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Therapeutic value of anti-cancer drugs: A critical analysis of Cochrane meta-analyses of the therapeutic value of chemotherapy for cancer

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Abstract

About one in three people in the western world die from cancer. Methods: Meta-analysis of the Cochrane meta-analysis on cancer chemotherapy. This study included all randomized clinical trials, where chemotherapy has been tested in comparison with no treatment (and including supportive care) and placebo (including harmless drugs). The primary outcome of interest is "global quality of life" and "mortality" (including "death" and "survival") as a function of study length and gender. The study included analyses of all dichotomous data using fixed effects relative risk (RR), an estimation of the 95% confidence interval (CI) as well as a calculation of the number needed to treat (NNT). Findings: The results showed that chemotherapy for cancer improved survival but only for men, and only in the short term (6-12 months, NNT=6-12). A strong publication bias makes even this very modest, positive effect uncertain. Women did not benefit from chemotherapy. Patients' 2-year survival was not improved. Quality of life was not included in any study after 1992.

Keywords: Cochrane, meta-analysis, oncology, chemotherapy.

Introduction

Chemotherapy is a chemical treatment for cancer, based on the understanding that cancer is caused by local mutations in cells making them divide out of the organism's control (1); when cancer cells are produced by such a biochemical error, they must be destroyed if the organism is to survive. This can be done by surgical removal of the cancer tissue, by radiation therapy, and by chemotherapy.

Another theory of cancer is the holistic cancer theory, based in the paradigm of holistic biology and medicine, where cancer is the end point of a more basic dysfunction within the biological system as a whole. A human being is a living organism and has

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not only a chemical and physical dimension but also psychic, social, sexual/energetic and spiritual dimensions. The complex dysfunction which has roots in all these different domains leads over time to uncontrolled cell divisions, caused by disturbances in the organisms informational system, and often also to molecular, chemical and genetic changes. It is this latter physicality of the change that is most often diagnosed as cancer while the underlying chemical/energy/informational disturbance is ignored. It is possible that this very narrow focus on the 'end point' only is partly responsible for the fact that the National Cancer Institute has abandoned the rallying phrase 'War on cancer', which clearly is very far from being won.

While the focus of the conventional model is on the alteration in DNA sequences, other approaches have considered a more holistic approach, as indicated above. The latter viewpoint considers the dysfunction leading to cancer as involving a disturbance of the information processes within the whole organism that comes from traumas involving emotional, mental, sexual and spiritual aspects of the human being (2-23). Of these aspects, holistic cancer researchers like Wilhelm Reich found sexuality to be the most important of these aspects (16,17). The holistic cure for cancer is to rebalance the person on all levels, to remove the burden on the organism's inner order, and thus to rehabilitate the informational system that informs the cells about their local functions, and thus to induce apoptosis and spontaneous remission (2,3,16-22).

Despite the 'war on cancer', progress has been excruciatingly slow. It is possible that this slow progress may be the result of a very narrow empiricism which is more akin to scientism than a broad-minded open empiricism which recognises that there is not only sensory experience, but also mental and spiritual experience, as suggested by Ken Wilbur in his book "The marriage of sense and soul" (24).

With a much broader overview of the pathogenesis of cancer not confined only to sensory input and measurements (narrow empiricism) it is possible that faster progress will be made and better outcomes achieved in the management of cancer, not as an end point diagnosis but as a dysfunction at the matter/energy/information interfaces.

Several research groups have researched the possibility of developing a psychosocial treatment of cancer (16-24). Such a cure has been in use by holistic physicians ever since Hippocrates and his students for the first time described this treatment in scientific terms around 300 BCE. Most of the research in holistic medicine has intended to test interventions based directly on an understanding of the mechanisms behind cancer. They has used casuistic reports, i.e. studies of single cases, and not on randomised clinical studies. Vandenbroucke has in a recent paper underlined that this does not mean that the quality of such studies is poor. Qualitative research is not as estimated but is just as enlightening as quantitative research (25-27). Some quantitative studies have been done in holistic treatment of cancer (see 17,18,20-24) and they strongly indicate that psychosocial treatment is an efficient treatment for cancer.

