989–1992, IDDM was diagnosed in 425 Sardinian children aged ≤14 years.

The climate in Sardinia is Mediterranean, with mild temperatures and a pronounced summer aridity. The fairly high altitude (half of the island is above 500 m) modifies the temperature and the distribution and total amount of rainfall. Average temperature during the summer is ~28°C, and during the cold season, it is ~10°C.

Statistical methods

The average annual incidence rates were calculated per 100,000 population per year. The mid-year populations aged ≤14 years were used as the denominator. The 95% CIs were estimated assuming the Poisson distribution of the cases. Age adjustment of the rates was done using 5-year intervals (0–4, 5–9, and 10–14 years) with the proportion being one-third for each group as the standard according to the previous approach by the Diabetes Epidemiology Research International Study Group (32).

Seasonal patterns in the incidence of IDDM were evaluated using the method as described by Jones et al. (33). The method fits sine waves to the incidence data with a fundamental period of one cycle per year, and when necessary, higher harmonics could be used. It also allows for different lengths of time intervals and different sizes of populations at risk.

The incidence model for group i at time t can be written as follows:

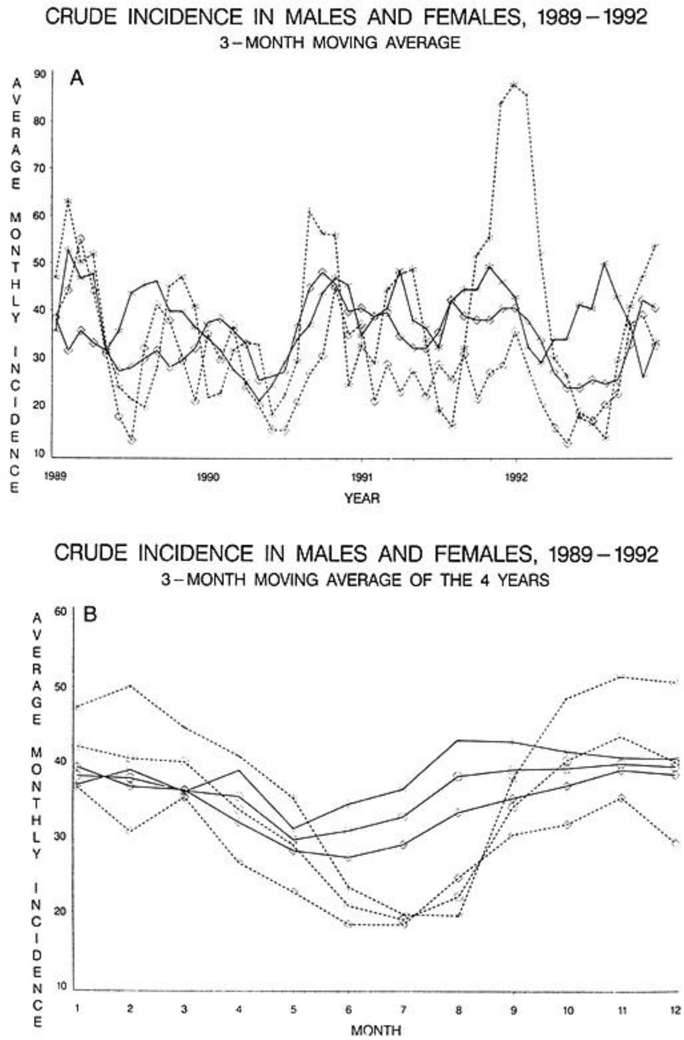

Figure 1—A: *The incidence of IDDM each month in Finland (—) and Sardinia (- - -), 1989–1992. Data are presented as 3-month moving averages for males* (○) *and females* (◇). B: *The monthly incidence of IDDM during 1989–1992 in Finland (—) and Sardinia (- - -). Data are presented as 3-month moving averages of the 4-year data for males* (○) *and females* (◇).

