Hardin Jones Biostatistical Analysis of Mortality Data for a Second Set of Cohorts of Cancer Patients with a Large Fraction Surviving at the Termination of the Study and a Comparison of Survival Times of Cancer Patients Receiving Large Regular Oral Doses of Vitamin C and Other Nutrients with Similar Patients Not Receiving These Doses

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Abstract

An analysis of survival times of a cohort of 134 cancer patients with advanced cancer, of whom 101 followed the regimen of vitamins and minerals prescribed by one of us (A.H.) when they were registered with him for psychiatric treatment and 33 (the controls) did not follow the regimen, was presented by us three years ago (Hoffer and Pauling, 1990). The members of this cohort have now been followed for an additional 31 months and the survival times in this extended study have been analyzed, leading to the conclusion that about 40% of the patients who followed the regimen are excellent responders, with survival times (after registration with A.H.) of 5 years or more, with 60% being good responders, with mean survival time about 4 times that of the controls. Data about 170 additional cancer patients who were registered with A.H. between 1 April 1988 and 31 December 1989 are also presented and analyzed. The fractions of excellent responders and good responders to the regimen of these patients, who have not been followed for so long a time as for the first cohort, are indicated to be about the same. A comparison is made of the effectiveness of this regimen with that of the daily intake of 10 grams of vitamin C and no others of the nutrients in the A.H. regimen (Cameron and Pauling, 1976, 1978), leading to the conclusion that vitamin C alone leads to only about 10% of excellent responders, as compared with 40% for the A.H. regimen.

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Introduction

One of us (A.H.) is a specialist psychiatrist who does not accept any primary patients; his patients have all been referred to him by other physicians for psychiatric treatment. Some of his patients are ambulatory patients with advanced cancer who have become severely depressed. At the first meeting with each patient he discusses the need to follow a good diet and also the regimen of high intakes of vitamin C, vitamin B_3, other vitamins, and also certain other nutrients that he recommends for all of his patients to control their psychiatric problems (Hoffer et al., 1957); the patients also continue to be under the supervision of their family physicians or oncologists for treatment of cancer. The regimen is based on the discovery made 45 years ago by A.H. and his associate, Dr. Humphry Osmond, that high doses of vitamin B_3 and vitamin C have value in controlling schizophrenia and to some extent also other psychiatric problems.

Some of the cancer patients registered with A.H. refused, for one reason or another, to follow his recommended regimen. A number of years ago A.H. noticed that those who did not follow the regimen were dying at about the rate expected for patients with advanced cancer, whereas those who followed the regimen seemed to be living much longer. He then wrote to L.P., suggesting that he make a

biostatistical analysis of the mortality data. It was seen that only about 10% of the controls were alive two years after registration with A.H., whereas nearly half of those who followed the regimen were still alive at that time (Hoffer and Pauling, 1990).

In 1956 the observation was made by the biostatistician Hardin Jones (1956) that the death rate for a homogeneous cohort of cancer patients is a constant:

$$-\frac{dN}{dt} = aN \qquad (1)$$

$$N = N_o e^{-\alpha t} \qquad (2)$$

$$S = \frac{N}{N_o} = e^{-\alpha t} \qquad (3)$$

Here N_0 is the number of patients in the cohort at time t = 0, N is the surviving number at time t, S is the surviving fraction, and **a** is the death rate. The mean survival time x is equal to or[1]. These equations are only roughly applicable to inhomogeneous cohorts. They can be used to develop methods of obtaining an average value of the expected survival time t and the hererogeneity of the cohort (Pauling, 1989).

Our first study (Hoffer and Pauling, 1990) was made on 134 cancer patients registered with A.H. between August 1977 and March 1988. This study was ended on 31 December 1989, so that each patient was followed for at least two years. Of the 134 patients, 33 (the controls) did not follow the regimen, and 101 (the Orthomolecular group) did. The analysis led us to conclude that the Orthomolecular patients with cancer of the breast, ovary, uterus, and cervix had life expectancy about 20 times that of the corresponding controls, and that those with other kinds of cancer had life expectancy about 12 times that of the corresponding controls. The analysis indicated some heterogeneity in each subcohort, but there seems to be little doubt that the patients who followed the regimen of daily oral intake of large amounts of nutritional supplements survived much longer than those who did not follow the regimen.