Unfortunately, strong commercial interests in chemotherapy have caused severe pressure on the whole field of cancer research, and holistic cancer researchers have often been severely discredited by their biomedical colleagues working close to the pharmaceutical industry, and even sometimes being sent to jail for using CAM-treatments and not chemotherapy. One such researcher is Hamer, who claimed in his work to have helped about one in seven of his cancer patients survive (NNT=7 for "cured") (21). Another holistic cancer researcher is Levenson, who in his work claimed to have helped patients improve their quality of life, reduce cancer-related pain and helped one in ten to survive. At least some of his patients seem to have had spontaneous remissions after he initiated his treatment (we estimate conservatively from his 75 presented case records that his treatment has the efficacy NNT=2 for improved quality of life, NNT=2 for less pain, NNT=10 for surviving longer, NNT=20 for "cured") (22-24). The Levenson retrospective study suffers from lack of satisfying objective data and lack of a solid, prospective resarch design. Nevertheless his results seems to be of the same magnitute of efficacy as the Hamer and the Spiegel study mentioned below.

The best and most fameous, randomised clinically trial (RCT) yet on psychosocial treatment of cancer, that also had the most impressive results, was published by Lancet in 1989 by Spiegel et al (NNT =2 for improved quality of life, NNT=2 for "surviving

longer", NNT=20 for "cured") (18); unfortunately this study has yet to be reproduced, as newer studies have been performed by people without Spiegels' quite unique ability to care for and bond to the patients; as the dimension "bonding between therapist and patient" according to Levenson is the most important psychosocial factors related to survival in cancer, it is a methodological disaster that later reproductions of the Spiegel study (18) have not included this, making it impossible to say if they actually reproduced Spiegel et al.'s study. In our Research Clinic for Holistic Medicine and Sexology we have recently seen examples of induction of spontaneious remission of cancer happening after holistic, existential healing (Antonovsky salutogenesis) (20). All in all, and in spite of the controversy around more solid documentation, there seems to be sufficient scientific evidence to conclude that holistic, psychosocial medicine can be of therapeutic value to cancer patients.

The commercial interests against psychosocial treatment, which since Abel's study (see below) have severely threatened commercial interests, are likely to play a role in the difficulties of reproducing the study of Spiegel et al. 1989. But the lack of a holistic philosophy in the study environment will also make such an attempt useless, as we recently have seen at the University Hospital, Copenhagen (Rigshospitalet) in Denmark, where such a study was stopped before completion, because the biomedical environment would not support this kind of psychosocial intervention, in spite of competent biomedical researchers like Mogens Claesson being involved (28).

On the other hand spontaneous remissions, a spectacular phenomena well recorded in the medical literature where a cancer suddenly completely disappears, seem to be quite a normal event in hospitals and private clinics for complementary and alternative medicine (CAM) (2,3,16-24). Good reviews are Boyd's: "The spontaneous regression of cancer"); Tilden, Everson and Warren's "Spontaneous regression of cancer" and O'Regan and Hirschberg': "Spontaneous Remission. An annotated bibliography" from the Institute of Noetic Science (29-31).

The private cancer hospital Humlegaarden in Humlebæk, Denmark, is such a place where spontaneous remissions have often happened during treatment as documented on the hospitals homepage, which is currently controlled and approved by the Danish health authorities (Sundhedsstyrelsen) (32).

If we take the works of Spiegel, Levenson and Hamer together we find that psychosocial treatment of cancer with holistic non-drug medicine (nonpharmaceutical CAM) improves quality of life (NNT=2), reduces cancer pain (NNT=3), increases survival (NNT=3), and induces spontaneous remission (NNT 7-20). A number of casuistic reports exist, i.e. with mind-body medicine of the subtype clinical holistic medicine (2,3,19,23).

The efficacy of cancer chemotherapy was thoroughly investigated by the competent German statistician Ulrich Abel from 1980-1995 (33-36). In 1992 Abel published a meta-analysis including all published and much unpublished data (33). Abel did not find a positive effect for chemotherapy, either on quality of life or on survival; on the contrary he found chemotherapy in general shortened patients' lives and destroyed their quality of life.

His study was the culmination of more than a decade of dedicated work; in the beginning he found many of the published cancer studies to be of poor quality and strongly biased. He therefore collected all original data, including that from many unpublished studies, from several hundreds of cancer researchers and included thousands of randomised clinical studies in the largest single study of chemotherapy for advanced epithelial cancers ever made. His study included all the major cancer types: lung (small-cell, non-small cell); colon/rectum; stomach; pancreas; bladder; breast; ovary; cervix uteri, and endometrial.

