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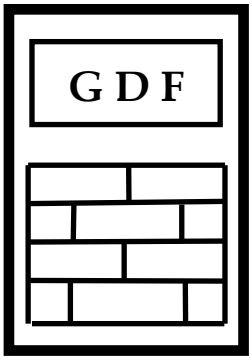

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Cancer erosion in German human society: 1980 – 2008

1. Summary

The recent studies on cancer erosion in different human communities [1-3] is continued on the incidence rate (IR) and mortality rate (MR) in Germany for the calendar periods of 1980-2006 and 1980-2008, respectively. All results obtained according to the previously established methodology are presented in graphic manner and short comments in view to better understand their significances. The development amplitude of all cancers is estimated by the three different representations (age cascade of cancers, S-rep and U-rep) previously defined on similar data from other countries. Now is the first time when results obtained from IR data are compared with the ones obtained from MR data. The main conclusions:

(i) both IR(t) and MR(t) have the same general age evolution, but different calendar evolution, so that IR(t) is much more sensitive to social events;
(ii) both age and calendar evolutions of IR and MR evidence again the strong coupling of cancer development processes of MP and FP;
(iii) the three representations differently reveal the social events evidencing their specific significances. Some new quantities are introduced for Universal representation in view to better evidence these social effects on cancer evolution;
(iv) analyzing all results, especially the phylogenies of Universal parameters, it results again that FP tends to "socialize" cancer, i.e. its resistance and tendency to cluster increase with cancer amplitude.

2. Raw statistical data

Statistical data of IR and MR as new annual cases for all cancers (C00-C97 excepting C44) reported to 100,000 persons on the same sex and 5 year segment of age were taken from the website of Robert Koch Institute – Germany [4]. The age ranges were 39-84 age years (ay) for IR and 4-84 ay for MR.

3. Incidence rate of all cancers: 1980-2006

Figure 1 presents the IR values at each age and sex group averaged on the all calendar period. These data allow estimating the main parameters for the three representations described previously [1-3]:

- the Age Cascade of Cancers (ACC);
- Sigmoidal representation (S-rep); and
- Universal representation (U-rep).

3.1. ACC

Figure 2 shows the ratio R(t) = IR(MP)/IR(FP) averaged for each age on the all calendar period. Due the limited range of age groups, it is possible to estimate only parameters r2 and r3 corresponding to C50 and C61, respectively.
Figure 3 shows the evolution of these parameters on the calendar period. These values are comparable with the previously calculated for other human communities [2, 3]. Values for r3(C61) are always bigger than r2(C50) and their ratio reveals the most important social events (Figure 4). This dependence appears like a "potential hollow" on the period of 1981-1999 formed by four distinct stages:

- 1981-1987 an abrupt decrease corresponding to a social relaxation;
- 1987-1991 with an almost constant value (bottom of the hollow) corresponding to an equal increase of C50 and C61 (Figure 3);
- 1991-1999 the abrupt increase corresponding to the increase of social stress in MP and a temporary relaxation in FP.
- after 1999 social stress in FP begins to increase, but with a lower slope than in MP.

3.2. S-rep

S-rep allows to estimate by nonlinear regression the saturation value, a, and the half time, t1/2 of IR(t) [1] with correlation coefficients (correl) better than 0.999. Figure 5 shows the values for a parameter for both sex groups on the considered calendar period. The following important facts must be pointed out:

- a(MP) > a(FP) in good agreement with r3 and r2 parameters;
- at 1999 both graphics show maximum values, more pronounced in FP, so that the ratio a(MP)/a(FP) shows a minimum value (Figure 6).

The difference in shape between graphics in Figures 4 and 6 is due by the fact that ASC reveals the exact IR on each age, while S-rep considers its limiting value for $t \to \infty$. It is important to note the average value of a(MP)/a(FP) in comparison with r3/r2 (Figure 4) and these ones for the other countries (Table 8 [5] and Table 7 [2], respectively).
Figure 7 shows values of t1/2 for both sex groups on the calendar period. It can observe that:

- t1/2(calendar period) has the same shape like parameter a for both MP and FP;
- t1/2 (FP) > t1/2(MP), but the two graphics appears as a social hysteresis on the calendar period because at 1980 and 2006 both sex groups have equal values;
- at 1999 both graphics show maximum values, more pronounced in FP.

These latest two facts show that FP has an increasing resistance to cancer up to 1999 and abrupt decrease after, while MP has an almost constant decrease of it on all the calendar period.

3.3. U-rep

As it was pointed out in the previous studies [1], U-rep considers only the $\theta(t) = IR(t)$ values up to approximately t1/2, so that:

- the age range considered was 14-64 ay and
- the initial values for all non-linear regressions were: N=-20, M=100, Ao=300 with correlation coefficients 0.99-0.999.

Figures 8-11 show the main ontogenic parameters according to their general significances:

$$M \sim \ln Ctr, -M/N \sim \ln ctr, Ao \sim \ln ctr, -N^2/M \sim CS \quad (3.1)$$

for both sex groups on the calendar period.
It results that (see the similar observations for Australia [1] and other countries [5]:

- $Ctr(FP) > Ctr(MP)$ on the almost all period;
- $ctr(FP) > ctr(MP)$;
- $CS(MP) \approx CS(FP)$;
- 1999 appears again as an important social transition for both sex groups, but 2002 appears as an additional transition year especially for MP.

It is important to observe some details in these behaviors, namely:

- FP senses the main transition since 1997 by a slight decrease first followed by an abrupt decrease of Ctr, ctr and reverse variation for CS at 1999 (see previous comments on them relationship [1-3]). Calendar year of 1999 appears in all FP ontogenic parameters as a singular point because the other points form a smooth variation.
- MP shows almost constant values up to 1999 when an abrupt increase of Ctr, ctr and decrease of CS up to 2002 after when reverse variations of these parameters occur up to 2006.

In view to better evidence some particular aspects of MP and FP behavior for cancer development, we can define the following derivate quantities:

$$dM = M(MP) - M(FP) \sim \ln(Ctr(MP)/Ctr(FP)) \quad (3.2)$$

$$d(-M/N) = -M/N(MP) + M/N(FP) \sim \ln(ctr(MP)/ctr(FP)) \quad (3.3)$$

$$dCS = CS(MP) - CS(FP) \quad (3.4)$$

Normalized Amplitude (NA) = (M+M/N)/(-N^2/M) ~ (ln(Ctr/ctr))/CS (3.5)

Relative Normalized Amplitude (RNA) = NA(MP) – NA(FP) (3.6).

The main purpose of these quantities is to better reveal the coupling strength of cancer development in MP and FP by comparing their amplitude for cancer development in standard conditions for kinetic entity (ctr) and coupling strength (CS) between inert and transforming components. As it was to expect, the first three quantities show the same general variations as the quantities of origin (Figures 12-14), but differing by relative values between MP and FP, namely:

dM ~ ln(Ctr(MP)) ; d(-M/N) ~ ln(ctr(MP)) ; dCS ~ CS(MP) (3.7)

dM and d(-M/N) have the same shape, while dCS has their mirror image.
On these graphics appears a dramatic social transformation starting at 1997 with two important extreme values at 1999 (also appearing as a singular point) and 2002. It is important to note that at 2006 all values are close to the previous trend defined by the period of 1980-1997.
Figure 15 shows that

NA(MP) > NA(FP), (3.8)

both of them having the same shape like M and –M/N in Figures 8 and 9, respectively. This fact is in good agreement with a(MP) > a(FP) in S-rep (Figure 5), but their shapes of variation differ.
Figure 16 shows RNA vs calendar period with the shape and characteristics similar with dCS (Figure 14).

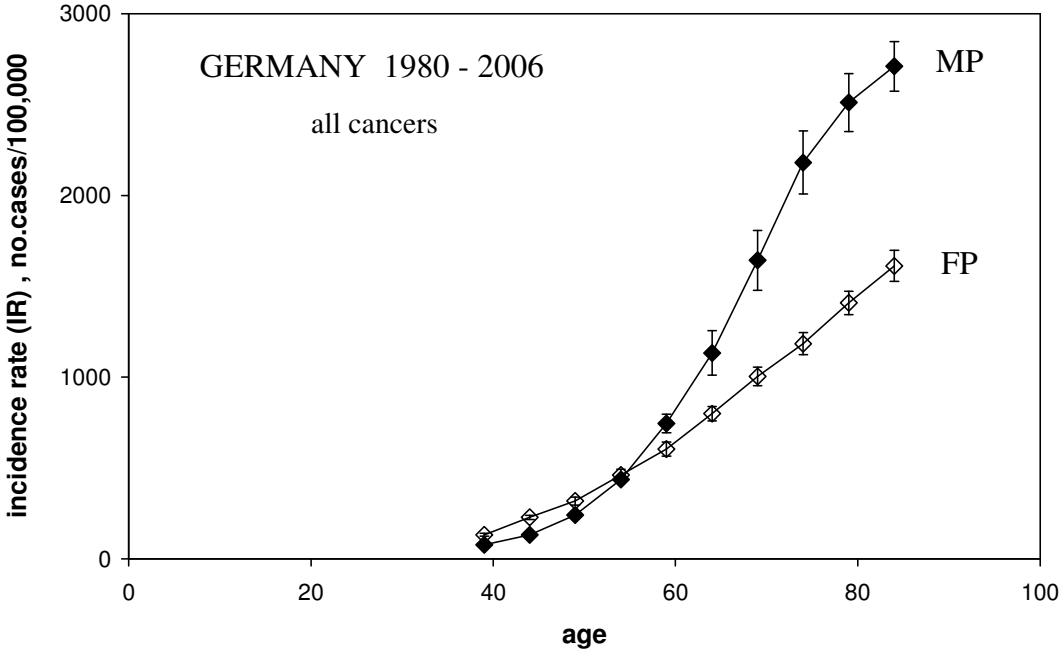
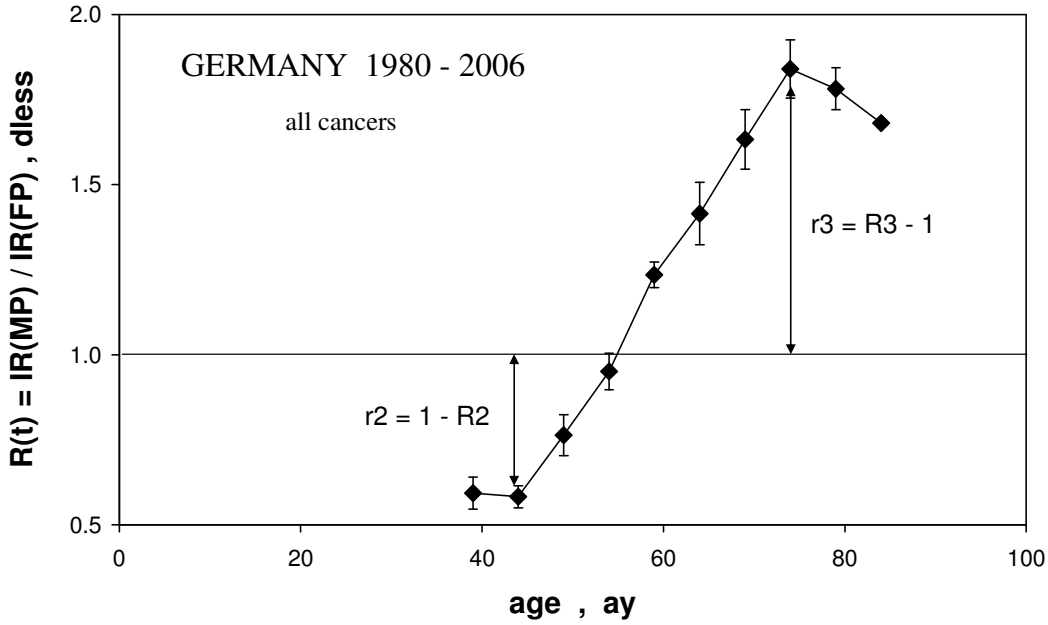


Figure 1.