$$\lambda_i(t) = a_i\left\{1 + b_i\left(t - \frac{T}{2}\right) + \sum_{h=1}^{p}\left[\alpha_{ih}\cos\left(\frac{2\pi ht}{P}\right) + \beta_{ih}\sin\left(\frac{2\pi ht}{P}\right)\right]\right\}$$

where α_{ih} equals $c_{ih}\cos(\Phi_{ih})$ and β_{ih} equals $-c_{ih}\sin(\Phi_{ih})$, a_i equals a parameter that allows the size of each group to be arbitrary, b_i equals $(t - T/2)$ the time trend, c_{ih} equals the amplitude of the cyclic curve, Φ_{ih} equals the phase angle, P equals the fundamental period of the seasonal model, h equals the harmonic of the fundamental frequency, and p equals the number of terms in the sum.

In this case, the 4-year data starting at 1 January 1989 has been divided into 48 intervals, at the time points $t1 = 31$, $t2 = 31 + 28$, $t3 = 31 + 28 + 31, \ldots$, a day as the unit of time and the fundamental period of seasonal model $P = 365$. This method allows an arbitrary shape for the seasonal effect by presenting the data as a short Fourier series up to three harmonics together with a possible linear trend. Likelihood ratio tests and Akaike's information criterion (AIC) (34) were used to determine the number of harmonics necessary to model the seasonal pattern adequately and to test differences among subgroups in the population. Maximum likelihood estimation based on Poisson distribution was used to estimate the parameters of the model. Seasonal pattern in incidence was also compared between males and females and between the three 5-year age-groups, each controlling for the other's effect.

RESULTS — During 1989–1992, the average annual incidence of IDDM was

Table 3—*Number of newly diagnosed cases of IDDM per month in children <15 years of age during 1989–1992*

	January	February	March	April	May	June	July	August	September	October	November	December
Finland												
Boys												
1989	21	14	30	14	15	10	19	25	12	20	17	12
1990	16	14	9	11	11	4	15	17	10	19	25	14
1991	17	12	19	19	22	6	17	17	18	20	17	24
1992	16	13	11	12	19	11	21	18	23	12	11	9
Girls												
1989	10	15	12	15	12	10	10	13	12	12	9	14
1990	15	15	15	12	12	6	13	13	17	23	17	14
1991	16	18	12	17	12	9	17	16	17	13	15	17
1992	16	15	14	11	7	10	11	9	9	12	18	20
Sardinia												
Boys												
1989	11	3	12	6	4	4	2	3	3	6	10	4
1990	3	2	4	6	3	4	1	4	7	13	2	7
1991	1	6	5	7	8	6	1	1	4	7	9	6
1992	19	10	5	6	2	3	2	1	2	9	6	5
Girls												
1989	3	5	5	7	5	0	2	3	7	5	2	4
1990	2	7	2	5	2	1	3	2	3	5	3	9
1991	1	4	2	4	2	4	2	5	3	4	1	5
1992	4	4	2	2	2	1	4	1	2	5	7	3

36.4/100,000 (95% CI 34.4–38.3) in Finland (Table 1) and 34.4/100,000 (95% CI 31.3–37.9) in Sardinia (Table 2). In both countries, the average incidence of IDDM was higher in males than in females. The incidence among Finnish females was higher than that among Sardinian females.

The 3-month moving averages of IDDM incidence are shown in Fig. 1*A* and the number of newly diagnosed cases for each month are shown in Table 3. There were six monthly peaks in incidence in males in Sardinia when the incidence exceeded 40/100,000 per month (early 1989, late 1989, late 1990, early 1991, and late 1991). Although the monthly variation in incidence was less in Finnish males than Sardinian males, high peaks in incidence were also observed during these periods. The month-to-month variation in incidence was more pronounced in Sardinia than in Finland but without any obvious pattern in the incidence (Fig. 1*A*). The low and high points in monthly incidence did not occur in the same months in these two populations.

