Chapter 2

Transyears Competing with the Seasons in Tropical Malaria Incidence

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Additional information is available at the end of the chapter

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Abstract

Communicable and non-communicable diseases show coperiodisms (shared cycles) with the sun's and earth's magnetism. About 11-year cycles and components with periods a few weeks or a few months longer than one year (near- and far-transyears, respectively) are the cases in point. Published data on the incidence of malaria in Burundi, Papua New Guinea, and Thailand are analysed by the linear-nonlinear cosinor to assess the relative prominence of transyears versus the calendar year. An about 2.3-year component characterizes malaria incidence in Burundi and Papua New Guinea (Thailand data were only sampled yearly). Long-term trends cannot be distinguished from the presence of an about 11-year cycle found in a 100-year long record from Chizhevsky on mortality from cholera in Russia, albeit its second harmonic is statistically significant in Burundi's data. Whereas far- and near-transyears characterize malaria incidence in Burundi more prominently than the calendar year, only a candidate near-transyear of small amplitude is barely detected in Papua New Guinea, where the calendar year is most prominently expressed. Both regions are located near the equator. Selectively-assorted geographic differences such as these, observed herein for a communicable disease, have been previously observed for non-communicable conditions, such as sudden cardiac death.

Keywords: Chronoepidemiology, Malaria, time series analysis, public health, infectious diseases

1. Introduction

Signatures of cycles in the sun's and the earth's magnetism, found in the aetiology of both communicable and non-communicable diseases, are selectively assorted geographically [1]. Far-transyears and near-transyears (components with periods a few months or a few weeks longer than the calendar year, respectively) are both known to characterize interplanetary and terrestrial magnetism and their biospheric signatures [1–3]. A geographic study of the incidence of sudden cardiac death reveals the prominence of the transyear over the calendar year in Minnesota and Tokyo, whereas the opposite holds in Hong Kong, North Carolina (USA), and the Republic of Georgia [2, 4].

About 11-year (Horrebow-Schwabe) cycles of relative sunspot numbers [5–7] have also been reported to characterize communicable diseases such as malaria, as suggested earlier by Dimitrov et al. [8]. In their analysis of cerebral malaria in Papua New Guinea (latitude between 0° and 12°S, longitude 140°–160°E), these authors also reported the presence of a strong calendar-yearly component, in the absence of a marked transyear. By contrast, a transyear over calendar year prominence at -3° from the equator characterized a time series of natality in Mindanao, Philippines (8°N, 125°E) [2,3]. In a study of malaria in Thailand, a period of about 4 years was prominent, while geographic differences prevailed; "seasonal" cycles were only synchronous in small clusters [9].

Gomez-Elipe et al. [10] forecast malaria incidence based on monthly case reports and environmental factors in Karuzi, a province of the Burundi highlands (at 3°6′5″ S, 30°9′53″ E), recorded from 1997 to 2003. The analysis is complicated by the occurrence of a large outbreak, resulting in outlying values. The authors developed a satisfactory model to predict malaria incidence (notifications of malaria cases from local health facilities) in an area of unstable transmission by studying the association between environmental variables (rain, temperature, and a vegetation index, NDVI) and disease dynamics. Their autoregressive integrated moving average model predicted malaria incidence during a given month based on the incidence during the previous month together with NDVI, mean maximum temperature, and rainfall during the previous month with a 93% forecasting accuracy (R^2adj = 82%, $P < 0.0001$). While their model was useful for forecasting the malaria incidence rate in the study area, we ask whether cycles in malaria incidence found in Karuzi are similar to those found in other geographic sites located near the equator, where populations are exposed to factors that strongly influence the origin and magnitude of malaria epidemics, such as a weakened immunity of the population associated with famine and massive displacements, failures of control measures and epidemiologic disease surveillance, and unstable environmental factors such as rainfall, temperature, and vegetation [11].

Herein, we revisit published data on the incidence of malaria in different geographic locations near the equator. For this purpose, we turn to data in Papua New Guinea [8], Thailand, and Karuzi, Burundi [10], to explore any differences in terms of the relative prominence of transyears versus the calendar year. Our meta-analysis raises the question whether space weather may also contribute to communicable diseases like malaria in certain geographic

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regions at certain but not at other longitudes and/or as a function of prevailing climatologic factors.

2. Materials and methods

Data from Papua New Guinea consist of the total monthly admissions for cerebral malaria and of those from selected facilities, recorded between 1987 and 1996 [8]. Data from Thailand are those reported by WHO (www.sears.who.int/EN/), available yearly between 1971 and 2010 for the percentage of microscopically diagnosed malaria positive slides found in blood smears examined, the number of cases of *Plasmodium falciparum* infections (including mixed infections), the number of *P. falciparum* infections per 100 slides examined, the percentage of *P. falciparum* infections per 100 malaria positives, and the number and percentage of malaria-related deaths, among others. Data from Karuzi, Burundi, are those published by Gomez-Elipe et al. [10], available from 1997 to 2003.