He investigated the outcomes in five different ways, and when he took all this together he found clear evidence that for almost all the common cancers chemotherapy only shortened the patient's life and destroyed their quality of life (see his "table 1 and 2" reproduced below (from 33)).

Abel also discovered that the strong commercial interests of the industry had lead to publication of only positive findings, so the whole field suffered from a very strong publication bias. According to Abel's study, cancer chemotherapy is not an evidence-based treatment.

Table 1. Direct evidence from randomized studies on the question of whether palliative chemotherapy prolongs survival. (Ø: There is no evidence of this type. + or ÷: The evidence is definitely a positive/negative response. (+) or (÷): Unclear evidence; on the whole rather positive/ negative. In case of (+) and (÷): the effect is, if any, small (from 33)

Type of study:	*Site Chemotherapy + X vs. X alone*	*Immediate vs. deferred therapy*	*Dose-effect studies (X = any treatment)*
Lung, small-cell	+	Ø	÷
Lung, non-small cell	(+)	÷	Ø
Colon/rectum	Ø	Unclear	Ø
Stomach	÷	Ø	Ø
Pancreas	÷	Ø	Ø
Bladder	Ø	Ø	Ø
Breast	÷	(÷)	÷
Ovary	Ø	Ø	Unclear
Cervix Uteri	Ø	Ø	÷
Endometrium	Ø	Ø	Ø

Table 2. Indirect evidence on the question of whether palliative chemotherapy prolongs survival. (Ø: There is no evidence of this type. + or ÷: The evidence is definitely a positive/negative response. (+) or (÷): Unclear evidence; on the whole rather positive/ negative. In case of (+) and (÷): the effect is, if any, small (from 30)

Type of study:	*Site randomized comparisons of different regimens*	*Non-randomised comparisons of patient cohorts*	*All 5 measures (total of the five measures)*
Lung, small-cell	+	÷	+ + ÷ ÷
Lung, non-small cell	Unclear	÷	(+) ÷ ÷
Colon/rectum	÷	÷	÷ ÷
Stomach	÷	÷	÷ ÷ ÷
Pancreas	÷	÷	÷ ÷ ÷
Bladder	÷	÷	÷ ÷
Breast	(÷)	÷	÷ ÷ ÷ (÷)(÷)
Ovary	+	÷	+ ÷
Cervix Uteri	÷	÷	÷ ÷ ÷
Endometrium	÷	÷	÷ ÷

It is worth noticing that until today nobody has been able to seriously question his work, his collection of data, his methods, his results, or his conclusions.

Abel thus found in his evaluation done in five different ways on the treatment effect of chemotherapy for the 10 most important cancer types, that cancer chemotherapy shortened the patients' life (23 times "÷"), and only two times that it prolonged life (2 times "+"); in these cases the benefit was only a few months longer survival. Only for one type of cancer, small cell lung cancer, was this tendency clear. In the long term as many patients died from their cancer with chemotherapy as without chemotherapy, indicating no clinical significance of the treatment even for small-cell lung cancer.

His findings led to the clear conclusion that chemotherapy in general only shortened life, did not prolong it at all and destroyed the patient's quality of life.

The continuation of cancer chemotherapy, in spite of clear and compelling evidence that chemotherapy harmed patients, is a logical consequence of the cancer physicians' hope for a chemical cancer cure,

and strong commercial interests leading to intensive continued research. Since 1992 literally thousands of cancer studies have been done.

Against this background we thought it important, twenty years later, to reproduce Abel's study, to see if cancer chemotherapy has improved significantly. To avoid the publication bias Abel discovered, we wanted to include Abel's data for the period before 1992 in our study, but Abel was not able to provide us with the data in spite of goodwill, due to a most unfortunate breakdown of the computer main frame, which happened shortly after he originally published his findings.

Therefore in the present analysis we will also have the persistent problem of publication bias. To be sure to only include studies of sufficient quality, and not to introduce selection bias, we have made this study a meta-analysis of all Cochrane meta-analyses of chemotherapy for cancer. This means that all studies included have passed the quality control of the Cochrane collaboration.

Methods

Cochrane Collaboration software for preparing and maintaining Cochrane reviews (Review Manager), and the basic review and meta-analysis principles recommended by the Cochrane Collaboration (37-39) were used in this study. The methodological quality of the studies was independently assessed by at least two authors. The data was extracted by two reviewers.

