Chemotherapy for cancer? Surprisingly, for most cancers, it should be avoided

The most important issue in having cancer is knowing when to say no to chemotherapy. The five pages below explains why it is prudent to decline chemotherapy for cancer most of the time it is offered.

Unfortunately, chemotherapy is given intensely - even in the last few weeks before the patient dies. In Denmark, prominent doctors have declared publicly that they would abstain from life-prolonging chemotherapy if they got lethal cancer, and few oncologists and nurses are willing to accept the chemo their patients endure for minimal benefit. I wonder why we do not offer patients the same privileges that we enjoy as health professionals. Ending our lives by spending time together with our loved ones would be much better than being pestered by the toxic effects of chemotherapy and frequent hospital admissions, and perhaps even dying in a hospital bed rather than at home.

The following pages constitute Chapter 10 in my book, *Gøtzsche PC. Survival in an overmedicated world: look up the evidence yourself. Copenhagen: People's Press; 2019*. Available on Amazon UK and Amazon USA, and elsewhere; exists also in Danish, Dutch, German and Swedish, and will appear in Italian, Korean and Spanish.

10 Treatment of cancer

We hear a great deal about progress against cancer, now called a chronic disease even though most people, by far, still die from their cancer despite being presented with convincing survival statistics. Yet little progress is actually being made, which is not the impression you get from newspapers and TV that often quite uncritically propagate highly misleading information from cancer charities.[1]

The propaganda is massive, and I shall therefore explain what is wrong with the type of data we see most often. It requires a little attention to look behind the facade and dissect the inflated messages, because there are several ways to measure progress - all of which have weaknesses.

One of the best things we can do is to look at the annual age-adjusted mortality of individual cancers. Mortality needs to be age-adjusted. Since we are getting increasingly older, more of us will die from cancer, no matter what we do.

The problem with this method is it is hard to know what people die from, especially when autopsies are no longer common. When a person has been diagnosed with a cancer, there is a risk the diagnosis will also be considered the cause of death if that person dies in an emaciated condition. But the cause of death could be another cancer or unrecognized heart disease.

The opposite can also happen. If you believe a patient is well - without recurrence - after treatment, you may think something else killed the patient.

However, what we see most often is a period of survival after the diagnosis has been made - 5-year survival, for instance. Unlike age-adjusted cancer mortality where bias, which is rarely extensive, can go both ways, bias in this case almost always leads to overestimations of the results

of screening for and treatment of cancer. The bias can easily be so large that interventions having no effects appear to be quite effective.

If the diagnosis is made earlier than previously, we will see an increase in 5-year survival even when the early diagnosis does not improve survival, and where the age-adjusted mortality of the cancer is therefore unchanged. Patients do not live longer; they live longer with the knowledge that they have cancer because the clock started earlier. Therefore, they are harmed by this type of early diagnosis.

We diagnose some cancers earlier than before because patients and doctors have become more aware of cancer symptoms. For breast cancer, for example, the average tumour size in Denmark was 33 mm in 1978-1979, but only 24 mm ten years later.[2] This decrease had nothing to do with screening for breast cancer, because it occurred before screening was introduced.

Here is an example of highly misleading propaganda: In 2008, a Danish newspaper announced that the 5-year survival for breast cancer had risen from 60% to 80% in 30 years.[3] Although they knew better, spokespeople from the Danish Breast Cancer Group and the Danish Cancer Society claimed that this was due to better treatments and screening. No one explained that a 5-year survival rate over a 30-year horizon is extremely misleading.

In 2016, a journalist wrote that, after being in last place in cancer survival, cancer treatment in Denmark was now at the same level as in our neighbouring countries.[4] The argument was that 5-year survival for breast cancer had risen from 12% to 18% in 20 years. But we now had screening for breast cancer in Denmark, which leads to 33% overdiagnosis.[5] That means many healthy women who would never have received this diagnosis in their lifetime if they had not gone to screening will get a diagnosis of breast cancer. As none of them would have died from the disease, this will improve 5-year survival, of course.

