

Studies on Increased Cancer Risk of Flight Personnel¹

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Dicentric chromosomes as chromosomal aberrations, as found more frequently in flight personnel, are a very impressive biological endpoint of radiation effects demonstrating quantitatively the high potency of ionizing radiation to damage the genome of human cells [Kuni 1994], but they are not correlated directly with a concrete disease. Therefore in this presentation a lot of publications concerning statistics of morbidity and mortality of pilots are analyzed. The main aim is not a discussion of the epidemiological methods and details, this will be the matter of Ms. Blettner as an epidemiological specialist [Blettner 1994]. My point of view is that of a physician searching for evidences of negative consequences of the high radiation burden to flight personnel, specially for an increased frequency of cancer. Therefore some own calculations with the published data are done respecting the rule: Newer trust a statistic which you not have falsified by yourself.

U.S. Navy Air Crew

In 1983 Hoiberg and Blood have presented a report about the hospitalisation rate of officers of the US Navy. Because of treatment in special medical institutions of the Navy or taking over the costs of medical treatment by the Navy the registration of the cases will be very complete. The hospitalisation rate was broken down in to age groups of three years from age 21 through 53 and adjusted to the number of individuals on active duty by year and age across the time period from July 1967 through December 1979, this are about 14 years. Using the **Individual Flight Activity Reporting Systems** the investigated group is divided in 22,417 aviators, first pilots or copilots and 9,483 other air crew mem-

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bers. Controls are 55,593 unrestricted line officers including officers on surface ships, submarine and special warfare officers and 46,565 staff corps officers including physicians, lawyers, chaplains and so forth.

Age-Specific Morbidity among Navy Pilots

Hoiberg, A., Blood, C.

Aviat. Space Environ. Med. 1983, 912-918 Hospitalisation rate per year and age of

22,417 Aviators: first pilots and copilots

9,488 Other air crew officers

55,593 Unrestricted line officers

46,565 Staff corps officers

Time period: July 1965 - December 1979: 14 years

Healthy worker effect 77%

Aviators: Increased rate of

Melanoma

Hodgkin's disease $p < 0.05$

Cancer of testis $p < 0.01$

Tab. 1: U.S. Navy Air Crew. Summary of data.

It is not surprising that Navy personal has a hospitalisation rate which is about 77% lower than that of the population. This may be a healthy worker effect². But in the internal comparison air crew members have a double increased rate, to which mainly the youngest and oldest age groups contribute. This

² Healthy worker effect: A working population has a lower morbidity and mortality than a reference group of the normal population standardized on age and sex. E.g. a healthy worker effect of 30% means, the mortality of the working population is 70% of the reference population.

effect was highly significant for pilots and also for the complete air crew each group compared with the both control groups together. In the younger air crew members mainly appendicitis, disorders of the tooth development and injuries by sport activities are seen very more frequently. Pilots had the highest rate for hemorrhoids and ischemic heart disease. Their rates for melanoma (black skin cancer), Hodgkin's disease (a malignant disease of the lymphatic system) and cancer of the testis were more frequent, the both latter diseases significantly respectively highly significantly.

Unfortunately in the table of the publication the hospitalisation rate is presented only for all cancer diseases together.

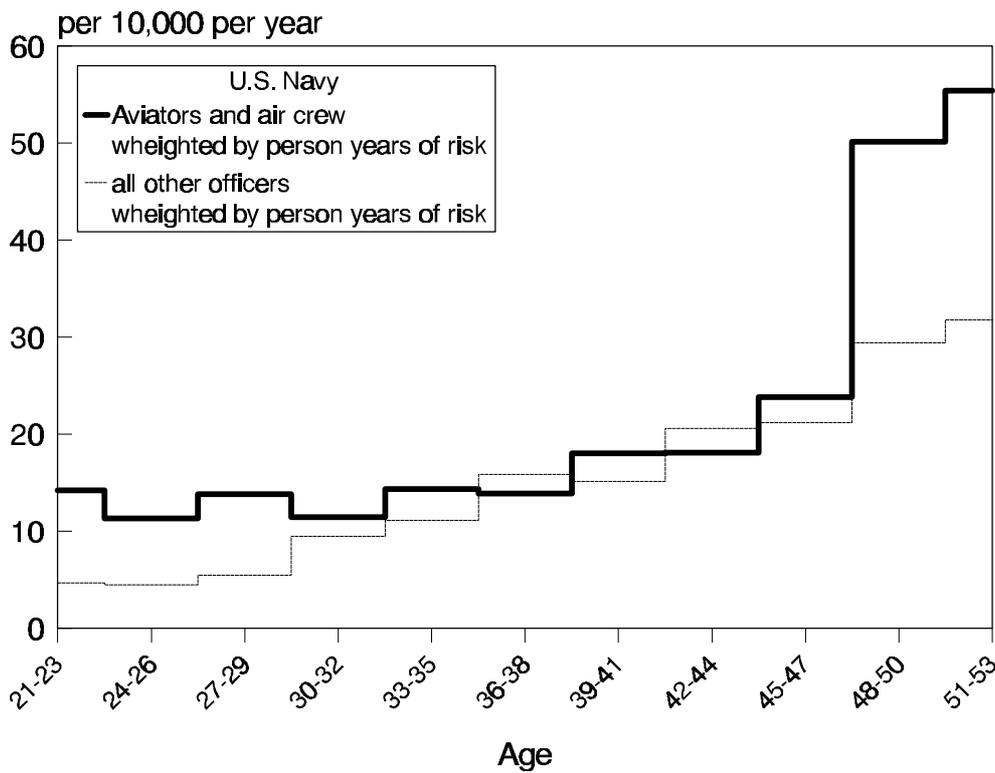


Fig. 1: Hospital Admissions with a diagnosis of cancer among aviators and other aircrew members combined and all other officers of the U.S. Navy
 The hospitalization rate is expressed per 10,000 of the group members in the specific age groups
 Data: Hoiberg, Blood 1983

In Fig. 1 the figures of the complete air crew are summarized by weighting each figure of the pilots and the other officers of the air crew by the person-years at risk of each age group and also the both groups of controls. In the age group of the elder of air crew in the more typical age suffering from cancer the cancer is much more frequently the cause of hospitalisation than in controls.