The Second Study

The number of cancer patients registered with A.H. in 1980 was 7. The annual number increased rapidly reaching 123 in 1990. There is evidence that the rapid increase resulted from the spread of the knowledge among both cancer patients and their primary physicians in Victoria, British Columbia, that cancer patients were benefitted by being referred to A.H. for psychiatric treatment. From 1 April 1988 to 31 December 1989 a total of 170 cancer patients had been registered with A.H., 20 controls and 150 who followed the regimen. The fraction in this cohort who followed the regimen is 88%, considerably greater than that in the first study, 75%. We suggest that this increase is the result of the recognition by the patients and their primary physicians that following the A.H. regimen is essential for increase in survival time and also for improvement in the quality of life.

The patients in this second study were followed until 31 December 1992, the termination date of the study. All patients had been under observation for at least two years after registration with A.H.

Results of the Analysis

Data about the 170 patients in the study, including the survival times after registration with A.H., are given in Table 1 (controls with cancer of the breast and related organs), Table 2 (controls with other kinds of cancer), Table 3 (patients with cancer of the breast and related organs who followed the regimen), and Table 4 (patients with other kinds of cancer who followed the regimen). The results are similar to those found in the first Hoffer study. Of the 20 controls (Tables 1 and 2), only 2 (10%) were still living at the termination of the study, whereas 53 (38%) of the 138 patients who followed the regimen were still alive at that time (Tables 3 and 4). As in the first Hoffer study, the extension of survival time for patients with cancer of the breast, ovary, uterus, and cervix (50% alive at the termination of the study) was greater than that for patients with other kinds of cancer (32%).

In order to get some additional information, we have striven to evaluate the mean survival times of the controls and the patients who followed the regimen by applying the methods provided by the Hardin Jones principle. These methods apply strictly to homogeneous cohorts under constant conditions, but the Hardin Jones plot of I n S versus t often provides interesting information for hetero-

Table 1. Values of the survival time for four women with cancer of the breast or ovary who were registered with A.H. on the date given in column 5 and received advice from him about diet and about the vitamin-mineral regimen, but who did not follow the regimen. The numbers t in the last column are the survival times in days from registration to death. The value t^+ = 1440+ indicates that the patient was alive at the date of termination of the study.

Number	Born	Sex	Organ	First Seen	t or t^+
161	1906	F	Breast	3/27/90	534
182	1932	F	Breast	9/26/89	142
234	1943	F	Ovary	7/26/88	44
269	1948	F	Breast	1/17/89	1444+

Table 2. Values of the survival time for 16 patients with cancer of several kinds who registered with A.H. on the date given in column 5 and received advice from him about diet and the vitamin-mineral regimen and who followed the regimen. The numbers t in the last column are the survival times in days from the date of registration to death and the values t^+ are the times in days from the date of registration to the date of termination of the study, at which time the patients were still alive.

Number	Born	Sex	Organ	First Seen	t or t^+
149	1926	F	Skin	8/11/89	1238+
173	1928	M	Bladder	12/13/89	64
190	1923	F	Lung	8/18/88	190
191	1904	M	Colon	6/6/88	101
200	1936	M	Lung	5/14/90	254
202	1927	F	Lung	1/9/89	187
205	1917	F	Thyroid	7/5/89	212
206	1962	M	Bowel	4/25/90	981 +
223	1948	M	Melanoma	5/27/88	56
229	1929	M	Rectum	6/28/89	258
243	1915	F	Bowel	7/20/89	57
253	1949	M	Brain	9/18/89	413
258	1934	M	Multiple myeloma	11/26/90	371
277	1918	F	Lung	6/27/89	233
279	1921	F	Colon	3/29/90	290
281	1930	F	Lymphoma	9/27/89	34

Table 3. Values of the survival time for 50 women with cancer of the breast, ovary, uterus, or cervix who registered with A.H. on the date given in column 5 and who followed the regimen. The numbers t in the last column are the survival times in days from registration to death and the numbers t^+ are the times in days from the date of registration to the date of termination of the study, at which time the patients were still alive.