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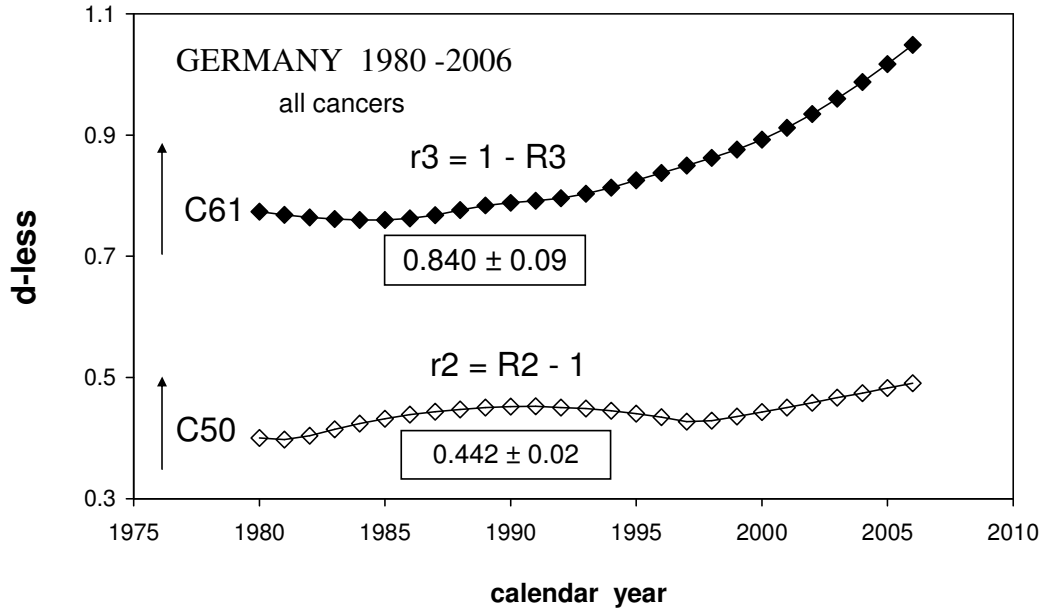

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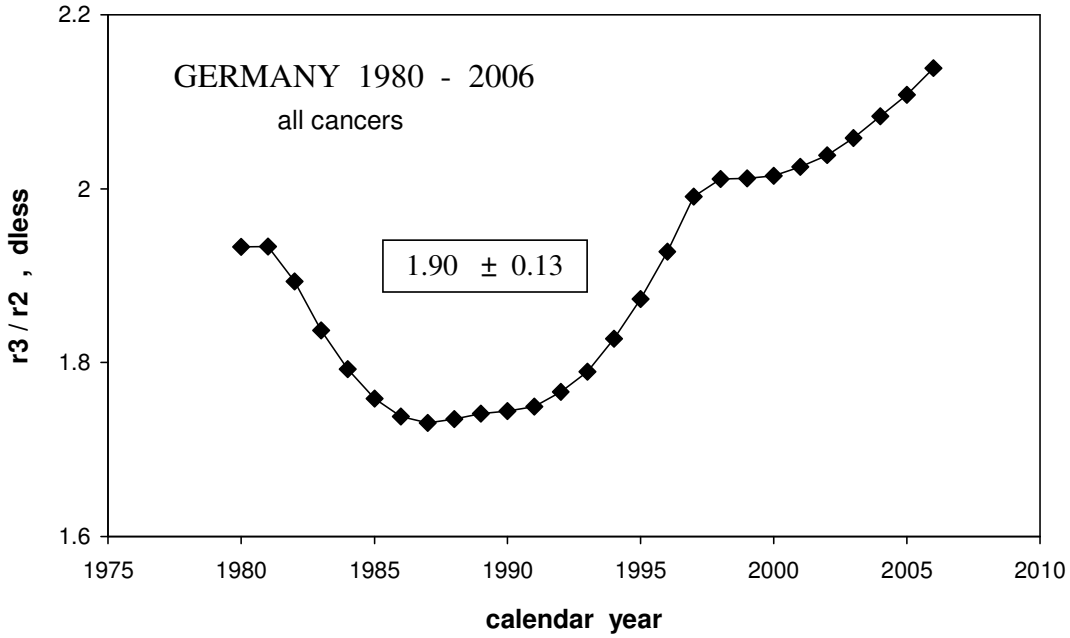

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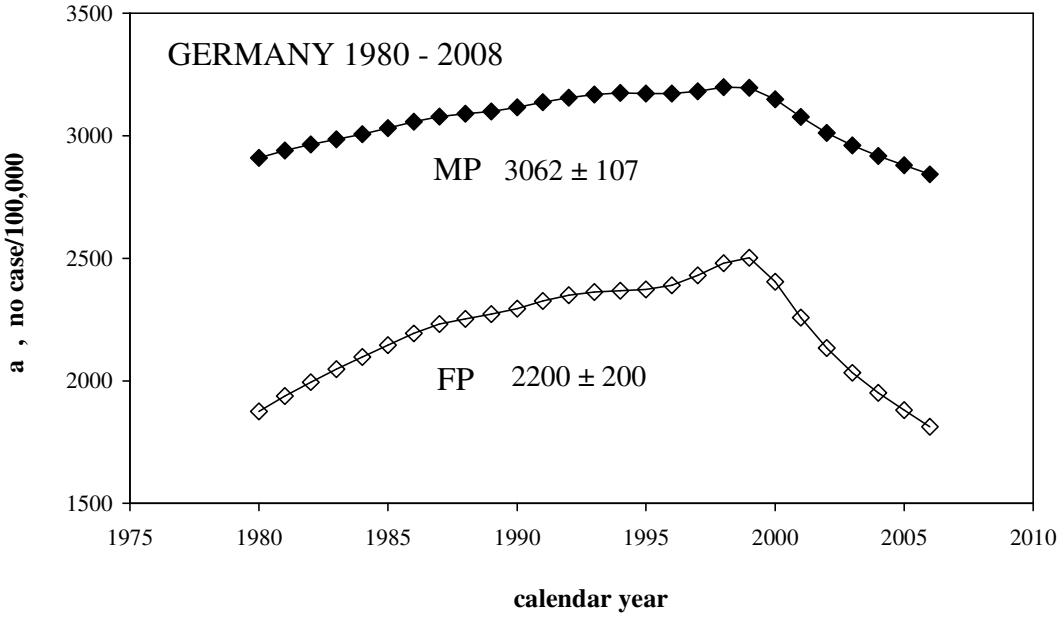

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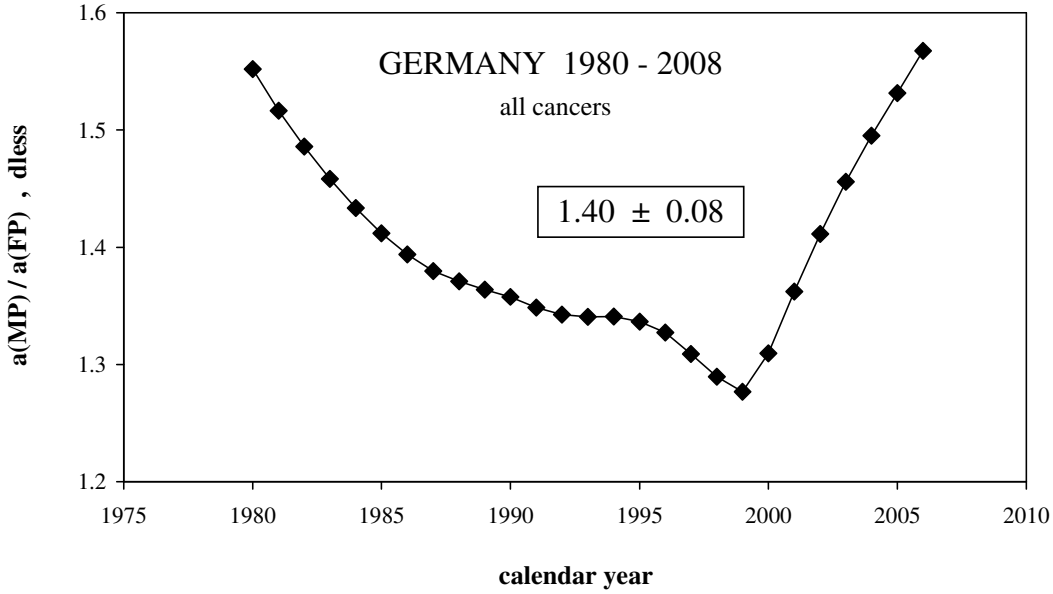

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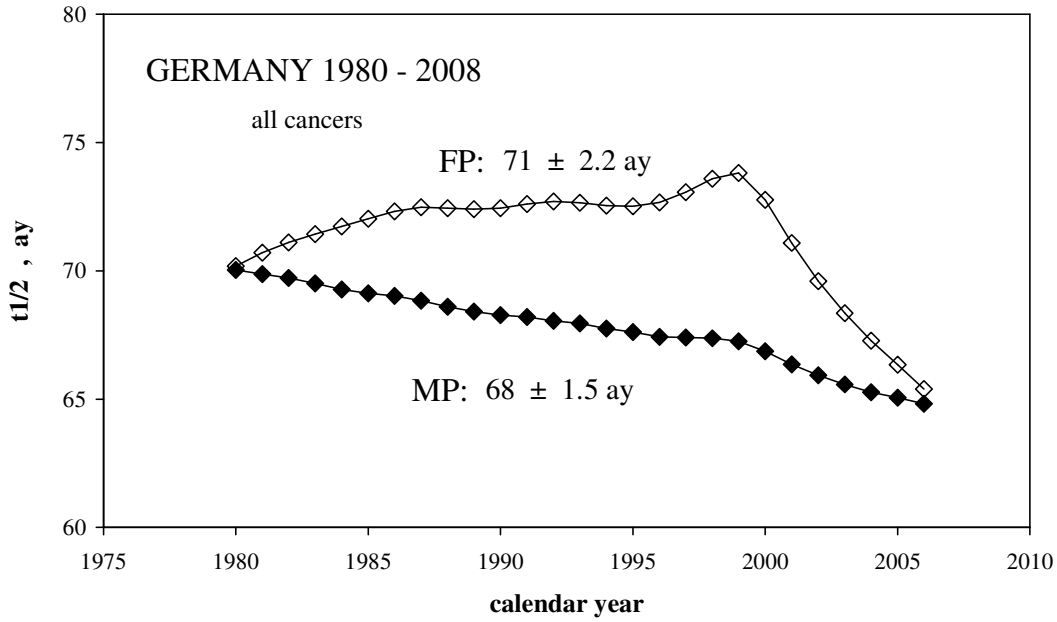