Data were analysed by the extended cosinor [12–15]. Least squares spectra examined the entire time structure (globally) to identify candidate cycles as spectral peaks. Nonlinear least squares based on Marquardt's algorithm [16] provided estimates of the periods involved with a measure of uncertainty as "conservative" 95% confidence intervals (CIs).

3. Results

After square root transformation, the monthly incidence of malaria in Burundi was characterized by a near- and far-transyear, and by components with periods of about 5.2 and 2.3 years. Results from the nonlinear analyses are summarized in **Table 1**. The corresponding model fitted to the data is illustrated in **Figure 1**. As illustrated in **Figure 2** (left and middle), the near- and far-transyears with periods of about 1.15 and 1.5 years, respectively, are more prominently expressed than the 1.0-year synchronized (calendar) component, as gauged by amplitude ratios.

The about 5.2-year component found in Burundi (**Figure 1**) may correspond to the second harmonic of the decadal cycle reported by Dimitrov et al. [8] for cases of cerebral malaria in Papua New Guinea. A component with a period slightly longer than 2 years was also reported by Dimitrov et al. [8] for the data in Papua New Guinea, together with a prominent yearly rhythm, as seen from least squares spectra of the original data and of the detrended data, obtained by removing either a linear or a quadratic trend (**Figure 3(A)–(C)**). The large-amplitude low-frequency component reflects a trend, a low-frequency cycle, or both, which may be difficult to separate in view of the brevity of the series. There is also a smaller spectral peak (below the noise level) that may correspond to a near-transyear, perhaps the second harmonic of the slightly longer-than-2-year component.

All components fitted concomitantly					
Period	**[95% CI]**		**Amplitude**	**[95% CI]**	
Original data					
4.78	3.89	5.68	7.04	3.68	10.40
2.26	1.95	2.58	4.80	1.38	8.21
1.50	1.34	1.66	4.82	1.44	8.19
1.13	1.02	1.24	3.90	0.63	7.17
After square-root transformation					
5.18	4.21	6.15	1.05	0.65	1.45
2.34	1.93	2.74	0.55	0.14	0.96
1.54	1.35	1.73	0.59	0.17	1.00
1.15	1.04	1.27	0.50	0.11	0.90

Table 1. Nonlinear results of monthly incidence of malaria in Burundi.