We searched Medline/PubMed and the Cochrane Library (CENTRAL) for all Cochrane reviews including studies investigating the effects of anticancer chemotherapy versus placebo (or harmless drugs) or no treatment (including care) for all cancers, and these studies formed the basis of the study at hand. Only randomized controlled trials were included, while quasi-randomized studies were excluded. All participants were people with a diagnosis of cancer, or previous cancer, irrespective of age, sex or severity of illness.

The search allowed us to include data from 48 randomised studies (chemotherapy vs. placebo, including harmless drugs) or no treatment (including supportive care) on the positive effects of chemotherapy for cancer including 5,965 patients (40-84). In this meta-analysis we did not include adverse effects and adverse events. We found no data on "global quality of life" in any of the selected studies. As it is well known from countless reports from cancer patients that chemotherapy destroys the patients' subjective quality of life, we have no reason to question Abel's thorough analysis and conclusions on this matter.

As inclusion necessitated at least a Category B on The Cochrane Handbook rating of allocation, a similar number of studies were excluded. The reason for reviewing studies based on quantitative methods only was the lack of qualitative research in the field.

Relative risk can be calculated as

$RR=P_1/P_0=(A_1/N_1)/(A_0/N_{0)})$ i.e. $RR=(287/453)/(177/379)=1.36$.

The confidence interval can be found from

$CI_{95\%}$= exp (ln RR +- 1.96* SE (ln RR)),

where SE = square root of $(1/a_1 – 1/n_1 – 1/a_0 – 1/ n_0)$. The Number Needed to Treat was found using the formula: NNT=1/RD, where RD= p_1-p_0 =$a_1/n_1 – a_0/n_0$.

Types of intervention

1. Any of the following: Any kind of chemotherapy, thus including any dose or mode of administration (oral or by injection).
2. No treatment, placebo (including treatment with drugs with very few adverse effects like hormones) or supportive care (including talk and touch therapy).

Types of outcome measures

1. Survival, death, mortality. Quality of life.

Methodological quality

1. Randomization

Not all studies described the methods used to generate random allocation. For some of the studies it was not clear that bias was minimized during the allocation procedure. At least 80% reported that the participants

allocated to each treatment group were estimated to be similar.

2. Blinding

Very few of the studies had an attempt to make the investigation blind or double-blind.

3. Treatment withdrawals

The description of those who left the study early was in general unclear, or sometimes absent.

4. Outcome reporting

Studies frequently presented both dichotomous and continuous data in graphs, or reported statistical measures of probability (p-values). This diminished the possibility of acquiring raw data for a synthesis. It was also common to use p-values as a measure of association between intervention and outcomes instead of showing the strength of the association. Although p-values are influenced by the strength of the association, they also depend on the sample size of the groups. Some of the continuous data were presented without providing standard deviations/errors (estimated about 20% of trials) or no data were presented at all (estimated about 10% of trials). Thus, much possibly informative data was not at hand; we estimated that 30% of the information was lost here.

5. Overall quality

Inclusion necessitated at least a Category B on the Cochrane Handbook rating of allocation. Few studies reached Category A, so most data must be considered to be prone to a moderate degree of bias.

Meta-analytical calculations

The meta-analysis was done in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines (34-36). The randomized-analysed endpoints used in the Cochrane reviews were used to group studies according to the above-mentioned outcome. Funnel plots were made for each outcome and to summarize the effect, relative risks (RR) and risk differences (RD) were calculated, and the number needed to treat (NNT) was calculated from RDs. To combine data in this meta-analysis the fixed effects model was used. We did not apply weighting for study quality, since we did not have any empirical basis for doing so.

Results

A search in the Cochrane Library 2009-06-02 for "cancer and chemotherapy" in the Cochrane Library gave 154 results (reviews and protocols) out of 5,785 records; among these were 117 Cochrane reviews. From these 47 Cochrane meta-analyses were selected as relevant based on the title (37-81). Of these five meta-analyses had useful data, which included 48 studies with randomisation of chemotherapy to placebo (or harmless drugs) or to no treatment (including supportive care). These 47 studies included 5,965 patients.