The average monthly incidence of IDDM calculated for the 4 years (Fig. 1*B*) was significantly lower in June than the yearly average among both sexes (P = 0.000 in males and P = 0.0064 in females) in Finland. In Sardinia, the incidence in June was significantly lower than the yearly average only among females (P = 0.0005). Among Sardinian males, the incidence in July (P = 0.0001) and August (P = 0.0208) was significantly lower than the yearly average incidence, whereas in October (P = 0.041) the incidence was significantly higher than the yearly average incidence.

To find out whether the variation in the IDDM incidence within the calendar year was random or whether a seasonal pattern exists, the incidence was modeled using the method by Jones et al. (33). The selection of best models for seasonal variation in the incidence was based on the AIC, with the minimum AIC being the best. The change in −2(log-likelihood) for models was tested using a χ^2 distribution with degrees of freedom equal to the difference in the number of parameters. Tables 4 and 5 show the values of −2(log-likelihood), the number of estimated parameters, and AIC from the analysis of seasonal variation in incidence, fitting different coefficients to each sex (two) and age-groups (three) with and without time trend for selected poolings.

In the first analysis, different coefficients were fitted to each of the three age-groups (0–4, 5–9, 10–14 years) and to both sexes for up to three harmonics with and without trend. The best fit in this test for the Sardinian data was the model with one harmonic without trend and with the minimum AIC of −20.40 (Table 4). For the Finnish data, the best-fit model was with null harmonics, no trend, and with the minimum AIC of 0.0 (Table 5). Seasonal patterns in incidence were also compared between males and females and among the three 5-year age-groups, each controlling for the other's effect. After several poolings of the incidence data, the comparison of the AICs showed that combining the two youngest age-groups and both sexes was acceptable for both the Sardinian (Table 4) and the Finnish data (Table 5). For the Sardinian data, the best fit was the model with two harmonics without trend and with the minimum AIC of −31.61 (Table 4). The summary of stepwise fitting of these models from zero to three harmonics is shown in Table 6. In Sardinia, there was a significant seasonal pattern in the IDDM incidence with two harmonics without trend in both age-groups and the minimum AIC of −20.00 in the age-group 0–9 years, and minimum AIC of −11.61 in the age-group 10–14 years. For the Finnish data, the best fit was also the model with two harmonics without trend and with the minimum AIC of −17.34 (Table 5). The age-group 0–9 years showed a significant seasonal pattern with one harmonic (mini-

Table 4—*Summary table for model selection, Sardinia*

	Number of harmonics	No trend: −2 log-likelihood	No trend: Number of estimated parameters	Trend: −2 log-likelihood	Trend: Number of estimated parameters	AIC: No trend	AIC: Trend
For six age-sex groups without pooling*							
	0	0.00	0	−3.71	6	0.00	8.29
	1	−44.40	12	−48.56	18	−20.40	−12.56
	2	−62.59	24	−67.51	30	−14.59	−7.51
	3	−70.82	36	−74.37	42	1.18	9.63
For four age-sex groups after pooling males and females							
	0	0.00	0	−2.01	3	0.00	3.99
	1	−38.61	6	−40.90	9	−26.61	−22.90
	2	−49.50	12	−53.06	15	−25.50	−23.06
	3	−54.00	18	−57.15	21	−18.00	−15.15
For three age-sex groups after pooling two lower ages and males and females†							
	0	0.00	0	−1.95	2	0.00	2.05
	1	−36.85	4	−38.56	6	−28.85	−26.56
	2	−47.61	8	−50.47	10	−31.61	−30.47
	3	−50.44	12	−53.11	14	−26.44	−25.11

*Age-groups: 0–4, 5–9, and 10–14 years; †age-groups: 0–9 and 10–14 years.

mum AIC of −13.93), but in the age-group 0–14 years, there were two harmonics (minimum AIC of −7.07).