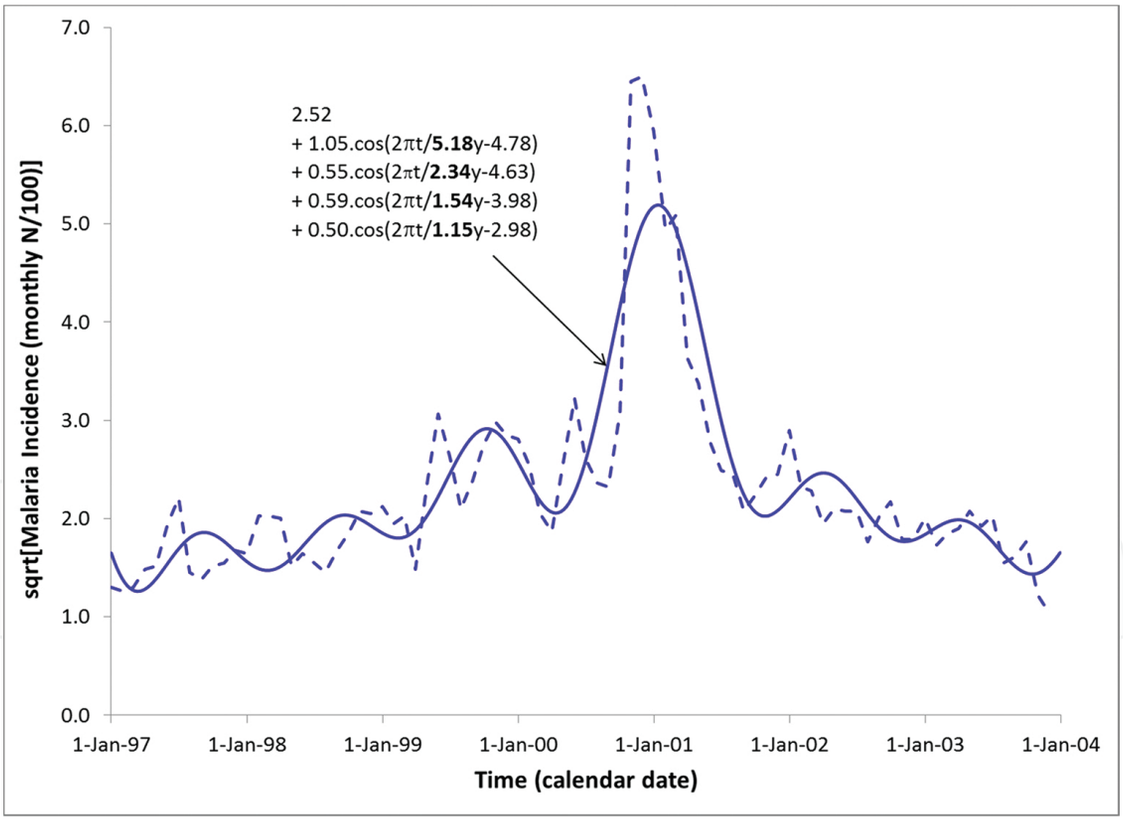

Figure 1. In view of a large outbreak resulting in influential (outlying) values, the monthly data on malaria incidence in Burundi recorded between 1997 and 2004 are transformed by taking their square root prior to analysis by the extended (linear-nonlinear) cosinor. Components with periods of about 5.2, 2.3, 1.5, and 1.15 years identified by least squares spectra and validated nonlinearly are included in a model plotted with the data. © Halberg Chronobiology Center.

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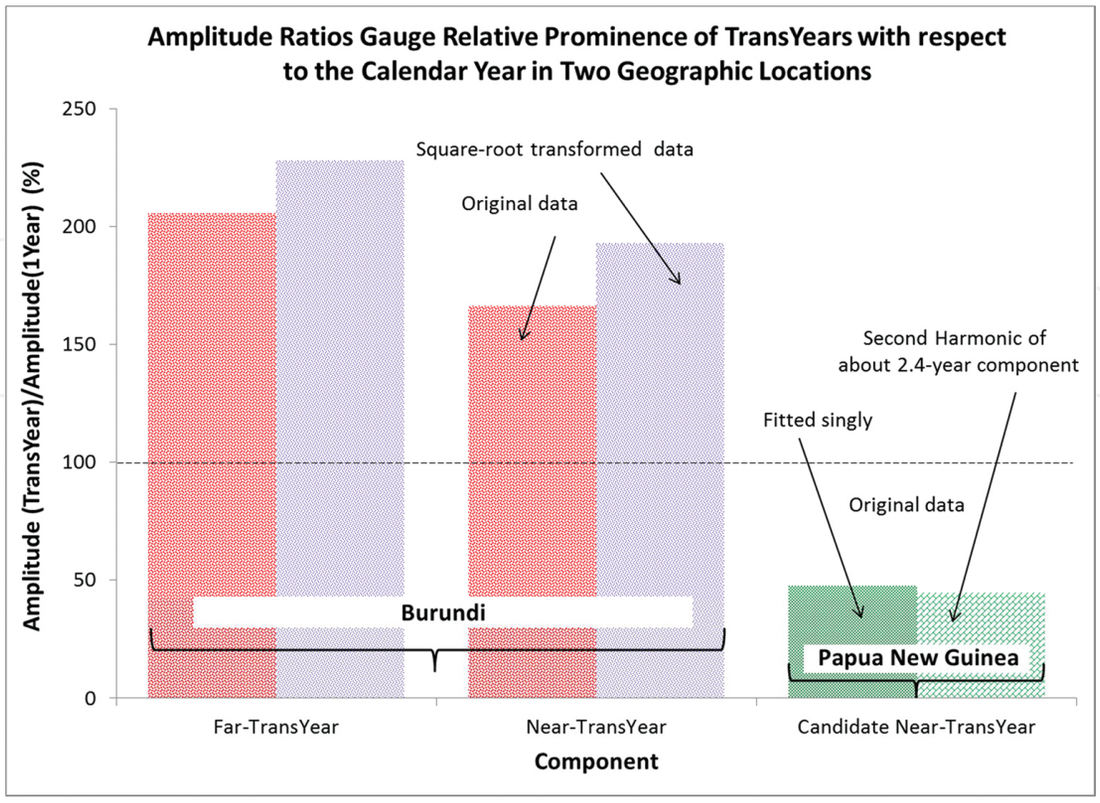
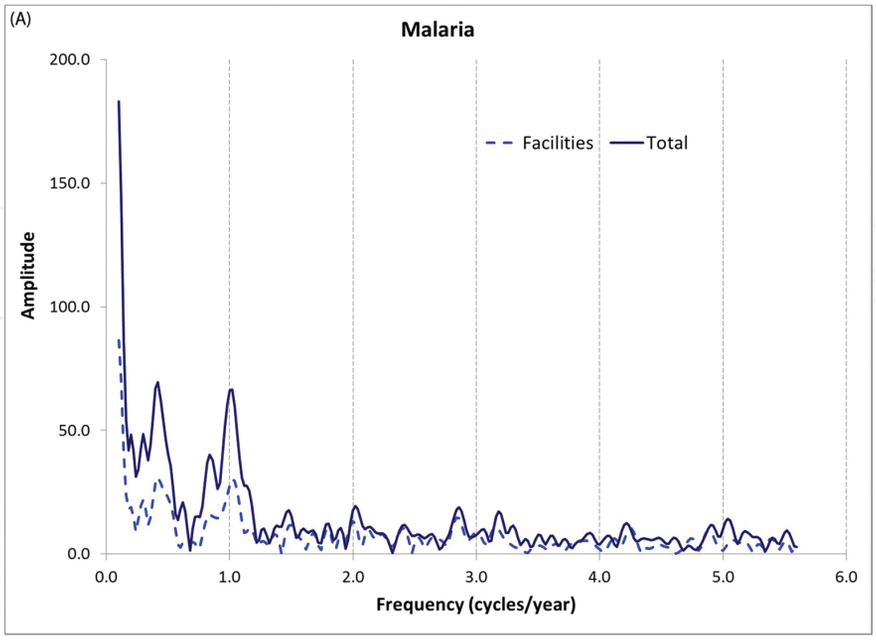