Number	Born	Sex	Organ	First Seen	t or t^+
135	1953	F	Breast	7/3/90	912+
143	1940	F	Breast	11/10/88	390
145	1931	F	Breast	8/9/89	1241 +
154	1943	F	Breast	8/8/90	797

Table 3. (continued)

Number	Born	Sex	Organ	First Seen	t or t^+
156	1939	F	Breast	7/12/89	218
158	1914	F	Breast	1/10/90	1086+
159	1919	F	Breast	7/18/90	897+
164	1935	F	Breast	8/23/88	528
166	1920	F	Uterus	8/11/88	250
167	1941	F	Breast	7/12/88	1491 +
170	1948	F	Ovary	5/4/89	688
175	1948	F	Breast	3/28/90	1009+
188	1945	F	Breast	5/23/89	1318+
195	1917	F	Breast	1/3/90	958+
196	1913	F	Breast	10/6/88	26
197	1918	F	Ovary	2/21/89	1409+
198	1931	F	Breast	7/23/90	892+
201	1946	F	Breast	5/3/90	945+
203	1926	F	Ovary	5/10/88	1108
208	1936	F	Breast	12/29/88	1432+
209	1936	F	Breast	3/16/89	1386+
215	1952	F	Breast	4/5/90	742
219	1917	F	Uterus	4/18/90	287
221	1947	F	Breast	10/11/88	1541 +
228	1915	F	Breast	6/20/88	1429+
236	1941	F	Breast	1/25/89	1436+
238	1935	F	Ovary	3/15/89	1004
241	1955	F	Breast	12/31/89	1096+
250	1955	F	Breast	7/24/89	1256+
251	1951	F	Breast	6/20/89	327
252	1947	F	Breast	5/17/90	923+
254	1930	F	Breast	6/6/90	873+
256	1950	F	Cervix	12/12/89	1113+
261	1929	F	Ovary	7/12/90	284
263	1951	F	Breast	6/6/89	824
274	1937	F	Breast	8/27/89	345
275	1954	F	Ovary	5/3/89	787
278	1943	F	Breast	7/13/88	1632+
286	1938	F	Breast	11/30/89	1127+
288	1930	F	Ovary	11/22/88	49
289	1943	F	Breast	7/24/90	410
291	1953	F	Breast	7/18/89	454
294	1953	F	Breast	3/6/90	3
295	1943	F	Breast	9/13/90	237
296	1920	F	Uterus	5/14/90	47
298	1926	F	Ovary	7/19/89	1442+
299	1942	F	Breast	9/11/90	842+
300	1935	F	Breast	11/21/90	771 +
301	1929	F	Cervix	10/23/89	1165+
303	1926	F	Breast	7/6/89	1274+

Table 4. Values of the survival time for 88 patients with cancer of several kinds who registered with A.H. on the date given in column 5 and who followed the regimen. The numbers t in the last column are the survival times in days from registration to death and the numbers t^+ are the times in days from the date of registration to the date of termination of the study, at which time the patients were still alive.