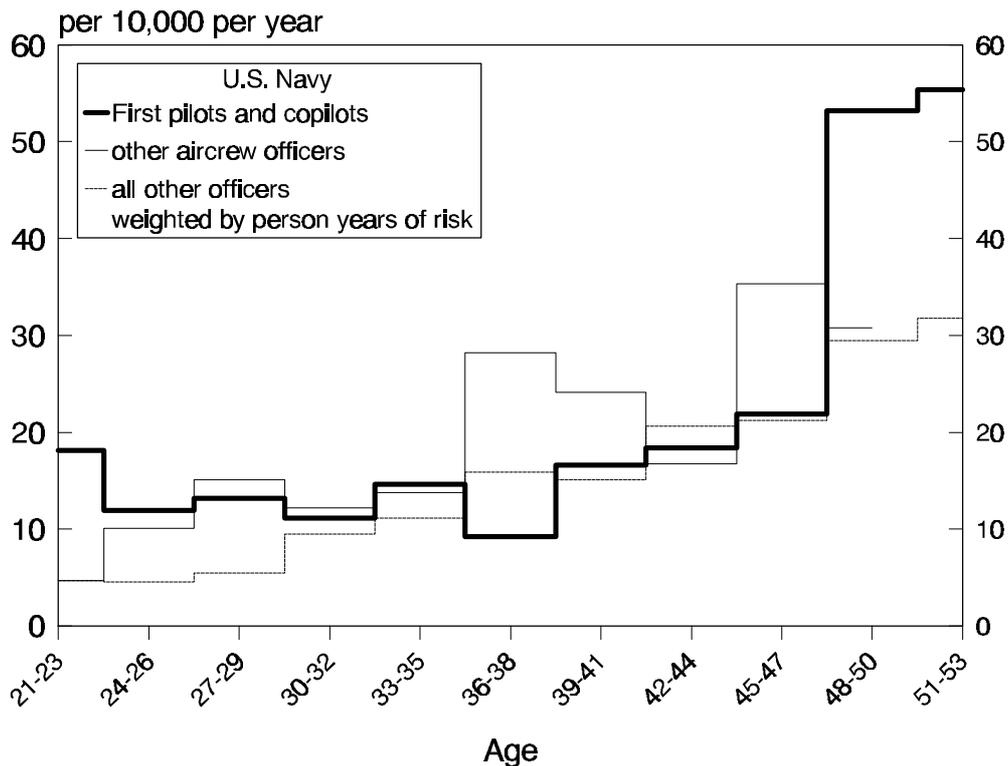


Fig. 2: Hospital Admissions with a diagnosis of cancer as in fig. 1 (p. 3), but for aviators and others air crew officers separately.

Additionally the pilots show a doubling in the youngest age groups (Fig. 2). Paying attention, that in an age from 20 through 30 the cancer of testis is the most frequent kind of cancer in males the assumption is possible, that this elevation is due to cancer of testis. Even assuming a latency period for cancer of testis induced by ionizing radiation as short as for leukemia it is very doubtful that the radiation burden is the primary cause for the significantly elevated frequency of this disease in pilots. It is also questionable, if the other air crew members are exposed to a proportional lower radiation dose. Therefore, it may be that specific factors of occupation, e.g. exposure to electromagnetic fields of high frequent waves may act as promotion factors. It is also possible that specifically occupational exposures during the Navy career of pilots is working as cofactors. This hypothesis is supported by the fact that the peak of the excess cancer morbidity of aviators is seen from age 21 through 26. This is earlier than the peak incidence of cancer of testis in other personal of the US Navy from age 25 through 34 [Garland et al. 1988].

Japan Airlines Cockpit Crewmembers

The biggest cohort of civil pilots analyzed originates from Japan [Kaji et al. 1993]. The group includes 2,327 males, employed in the period from 1.8.52 through 31.12.88. Only 59 persons, 2.5 percent of

the cohort, have died. Though the mean age of follow up was low, 42.1 years, only 191, 8.2 percent are retired. Therefore the mean period of employment, only 13.8 years, characterize also a short follow up time in the same order of magnitude. The mean age at first flight was 29.5 years.

Mortality Experience of Cockpit Crewmembers from Japan Airlines

Kaji, M., Tango, T., Asukata, I., Tajima, N., Yamamoto, K., Yamamoto, Y., Hokari, M.

Aviat. Space Environ. Med. 1993, 748-750 Mortality of

2,327 Male Japanese (59 deaths: 2.5%, mean 45.9y)

2,136 Active (43 deaths, mean 39.4y)

191 Retired (16 deaths, mean 63.4y)

Time period: August 1, 1952 - December, 31 1988: 36 years

Age at follow up 42.1 years

Age at first flight 29.5 years

Working time 13.8 years

Healthy worker effect

all causes 34%, corrected by air crash 63%

cancer 13%

Deaths by air crash 81 per 100,000 person-years

Cancer

rel. mortality 33.8%

corrected by air crash 61%

Stomach cancer SMR 120 (n.s.)