The observed (pointwise) and estimated seasonal patterns in Finland and Sardinia for sexes pooled in two age-groups (0–9 and 10–14 years) with an overall 95% CI for the curves are shown in Figs. 2 and 3. There are some points that fall outside the CI, indicating that pointwise month-to-month variation is great and the model is not perfect, although it is the best fit. In Sardinia, there were two distinct cycles during the calendar year, with a decreased incidence during warm months in both age-groups (0–9 and 10–14 years). In the age-group 0–9 years, the incidence was low during the period from April to August

Table 5—*Summary table for model selection, Finland*

	Number of harmonics	No trend: −2 log-likelihood	No trend: Number of estimated parameters	Trend: −2 log-likelihood	Trend: Number of estimated parameters	AIC: No trend	AIC: Trend
For six age-sex groups without pooling*							
	0	0.00	0	−7.07	6	0.00	4.93
	1	−23.84	12	−30.46	18	0.16	5.54
	2	−40.33	24	−46.42	30	7.67	13.58
	3	−50.16	36	−56.48	42	21.84	27.52
For four age-sex groups after pooling males and females							
	0	0.00	0	−3.57	3	0.00	2.43
	1	−19.96	6	−21.96	9	−7.96	−3.96
	2	−34.18	12	−35.61	15	−10.18	−5.61
	3	−39.62	18	−41.16	21	−3.62	0.84
For three age-sex groups after pooling two lower ages and males and females†							
	0	0.00	0	−2.45	2	0.00	1.55
	1	−19.27	4	−20.64	6	−11.27	−8.64
	2	−33.34	8	−34.03	10	−17.34	−14.03
	3	−37.75	12	−38.60	14	−13.75	−10.60

*Age-groups: 0–4, 5–9, and 10–14 years; †age-groups: 0–9 and 10–14 years.

Table 6—*Summary for stepwise fitting of the model for age-groups 0–9 and 10–14 years with pooled boys and girls in Sardinia and Finland, 1 January 1989 to 31 December 1992*

	Number of harmonics	Age-group 0–9 years −2 log-likelihood	AIC	Age-group 10–14 years −2 log-likelihood	AIC
Sardinia					
	0	0.00	0.00	0.00	0.00
	1	−23.09	−19.09	−13.76	−9.76
	2	−28.00	−20.00	−19.61	−11.61
	3	−30.54	−18.54	−19.90	−7.90
Finland					
	0	0.00	0.00	0.00	0.00
	1	−17.93	−13.93	−1.34	2.66
	2	−18.28	−10.28	−15.07	−7.07
	3	−19.14	−7.14	−18.61	−6.61