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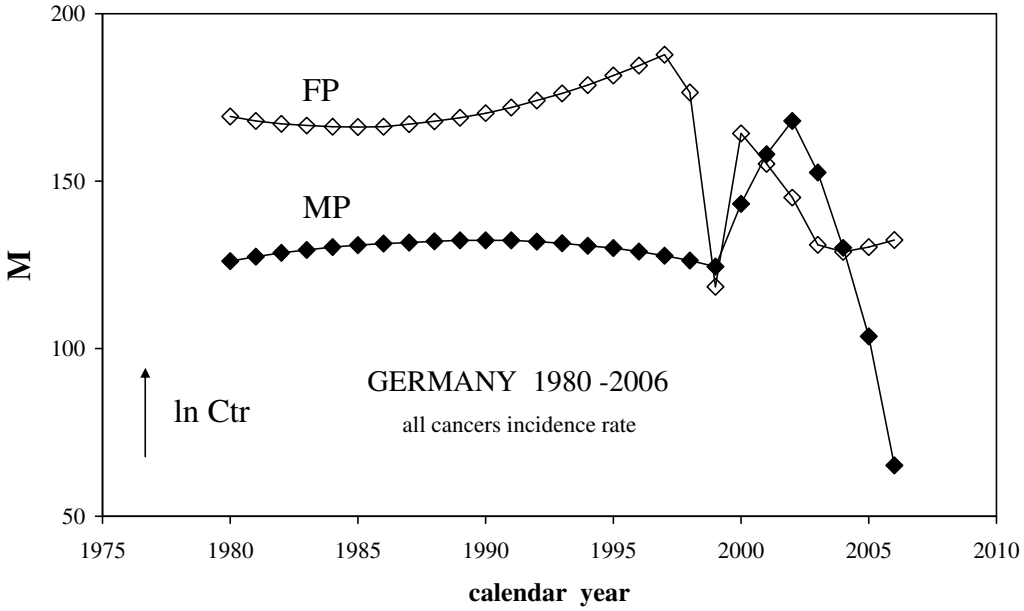

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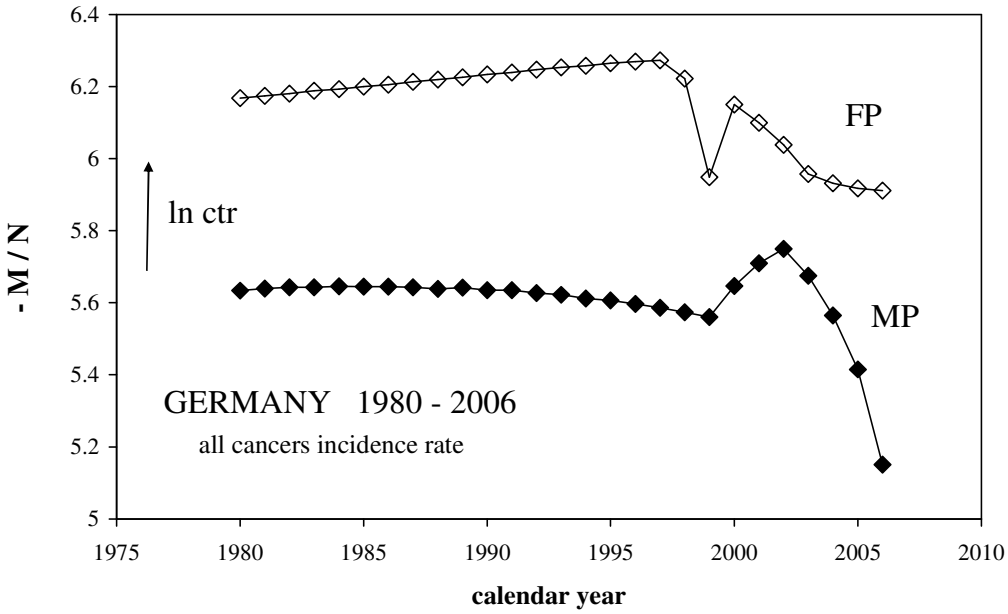

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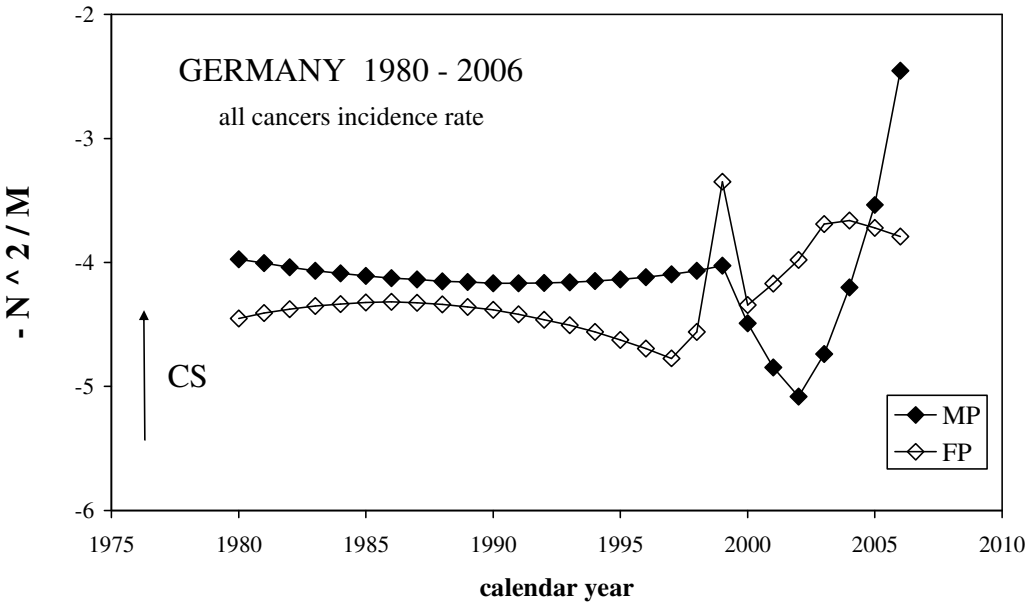

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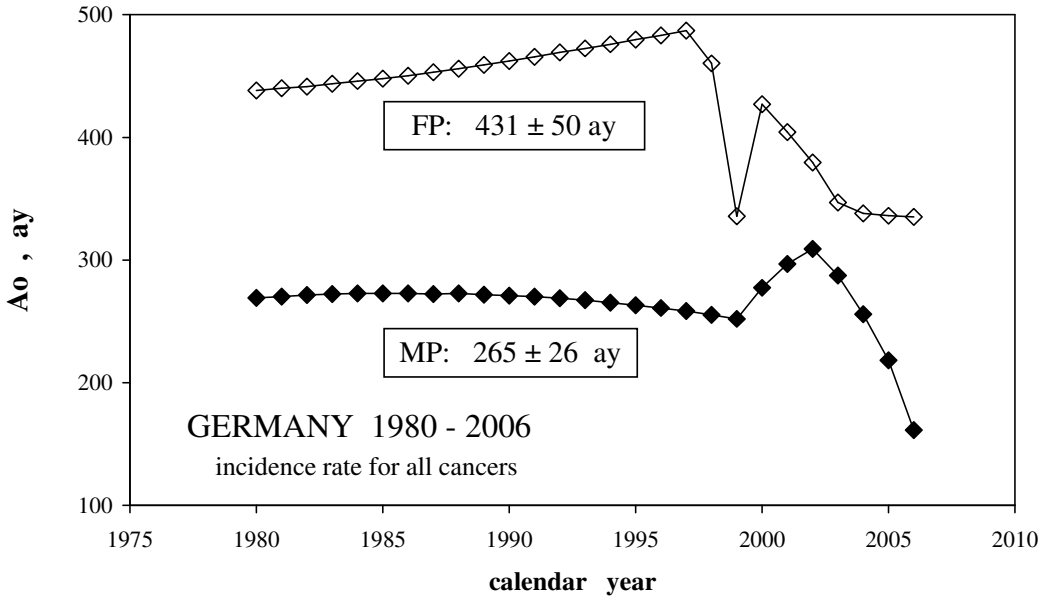

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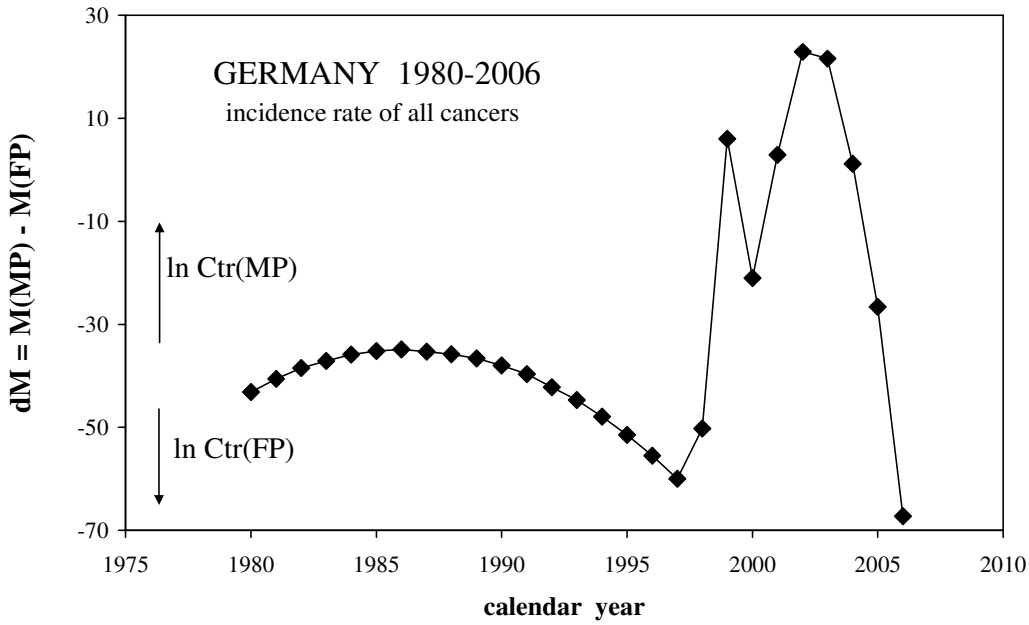

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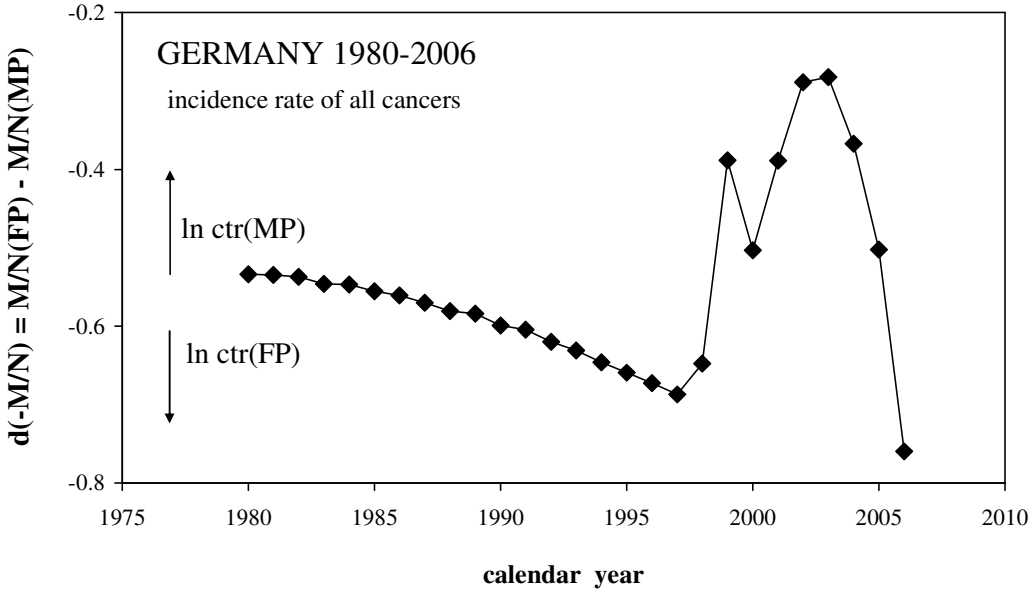