Figure 2. Amplitude ratios compare the relative prominence of the far- and near-transyear versus the calendar year in malaria incidence in Burundi (left and middle) and in Papua New Guinea (right). Despite the fact that both geographic sites are located near the equator, transyears are more prominent in Burundi but are only barely detected in Papua New Guinea. © Halberg Chronobiology Center.



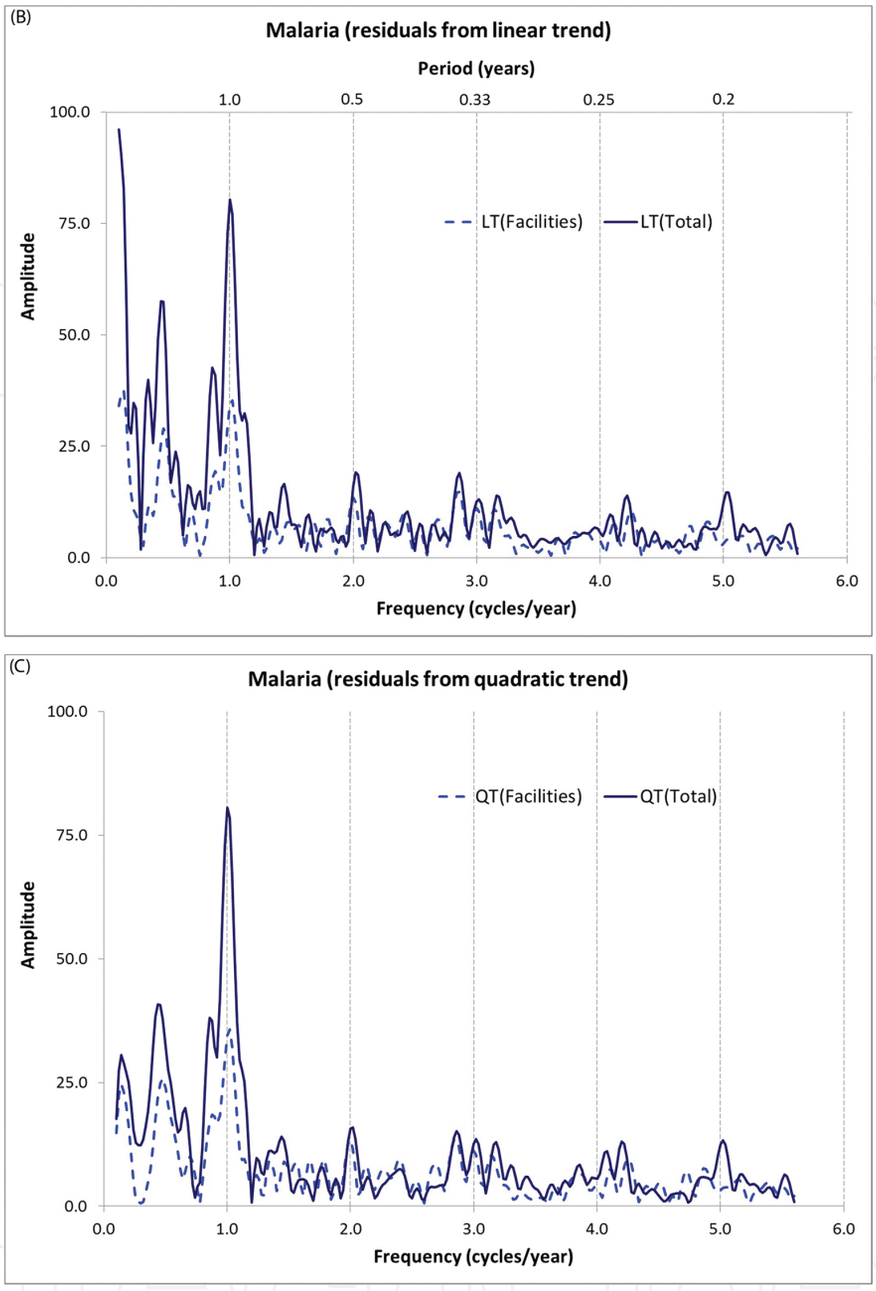


Figure 3. (A) Least squares spectrum of the monthly incidence of cerebral malaria in Papua New Guinea (original data). Spectral peaks correspond to a prominent 1-year component and a cycle with a period slightly longer than 2 years. The large amplitude of the low-frequency component may reflect the increasing trend seen in a plot of the data as a function of time (not shown). © Halberg Chronobiology Center. **(B)** Least squares spectrum of the monthly incidence of cerebral malaria in Papua New Guinea (residuals from a linear trend). In addition to the spectral peaks corresponding to the year and about 2.3-year components seen in the spectrum of the original data (**Figure 3(A)**), there is a smaller peak corresponding to a cycle with a period of about 1.15 years, which may also be the second harmonic of the about 2.3-year cycle. © Halberg Chronobiology Center. (**C)** Least squares spectrum of the monthly incidence of cerebral malaria in Papua New Guinea (residuals from a quadratic trend). Spectral peaks corresponding to the yearly and about 2.3-yearly components remain visible, while the low-frequency amplitude is considerably reduced by comparison to spectra of the original data and of residuals from a linear trend. With a series spanning no more than 10 years, it is not possible to distinguish between a quadratic trend and a cycle with a period of about 10 years or longer. © Halberg Chronobiology Center.

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	Facilities						Total					
	Period	[95%	CI]	Amplitude	[95%	CI]	Period	[95%	CI]	Amplitude	[95%	CI]
	Trial period = 2 years											
Original	2.392	2.084	2.700	30.93	-1.07	62.94	2.420	2.127	2.714	70.05	4.10	135.99
+LinTrend	2.147	1.961	2.332	29.30	7.67	50.93	2.229	2.019	2.440	58.76	14.02	103.50
+QuadTrend	2.104	1.900	2.308	26.24	4.56	47.91	2.228	1.977	2.478	42.14	3.87	80.40
	Trial periods = 10, 2 and 1 year(s)											
Original	15.346	8.607	22.085	93.50	63.98	123.02	17.629	8.924	26.333	247.54	118.83	376.26
	2.055	1.840	2.270	22.88	2.11	43.65	2.448	2.190	2.707	41.14	8.30	73.98
	0.985	0.952	1.017	33.80	13.14	54.46	0.992	0.970	1.013	77.53	45.86	109.19
+LinTrend	7.895	4.377	11.414	35.44	13.66	57.21	***11.879***	***1.871***	***21.887***	***116.30***	***-12.49***	***245.09***