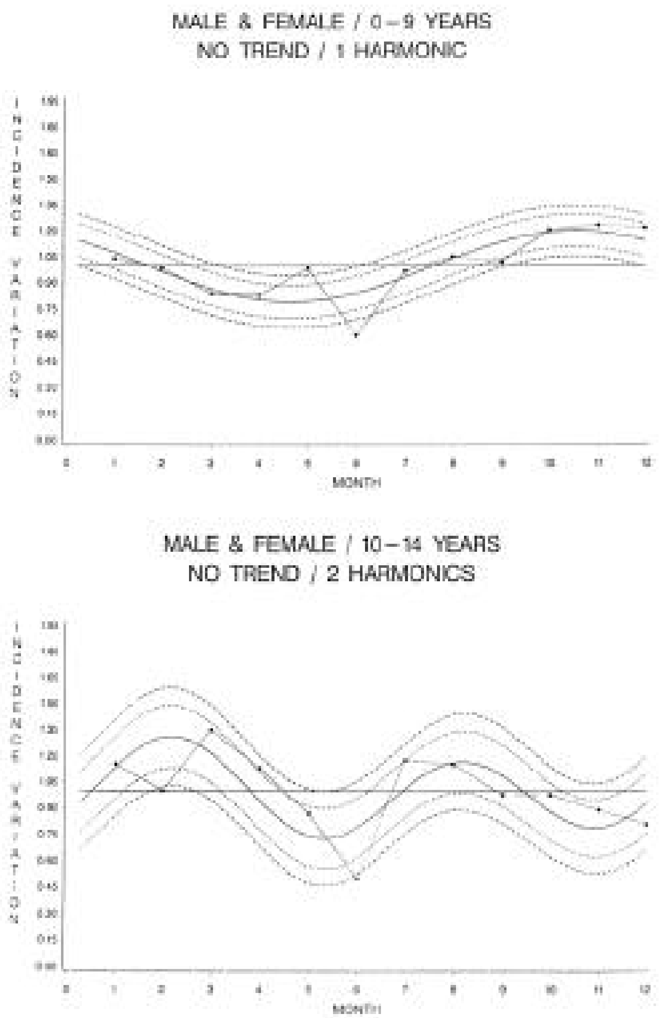

Figure 2—*Estimated and observed (—) seasonal pattern in the diagnosis of IDDM in both sexes in Sardinia, 1989–1992. The value 1 on y-axis denotes the mean of the incidence during the entire study period for the particular age-group. The inner interval of the two CIs shown is the pointwise 95% CI, and the outer interval is a 95% CI for the model. The equations for the seasonal patterns are as follows: males and females aged 0–9 years* $\lambda(t) = 1 + 0.3876\cos(2\pi t/365) - 0.0635\sin(2\pi t/365) - 0.1945\cos(4\pi t/365) + 0.0309\sin(4\pi t/365)$*; males and females aged 10–14 years* $\lambda(t) = 1 + 0.3316\cos(2\pi t/365) + 0.1737\sin(2\pi t/365) - 0.0877\cos(4\pi t/365) - 0.2418\sin(4\pi t/365)$.

and higher during early spring and fall. Among older children (aged 10–14 years), the decrease in incidence was seen about 1 month later than it was seen in younger children during the period from May to September, while during the rest of the year, the incidence in older children followed the pattern of younger children. Among the younger children (aged ≤9 years) in Finland, there was only one distinct cycle within the calendar year, with lower rates during the early spring and summer (from March to July) and higher rates during the rest of the year. Among children aged 10–14 years, there were two distinct cycles during the calendar year, with nadirs in incidence during the periods from April to July and from October to December through January.

CONCLUSIONS — During 1989–1992, the incidence of IDDM in children aged ≤14 years fluctuated to some extent within a calendar year in Sardinia and in Finland, countries with the highest rates of IDDM in the world but with different climates and genetic backgrounds of their populations (25,26,35). The incidence rates were similarly high and higher in males than in females in both countries. A seasonal pattern in the incidence was examined using statistical methods that have been developed and applied to analyze the seasonal pattern in incidence in the Denver IDDM registry (33). This method allows to test whether seasonal patterns exist among all study subjects, in males and females, and in age-groups. It can also be used to test whether two or more groups have the same seasonal pattern in incidence. Although the number of cases in Sardinia was only one-third of that in Finland, there were enough cases for modeling the IDDM incidence. However, the results must be interpreted cautiously, taking into account that the model of seasonal pattern in incidence is based on a low number of cases in Sardinia and thus has less reliability and precision than the model based on Finnish IDDM data.