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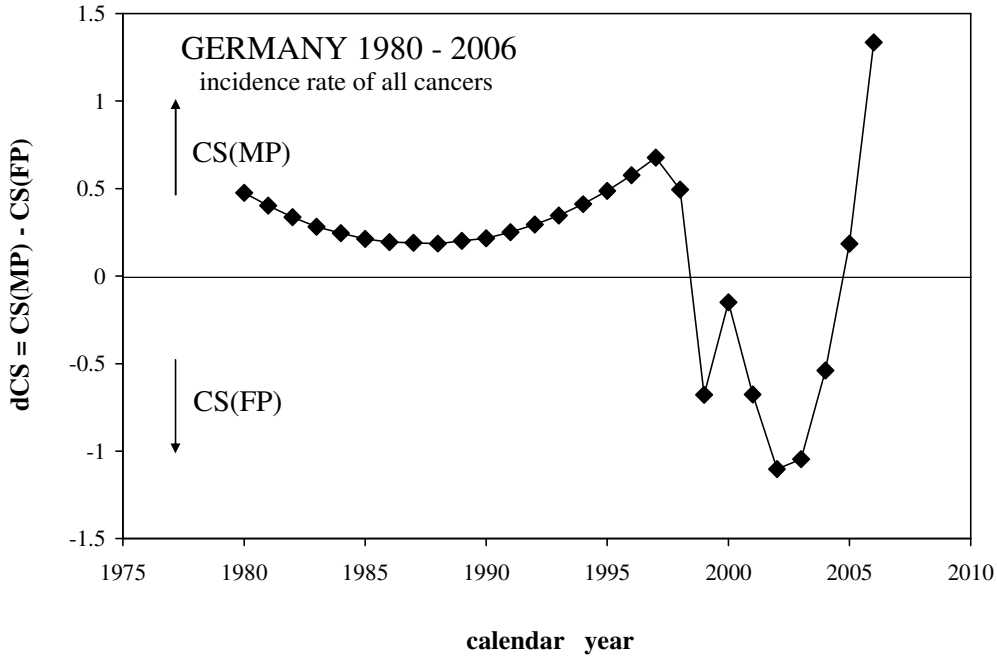

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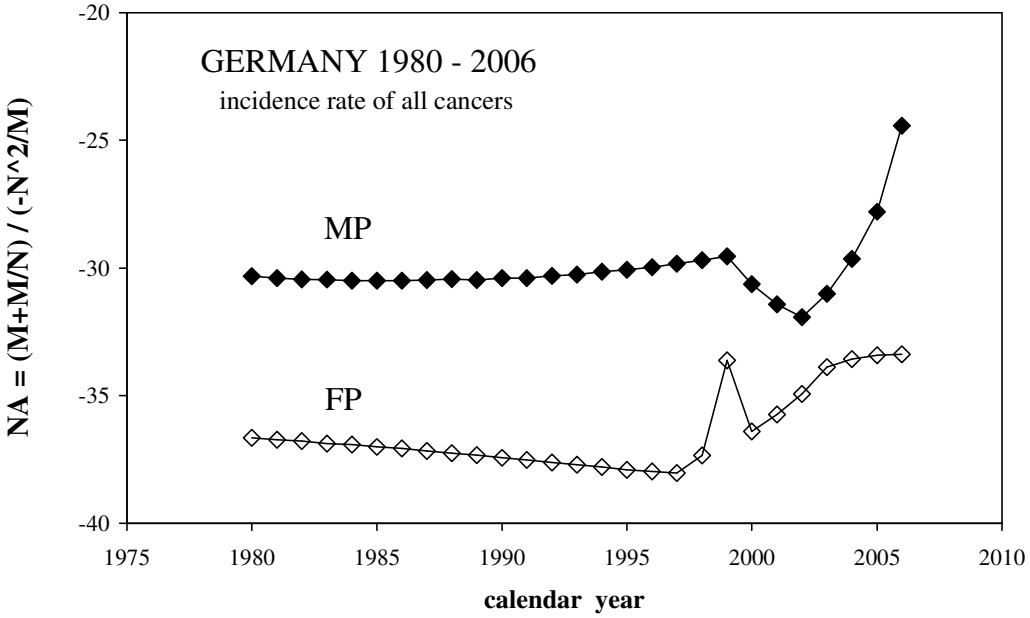

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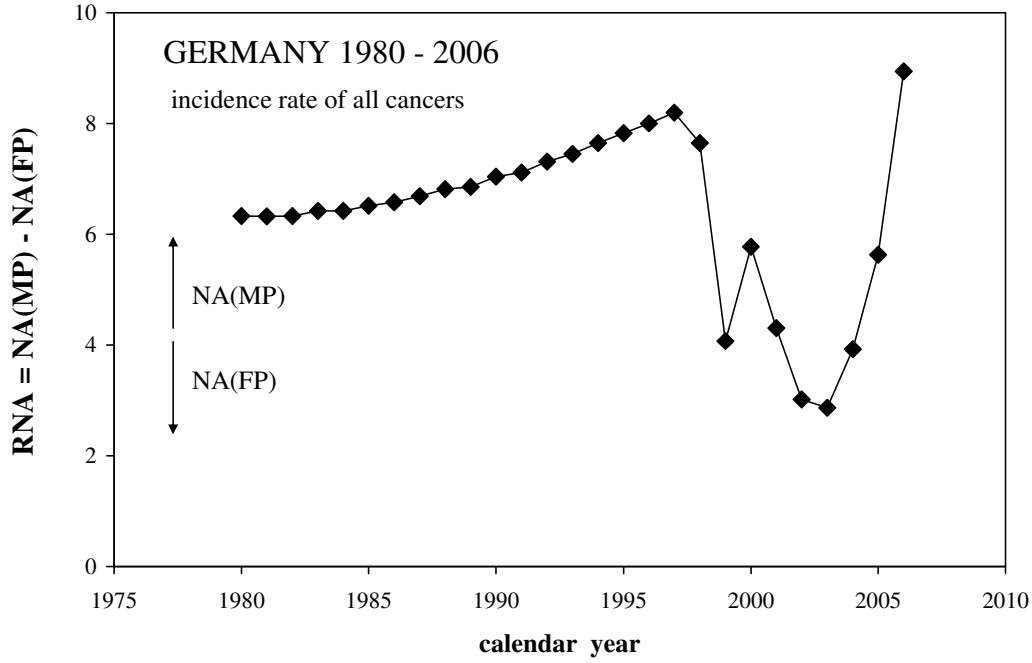


Figure 16.

4. Mortality rate of all cancers: 1980 – 2008

It was expected that MR data show a different process nature and amplitude than IR data. However, MR(t) (Figure 17) looks very similar to IR(t) (Figure 1), so all retrieval algorithm previously described by the three representations is available here.

4.1. ACC

Figure 18 shows the complete age cascade of cancers by the similar ratio:

$$MR(t) = MR(MP) / MR(FP) \quad (4.1)$$

averaged for each age on all calendar period. Its shape is also similar with the general fit previously analyzed for IR(t) data from other countries (Figure 2, [2]), but it is shifted to MR(t) = 1.2. It is important to compare the results obtained in the previous chapter (Figure 2) with the similar ones obtained according to the main contributions of mr2 and mr3 corresponding to C50 and C61, respectively.
Figures 19 and 20 show the calendar evolution of these two quantities and their ratio. No particular modification in mortality behavior can be revealed, excepting the continuous decrease of the ratio mr3/mr2 and its average value is closer to the golden ration (1.618…) than the r3/r2 (Figure 4), as it was previously observed for IR(t) [5].

4.2. S-rep

S-rep was applied in the same conditions as previously (chapter 3.2.). Figure 21 shows the calendar evolution of parameter a for both sex groups where two prominent maximum values can be evidenced, namely at 1997 (MP) and 1998 (FP). On the other hand, in general a(MP) > a(FP) excepting for the period of the two maximum values where FP mortality amplitude exceeds the MP one. This can be better observed in calendar evolution of their ratio (Figure 22).
Figure 23 shows the calendar evolution of t1/2 for both sex groups where these particular behaviors are also revealed. By comparing with Figure 7, it results a shift of 1-2 years between the maximum values from IR and MR:

$$\begin{aligned} &\text{MP: } 2 \text{ years} = \\ &= \text{calendar (max t1/2(IR))} - \text{calendar (max t1/2(MR))} \\ &\text{FP: } 1 \text{ year} = \text{calendar (max t1/2(IR))} - \text{calendar (max t1/2(MR))} \end{aligned} \quad (4.2)$$

As it was expected we observe that:

t1/2 (MR) > t1/2 (IR) (4.3)
MR: t1/2 (FP) > t1/2 (MP)

which proves once again that FP is more resistant to cancer than MP.

4.3. U-rep

U-rep is applied in the same conditions as for IR(t) (chapter 3.3.).
Figures 24 – 27 show the calendar evolution of the basic ontogenic parameters which do not present any important behavior modifications. This fact is substantiated also by the standard deviations associated with their values averaged on the overall calendar period.
However, their relative variations as defined previously by eqns. (3.2)-(3.4) and (3.6) show prominent extreme values placed at 1998 and 2000 corresponding to:

FP 1998: max (ln Ctr, ln ctr), min (CS) (4.4)
MP 2000: max (ln Ctr, ln ctr), min (CS).

It results again as for IR(t) that

NA(MP) > NA(FP) (4.5)

in contrast with

M(FP) > M(MP) (4.6),

but calendar evolution of NA is almost smooth for both sex groups (Figure 31).
Figure 32 shows the calendar evolution of RNA where the two maximum values appear again:

1998: NA(MP) and 2000: NA(FP) (4.7).

However, the average value on the overall calendar period has a relative small standard deviation.