We were shocked to find that the majority of studies from 1992-2009 randomised chemotherapy to chemotherapy (old vs. new drugs, local versus systemic treatments, high dose vs. low dose, polypharmacy vs. single drug treatment etc). From an ethical point of view this is totally unacceptable where it is well known from Abel's thorough study that chemotherapy only shortens life and destroys quality of life. From this study it is logical to expect that modern chemotherapy, which is still poisonous to human cells, will also be harmful, shortening the patients' life and destroying their quality of life. Even more shocking to us was the lack of quality of life indicators in most studies, as if the physicians no longer cared about the patients' quality of life.

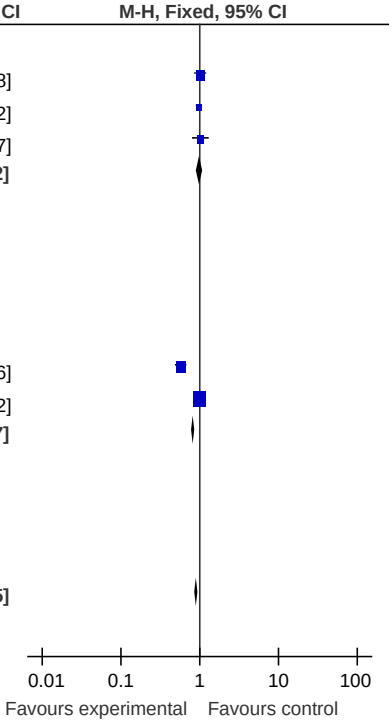
Positive effects

Table 3 shows our findings. We found that the effect of chemotherapy on survival is significant in the short term (6 month (NNT=5.77) and 12 month (NNT=11.9)) but insignificant in the long term (24 month, NNT=50.0)). We found a strong correlation to gender; the effect of chemotherapy on survival was insignificant in women (NNT=167) and significant (NNT=5.85) in men. Thus chemotherapy prolongs life for a few months for one man out of six to twelve but it does not significantly help patients to survive, and the few months of life-prolongation must be balanced

with the from Abel's study well-known, significant, destructive impact on patients' quality of life, indicating negative Quality of life-Year (QALY) and Healthy Life Year (HLY) outcomes of chemotherapy. As we know from Abel's work as mentioned above that there is a very strong publication bias, with many studies showing negative results never being published, even the few month of life prolongation is connected with a strong uncertainty, which all in all make us conclude that chemotherapy does not significantly improve survival in cancer.

Table 3. Chemotherapy vs. placebo (including harmless drugs) or no treatment (including care): Survival as a function of length of study (6,12 and 24 month) (All studies included in the Cochrane cancer metaanalysis, see text))

	Chemotherapy		Placebo/no treatment			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
1.3.1 Women							
CD1419 2.1. Sarcoma	180	413	182	423	20.7%	1.01 [0.87, 1.18]	
CD2093 4.3 Pancreatic	57	59	69	69	7.4%	0.97 [0.91, 1.02]	
CD2747 1.2Met.Breast	112	349	104	330	12.3%	1.02 [0.82, 1.27]	
Subtotal (95% CI)		**821**		**822**	**40.5%**	**1.01 [0.91, 1.12]**	
Total events	349		355				
Heterogeneity: Chi² = 2.07, df = 2 (P = 0.35); I² = 4%							
Test for overall effect: Z = 0.11 (P = 0.91)							
1.3.2 Men							
CD1419 2.1. Sarcoma	142	332	180	241	24.0%	0.57 [0.50, 0.66]	
CD2093 4.3 Pancreatic	328	334	290	295	35.5%	1.00 [0.98, 1.02]	
Subtotal (95% CI)		**666**		**536**	**59.5%**	**0.83 [0.79, 0.87]**	
Total events	470		470				
Heterogeneity: Chi² = 340.76, df = 1 (P < 0.00001); I² = 100%							
Test for overall effect: Z = 7.39 (P < 0.00001)							
Total (95% CI)		**1487**		**1358**	**100.0%**	**0.90 [0.85, 0.95]**	
Total events	819		825				
Heterogeneity: Chi² = 144.70, df = 4 (P < 0.00001); I² = 97%							
Test for overall effect: Z = 3.90 (P < 0.0001)							
Test for subgroup differences: Not applicable							



Adverse effects

We did not include adverse effects and adverse events in this study. The measure of global quality of life includes these negative effects (except treatment-related deaths); therefore we know from Abel's study that all positive and all negative effects taken together for the patients come out negatively, as a reduced quality of life.