Twenty years ago, we only had screening for 20% of the country. For simplicity's sake, if we assume that the 5-year survival rate of 18% comes from a population that is not screened, and 12% comes from a screened population, the calculation is easy. Without screening, 18% of 100 women with breast cancer die over five years, i.e. 18 women. With screening, 12% of 133 women die (the same 100 plus 33 healthy, overdiagnosed women), which equals 16 women or almost the same. That is not to say there has been no progress in the treatment of breast cancer, but the calculation shows that 5-year survival after a breast cancer diagnosis is highly misleading. The true progress must be far less than the difference between 18% and 12%.

Sometimes the mortality of cancer is compared to the incidence of cancer, but such comparisons can be similarly misleading as 5-year survival, or even more so, and for the same reasons. As an example, the mortality rate of malignant melanoma has been fairly constant for many years, whereas the incidence has been steeply increasing.[6,7]

If cancers were always the same, that would be an outstanding progress in the treatment of malignant melanoma, but that is not the case. The explanation is that many more diagnoses are being made because people are more likely to get their brown spots examined. Almost all of these additional cancers are harmless.[6,7]

The best thing we can do to find out whether a treatment of cancer has any benefit is to do a randomized trial. If we do a randomized trial, there is no problem in using 5-year survival because everyone has cancer to begin with, and the randomization ensures that the two groups are comparable for prognostic factors.

So, what do the randomized trials tell us? A 2004 meta-analysis of 250,000 adult cancer patients treated with chemotherapy in randomized trials showed an effect on 5-year survival for testicular cancer (40%), Hodgkin's disease (37%), cervical cancer (12%), ovarian cancer (9%) and lymphoma (5%).[8] That is reassuring but these cancers represented less than 10% of all cancer cases. In the remaining patients, 5-year survival increased by less than 2.5%, which corresponded to only three months. New drugs for solid cancers approved by the European Medicines Agency increased survival by only one month compared to other regimes.[8]

Breast cancer was not among those cancers where a worthwhile effect of chemotherapy was shown. Yet, that is not what people think. We constantly hear about breast cancer, and people think screening works - which it does not (see Chapter 7) - and that chemotherapy is effective - which it is not. I, too, fell victim to the propaganda. I knew that chemotherapy increased survival and thought it was a substantial effect, and I even recommended it to a patient worried about serious harms. That was before I wrote this book. When I looked up the evidence, I got shocked.

If you google *chemotherapy breast cancer*, the first entry goes to the American Cancer Society, which begs you to *DONATE* in white letters on a red background. You should not donate because the society is obscenely wealthy and spends a lot of money on its own people, just like the cancer society does in my country. By 1989, the society's cash reserves were worth more than $700 million; 74% of its budget was spent on "operating expenses," including about 60% for generous salaries, pensions, executive benefits and overhead.[1] Furthermore, the society has partners that include drug companies like Pfizer, Bristol-Myers Squibb, Abbvie, Merck, Quest Diagnostics, AstraZeneca, Abbott, Eli Lilly, and Genentech. Some of these companies earn exorbitant amounts of money selling chemotherapy at extremely inflated prices that do not reflect research and developments costs.[9] Even Morgan Stanley, which played a major role in the global financial crisis in 2009, is one of the partners. What a group of playmates.[10]

The American Cancer Society once announced that early detection of breast cancer results in a cure "nearly one hundred percent of the time."[11] That was an error of "nearly one hundred percent," since mammography screening does not lead to cures.

The society says nothing about the effects of chemotherapy, only when chemo should be used, and despite providing a long list of serious harms, it omits the statistics regarding their frequencies. The text starts out by saying that, "Chemo drugs can cause side effects." Can? Has anybody ever heard about a patient who did *not* get harmed by chemo? No. There is no free ride.

If you add *cochrane* to the Google search, the fourth record takes you to a page that says there are 17 Cochrane reviews of chemo for breast cancer, divided according to whether the cancer was advanced or not. The American Cancer Society noted that polychemotherapy is often used and the first Cochrane review found that the addition of one or more chemotherapy drugs to a regimen caused greater shrinkage of tumours seen with imaging, but increased toxicity.[12] There was insufficient evidence to determine an effect on overall survival or length of disease progression. The hazard ratio for survival (similar to the relative risk) was about one, 0.96 (95% confidence interval 0.87 to 1.07, P = 0.47), and time to progression was also unchanged, 0.93 (0.81 to 1.07, P = 0.31).