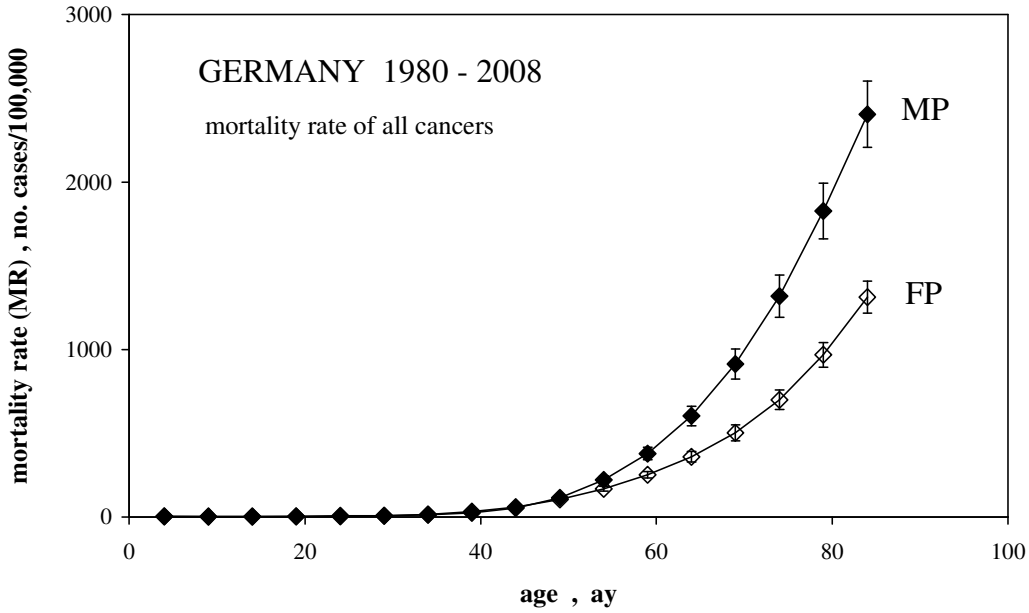
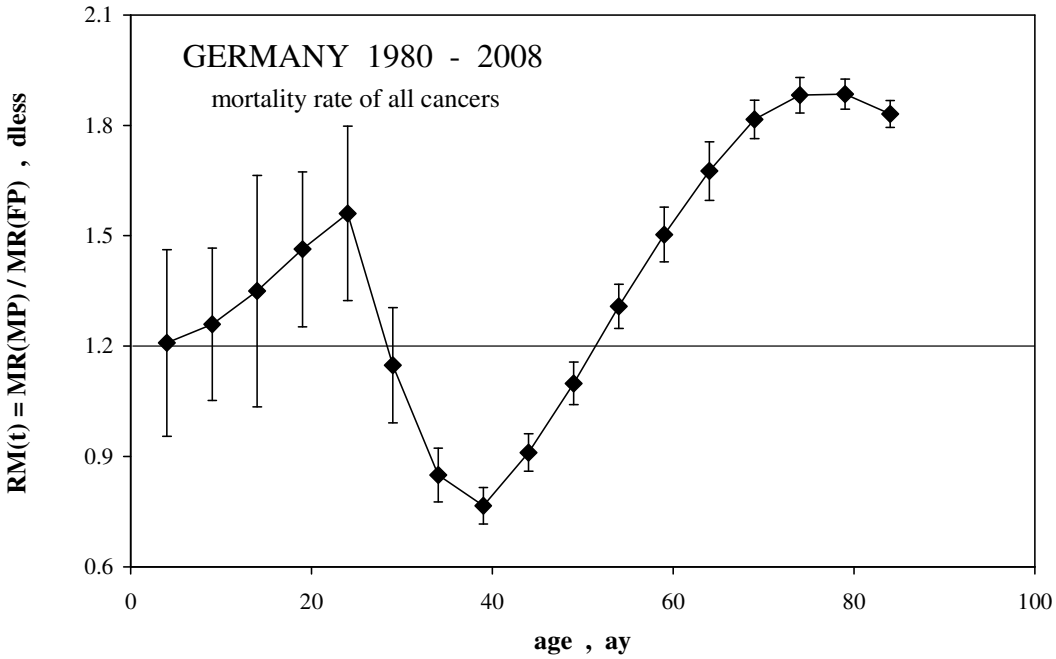


Figure 17.



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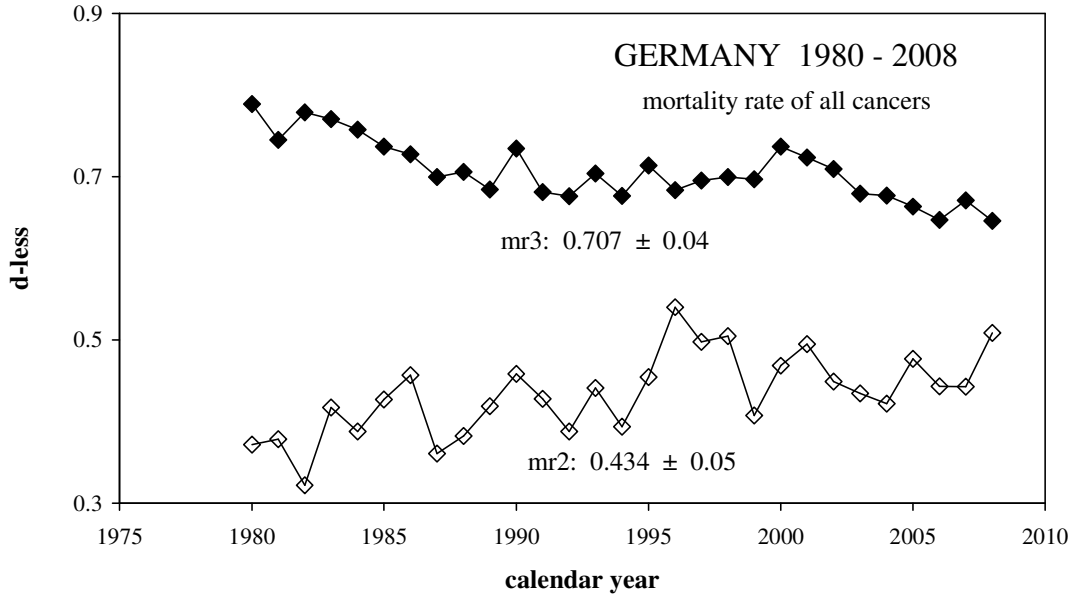

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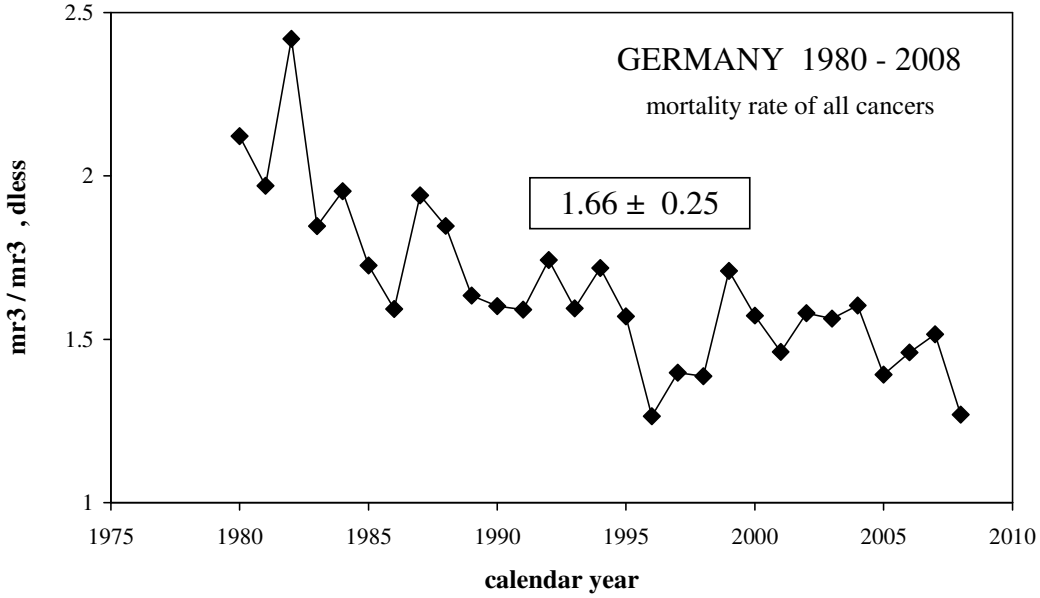

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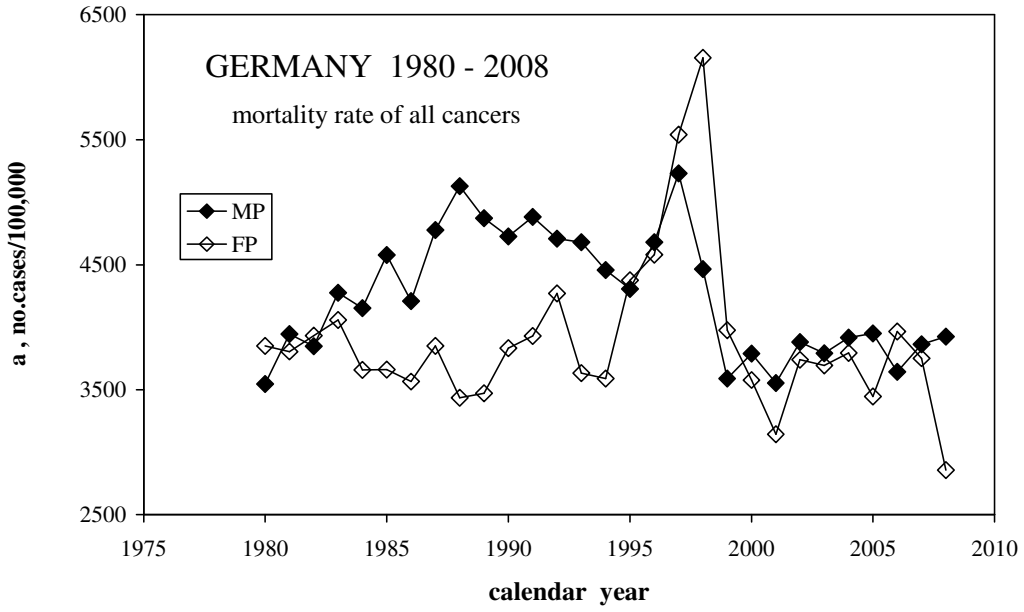

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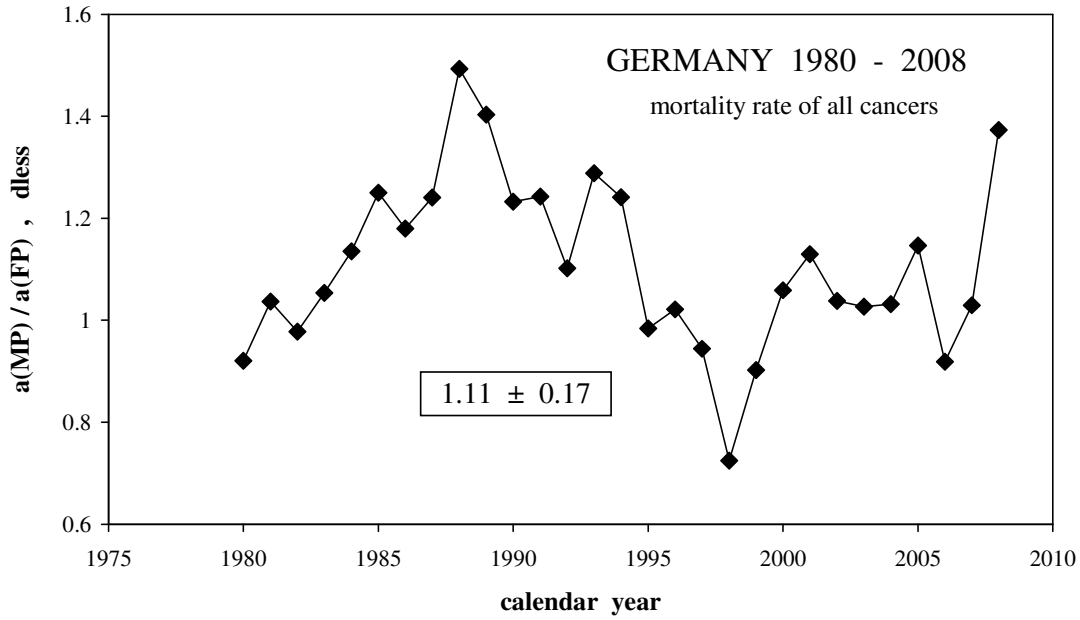