Number	Born	Sex	Organ	First Seen	t or t^+
136	1932	M	Lung	8/2/89	135
137	1921	M	Kidney	6/18/90	77
138	1934	F	Lung	12/5/89	364
139	1913	M	Lung	9/29/88	356
140	1936	M	Lung	6/28/88	159
142	1919	F	Thyroid	11/8/89	1149+
144	1929	F	Lung	2/27/90	136
146	1917	F	Colon	4/10/89	1361+
147	1915	M	Brain	3/31/89	42
148	1925	M	Prostate	12/18/90	744+
150	1901	F	Bone	7/19/90	395
151	1927	M	Lung	7/11/89	130
152	1956	M	Colon	6/13/89	1280+
153	1916	M	Prostate	11/7/89	1150+
155	1947	F	Melanoma	7/5/90	183
157	1939	F	Colon	10/18/980	2054
160	1974	F	Hodgkins	2/20/90	1045+
162	1921	F	Bowel	5/15/90	549
163	1918	M	Lung	8/9/89	152
165	1934	M	Parotid	6/20/89	299
171	1928	F	Blood	4/11/88	133
172	1958	M	Testes	12/12/89	1084+
174	1931	M	Colon	11/7/89	47
176	1927	M	Lung	5/25/88	375
177	1916	M	Stomach	4/6/88	53
178	1920	M	Leukemia	8/23/88	456
179	1915	F	Leukemia	12/4/90	758+
180	1912	M	Bladder	10/2/90	617
181	1950	F	Colorectal	11/1/90	791+
183	1916	F	Lung	10/3/90	820+
184	1928	M	Colon	5/31/90	95
185	1915	M	Lung	5/16/90	178
186	1922	M	Pancreas	9/18/90	107
187	1937	F	Brain	9/10/90	843
189	1952	F	Hodgkins	4/17/90	989+
192	1927	M	Lung	12/20/88	450
193	1912	F	Liver	6/7/89	1303+
194	1936	M	Bowel	10/10/90	41
199	1923	F	Bowel	5/23/89	678
204	1942	M	Colon	8/11/89	229
207	1930	M	Lymphoma	11/1/88	614
210	1913	M	Bladder	10/20/88	766
212	1928	M	Colon	6/22/89	923
213	1959	M	Lung	3/22/90	369
214	1948	F	Lymphoma	2/2/89	863
216	1922	F	Lung	10/12/89	151

Table 4. (continued)

Number	Born	Sex	Organ	First Seen	t or t^+
217	1942	F	Bowel	5/1/90	973+
218	1920	M	Prostate	12/5/90	755+
220	1921	F	Colon	5/1/89	106
222	1926	M	Pancreas	11/28/88	27
225	1931	M	Lung	4/26/90	81
226	1942	F	Bowel	4/3/90	325
227	1925	F	Skin	2/1/89	276
230	1914	F	Cecum	8/27/90	102
231	1928	M	Prostate	2/28/89	323
232	1918	F	Lymphoma	10/15/90	215
233	1917	M	Lung	9/6/90	242
235	1930	F	Colon	10/27/88	779
237	1922	M	Esophagus	4/7/88	130
239	1946	M	Lymphoma	9/20/90	803
240	1922	M	Lung	1/31/89	280
242	1947	F	Adrenal	10/3/88	615
244	1976	F	Leukemia	6/4/90	941+
245	1920	F	Leukemia	6/7/89	270
247	1924	F	Bladder	5/30/88	138
249	1912	F	Colon	4/24/90	319
257	1948	F	Thyroid	8/30/88	1584+
259	1947	M	Skin	8/28/89	1221+
260	1932	M	Prostate	4/19/90	616
262	1956	F	Pancreas	8/29/90	53
264	1928	M	Colon	11/27/90	366
265	1927	M	Colon	10/26/88	50
266	1918	M	Prostate	12/15/88	1477+
267	1920	M	Prostate	11/22/89	1137+
268	1914	M	Colon	8/30/90	431
270	1921	F	Multiple myeloma	8/30/89	1219+
272	1942	F	Colon	6/13/90	477
276	1930	M	Lymphoma	6/25/90	920+
280	1934	M	Prostate	6/8/88	1667+
282	1927	F	Brain	8/4/88	528
283	1928	F	Tongue, lung	12/11/90	612
284	1922	M	Prostate	3/26/90	1011 +
287	1931	M	Lung	9/5/90	132
290	1938	F	Colon	9/2/88	221
292	1947	M	Colon	6/7/90	265
293	1928	F	Lung	5/11/90	485
305	1934	M	Lung	8/3/89	25
325	1950	F	Jaw	6/16/88	1659+

Table 5. Results of the continued observation to November 1992 of the 50 patients in the first Hoffer study who were alive on 31 December 1989 (the termination date for that study). During this period of 1035 days, 12 of the 50 patients died and 38 continued to survive. Category I is the subgroup of patients with breast cancer and related cancers who did not follow the Hoffer Orthomolecular regimen, II those with other kinds of cancer who did not follow the regimen, III those with cancer of the breast, etc., who followed the regimen, and IV those with other kinds of cancer who followed the regimen. The numbers in the second column identify the patients.