We always prefer absolute risks to relative risks (e.g. a risk ratio or hazard ratio), and a large meta-analysis from 2005 provides this.[13] This study is about early breast cancer, which means that the cancer and any affected lymph nodes can be surgically removed and includes both chemotherapy and hormonal therapy. It runs for more than 31 pages in *The Lancet*, which would

take many hours to read and digest. But that is not necessary. A graph shows that, for women aged 50 to 69 years who received polychemotherapy, the breast cancer mortality is 47.4% after 15 years, compared to 50.4% in women who did not get multiple drugs. Not much of a difference, but it is reassuring that half of the women with early breast cancer had not died from breast cancer after 15 years.

Yet, that does not mean that half the women are still alive after 15 years. Some died from other causes, including the chemotherapy they received, which is why breast cancer mortality is a flawed outcome. *Thus, the most important outcome in cancer trials is always total mortality.* We do not know whether polychemotherapy reduces total mortality because the 31-page paper does not tell us. The readers are referred to figures 1, 6 and 8 in a web appendix not included in the paper.

Then began a bizarre type of academic playing hide-and-seek. Nowhere in the paper was even a hint about how to find the appendix. I looked up the abstract on PubMed but there was no sign there, either. I have free access to *The Lancet* via the university library and I desperately tried all the options I could find on the website. I even went into the issue of the journal where the paper was published, yet no link to any appendix was to be found. There was a PDF without a link to an appendix and a *Detailed Record* that led nowhere. An entry called *Related Information* was dead. I was totally stuck.

In my desperation, I forgot what measures I had tried. At one point, I was at a website with various options that included links to a summary and supplementary material. But when I clicked on supplementary material, I was taken back to the summary! I tried several times with the same result. It was only when I scrolled down to the bottom of the screen that I suddenly realized I needed a password in order to get in. Since I had a password for *The Lancet*, I finally succeeded and found what were called the appendices to the paper. Thus, even though I had free access to the journal via my university, I did not have free access to finding out if polychemotherapy reduces mortality. That was really bizarre.

But my troubles were not over. There were three PDF files. As the first one was called *Annex-Figures 1-13*, this should be the one I was looking for. But it was not what it was supposed to be. There were 249 pages of graphs and often more than one graph on each page, with no meaningful legends to help me find what I was after. I could not find any figures 1, 6 and 8. The first graph showed annual event rates, but there was no information whether these events were total mortality, breast cancer mortality, recurrence of the cancer or something else.

Another PDF told me that the information I was looking for was to be found on another website, outside the journal's control! The third document - 142 pages long - contained some other information.

I looked out the window and swore loudly but did not want to give up. I started browsing the many hundreds of graphs. Nowhere was anything called figure 1, 6 or 8. But on page 17, I found the graph on breast cancer mortality I had also seen in the paper, with a 3% difference in breast cancer mortality after 15 years (50.4% versus 47.4%). The next graph was actually labelled *"Any death*," which was 55.7% versus 53.6%, i.e. a difference of 2.1%. I knew it! Of course, total mortality was higher than for breast cancer alone and - of course - the mortality benefit was lower because some women were killed by the chemo.

Why were there no data on the only unbiased outcome - total mortality - in the 31-page *Lancet* paper? And why were these data so well-hidden that only people as stubborn as me could find them?

This story illustrates what has been documented many times before: academia can be just as biased as the drug industry and just as 'skilled' at hiding the most important facts.

If that woman with breast cancer asked me today, I would tell her that I would not recommend polychemotherapy, and probably not an individual chemotherapeutic drug either, considering the meta-analysis of treatment of various cancers mentioned above.[8] Taxanes do have some effect compared to other chemotherapies, which a Cochrane review shows,[14] but the question is whether these small effects make it worthwhile to get chemo.