	2.147	1.925	2.370	24.73	3.24	46.23	***2.338***	***2.079***	***2.596***	***41.20***	***7.44***	***74.96***
	0.986	0.953	1.019	33.43	12.55	54.32	***0.993***	***0.971***	***1.016***	***77.20***	***44.40***	***110.00***
+QuadTrend	6.160	2.488	9.831	24.81	0.15	49.47	5.161	3.597	6.725	35.28	0.88	69.69
	2.126	1.892	2.360	25.36	3.22	47.50	2.190	1.970	2.409	41.46	8.50	74.42
	0.987	0.954	1.021	34.12	12.43	55.82	0.996	0.975	1.018	80.29	47.96	112.63
	Trial periods = 10, 2 and 1(fixed) year(s)											
Original	15.614	8.684	22.544	94.12	63.97	124.28	21.895	5.081	38.708	309.80	0.33	619.26
	2.056	1.852	2.260	23.46	3.29	43.62	2.200	1.980	2.419	38.13	7.06	69.21
	1.000			32.42	12.40	52.44	1.000			77.49	46.83	108.16
+LinTrend	7.822	4.518	11.127	35.02	14.10	55.94	***11.405***	***2.988***	***19.821***	***106.28***	***15.08***	***197.47***
	2.137	1.926	2.347	25.13	4.27	45.99	***2.265***	***2.036***	***2.493***	***41.27***	***8.52***	***74.01***
	1.000			32.37	12.13	52.62	***1.000***			***77.00***	***45.43***	***108.56***
+QuadTrend	6.036	2.846	9.226	24.63	1.54	47.72	5.149	3.666	6.632	35.45	2.27	68.64
	2.117	1.898	2.337	25.81	4.30	47.33	2.185	1.977	2.393	41.61	9.82	73.40
	1.000			33.27	12.16	54.37	1.000			80.06	48.92	111.20
	Trial period = 1.2 years											
Original	1.189	1.031	1.346	15.84	-6.75	48.44	1.187	1.058	1.316	40.22	-27.36	107.81
+LinTrend	1.136	1.052	1.220	19.40	-3.05	41.84	1.154	1.074	1.235	43.06	-3.13	89.24
+QuadTrend	1.130	1.044	1.215	18.64	-3.52	40.80	**1.152**	**1.078**	**1.226**	**38.61**	**0.84**	**76.37**
	Trial period = 2.4(&2ndH) years											
Original	2.397	2.162	2.631	30.72	-6.26	67.70	2.405	2.197	2.612	69.37	-6.57	145.31
	1.198			15.39	-21.34	52.12	1.202			38.49	-37.30	114.28
+LinTrend	2.220	2.077	2.363	26.78	2.68	50.87	2.287	2.147	2.428	54.38	5.26	103.51
	1.110			15.93	-8.10	39.97	1.144			38.98	-10.19	88.16
+QuadTrend	1.982	1.925	2.040	23.21	3.03	43.40	***2.300***	***2.164***	***2.436***	***39.01***	***-1.81***	***79.84***
	0.991			35.91	15.58	56.24	***1.150***			***36.29***	***-3.61***	***76.20***
	Trial period = 10,2.4(&2ndH) years on residuals from 1-year fit											
Original	14.160	8.695	19.625	88.98	65.46	112.51	17.656	9.159	26.153	245.83	121.36	370.30
	2.357	2.110	2.603	19.79	-1.41	40.98	2.408	2.240	2.577	40.60	9.60	71.60
	1.178			7.90	-12.43	28.22	1.204			18.59	-11.26	48.45
+LinTrend	**8.008**	**4.596**	**11.421**	**35.59**	**15.31**	**55.87**	12.612	0.755	24.470	118.08	-28.72	364.87
	2.165	**2.048**	**2.283**	**23.80**	**3.95**	**43.66**	2.204	2.095	2.314	38.99	8.10	69.87
	1.083			**16.21**	**-2.85**	**35.27**	1.102			28.80	-0.59	58.18
+QuadTrend	6.042	3.160	8.923	24.49	3.33	45.65	5.133	3.829	6.437	35.08	4.44	65.71
	2.160	2.042	2.278	24.38	4.03	44.73	2.195	2.097	2.293	39.90	10.60	69.21
	1.080			16.94	-2.79	36.67	1.097			30.62	2.22	59.03