Cate-gory	No.	Recent condition	t or t+	Category	No.	Recent condition	t or t+
I	31	Died 1/12/90	1520	IV	74	Alive 1/11/92	3410+
II	112	Alive 1/11/92	2560+		55	Alive 1/11/92	2400+
III	5	Alive 12/31/92	2340+		60	Alive 1/11/92	3500+
	10	Died 10/5/91	2110		62	Alive 8/11/92	2690+
	19	Alive 1/11/92	3530+		63	Alive 3/26/91	2220+
	23	Alive 1/11/92	3800+		88	Alive 1/11/92	2190+
	27	Alive 1/11/92	3260+		91	Died 3/7/92	4480
	35	Alive 1/11/92	3620+		93	Alive 1/11/92	2220+
	38	Alive 1/11/92	2890+		117	Died 6/7/91	1530
	40	Alive 1/11/92	2560+		118	Alive 1/11/92	1860+
	41	Alive 1/11/92	2980+		124	Alive 12/31/91	1370+
	44	Died 2/7/92	2860		129	Died 8/25/92	1729
	48	Alive 1/11/92	2100+		84	Alivel/11/92	5205+
IV	1	Alivel/11/92	3105+		86	Alive .1/11/92	4230+
	11	Alive 1/12/91	2800+		87	Alive 1/11/92	3835+
	15	Alive 1/11/92	2375+		95	Alive 1/11/92	2220+
	18	Alive 1/11/92	4500+		97	Died 11/15/90	1140
	22	Alive 11/15/92	3360+		98	Died 12/6/92	2175
	37	Alive 1/11/92	4230+		104	Alive 1/11/92	1800+
	43	Alive 1/11/92	2160+		105	Died 6/15/92	1840
	49	Alive 1/11/92	3045+		121	Died 5/29/92	1520
	58	Alive 1/11/92	2160+		122	Died 3/15/91	1325
	66	Alive 1/11/92	3165+		125	Died 9/14/91	1445
	70	Alive 1/11/92	2130+		126	Alive 1/11/92	1825+
	73	Alive 1/11/92	2310+		132	Alive 1/11/92	2010+

geneous cohorts.

For the 16 control patients in Table 2, the points for the first 14 on the Hardin Jones plot are reasonably well approximated by a straight line, with slope corresponding to the value 274 d (9 mo), for the mean survival time x. (The last two points are for the two surviving patients, with t^+ = 981+ and 1238+d; they constitute a separate long-lived subcohort.) There are two unusual features of this plot. First, the intercept of the straight line at S = 1 comes not at time of registration, t = 0, but at t = 16 d. This lag is found also for other cohorts. Our suggested explanation is that the malaise of patients close to death prevents some of them from registering for treatment by A.H. The second feature is that the values of I n S can be expressed better by two lines than by one. This fact is usually accounted for by the assumption that there are two subcohorts, with different values of x, but this explanation is ruled out by the fact that the second value of x, 175 d, is less than the first value, 274 d, which applies to the first five points. A change of slope in the observed direction clearly indicates that there has been some change in the environment of the patients at about 100 days after registration. These control patients had stopped their intake of vitamins early, usually by 30 days after registration, but they may well have followed A.H.' s other advice, especially about the selection of foods, for a longer time, perhaps 100 d, after which their condition would deteriorate, leading to the observed increase in death rate by over 50%. This effect is found also for the other control groups in this study and our first study, but not in the groups that followed the Orthomolecular regimen.

Since by the end of 1992 three years had elapsed since the termination date of the first Hoffer study, we decided to obtain additional information about the progress of the 50 patients who were alive at that termination date. This information is given in Table 5. Each patient in the first Hoffer trial has been followed for a minimum of 4.6 years (a maximum of 15 years).