Tab. 2: Japan Airlines Cockpit Crewmembers. Summary of data.

The mean cause of death was accident, 49%, specially air crash, 44.1%. Therefore the mean age of death is very low with 45.9 years. In spite of this the cohort shows a healthy worker effect of 34%. Death by air crash has with 81 per 100,000 person-years a figure ten times greater than the mean frequency of occupational death due to all causes together in a big German air line in the period from 1970 through 1980. After substitution of the extraordinary high mortality figure from air crash by a

mean value of other occupations³ the enormous distortion of the mortality statistics by the high accidental rate becomes visible. The healthy worker effect increases to 63%.

Death by cancer shows an healthy worker effect of 13%. This seemingly favourable finding changes its face in the glance of the corrected healthy worker effect of 63%. The relation shows a relative increase of cancer mortality of more than two times the usual proportion, the relative cancer mortality⁴ is 61%. In the total cohort this figure is nearly the same as in the subgroup of retired pilots, also with a clearly elevated figure of 62.5%.

The main groups of cancer death is cancer of the stomach, typically in Japan. The SMR⁵ is 120, in spite of the fact that the members of Japan airlines with an age of 40 and more are screened yearly by radiological and/or gastroscopic examination since 1960. It is remarkable that Japans people in USA are suffering also from cancer of the stomach more frequently but the figure is half as large than in Japan [Shimizu et al. 1987]. The Japanese pilots may be more often exposed to not Japanese food as normal inhabitants. Therefore the highly incidence of stomach cancer death has a certain importance.

Canadian Pacific Airlines Pilots

1990 a study of pilots of the Canadian Pacific Airlines, now Canadian Airlines International, was published [Band et al. 1990]. The cohort consists of 913 males, employed for at least one year from 1.1.1950 through 31.10.1988. With a mean age of 49.9 years only 8% of the cohort had died. Because on earlier begin of employment than in the study from Japan, mean 25.8 years, the mean time of working was longer with 16.7 years. The healthy worker effect was 20%. The mean age at death is not presented and cannot derived from the data.

³ 2.6 instead of 26 deaths

⁴ Relative cancer mortality: Proportion of cancer as cause of death to all causes of death.

⁵ SMR: **S**tandardized **m**ortality **r**ate. Mortality of an analyzed group compared with the mortality of the normal population standardized by age and sex. SMR=100 (or sometimes SMR=1.0): The mortality of the analyzed group is equal to that of the reference population

Mortality and Cancer Incidence in a Cohort of Commercial Airline Pilots

Band, P.R., Spinelle, J.J., No, V.T.Y., Moody, J., Gallagher, R.P.

Aviat. Space Environ. Med. 1990, 299-302

Mortality of
913 Male pilots Canadian Pacific Airlines

employment 1y and more

71 deaths: 8%

Time period: January 1, 1950 - October, 31 1988: 38 years

Age at follow up 49.9 years

Age at first hire 25.8 years

Working time 16.7 years

Healthy worker effect

all causes 20%, corrected by air crash 45%

Deaths by air crash 135 per 100,000 person-years < 60y

Cancer

rel. mortality 22.5%

corrected by air crash 32.6%

Rectum cancer SMR 435 (p = 0.033)

Brain cancer SMR 417 (p = 0.017), SIR 345 (p = 0.03)

Hodgkin's disease SIR 454 (p = 0.03)

Tab. 3: Canadian Pacific Airlines Pilots. Summary of data.

The statistic also was distorted by a high relative mortality of 32% by air crash. Adjusted to person-years at risk under age 60 years the mortality rate of 135 per 100,000 person-years is a lot higher than the Japanese figure. Corrected with an usual death rate of occupational accident⁶ the healthy worker effect increases to 45%.

It is not possible calculating the healthy worker effect for all cancer deaths together with the published data. For the 75% of kinds of cancer, appearing with at least two cases in the mortality table, the mortality shows an SMR of 149%. This is mainly due to cancer of rectum and brain tumours with a

⁶ 11.08 instead of 23 deaths

significant elevation of the mortality of about four times. After correcting by the extraordinary mortality by air crash the relative cancer mortality is clearly elevated to 32.6%.

A special feature of this study is the additional recording of cancer diseases. Such incidence study has the advantage to cover types of cancer with low mortality, as e.g. cancer of skin and testis, and in a young cohort, as presented, cases of disease, which are not finished with death at the time of follow up. Hereby additionally, like in the study of the military pilots of the US Navy, a significant elevation of Hodgkin's disease with SIR of 454% is seen. Also cancer of testis with SIR⁷ of 174% and Melanoma with SIR 196% was observed more frequently, but not significantly, perhaps because the low absolute count of cases. Significantly increased are the non-melanoma skin cancer with an SIR of 159%.

The authors emphasised that the skin cancer was seen at the trunk three times than expected and fewer in the face, head and neck, a highly significant alteration of the distribution.

This is the opportunity inserting a notice about military pilots of the US Air Force suffering from melanoma disease significantly more frequently with an increased localisation in skin areas not exposed to sun as genitalia, rectum [Krain 1991].

British Columbia Pilots

Also from Canada a further mortality study originates, examining all deaths in British Columbia in the period from 1950 through 1984, also 34 years, in which the occupation was declared as pilot [Salisbury et al. 1991]. The advantage of this study is a much bigger number of cases. While the cohort study of the Canadian Pacific Airlines is based on 71 cases, originating to 75% from British Columbia, this study covers 402 death, 7.5 times more. But this is purchased by a lot disadvantages. Retired persons and pilots changing their occupation before death, also particularly elder persons with an increased risk of cancer, are underrated. Further the calculation of the absolute figure of expected cases is not possible. It remains solely the possibility calculating the relative frequency of causes of death with the method of the proportional mortality rate⁸. With this condition it is nor surprising that 68% of the death are observed at an age under 66 y and 58% of the deaths are due to air crash. Also 63.9% of all other deaths concern males of an age under 66 years, elucidating the characteristics of this study.