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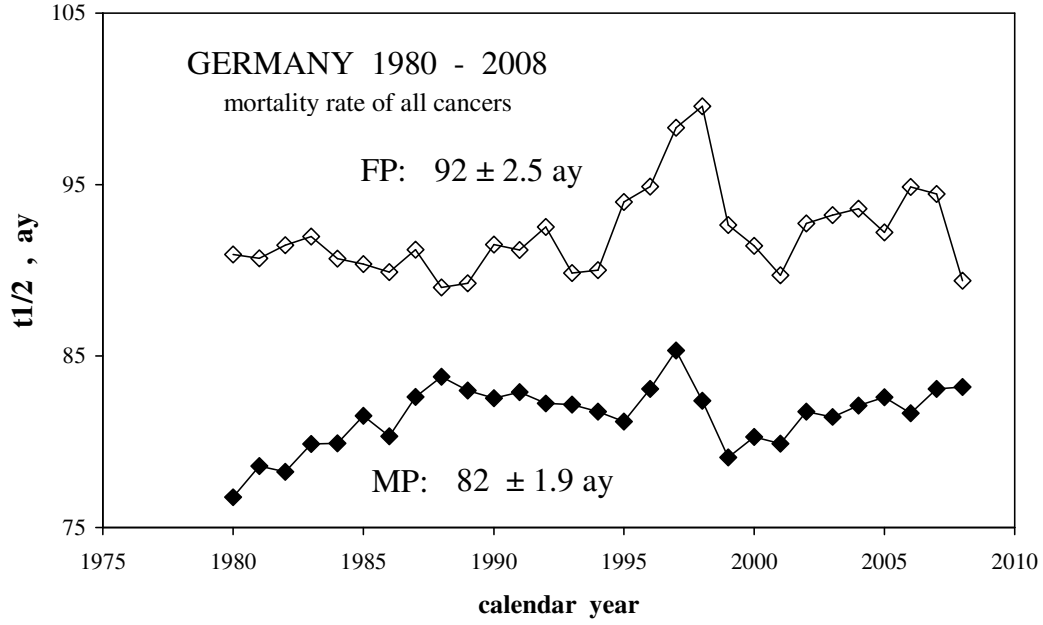

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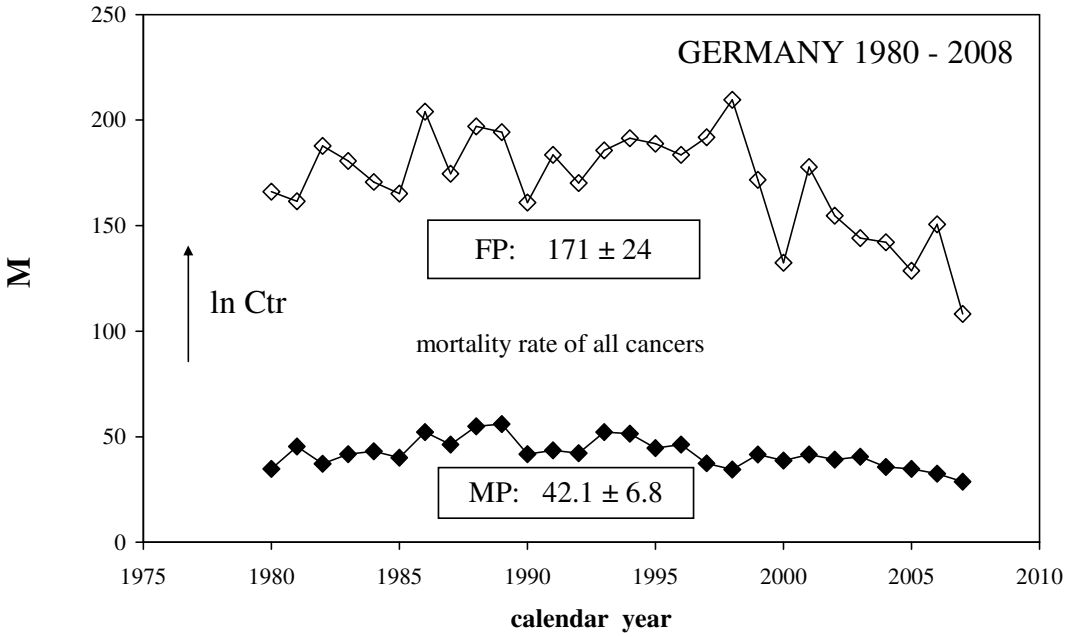

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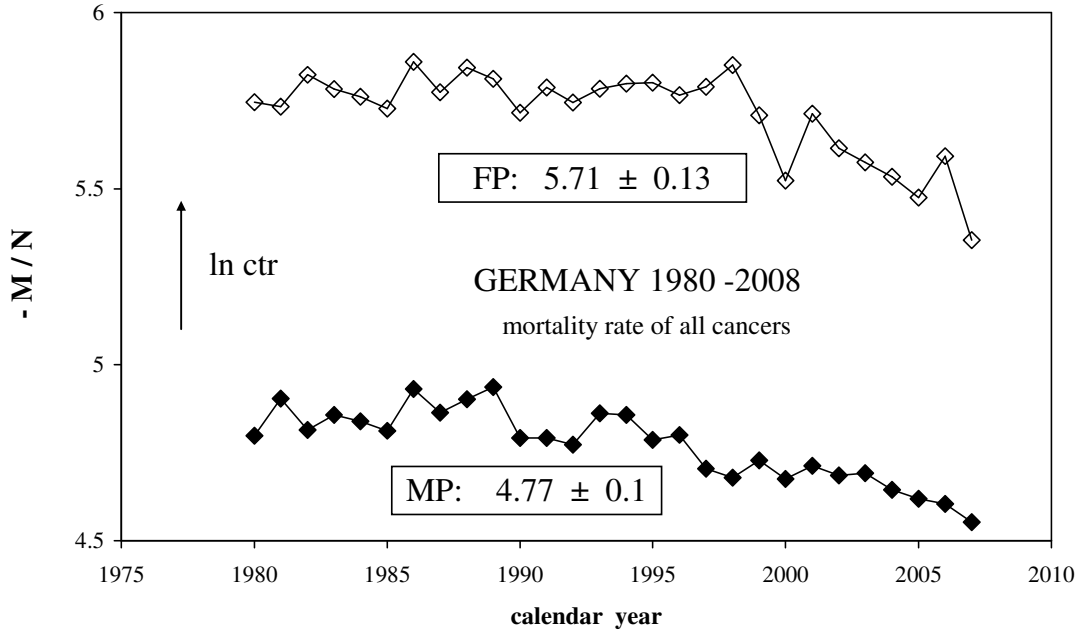

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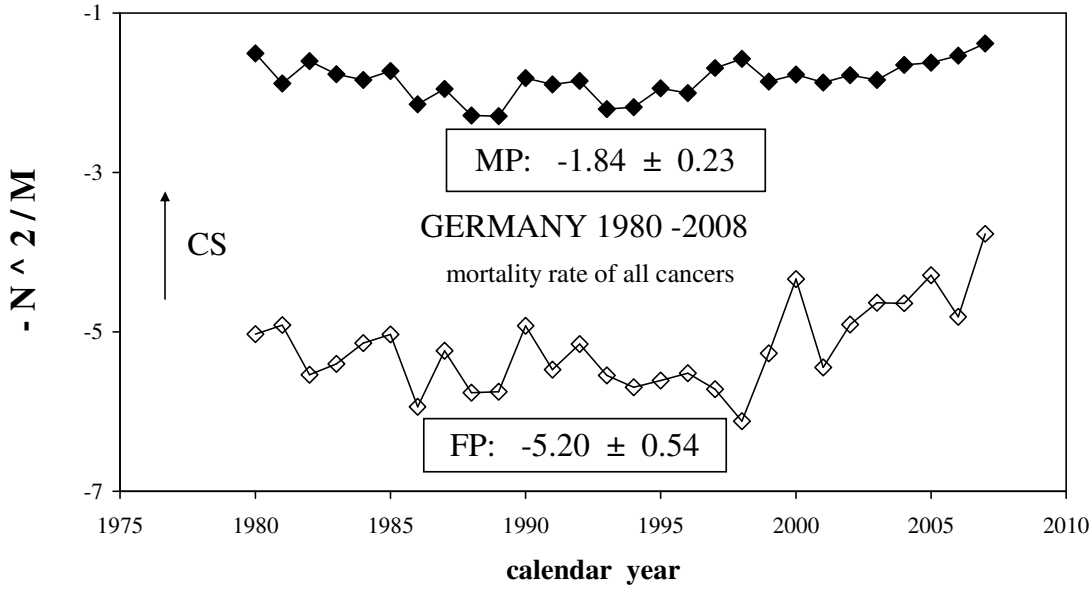

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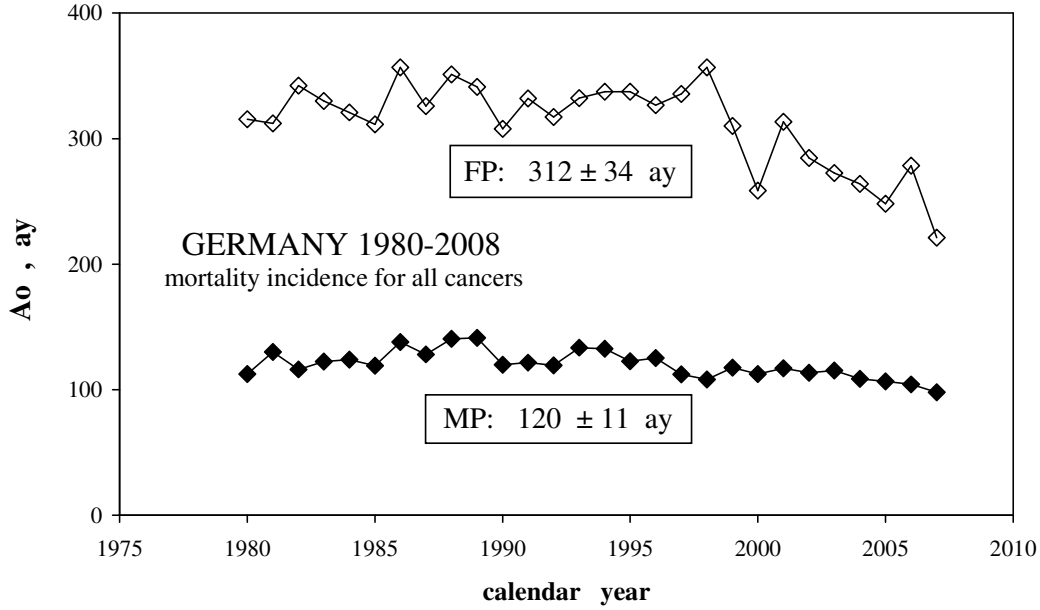

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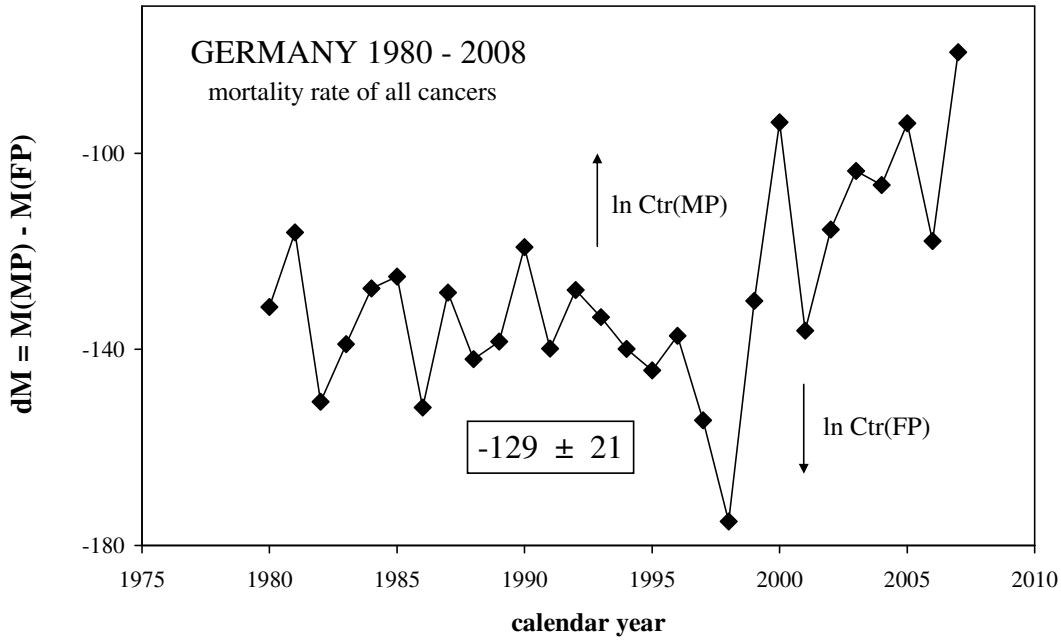