In the reanalysis of the first Hoffer study we selected three dates to determine the intervals over which to apply Equation 1: 1 April 1988, the closing date for enrollment in the first Hoffer study, 1 January 1990, the termination date of the study, and 1 November 1992, the extended termination date. The time intervals are 640 d, 1040 d, and (overall) 1680 d. For the patients with cancer of the breast, uterus, etc., who followed the regimen the numbers of survivors at the three selected intervals are 30, 22, and 18 (from the original cohort of 40). Application of Equation 1 is made as shown by the following example for the third (overall) time interval, with length 1680 d. There are 30 patients alive at the beginning of this interval and 18 at the end. The value of S, the relative fractional survival, is 18/30 = 0.60. Equation 1 then leads to a = 0.000304 d^{-1} for the rate constant and to its reciprocal, 3290 d = 9.0 yr, for the mean survival time. Similar calculations for the 640 d and 1040 d intervals (Table 5; 22 alive at the intermediate time) lead to values 5.7 yr and 14.2 yr for the mean survival time, *x*. These values of *x* are, of course, averages (the reciprocals of the means of the reciprocals of the values of *x* corresponding to the several subcohorts that constitute the inhomogeneous cohort). The increase in the value of x from 5.7 yr to 14.2 yr shows clearly that the cohort is not homogeneous.

The second value of x, 14 years, is so large as to suggest strongly that the patients have overcome their disease - have, one might say, been "cured". In fact, the usage has sometimes been followed by saying that if a patient receiving a cancer treatment is apparently well after 5 years, the patient may be described as having been cured.

The number of patients is not large enough to permit a very detailed analysis of the data. We make the assumption that each cohort consists of two subcohorts, one of excellent responders to the regimen, and the other of good responders.

To find the number of excellent responders, we check the number of the original 40 patients in this cohort who survived more than 5 years. This number is 20. Accordingly, we conclude that about 50% (20/40) of these patients with cancer of the breast, etc., are excellent responders to the regimen and can anticipate recovering from the disease.

For comparison, we look at the 11 controls, the similar patients who did not follow the regimen. Ten of these patients had lived only a short time after registration, a median of 0.37 years (135 days). The survivor (the only patient in the study with cancer of the Fallopian

tubes) had lived for over 4 years.

A similar analysis has been carried out for the 61 patients with other kinds of cancer. The numbers of survivors at the three selected dates are 37, 26, and 20. The values of the mean survival time x for the intervals 640, 1040, and 1680 d (Table 6) are 5.0, 10.9, and 7.5 y. Here, as with the other cohort, there is strong indication that the cohort is inhomo-geneous, and that it includes a large subcohort with mean life expectancy greater than 5 years. With 20 of the 61 patients having survived for more than 5 years after registration, we take the fraction of excellent responders to the regimen to be about 33%.

We have concluded that 50% of the breast, etc. cancer patients who followed the regimen are excellent responders, with mean survival time as great as about 15 years. Assuming that the other 50% constitute a single subcohort, we have analyzed the survival times to obtain the value 1.7 years (630 d) for x for this subcohort. A similar analysis for the controls gives x = 0.4 years (150 d). Accordingly the mean life expectancy for this subcohort is about four times that of the controls, and those patients can be described as good responders, though not excellent responders.

A similar treatment of the 67% of the patients with other kinds of cancer who are not excellent responders yields the value 1.5 years (550 d) for the mean life expectancy, which is four times that for the corresponding controls, 0.4 years (140 d). Accordingly the patients in this subcohort can also be described as good responders, although not excellent responders.

The same analysis cannot be applied to the second Hoffer study because the period of observation of the patients is much shorter. The fraction of the patients with breast cancer and related cancers who were alive at the termination of the study and who had followed the regimen (Table 3) is 56% (28/50). This value suggests that the subcohort of excellent responders may constitute as much as 50% of the cohort, as suggested for the first Hoffer study, but probably is somewhat smaller. For the patients with other kinds of cancer who followed the regimen (Table 4) the fraction of survivors is 30% (26/88). This value can be taken as an upper limit of the fraction of excellent responders, which accordingly is smaller than suggested for the first Hoffer study, 33%. The good responders in each cohort probably have about the same mean survival times as for the first study, about 1.6 years, 4 times that for the controls.