⁷ SIR: **S**tandardized incidence rate. Analogous figure as SMR (ref. 5 , p. 6) but for the incidence of a disease.

⁸ PMR: **P**roportional mortality rate. Proportion of the relative mortality of a certain cause, e.g. cancer, in an analyzed group compared with the relative mortality of this cause in the normal population.

Mortality among British Columbia Pilots

Salisbury, D., Band, P.R., Threfall, W.J., Gallagher, R.P.

Aviat. Space Environ. Med. 1991, 351-352 Causes of deaths with declared occupation pilot

402 Males

Time period: 1950 - 1984: 34 years

68% Age < 66 years

58% by air crash

Other: 63.9% Age < 66 years

Cancer

rel. frequency 12.7%, corrected by air crash 28.9%

all causes PMR 89, corr. PMR 203 (sign.)

Colon cancer PMR 152, corr. PMR 333 (sign.)

Lung cancer PMR 109, corr. 265 (sign.)

Tab. 4: British Columbia pilots. Summary of data.

This distortion by air crash is also the cause, that seemingly only 89% of the expected cancer deaths were observed. The authors have made no correction. After doing this⁹ the relative cancer mortality increases to 28.9%, this is 2.03 times the expected value in this group of 14.25%. This is also valid for distinctly listed kinds of cancer, cancer of colon (SMR 333), of lung (SMR 265), melanoma (SMR 474), Hodgkin's disease (SMR 208) and brain tumour (SMR 228). The finding of an increased frequency of all cancers together and of cancer of lung and colon becomes significant after the correction by air crash. Cancer of rectum remains in the expected magnitude (SMR 103), at which the authors discuss the possibility of misclassification of rectum cancer as colon cancer.

⁹ 7.3 instead of 233 deaths

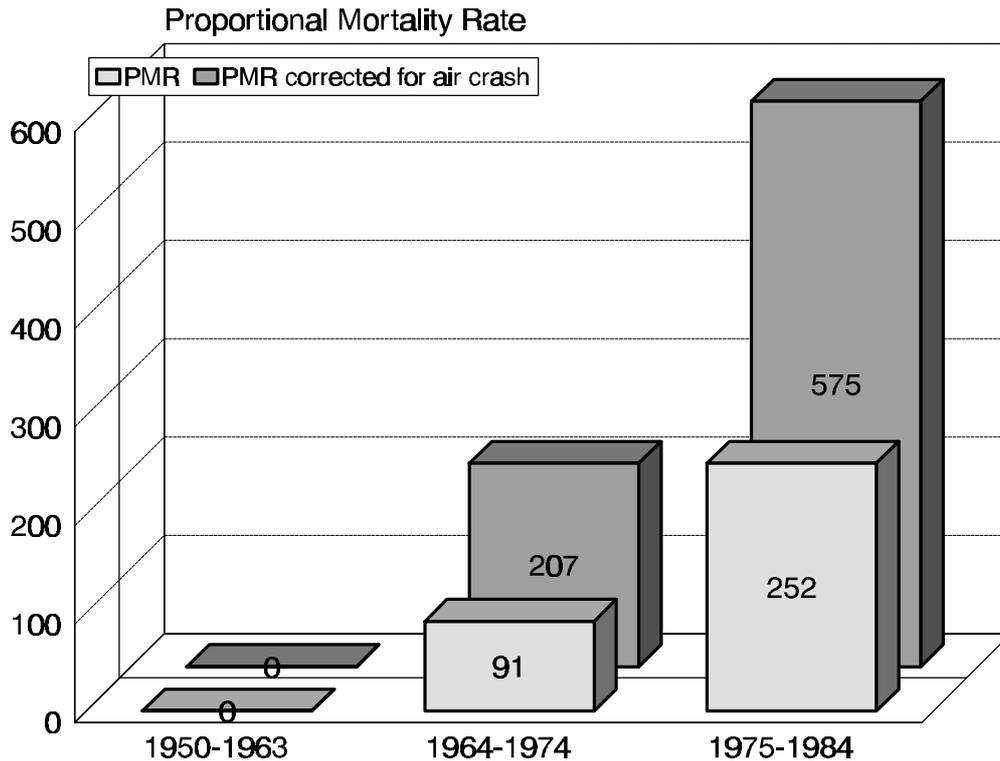


Fig. 3: Brain tumour as cause of death among British Columbia pilots in various time periods. Original observation and data after correction for the unusual high mortality by air crash.

[Data: Salisbury et al. 1991]

Of interest is an increasing trend of brain tumours over the periods 1950 through 1963, 1964 through 1974, 1975 through 1984 (Fig. 3). After correction by air crash, the trend of which shows a constant rate over the whole time, the increasing trend of PMR of brain tumour becomes still more dramatically.

The authors discuss in this context that not before 1960 high flight levels become common and they assume a latency period of ten years explaining the increasing frequency of brain tumours as a consequence of increasing radiation burden.

The constant relative mortality by air crash over a period of three decades, totally different from the international trend with a decreasing frequency of death by air crash, adjusted by person-years, elucidates once more the questionable method of the data sampling in this study. The pilot apparently are seldom professionals of great airlines but mainly, according to the authors, bush pilots.