Table 2. Nonlinear results from several models fitted to monthly incidence of malaria in Papua New Guinea.

Nonlinear results from several models fitted to the data in Papua New Guinea are summarized in **Table 2**. A 1.0-year synchronized component is most prominent, whereas transyears are not detected with statistical significance (**Figure 2**, right). As seen from **Table 2**, the period of the circannual component has a CI overlapping the exact 1.0 (calendar) year. Accordingly, its period can be fixed in composite models. The period of the about 2.3-year component assumes consistent estimates irrespective of the model considered. As expected from the brevity of the series spanning only 10 years, this is not the case for the decadal component. Indeed, the low-frequency (about 10-year?) component is somewhat problematic: analyses of the original data tend to estimate its period between 17 and 22 years, shortened to about 11 years in some models including a linear trend, or toward 5 years when considering a quadratic trend. Nevertheless, for the total number of cases, the period estimate converges toward 11.4 years when a linear trend is included in the model, albeit with a very wide CI. A near-transyear with a period of about 1.15 years is also detected when fitted as a single

component or as the second harmonic of the about 2.3-year cycle, but its amplitude is much smaller than that of the yearly rhythm and it cannot be detected with statistical significance as part of a composite model including the yearly and decadal cycles. Only in the case of facilities when a linear trend is included in the model and analyses are carried out on residuals from the yearly component is the near-transyear detected with borderline statistical significance, the decadal cycle having an estimated period of 8.0 [CI: 4.6, 11.4] years.

As a compromise, a model consisting of a linear trend, a fixed 1-year component and about 10-year and 2.3-year components was used to approximate the data. For all cases (total), the period estimates were 11.4 [CI: 3.0, 19.8] and 2.26 [CI: 2.04, 2.49] years. Using these estimates, a composite model was fitted by the linear cosinor, including the candidate 1.1-year component. The model as a whole and all its components are detected with statistical significance for both facilities and all cases (P<0.001). Results from this multiple-component fit were used to approximate the data, as illustrated in **Figure 4**.

Whatever model is considered, malaria in Papua New Guinea is characterized by a prominent yearly component, a cycle with a period slightly longer than 2 years and a trend that may correspond to a longer cycle, possibly with a period of about 10 years. No far-transyear is detected and a near-transyear may be the second harmonic of the about 2.3-year cycle, much less prominent than the calendar year, in sharp contrast with results in Burundi, also located near the equator. Thus the incidence of malaria differed not only by the absence in Burundi of a calendar-year component found in Papua New Guinea, but also by the presence of prominent far- and a near-transyears in Burundi, but only a candidate near-transyear in cerebral malaria incidence in Papua New Guinea. Accordingly, the near-transyear-to-calendar year amplitude

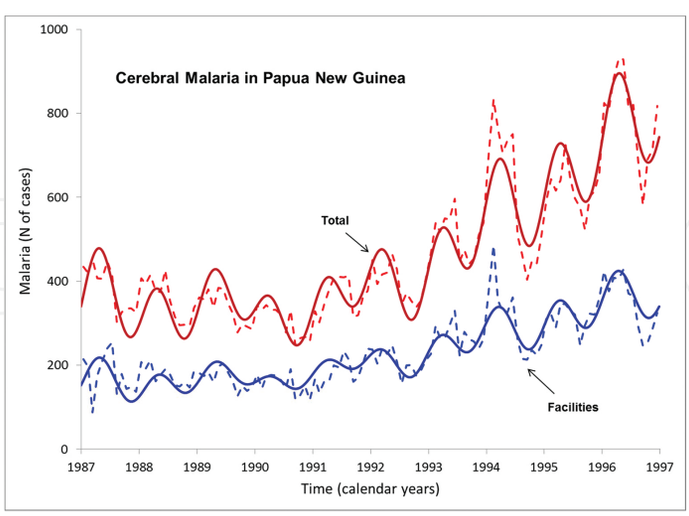

Figure 4. Monthly data on the incidence of cerebral malaria in Papua New Guinea are fitted with a model consisting of a linear trend, a 1.0-year synchronized rhythm, about 11.4-year and about 2.3-year components, and a candidate 1.1-year near-transyear. Whereas the contribution of each component to the composite model can be seen by the naked eye, this is not the case for the near-transyear that only has a very small amplitude. © Halberg Chronobiology Center.