Discussion

During the last 17 years A.H., a psychiatrist, has had about 500 patients with advanced cancer referred to him for psychiatric treatment. He recommended to each of them the regimen that he recommends to all of his patients - improvement in the diet and a regimen involving the regular intake of rather large amounts of dietary supplements (vitamins and other nutrients). About 80% of the patients followed his regimen, and about 20% (the "controls") did not do so. In addition, the patients were under medical care by the primary physician and, for some, the oncologist.

A.H. observed that the cancer patients who followed his regimen lived longer after registration with him (at which time his regimen was begun by the patients) than those who did not follow the regimen. He sent data about 134 patients who had been registered with him up to the end of March 1988 to L.P. for statistical analysis of the survival times. The results of this analysis were published. They showed that the patients who followed the regimen had much longer survival than the controls. The study of this cohort has been continued in the present report.

A somewhat larger cohort of 170 patients registered with A.H. between April 1988 and the end of December 1992 (15 controls, Tables 1 and 2, and 155 patients who followed the regimen, Tables 3 and 4). These data have now been subjected to statistical analysis, with results similar to those found for the first cohort.

These results can be summarized by the following statements. The controls in both the Hoffer studies have a mean survival time (after the date of registration with A.H.) of 135 days. The patients who followed the regimen can be divided into two subcohorts, the excellent responders and the good responders. In the extended first study about 50% of the patients with cancer of the breast and related organs are estimated to be excellent responders, with mean survival time greater than 5 years (1827 days), with the other 50% being good responders, with mean survival time 630 days. For the patients with other

kinds of cancer it is estimated that about 33% are excellent responders, with mean survival time greater than 5 years, and 67% are good responders, with mean survival time 540 days. These estimates apply also, at least roughly, to the patients in the second study. The good responders have mean survival time about 4 times that of the controls.

In our 1990 paper we pointed out that the Hoffer regimen gave longer survival times than the Cameron regimen, which involved only vitamin C, 10 grams per day, with no other supplements. Cameron's studies were carried out from 1973 on in Vale of Leven Hospital, Lochlomondside, Scotland. The patients had all reached the untreatable stage, when the physicians reached the decision that no potentially curative or palliative treatment was likely to be of value. In 1976 a paper was published giving the survival times of 100 untreatable cancer patients who had followed the regimen of 10 grams of vitamin C per day and also for 1000 matched control patients who had reached the untreatable stage, in the same hospital, but who did not receive vitamin C (Cameron and Pauling, 1976), and two years later, a second paper was published reporting the increases in survival times during the additional two years of observation (Cameron and Pauling, 1978). Only one of the 1000 controls had lived more than 2 years (survival time 341 days), and the mean survival time, after the date of untreatability, was 38 days. Of the 100 patients taking vitamin C, 7 were still living after the extended period of observation and 3 others had survived more than 2 years. Our estimate of the number of excellent responders to vitamin C alone is 10%. The mean survival time of the other 90%, the good responders, is 186 days, 4.9 times that for the 1000 controls.

The main difference between the results of the Hoffer studies and the Cameron studies is that the fraction of excellent responders is about 4 times as great for the Hoffer regimen (50% for patients with cancer of the breast, etc., 33% for those with other kinds of cancer) as for the Cameron regimen (10%). The good responders (about 60% for Hoffer, 90% for Cameron) seem to be benefitted by about the same amount (mean survival time 4 or 5 times the values for the controls). These differences suggest that an additional 30% of patients with advanced cancer may be "cured" (with survival times of five years or more, after reaching an advanced stage of the disease) by following the more extensive Orthomolecular regimen prescribed by Hoffer rather than only the vitamin C regimen prescribed by Cameron.

In the Hoffer studies patients with cancer of the breast and related organs were observed to respond somewhat better to the Hoffer regimen than patients with other kinds of cancer. This difference was not observed in the Cameron study. The numbers of patients with other kinds of cancer are too small to permit reliable conclusions to be drawn about the relative effectiveness of the regimens for controlling different kinds of cancer. We can, however, state that there is evidence that the regimens have some value, often great value, for all cancer patients, as an adjunct to appropriate conventional therapy.