British Airways Pilots

These findings are confirmed one year later principally by a study, which analyzes the cause of death of 411 male pilots of the British Airways by the method of PMR [Irvine, Davies 1992]. The authors covered the period from 1966 through 1989, also 23 y and followed up the status of vitality of active and retired pilots. Additionally the authors removed the highly significantly elevated frequency of death by air crash before calculation of PMR. 36 death by air crash¹⁰ refers to a PMR¹¹ 11,467!

The Mortality of British Airways Pilots,

1966-1989: A Proportional Mortality Study

Irvine, D., Davies, D.M.,

Aviat. Space Environ. Med. 1992, 276-279 Causes of deaths

411 Males

Time period: May 1, 1966 - December, 31 1989: 23 years

Air crash PMR 11467

Cancer PMR corr. by air crash

PMR 131 (sign.)

Colon cancer PMR 230 (sign.)

Melanoma PMR 668 (sign.)

Prostate cancer PMR 212 (sign.)

Brain cancer PMR 268 (sign.)

Non specified PMR 208 (border of sign.)

Tab. 5: British Airways pilots. Summary of data.

¹⁰ instead of 0.31 expected cases

¹¹ In the original paper the PMR is expressed as fraction of one, e.g. PMR=1.0 instead of PMR=100. Allowing for a better comparison with the results of the other papers, the values of PMR presented here are multiplied times 100.

All cancer together were significantly more frequent the cause of death (PMR 131), with main contribution of colon cancer, melanoma, cancer of prostate and brain tumour. Cancer of not specified courses was at the border of significance. More frequently, but not significantly, was seen cancer of oral cavity, oesophagus, liver, lung, pancreas, pleura, of the lymphatic and hematological system including Hodgkin's disease. Also in this study cancer of the rectum is seen more seldom as expected.

Synopsis

Now a synopsis is presented combining mainly the four studies from Canada, Great Britain and Japan broken down by kind of cancer. The smallest possible denominator is an analysis by PMR, because the SMR values can be converted to PMR. The missed values for expected cases in the Japanese study are supplemented by a weighted mean from the other studies. Weighting factors are the proportion of the number of deaths observed in the study, corrected by air crash, to the sum of the corrected numbers of deaths of all studies.¹² Also the PMR values are combined by weighting with the proportion of the corrected number of deaths. Significance of the PMR values was assessed by comparison with the Poisson distribution observing a 95% confidence interval¹³. Of course this method of combining different studies is not absolutely exact, it looks somewhat like the addition of apples and pears, but it enables to recognize at least semiquantitatively a correspondence in the results.

¹² Canada: 49.08; Japan: 35.6; British Columbia: 176.3; Great Britain: 376.31; total 637.29)

¹³ Comparing the results presented here with the original papers pay attention for the 90% confidence interval used in the study of Band et al. among the Canadian Airlines pilots. All other authors, even Irvine et al., used the 95% confidence interval.

Brain Tumour

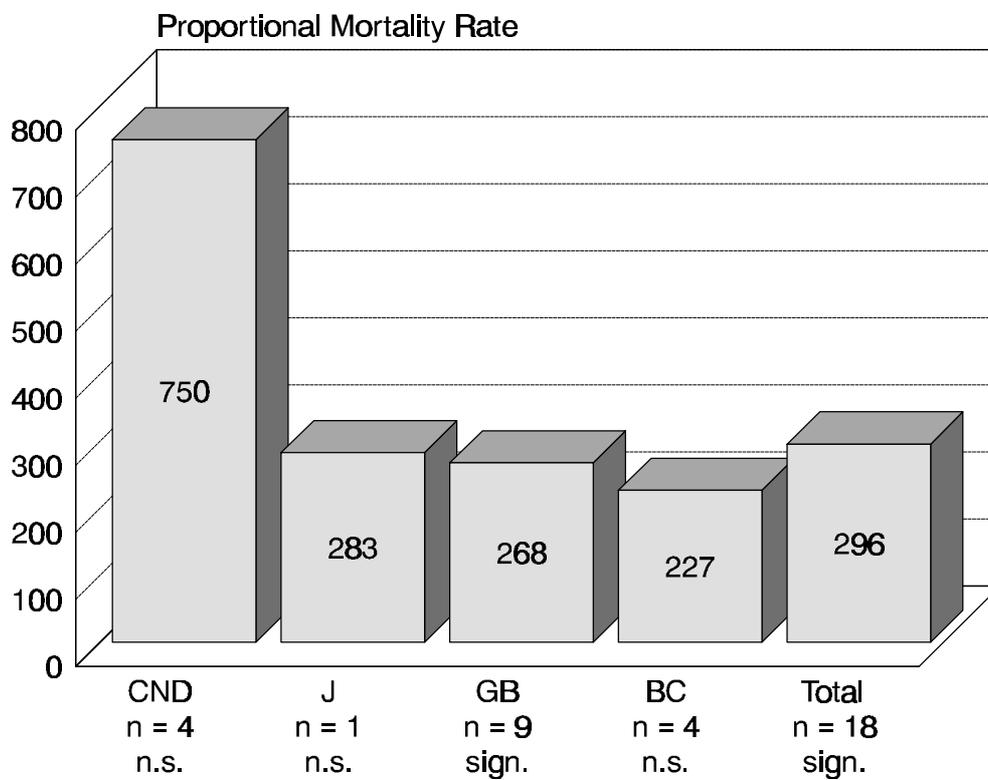


Fig. 4: Proportional mortality rate (PMR) of brain tumour in various studies

CDN: Canada [Band et al. 1990]