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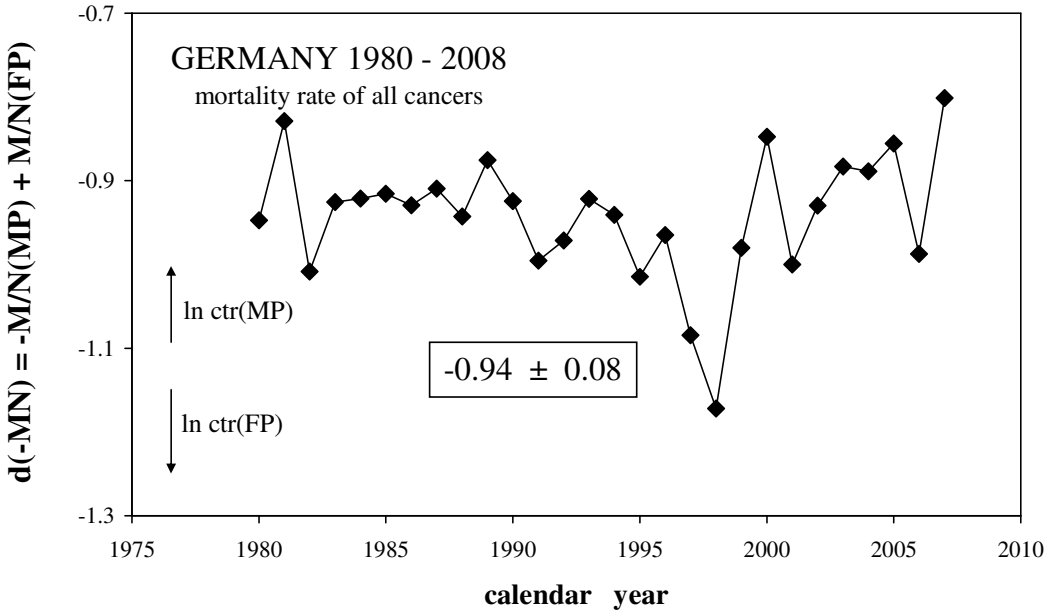

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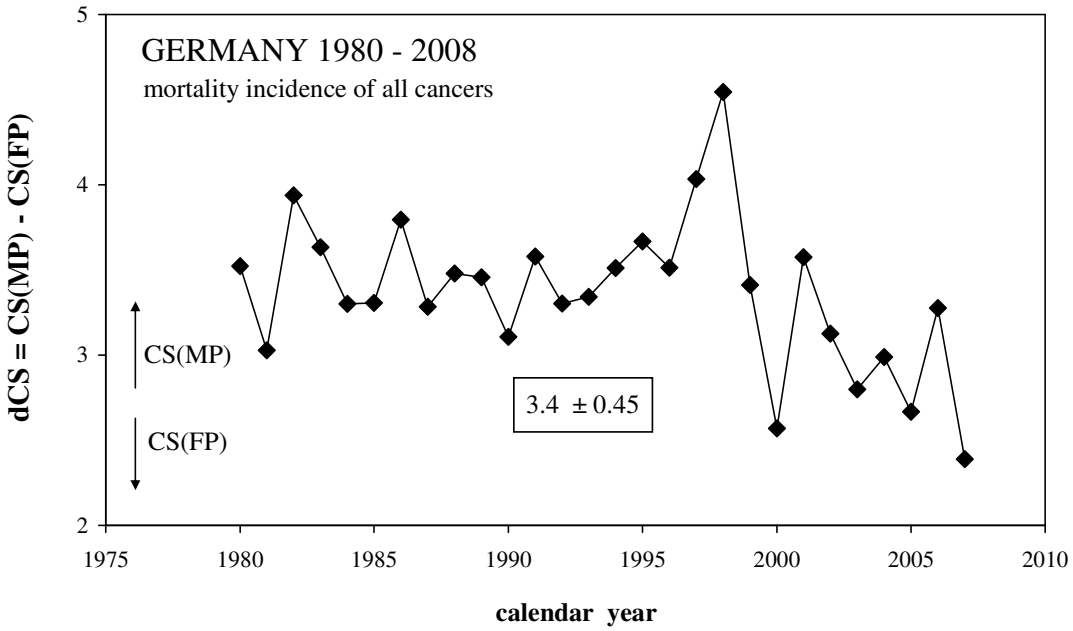

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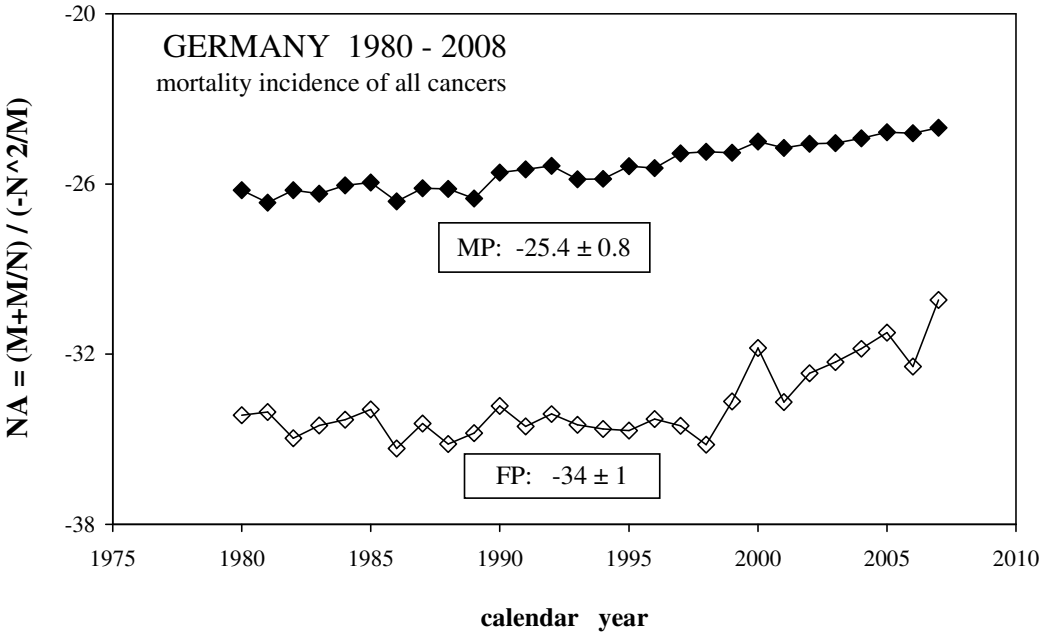

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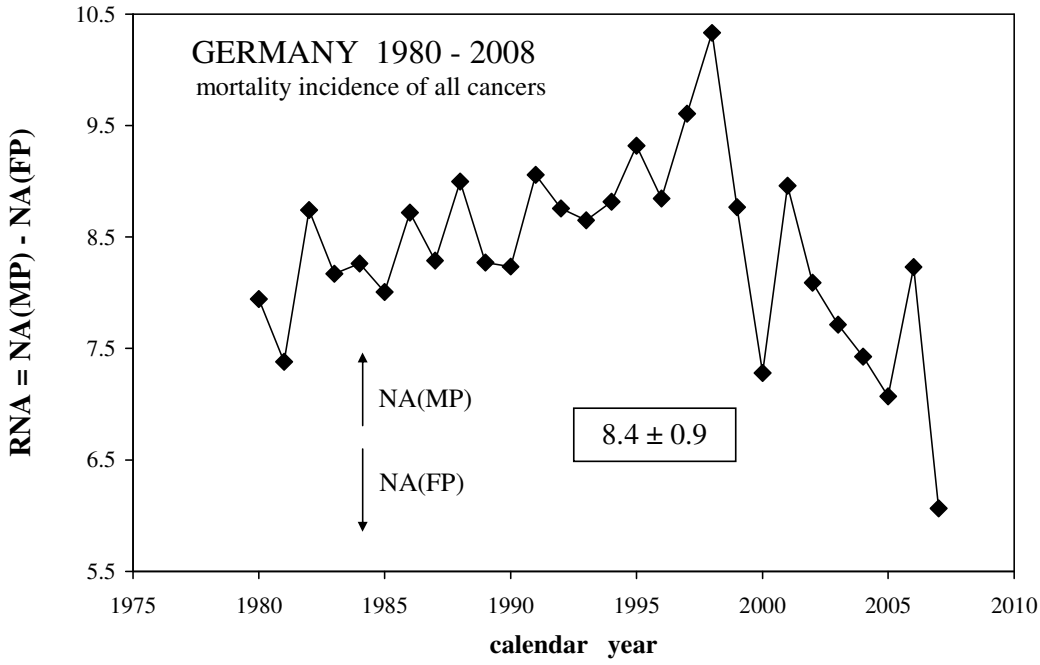

Figure 32.

5. Cancer phylogeny

Tables 1 and 2 present the first phylogeny parameters obtained for Universal ontogenic parameters of IR(t) and M(t), respectively. These values must be compared with the previously reported values obtained for different countries and regions from the world (the most recent values for Australia, Table 3 [1]).
In the present study it is possible to compare these parameters for IR and MR, so this can be revealed much better by their graphic representation. Additionally, the second phylogenies can be estimated.
Figures 33-37 present graphically the first phylogenic parameters from Tables 1 and 2. All second phylogenies appear to be clearly different for IR and MR excepting for L(ln ctr, Ao) (Figure 37).
Taking into account that IR and MR are expressed in the same units and the definition of parameters (n1, m1), it is possible to compare their values for the points in each graphic.
The following relationships are revealed:

- the slope ln ctr/ln Ctr: (MR-MP) » (IR-FP) ~ (IR-MP) > (MR-FP) and n2(IR) > 0, n2(MR) < 0 (Figure 34);
- the slope CS/ln Ctr: (IR-FP) >~ (MR-FP) > (IR-MP) > (MR-MP) and n2(IR) ~ n2(MR) < 0 (Figure 35);
- the slope Ao/ln Ctr: (IR-FP) » (MR-MP) > (MR-FP) ~ (IR-MP) and n2(IR), n2(MR) < 0 (Figure 36);
- the slope Ao/ln ctr: (IR-FP) > (MR-FP) > (IR-MP) > (MR-MP) and n2(IR) = n2(MR) < 0 (Figure 37).

In other few words these relationships show that the resistance to cancer and tendency to cluster (CS) increase at FP with cancer amplitude. This result is in good agreement with the fact that t1/2 and Ao have significant higher values for both FP (IR, MR) which means that FP tends “to socialize” its cancer.