ratio, if the presence of a near-transyear in Papua New Guinea is accepted, was smaller than 100% (**Figure 2** (right)).

Variable	Period	[95% CI]		Amplitude	[95% CI]		[1-parameter limits]	
API	17.21	12.97	21.45	0.98	0.00	1.95	0.51	1.45
	9.60	7.64	11.56	0.66	-0.24	1.56	0.23	1.09
SPR%	18.42	13.70	23.13	1.02	-0.07	2.12	0.50	1.55
	10.07	8.02	12.12	0.73	-0.28	1.73	0.24	1.21
SfR	16.62	11.36	21.88	0.13	-0.03	0.30	0.05	0.21
	8.27	7.24	9.30	0.15	-0.01	0.32	0.07	0.23
Pf%	25.71	18.97	32.44	4.84	2.11	7.57	3.53	6.15
	9.15	8.14	10.16	3.18	0.49	5.87	1.89	4.48
Pf%	22.70	13.29	32.11	5.50	0.40	10.60	3.35	7.66
	15.94	11.04	20.84	3.71	-1.57	8.99	1.48	5.94
	8.81	8.02	9.60	2.80	0.91	4.69	2.00	3.60

All models fitted with a linear trend.

API: Annual parasite incidence (malaria positives in 1000 population).

SPR%: Slide positivity rate (positives per 100 slides examined).

SfR: Slide falciparum rate (Pf infection per 100 slides examined).

Pf%: Pf infections per 100 malaria positives.

Table 3. Nonlinear results of yearly incidence of malaria in Thailand.

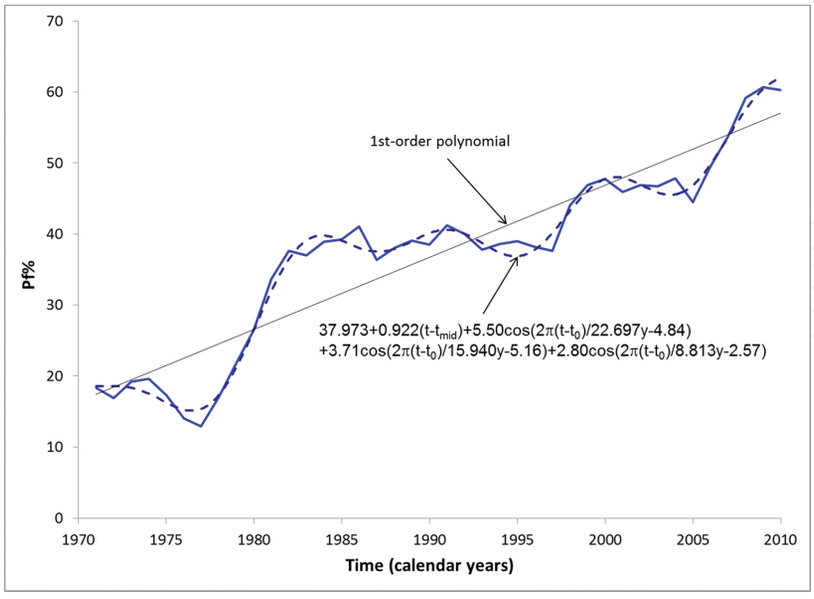

Figure 5. The yearly data on the percentage of *Plasmodium falciparum* infections (expressed per 100 malaria positives) in Thailand are fitted with a model consisting of a linear trend and cycles with periods of about 22.7, 15.9, and 8.8 years. © Halberg Chronobiology Center.

Tentative decadal components were also found by linear-nonlinear cosinor in the yearly data from Thailand (**Table 3**). Results for the percentage of *P. falciparum* infections per 100 malaria positives are illustrated in **Figure 5**.

4. Discussion

Malaria is transmitted in tropical and subtropical areas where Anopheles mosquitoes can survive and multiply. Malaria parasites can complete their growth cycle in the mosquitoes. Temperature is particularly critical. Generally, in warmer regions closer to the equator, transmission is more intense, and malaria can be transmitted year-round. It is not surprising then that components with periods other than 1 year may also be detected, reflecting the influence of solar and other factors not directly related to temperature.