J: Japan [Kaji et al. 1993]

GB: Great Britain [Irvine et al. 1992]

BC: British Columbia [Salisbury et al. 1991]

Total: All studies combined with weighted PMR.

n.s.: not significant

sign.: significant with $p < 0.05$

Only significant in one individual study the significance is also seen in the combination of all four [Fig. 4]. This kind of tumour is also seen more frequent after radiation burden, but very seldom. Normally only 1.5% of cancer death are due to brain tumours. Therefore this penetrant finding raises the question of specific causes in the flight environment. The discussion must be extended to the promotion effect of fields of electromagnetic waves with high frequency [Clearly et al. 1990]. Experiments with rhesus monkeys, observing the mortality experience of nine years, show in a group exposed to proton radiation of 55 MeV in seven of ten cases with death by malignant tumours a brain tumour (glioblastoma) [Krupp 1976]. Therefore the possibility must be discussed that the specific field of radiation in high flight levels causes a different pattern of organ cancer than X-rays or gamma rays alone.

Cancer of colon and rectum

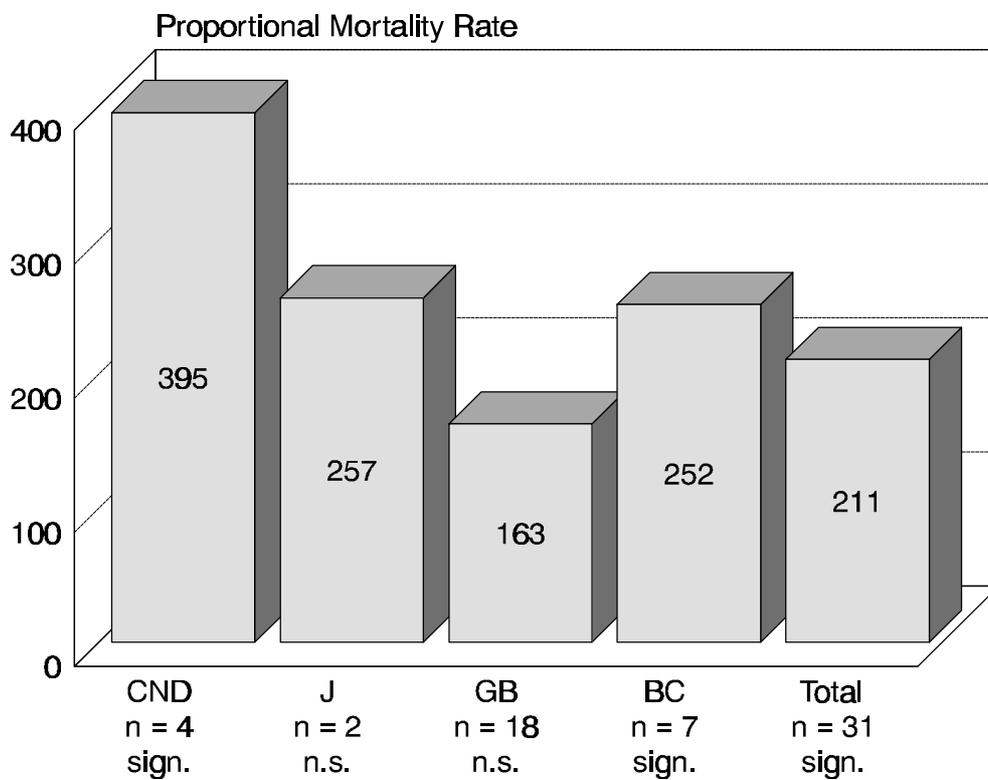


Fig. 5: Proportional mortality rate (PMR) of cancer of colon and rectum.
Details cf. fig. 4, p. 13.

This two entities are put together for compensation of a possible misclassification of rectum cancer. In all four studies combined as in two individual studies the increased PMR is significant (Fig. 5). Cancer of colon and rectum are responsible for about 12% of male cancer death, the fourth entity in the frequency statistic. An increased frequency is usually seen after radiation burden and the colon is therefore listed in the new 1990 recommendations of ICRP of weighting factors for tissues and organs [ICRP 60 1991]. But this does not exclude specific cofactors due to the life style of pilots and specific occupational conditions as disruption of the circadian rhythm, long working in sitting positions, unusual food and so on.