Table 1. First phylogeny for incidence rate (IR) of all cancers in Germany 1980-2006. By definition L(x, y): y = n1*x + m1

		n1	m1	correl
L(N, M)	MP	-6.21 ± 0.047	-13.7 ± 1.1	0.9993
	FP	-7.21 ± 0.064	-27.4 ± 1.7	0.9990
L(M, -N)	MP	0.161 ± 0.0012	2.20 ± 0.16	0.9993
	FP	0.139 ± 0.0012	3.80 ± 0.20	0.9990
L(M, Ao)	MP	1.44 ± 0.077	78 ± 10	0.966
	FP	2.66 ± 0.097	-0.9 ± 16	0.984
L(M, -M/N)	MP	0.00577 ± 0.00044	4.86 ± 0.058	0.934
	FP	0.00623 ± 0.00030	5.14 ± 0.049	0.973
L(M, N^2/M)	MP	0.0254 ± 0.00043	0.813 ± 0.057	0.996
	FP	0.0185 ± 0.00040	1.263 ± 0.066	0.994
L(-M/N, Ao)	MP	239 ± 6	-1076 ± 34	0.992
	FP	422 ± 5	-2163 ± 33	0.998

Table 2. First phylogeny for mortality rate (MR) of all cancers in Germany 1980-2008.

		n1	m1	correl
L(N, M)	MP	-5.36 ± 0.077	-5.09 ± 0.68	0.997
	FP	-6.58 ± 0.048	-25.4 ± 1.4	0.9993
L(M, -N)	MP	0.187 ± 0.0027	0.95 ± 0.11	0.997
	FP	0.152 ± 0.0011	3.86 ± 0.19	0.9993
L(M, Ao)	MP	1.57 ± 0.062	54 ± 2.6	0.980
	FP	1.40 ± 0.051	73 ± 8.9	0.983
L(M, -M/N)	MP	0.0128 ± 0.0016	4.23 ± 0.067	0.848
	FP	0.00502 ± 0.00027	4.86 ± 0.047	0.964
L(M, N^2/M)	MP	0.0338 ± 0.0011	0.415 ± 0.047	0.986
	FP	0.0224 ± 0.00039	1.378 ± 0.067	0.996
L(-M/N, Ao)	MP	99 ± 7.6	-352 ± 36	0.931
	FP	272 ± 5.3	-1243 ± 30	0.995

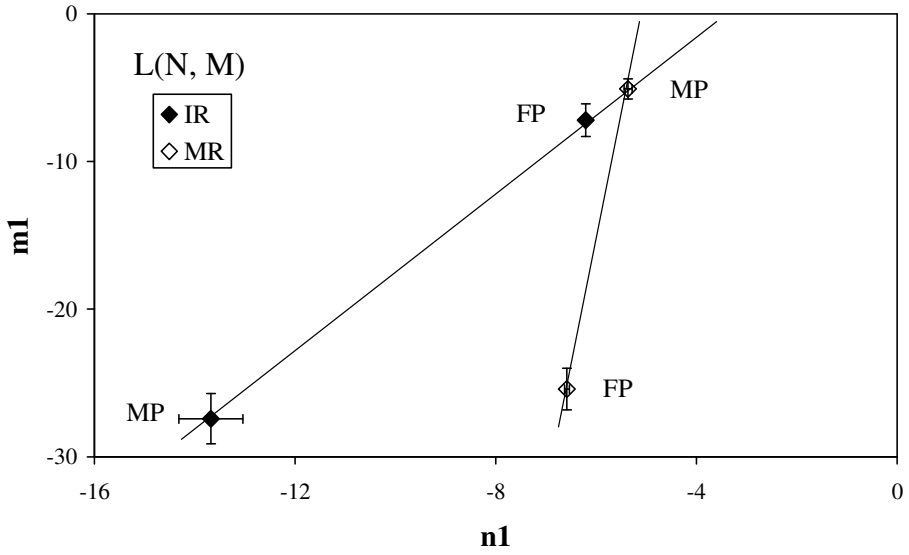

Figure 33.

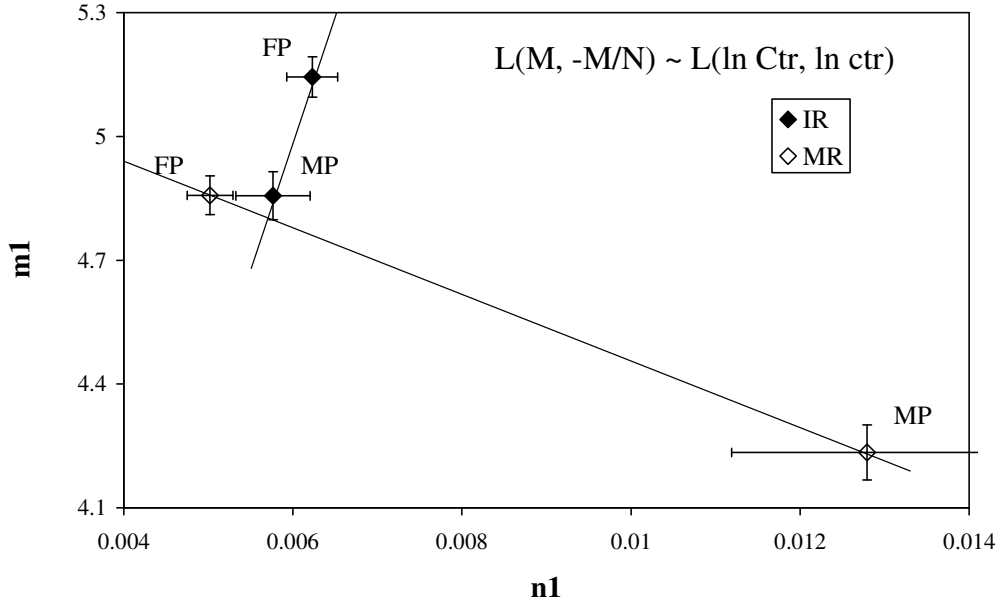

Figure 34.

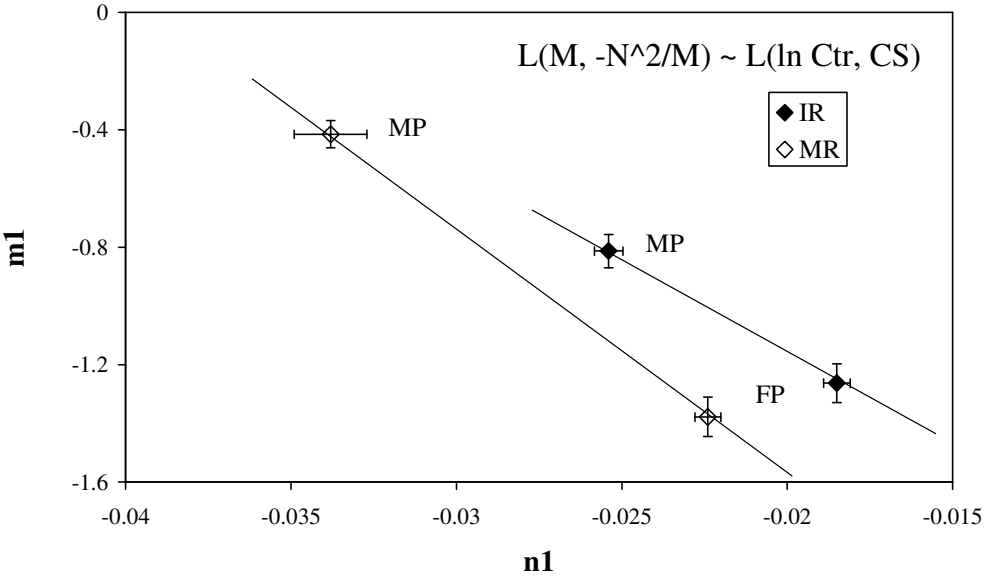

Figure 35.

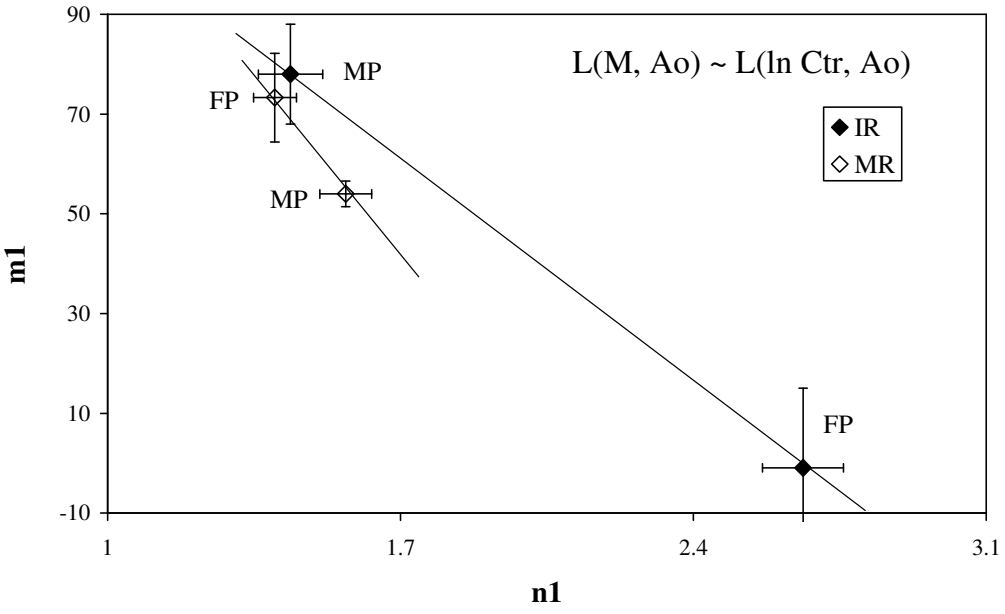

Figure 36.

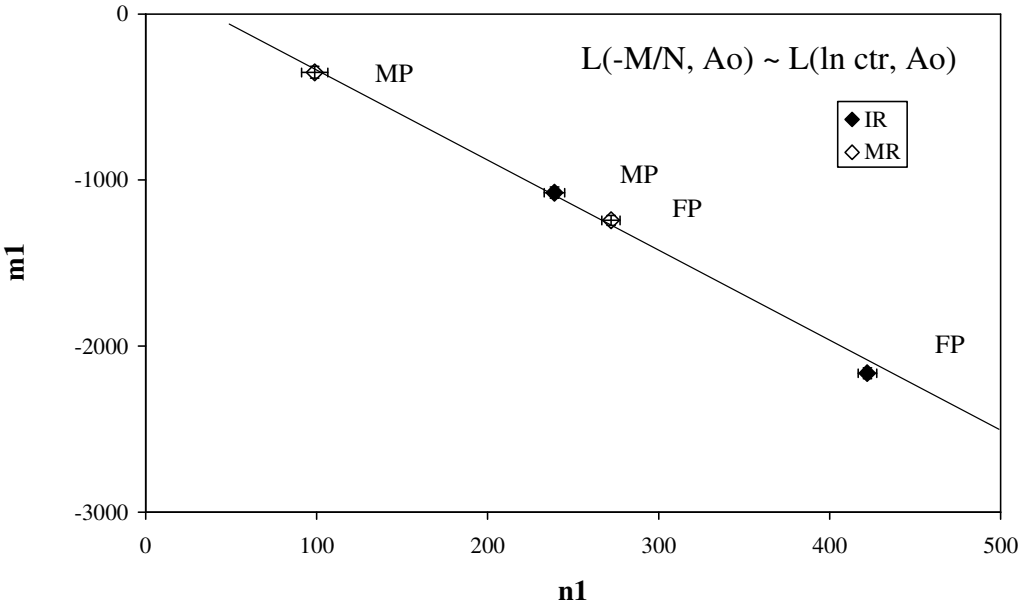

Figure 37.

5. References

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