We recommend that all cancer patients begin the Orthomolecular regimen as early in the course of the disease as possible. The Hoffer regimen (varying somewhat from patient to patient), in addition to including fruits and vegetables in the diet, includes the following Orthomolecular substances (the amounts listed are the daily intake, usually taken in three doses):

The Average Hoffer Regimen, Daily Intake
(g = gram, mg = milligram, I.U. = international units)

Vitamin C (ascorbic acid, sodium ascorbate, calcium ascorbate, mixture)	12 g
Vitamin B_3 (niacin, niacinamide)	1.5 to 3 g
Vitamin B_6 (Pyridoxine)	250 mg
Folic acid	5 to 10 mg
Other B vitamins	25 or 50 times the RDAs
Vitamin E	800 LU.
Beta carotene	25,000 I.U. to 50,000 LU.
Selenium	0.2 to 0.5 mg
Zinc sulfate	220 mg
Sometimes calcium, magnesium, or a mineral tablet	

One may ask whether all of the nutrients in this regimen are needed for the control of cancer. There is no doubt about the importance of a high intake of vitamin C; early evidence is summarized by Irwin Stone in his 1972 book *The Healing Factor: Vitamin C Against Disease*, and much more evidence has been published during the last twenty years. There is also evidence that the other nutrients in increased intake have value in

helping to prevent or treat other diseases. Having in mind that these nutrients are not very expensive, in comparison with many drugs, we recommend that the complete regimen given above be followed by all cancer patients. All or nearly all of the nutrients are available without a prescription. We suggest checking the prices and not buying the high-priced preparations, even though claims of increased efficacy may be made for them.

Niacin (nicotinic acid) when first taken causes a flushing (tingling, redness) of the skin. If the large doses are taken regularly, this flushing usually does not occur after two or three days. The patient may prefer to take niacinamide, which, however, may not be quite as effective. Vitamin C is a laxative. If the intake of 4 grams three times a day causes an inconvenient amount of looseness of the bowels, the dosage should be decreased somewhat. A larger intake, up to the bowel-tolerance limit, may have additional value.

We conclude by repeating our recommendation that every cancer patient follow this regimen, beginning as early in the course of the disease as possible. Persons who have not developed cancer may find it wise to follow the regimen, perhaps with somewhat reduced amounts of the nutrients, to prevent or slow down the development of cancer and other diseases and to improve their general health and increase the length of their period of well-being and enjoyment of life.

References

1. Cameron E and Pauling L: Supplemental ascorbate in the supportive treatment of cancer: Prolongation of survival times in terminal human cancer. *Proceedings of the National Academy of Sciences USA* 73:3685-3689, 1976.
2. Cameron E and Pauling L: Supplemental ascorbate in the supportive treatment of cancer: Re-evaluation of prolongation of survival times in terminal human cancer. *Proceedings of the National Academy of Sciences USA* 75:4538-4542, 1978.
3. Cameron E and Pauling L: Experimental studies designed to evaluate the management of patients with incurable cancer. *Proceedings of the National Academy of Sciences USA* 75:6252, 1978.
4. Hoffer A and Pauling L: Hardin Jones biostatistical analysis of mortality data for cohorts of cancer patients with a large fraction surviving at the termination of the study and a comparison of survival times of cancer patients receiving large regular oral doses of vitamin C and other nutrients with similar patients not receiving those doses. J. *Orthomol. Med.* 5:143-154, 1990.
5. Hoffer A, Osmond H, Callbeck MJ and Kahan I: Treatment of schizophrenics with nicotinic acid and nicotinamide. *J. Clin. Exper. Psychopath.* 18:131-149, 1957.
6. Jones HB: Demographic consideration of the cancer problem. *Trans. N. Y. Acad. Sci.* 18:298-333,1956.
7. Pauling L: Biostatistical analysis of mortality data for cohorts of cancer patients. *Proceedings of the National Academy of Sciences USA* 86:3466-3488, 1989.
8. Stone I: *The Healing Factor: Vitamin C Against Disease.* Grosset and Dunlap, New York, 1972.