Melanoma

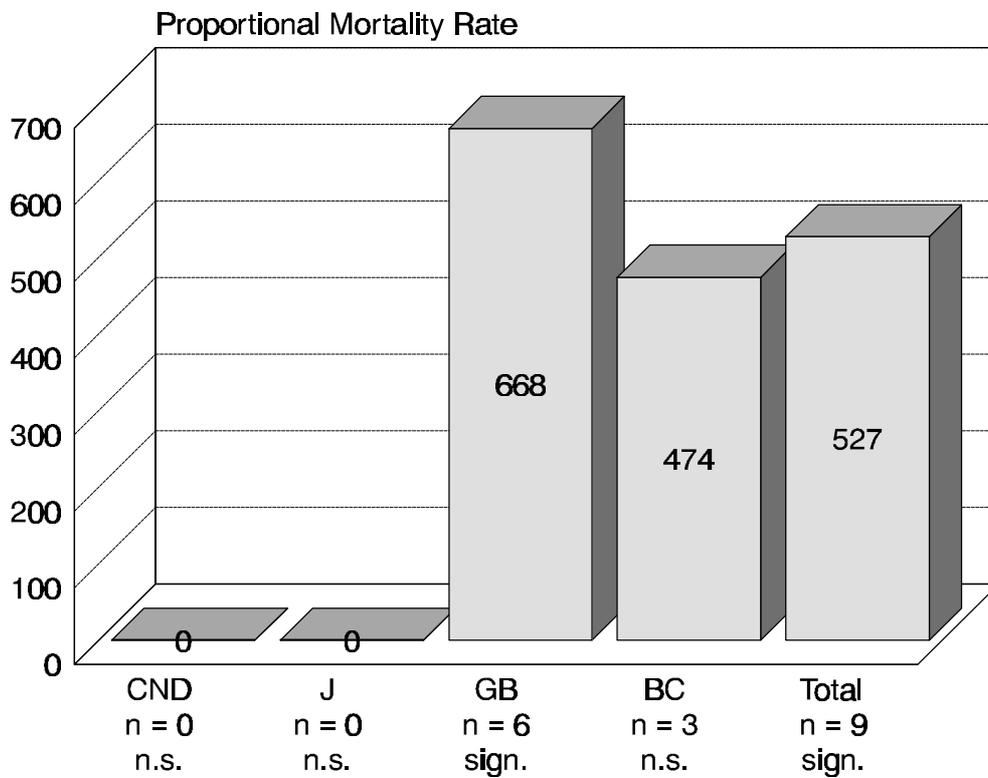


Fig. 6: Proportional mortality rate (PMR) of melanoma.
Details cf. fig. 4, p. 13.

The significant finding in one individual study remains significant after adding the non significant figure of a second study and after dilution by zero findings in the two others (Fig. 6). Additionally we have to remember on the significant elevated frequency in the US Air Force and the non significant elevation in the US Navy. This seldom tumour is also seen more frequent in some statistics after radiation burden. Like in the case of brain tumours the higher frequency of this tumour raise the question of specific cofactors or promotion factors. This suspicion is supported by the more frequent appearance of this tumour in regions of skin not or not usually exposed to sun. I don't agree without reservation reading in the paper about the British Airways pilots: "The marked excess of this cause of death is compatible with the lifestyle of pilots where excessive sun bathing may occur on stop-overs or holidays." [Irvine, Davies 1992]. Supposed this statement is valid an important contribution of ionizing radiation is not excluded. Incidence studies of skin cancer after exposure to medical X-rays in children has shown that the elevated frequency per dose in sun exposed areas is ten times the elevation in protected areas [BEIR V 1990].

Malignant Tumours of the Haematopoetic and Lymphatic System

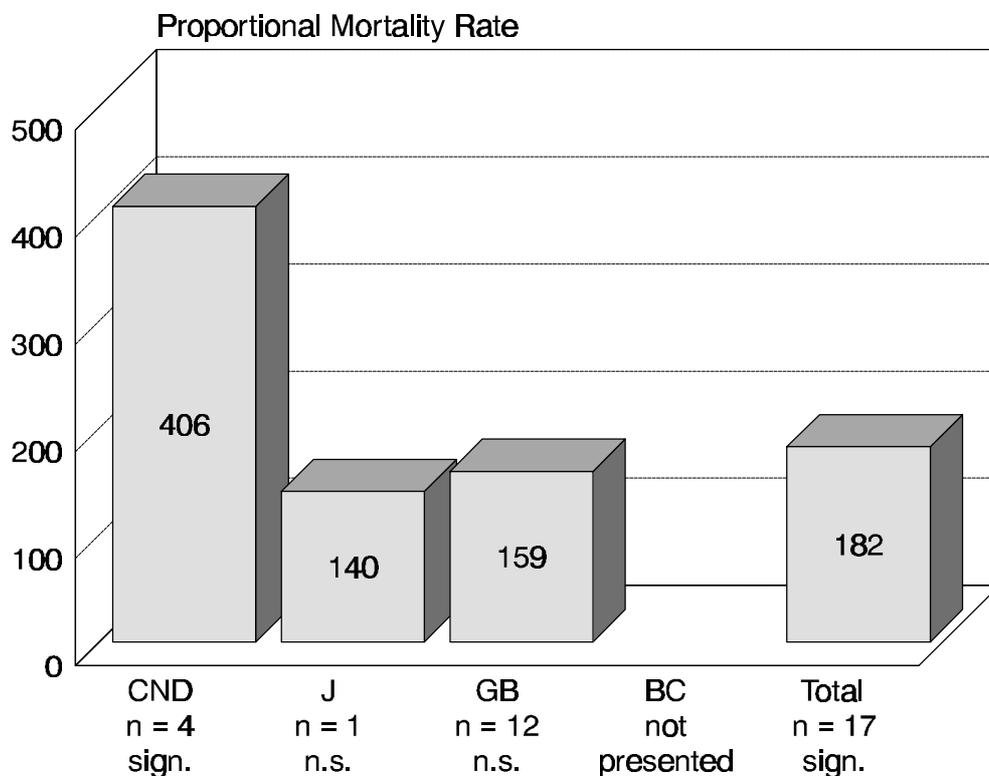


Fig. 7: Proportional mortality rate (PMR) of malignant tumours of the haematopoetic and lymphatic system.
Details cf. fig. 4, p. 13.

The significance of the elevation in one individual study remains after the combination of three studies (Fig. 7). The study from British Columbia gives no contribution to this entity. These seldom diseases, normally with less than five percent share on cancer death, are typical consequences of radiation burden, thereafter they share with more than ten percent of the excess cancer death [BEIR V 1990].