Although a clear seasonal pattern in IDDM incidence for sexes pooled and for two age-groups (0–9 and 10–14 years) was found in both countries, the pattern of seasonal variation in incidence deviated. In Sardinia, there were two distinct cycles during the calendar year, with a decreased incidence during warm months in both age-groups (0–9 and 10–14 years). Among younger children (aged ≤9 years), a low

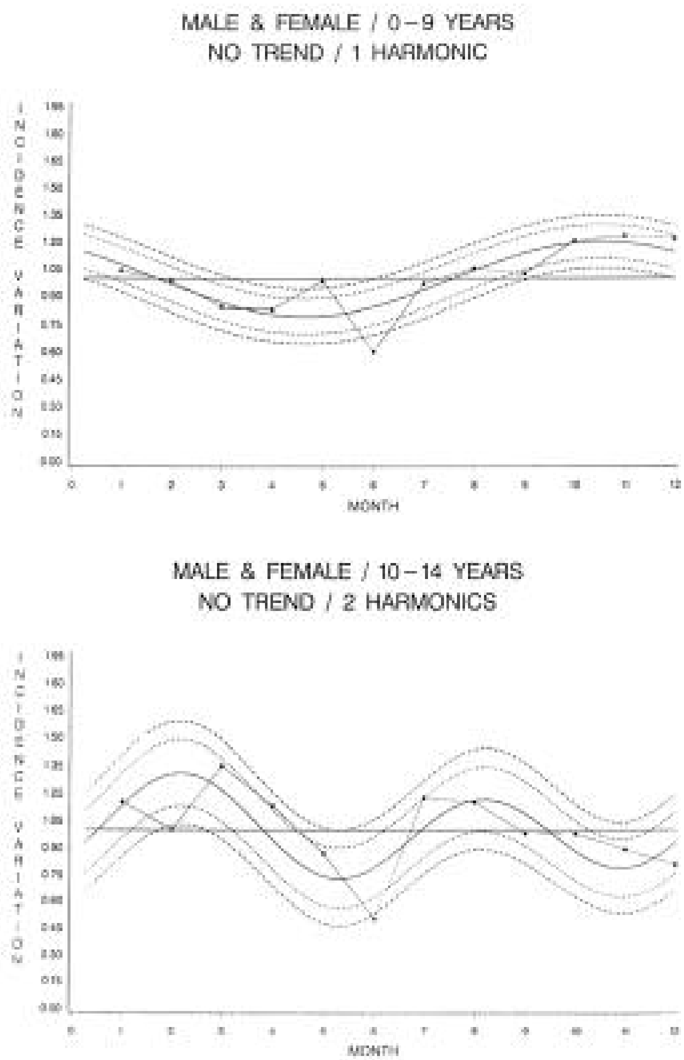

Figure 3—*Estimated and observed (—) seasonal pattern in the diagnosis of IDDM in both sexes in Finland, 1989–1992. The value 1 on y-axis denotes the mean of the incidence during the entire study period for the particular age-group. The inner interval of the two CIs shown is the pointwise 95% CI, and the outer interval is a 95% CI for the model. The equations for the seasonal patterns are as follows: males and females aged 0–9 years:* $\lambda(t) = 1 + 0.1457\cos(2\pi t/365) - 0.1451\sin(2\pi t/365)$; *males and females aged 10–14 years:* $\lambda(t) = 1 + 0.059\cos(2\pi t/365) + 0.0501\sin(2\pi t/365) - 0.1293\cos(4\pi t/365) + 0.2027\sin(4\pi t/365)$.

incidence from April to August and a higher number of cases diagnosed during the fall, winter, and early spring was the most visible seasonal pattern. Although the seasonal pattern from May to September among older children (aged 10–14 years) was nearly identical to that among younger children, the decrease in incidence was ~1 month later in older children as compared with younger children.

In Finland, the seasonal pattern in the IDDM incidence deviated from that in Sardinia among the younger children (aged ≤9 years). In Finland, there was only one distinct cycle within the calendar year, with lower rates during the spring and early summer and higher rates during the rest of the year. The nadir in the IDDM incidence in the spring or early summer among younger children was seen 1–2 months earlier than in Sardinia. Among children aged 10–14 years, two distinct cycles were found during the calendar year, as was also seen in Sardinia, but the seasonal pattern in incidence was almost the opposite of that among children in Sardinia in the same age-group. In Finland, the first nadir in the incidence during the calendar year was ~1 month earlier than in Sardinia. During August through October, the incidence in Finland was increased, but this was the period of low incidence in Sardinia. Coincidentally with the nadir in incidence in Finland, around November was a period of high incidence in Sardinia.