Discussion

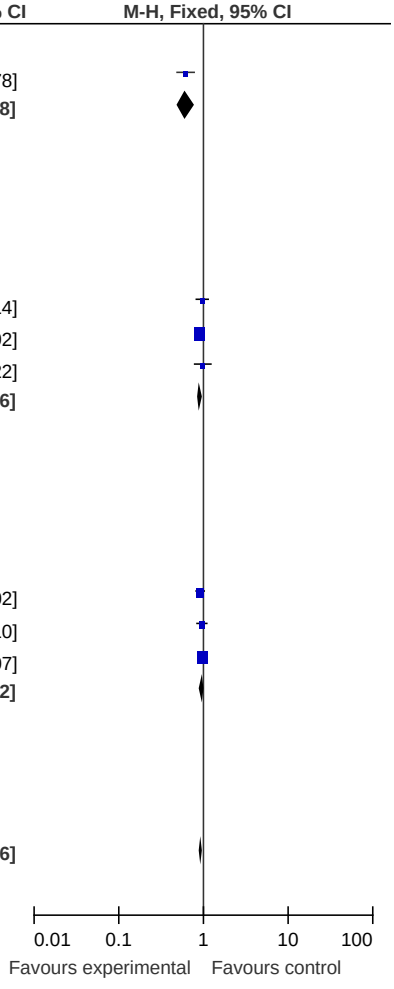
We are in a peculiar situation where Abel already 20 years ago found that chemotherapy did not help cancer patients. Quite the opposite: he found it evident that chemotherapy shortened patients' lives and destroyed their quality of life. Abel also found a strong publication bias, which is logical as there are no commercial interests in publishing studies with negative outcomes.

Our findings are based on less data than Abel's study; in spite of the lack of rationale for it, most studies of chemotherapy today are done as chemotherapy vs. chemotherapy, and studies of

chemotherapy vs. placebo or no treatment has become rare. However we still found 48 studies that could be used for our analysis, with over 6,000 patients, which we considered enough for a valid analysis.

Table 4. Chemotherapy vs. placebo (including harmless drugs) or no treatment (including care): Survival as a function of gender (women, men, 12 months) (All studies included in the Cochrane cancer metaanalysis, see text)

	Chemotherapy		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.2.1 6 months							
CD2093 1.1Pancreatic	68	208	115	217	5.6%	0.62 [0.49, 0.78]	
Subtotal (95% CI)		**208**		**217**	**5.6%**	**0.62 [0.49, 0.78]**	
Total events	68		115				
Heterogeneity: Not applicable							
Test for overall effect: Z = 4.08 (P < 0.0001)							
1.2.2 12 months							
CD2093 1.2Pancreatic	119	208	128	217	6.2%	0.97 [0.83, 1.14]	
CD2139 4.1Non-s Lung	448	522	645	668	27.9%	0.89 [0.86, 0.92]	
CD2747 1.2Met.Breast	104	330	112	349	5.4%	0.98 [0.79, 1.22]	
Subtotal (95% CI)		**1060**		**1234**	**39.5%**	**0.91 [0.87, 0.96]**	
Total events	671		885				
Heterogeneity: Chi² = 3.06, df = 2 (P = 0.22); I² = 35%							
Test for overall effect: Z = 3.64 (P = 0.0003)							
1.2.3 24 months							
CD1419 1.4 Sarcoma	328	767	363	777	17.8%	0.92 [0.82, 1.02]	
CD2747 1.3Met.Breast	193	349	190	330	9.6%	0.96 [0.84, 1.10]	
CD3188 1.1 Ml.Myeloma	557	1079	549	1048	27.5%	0.99 [0.91, 1.07]	
Subtotal (95% CI)		**2195**		**2155**	**54.9%**	**0.96 [0.90, 1.02]**	
Total events	1078		1102				
Heterogeneity: Chi² = 1.10, df = 2 (P = 0.58); I² = 0%							
Test for overall effect: Z = 1.41 (P = 0.16)							
Total (95% CI)		**3463**		**3606**	**100.0%**	**0.92 [0.89, 0.96]**	
Total events	1817		2102				
Heterogeneity: Chi² = 18.79, df = 6 (P = 0.005); I² = 68%							
Test for overall effect: Z = 4.02 (P < 0.0001)							
Test for subgroup differences: Not applicable							



Nothing seems to have changed since Abel's study in 1992. Most of the decline in cancer noted and touted by media and even the oncology establishment have been due to smoking cessation, early stage diagnosis and to improvement in overall health care.