Our interest in the relative contributions of the seasons vs. helio-, interplanetary and terrestrial magnetism was stimulated by the report by Dimitrov et al. [8] of a sharp calendar-yearly peak in the spectrum of monthly admissions of cerebral malaria in Papua New Guinea (latitude -6°; 1987–1996) with no comparable transyears (components longer than a year with a CI of their period not overlapping the calendar year). Decadal and longer cycles cannot be examined in the short series of malaria incidence in Burundi analysed herein, although, as noted, an about 5-year cycle can be the second harmonic of the Horrebow-Schwabe cycle. An about 2-year component is also found in interplanetary and geomagnetism as well as in the El Niño Southern Oscillation (ENSO) and may show cross-wavelet coherence with malaria in certain regions of Thailand [9].

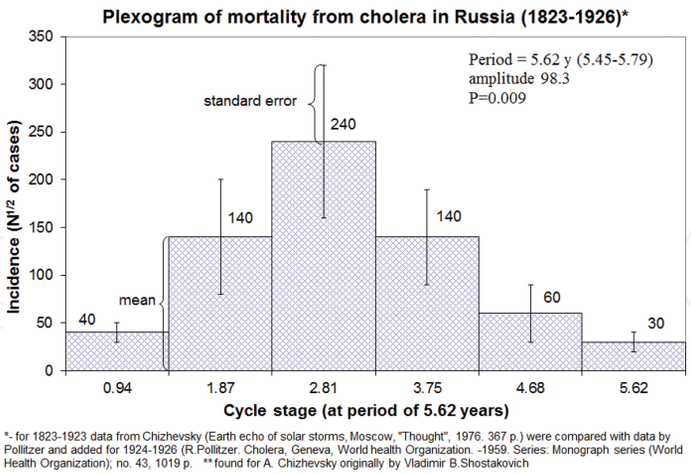

Figure 6. An about 5.6-year component was also detected in yearly data from Chizhevsky on mortality from cholera in Russia [19, 20]. © Halberg Chronobiology Center.

An about 5-year component in his time series on cholera incidence was communicated to Alexander Leonidovich Chizhevsky [17] by Vladimir Boleslavovich Shostakovich (**Figure 6**) [18]. Decadal and multidecadal signatures are found in diphtheria, croup, relapsing fever, and

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cholera at a time when these diseases were rampant in meta-analyses [18] of statistics assembled descriptively by Chizhevsky [17]. Chizhevsky also reports on data from Dr. SI Ivanchenko regarding the incidence of malaria in the North Caucasus from 1916 to 1930. He noted an inverse relationship between the incidence of malaria and air ionization. Albeit short, the record can be characterized by a decadal component, as illustrated in **Figure 7**.

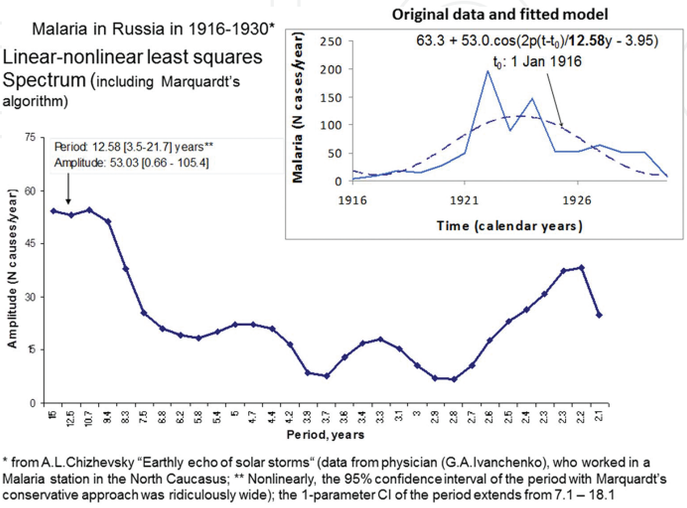

Figure 7. A decadal component characterizes the incidence of malaria in Russia between 1916 and 1930, as seen from the low-frequency spectral peak, resolved nonlinearly as an about 12.6-year component, which is fitted to the data (top right). Note a secondary smaller spectral peak corresponding to a period of about 2.3 years, as observed also in the data from Burundi (**Figure 1**) and Papua New Guinea (**Figure 3**). © Halberg Chronobiology Center.

In the case of malaria, it is surprising to see the presence of a calendar yearly component in the tropical region of Papua New Guinea, which is absent in Karuzi, Burundi (at 3° from the equator at a latitude, but not a longitude similar to that of Papua New Guinea). The original publication on malaria in Burundi [10] used data on rain and temperature and a vegetation index to predict malaria incidence. The terrestrial environmental variables could also be related to solar activity, as reviewed by Clayton [19] and Abbot [20].

Both the near- and far-transyears are features of the solar wind's speed and of geomagnetics. Space weather and geomagnetism may act via rainfall and its consequences. Just as helio-, interplanetary, or geomagnetism can influence sudden cardiac death [2], they may also influence communicable diseases, probably via the host, whose steroidal defence shows a decadal cycle [21] and/or by the invading microorganism. Bacterial mutations can also undergo a cycle mirroring that of sunspots [22–24].

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