A seasonal variation in the onset of IDDM, with higher rates during cooler seasons (autumn and winter) and lower rates during the summer, has previously been described by other investigators (2–16,28, 36–40). Our results showed that in both countries there were no high peaks in incidence during the cool months that significantly deviated from the overall incidence. Since the 1920s, there has been increasing interest in the possibility that a viral infection may play a role in the onset of IDDM (17,18,41,42). However, virological studies in patients have not yet produced convincing evidence to prove this hypothesis, although the possibility of numerous viruses in the etiology has been suggested.

In Sardinia, the higher incidence particularly around March and April could be explained by a precipitating effect of nonspecific infections in people who already have an appreciable degree of β-cell destruction and possibly experienced infections during the preceding winter (42,43). In recent years, it has been reported that a yearly peak in the incidence of rubella, chickenpox, and mumps occurs in the spring among children ≤14 years of age (44). However, the highest number of IDDM cases has been diagnosed among children aged ≤9 years in October, a month when the weather is still generally mild and viral infections are infrequent. It can be speculated that seasonal variation in the incidence of IDDM in Sardinia would be partly a consequence of the summer holidays, because schools are closed from the beginning of July to late September. Family holidays and trips may cause a delay in noticing early symptoms in children and a delay in diagnosis until October, when viral infections in Sardinia are infrequent (44).

In Finland, there was a seasonal pattern with one nadir among younger males and two nadirs among older males. This does not fit the assumption that the seasonal variation in incidence is caused by a viral infection. The occurrence of diseases caused by viruses, such as mumps, measles, and coxsackie B, that have been proposed to trigger IDDM shows an epidemic pattern and the duration of the high-incidence period is often short. However, the very high and relatively stable incidence of IDDM in Finland supports the assumption that if a viral infection were involved in the etiology of diabetes, such a virus should be endemic in the country. The high and stable incidence of IDDM would also require the presence of chronic or recurrent infections and thus a high endemic level of infections in the country. Almost all of Finnish children aged ≤14 years have been vaccinated against several common viruses, such as mumps, that have previously been described as causing occasional epidemics. However, despite such a vaccination program, the incidence of IDDM has remained high and is still increasing in Finland, especially among the youngest age-groups (22). Our results suggest that if a viral infection causes the β-cell damage, the behavior of such a pathogen is very atypical of viruses, which usually cause short-term epidemics in susceptible populations.

It is very likely that the seasonality in the diagnosis of IDDM is not related to causal factors that trigger IDDM, but may be associated with the expression of symptoms in people who already are at an advanced stage in developing the disease, which may take months or years. Many physiological parameters (for instance, blood glucose, blood lipids, blood pressure, and body weight) and health habits (diet and physical activity) have a seasonal pattern. This may explain the seasonal effect that we observed in the diagnosis of IDDM. The beginning of school holidays in June in Finland may explain the low rate of newly diagnosed IDDM in children in this month (25). The low incidence of IDDM during the summer months is a real phenomenon made plausible not only by the usually low frequency of potentially precipitating infections (43) but also by a parallel phenomenon in an animal model in which the incidence of diabetes is reduced in the NOD mouse exposed to raised environmental temperature (45).

Differences in the seasonal pattern of the IDDM incidence between Sardinia and Finland cannot be explained by differences in climate and temperature, the longer warm period in Sardinia, or differences in other climatic phenomena. The results do not provide evidence in favor of a specific viral etiology of IDDM. There may be triggering events at certain times but they are likely to be unspecific. Nevertheless, the question remains unsolved as far as why the incidence of IDDM in these two populations is equally high despite differences in climate, environment, and genetic background.

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