The Annual Report to the Nation on the Status of Cancer 1975-2000 disclosed that no further declines in the incidence rates after 1995 or in mortality rates after 1998 were noted (85).

As pointed out by Faguet in his book 'The war on cancer' (86) the cell-kill paradigm has failed to achieve its goals, using a model, which is based on 'flawed premises, with unattainable goals, cytotoxic chemotherapy in its present form will neither eradicate cancer nor alleviate suffering.'

It is surprising that so few cancer researchers have studied Abel's papers and books; none of the Cochrane meta-analysis used Abel as a reference. The focus on tumour shrinkage rather than on patient survival and quality of life has detracted oncologists from the primary purpose of 'doing no harm' and also of being completely honest with regard to outcomes.

While the bias towards the use of chemotherapy has become so entrenched within the oncology community, tied up as it is with the whole industry and the commercial success of that community, it has become very difficult for oncologists to extricate themselves from the stranglehold that this chemotherapy paradigm has become.

It seems that the international cancer society collectively has simply ignored Abel's important findings from 1992, which we do understand from a commercial angle, but which we find extremely problematic. There needs to be better regulation of how money is allocated to cancer research and more non-drug approaches should be in included. In general is seems safe to conclude that the industry has had its chance to prove that efficient chemotherapy can be developed, and has failed. The reason why chemotherapy after 1992 has not been substituted with psychosocial treatment, which at least seems to improve quality of life, and possibly also survival, is undoubtedly the conservatism of the medical system, backed up by physicians working closely together with the powerful pharmaceutical cancer industry.

A political analysis shows that the media plays a central role in keeping cancer chemotherapy on the market (87). The link between the media and the industry might be so strong that it is not politically possible for a single nation to stop using chemotherapy on its own, as the industry and the cancer physicians have the power to turn a government over, simply by claiming that it "kills cancer patients by refusing the life-saving cure". The systematic and strategic massive misinformation of the population on the effect of chemotherapy during the last 20 years has made patients believe in chemotherapy, in spite of no evidence of positive effects of chemotherapy in general.

What is needed to improve the situation for patients is international cooperation of all organisations of oncologists and of international governmental health organs. The pharmaceutical industry is in business to make money and this may not serve the patients' best interests.

WHO is unfortunately working so closely with the pharmaceutical industry that it is not likely to be able to play a role in this important process; we must strongly recommend that WHO is not involved in such collaboration.

The major problem of Ulrich Abel was to get studies of sufficient quality for review; what he did in the end was to collect all original data from all cancer researchers, to complete the review he made. Shortly after his study was published the computer main frame crashed and all data was lost (88), presumably because of industrial sabotage(if there is no evidence for this statement then perhaps leave it out). As a result of this all the original data was lost. But we still have his analysis conclusions, and we have no reason to doubt his honesty or integrity as scientist. Abel showed in 1992 that chemotherapy didn't prolong life as expected, which means that chemotherapy has not proven its worth as a standard treatment for cancer.

Today we are fortunate that cancer research has been done in the Cochrane meta-analysis, making it easy to identify the relevant studies of sufficient quality to qualify for entry into a general review or meta-analysis. But still we need to accumulate all unpublished data to get the truthful picture.

Finally, we find it peculiar that none of the Cochrane meta-analysis has a reference to Abel's work, as he was the first to do a meta-analysis of chemotherapy for most types of cancers. It is as if the researchers making the Cochrane meta-analyses either have not done their homework, or more likely that they intentionally have neglected Abel's study. Not to include important sources, for whatever reason, is introducing an important bias. We therefore must conclude that the Cochrane meta-analysis of chemotherapy for cancer in general seems to be biased for chemotherapy.

The outcome "quality of life" was almost never found in the studies from 1990-2009, but many adverse effects of the drugs strongly indicated that quality of life, as in Abel's study, was not improved, but rather destroyed, by chemotherapy. In spite of the data lacking from the studies, some researchers still paradoxically concluded that chemotherapy improved patients' quality of life.