Cancer of Lung

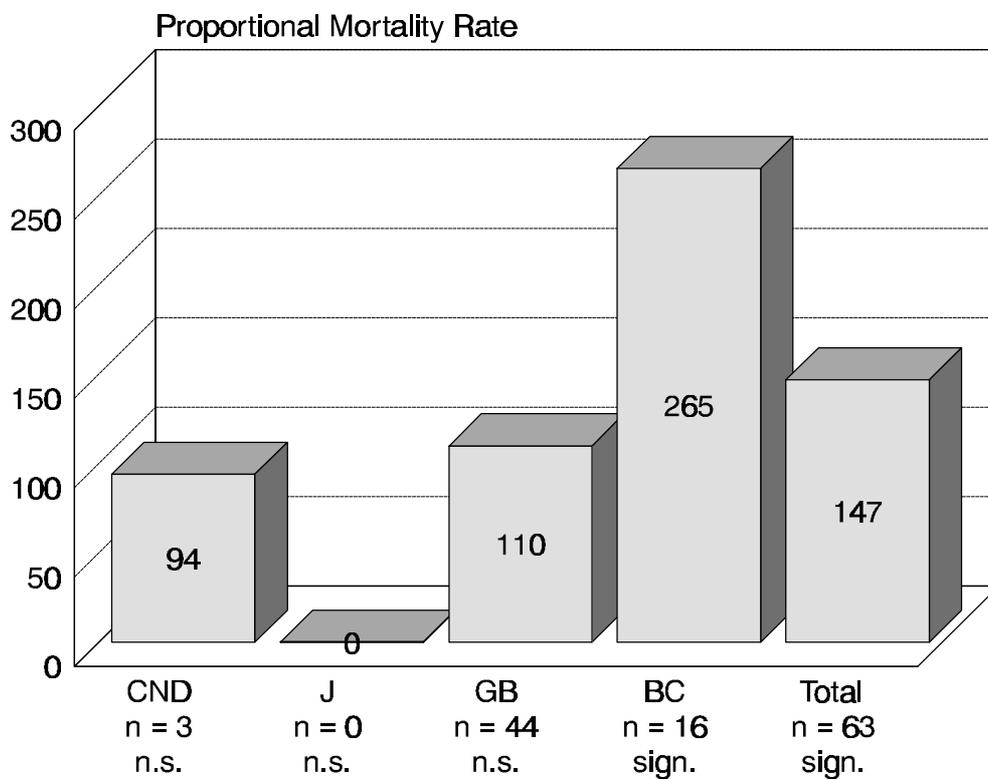


Fig. 8: Proportional mortality rate (PMR) of cancer of lung.
Details cf. fig. 4, p. 13.

This tumour, being the most frequent cause of cancer death in males, is only significant in one individual study and remains significant in the combination of all four combined (Fig. 8). Usually in mortality statistics of a population working in conditions with a restriction of the possibility to smoke an exceptionally increased healthy worker effect can be observed. Therefore this finding is alarming and compatible with the heavy exposure to ionizing radiation.

All cancers

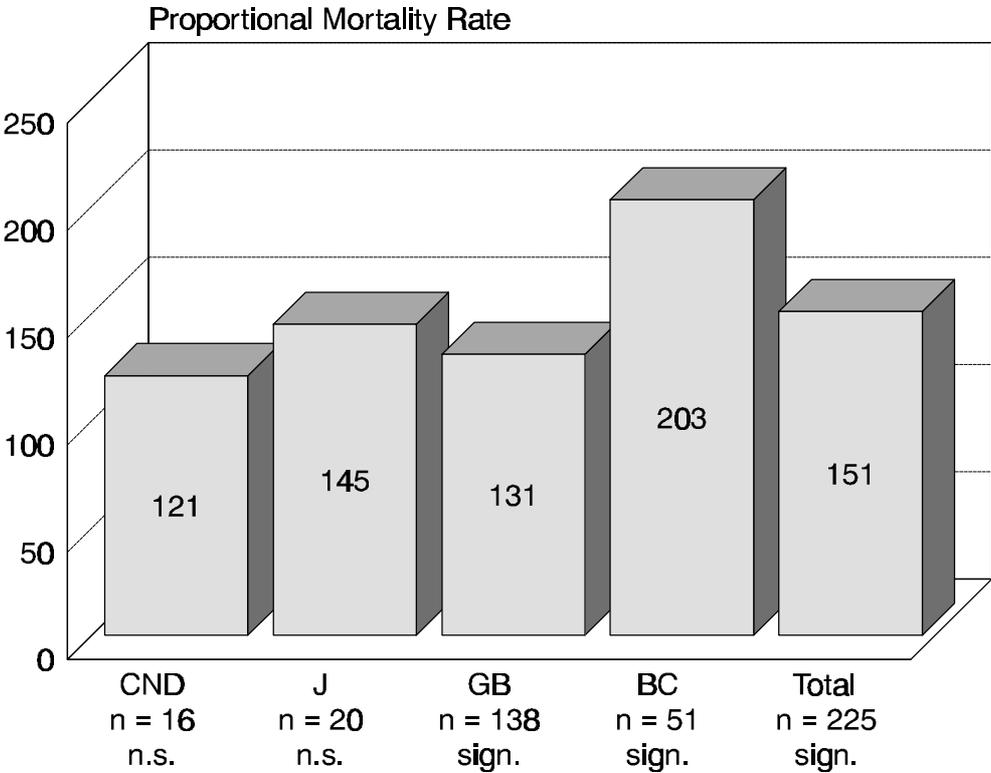


Fig. 9: Proportional mortality rate (PMR) of all cancers. Details cf. fig. 4, p. 13.

The elevated frequency significant in two single studies is also significant in all four studies combined [Fig. 9]. This fact and the specific expression of the manifestation in the different organ systems calls for further investigations as basis of the possibility of specific prevention.

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