It would take some time to find out the effects of single agent chemotherapies because there are so many of them. You would also need to learn some basic issues, like the difference between adjuvant therapy and neoadjuvant therapy (which means chemo before surgery). There are also many forms of breast cancer. Therefore, the easiest way forward will be to ask your doctor what the precise effect is compared to no treatment. The doctor should be able to respond.

People - including most doctors - often say that a small average benefit can be worthwhile because some patients benefit more than others. "Perhaps I will be one of the lucky ones who adds 6-12 months to my life, not the 1-3-month average." Sometimes patients refer to other people who lived many years after polychemotherapy.

That is a false hope. Some patients live especially long because cancer is highly variable, with highly varying growth rates.[1] Some women are therefore predestined to live much longer than others. It has nothing to do with the treatment. We can only make rational decisions if we base them on the average life extension obtained in randomized trials.

The most important issue in having cancer is knowing when to say no to chemotherapy. The fact that chemo is given intensely - even in the last few weeks before the patient dies - has been documented many times.[15] Ending our lives by spending time together with our loved ones would be much better than being pestered by the toxic effects of chemotherapy and frequent hospital admissions. Dying in a hospital bed is worst of all. We want to die in our homes - which my mother did from an ulcerating breast cancer - rather than getting the last dose of chemo on our way to the morgue. That was how we jokingly described that kind of excessively interventionist approach when I was a cancer doctor.[16] My mother preserved her dignity, self-determination and independence until the very last moment, which was important to us.[9]

In Denmark, prominent doctors have declared publicly that they would abstain from life-prolonging chemotherapy if they got lethal cancer,[9] and few oncologists and nurses are willing to accept the chemo their patients endure for minimal benefit.[9,17] I wonder why we do not offer patients the same privileges that we enjoy as health professionals. A woman, only 39 years old, who recently died of breast cancer, said after four courses of chemo, "If this is my last spring, I'd like to put myself in the middle of it instead of having to go to hospital all the time."[16] It was her last spring.

There is something badly wrong with the way we approach incurable cancer (which almost all cancers are), and I will end this chapter with two recent stories from my nearest family which illustrate how absurd it can be to fight a battle you cannot win.[16]

Obituaries often say: "He lost the battle against cancer." I would prefer we left out the war rhetoric and said something positive like: "He had a good life."

My two relatives battled until the very last moment. One, a 67-year-old man was diagnosed with incurable stomach cancer with metastases to the kidney and the liver. As far as I can tell, absolutely nothing could be reasonably done, yet the patient underwent many diagnostic tests, which, due to their invasive nature, aggravated his condition. Several types of chemo were tried, and at one point the patient and his wife were told that he would be offered life-prolonging treatment. They both perceived this message very positively - like a four-year extension of life. The reality was it was extremely unlikely any life extension would be obtained; in fact, it would be more likely the chemo would kill him. Yet this false hope led to a series of additional chemo regimens that pestered the last six months of his life. He did not experience one single tolerable day and was constantly plagued by the harmful effects of the chemo. That was not dignified - not a good death.

My other relative, a 64-year-old man, had cancer in the pancreas with metastases, which is also incurable. He was willing to do everything possible and underwent 27 radiation treatments in Denmark, after consulting a new doctor each time. He then asked to be operated in Germany which was at no expense to him because of a cooperation agreement between the two hospitals. However, the doctor who operated on him experimented by mixing white blood cells with the cancer cells and reintroducing them into the patient via monthly injections in order to strengthen his immune system. That treatment was certainly not free. The patient died a year and a half after the diagnosis was made, convinced that these interventions had prolonged his life. Nobody knows for sure, but it is fairly unlikely.

Adding to all this misery, we have totally spineless drug regulators who approve new cancer drugs without having a clue whether they are better or worse than those we already have.[9,18] This broken system has resulted in huge expenditures on cancer drugs with certain toxicity but uncertain benefit. Even when randomized trials have been performed and marginal advantages have been found, these trivial differences may disappear when the drugs are used in real life on patients suffering from co-morbidity.[18]

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