Conclusions

In 1992 Abel published his findings that chemotherapy was not beneficial for survival and quality of life and that in general the opposite was actually the case: Chemotherapy was harmful to the

patients. This was found for all epithelial cancers – 80% of all cancers, including cancer of the lung (small-cell, non-small cell), colon/rectum, stomach, pancreas, bladder, breast, ovary, cervix uteri, and endometrial. We have repeated Abel's study, but included all types of cancers in general. We have found no evidence whatsoever that the situation has changed since 1992.

The pharmaceutical industry has changed its patterns of clinical studies from testing chemotherapy against no treatment or placebo to almost always testing it against other types of chemotherapy, or against surgery and/or radiation therapy. This strategy is understandable as the industry has a business to protect, but seen from the interests of the patients this is highly regrettable, and from an ethical perspective completely and utterly unacceptable.

Since 1992 we have known that the treatment of most types of cancer with chemotherapy is not evidence based. We have repeated Abel's study for all cancers, and we have reached the same conclusion as Abel did 17 years ago. Even for the few cancers where chemotherapy seems to improve survival this is only for a few months, with no effect on long term survival. Only about 4% of all cancers are potentially curable with biomedical methods and fewer than 50% of them will achieve a 5-year survival (see 86). We also found that women in general do not benefit from chemotherapy.

In this situation, where a strong industry continuously and by all means promotes a type of drug that we know is harmful to the patients, we need strong governmental restrictions on the use of chemotherapy, and immediate research programs for the psychosocial treatment of cancer.

We suggest a review of the standards of practice using chemotherapy, a return to basics in which cancer protocols include a non-drug treatment group which has an active QOL program.

What concerns cancer patients is quality of life and survival. Given the meagre impact of chemotherapy on the majority of cancers, quality of life then becomes a major issue. It is possible that whatever good results have been seen in overall mortality figures may be due to a decrease in smoking, early stage diagnosis and a general improvement in lifestyle management including diet and stress management together with more emphasis on exercise and nutritional supplements.

In contrast to chemotherapy, psychosocial interventions for cancer have no side effects and seem in general to be of large and significant, therapeutic value (2,3,16-24). As far as we know today, psychosocial intervention, together with an improvement in overall healthcare, may achieve the same or probably much better outcomes than chemotherapy.

The issue of cancer cure, palliation and quality of life has not been approached in a way that helps doctors and patients make clear choices. Oncologists very often will justify further treatment to provide immediate palliative relief of symptoms when it is clear that this has nothing to do with a cancer cure and may not improve, and might even depress, quality of life in the long term. Quality of life improving interventions when practised in a patient-centred way using the most efficient non-drug therapeutic techniques and allowing the patient to deal with repressed emotions, letting go of negative beliefs and finding a new purpose of life as developed by one of the author's has the potential of shifting the way the body deals with the cancer and seems able to prolong life and even shift the organism into a spontaneous remission.

The poor results of chemotherapy despite the enormous amounts of money involving the largest number of researchers ever assembled to conquer a disease suggest that the war against cancer has not only been misdirected, but the results obtained even exaggerated. There is little evidence that chemotherapy will have better overall patient survival than placebo, and the chances are that QOL approach may be more efficacious, with a major decrease in morbidity and patient suffering. All further research in chemotherapy should include chemotherapy vs. placebo, especially in the form chemotherapy vs. active QOL improvement. Without this evidence we may be doing more harm to our patients while only serving the interest of drug companies who make enormous profits from these medications.

Recommendation for further research

Further research is needed to develop the optimal mind-body medicine cures for the different cancer types, but we already have well-researched approaches that can be used for standard treatment to improve cancer patients' quality of life, like the psychosocial group intervention developed at Stanford University by David Spiegel (18), the mind-body treatment developed by Levenson (22-23) or the individual treatments with clinical holistic medicine developed at the Research Clinic for Holistic Medicine in Denmark (2,3,20). All in all there seems to be sufficient scientific evidence to conclude that holistic, psychosocial medicine can be of therapeutic value to cancer patients. Induction of spontaneious remission with holistic medicine has been observed in the clinic and seems to be a possiblity in the future. One way to go in future research might be to reproduce the shamanistic one-session healings with the most severe and chronic, mental and somatic diseases (89). It is important to notice that holistic and shamanistic healing work does not have all the serious adverse effects that is so intimately connected with the biomedical treatment of cancer, including anti-cancer chemotherapy (90).

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