

Response to Frass et al.

Dear all,

thanks for your elaborate answer. Please find my comments below, for there is a major point of some impact where we strongly disagree.

General

First of all, yes, you are right, the Stupp paper contains patients that underwent surgery. My mistake, compiling my response I just checked this point in the abstract and there only chemotherapy and radiotherapy got mentioned. Sorry for that.

Then I take it, that for MRCC and MSARC the data given for 'time from diagnosis to homeopathic treatment' on one hand and 'reached survival' or 'expected survival' on the other do not refer to the same point in time as '0'. This makes analysis a little tricky as will be shown further down.

In fact, I must confess, there is some further incongruity in your data, that renders proper analysis difficult. See, in table 3 expected survival is given 'according to experts assessments and literature data', for instance PC-patients show either 8 or 22 months. In table 4 however expected median survival 'according to literature data' is given for the same patients as 6.6 months, smaller as any of the data of table 3. The P-Values in Table 4 seem to be based on still another set of figures defined as 'individually estimated survival times according to experts' assessments' without those data to be found anywhere in the paper. For my considerations here I stick to the statistical data because Gaertner et al. deploy them as comparison to their results in graph (Fig. 2) and table (Tab. 4).

Method of reanalysis

You indicate that my calculations were wrong without giving too much of a reason. Note: I do not challenge the source of your control data neither the competence of the scientists that evaluated them. Nor do I challenge standing and persuasion of the authors of the paper considered here. Rather I criticize the way Gaertner et al. deploy the data from literature as control. To the best of my ability I will give the reasons for why I think my calculations are correct, I would ask you to indicate where you think this reasoning to be faulty.

Gaertner et al. want to check if patients suffering from cancer might have fared better after adjunct

homeopathic treatment and use survival time after first diagnosis as a fixed endpoint to prove it. As control they use statistical data from literature. So the authors would have to prove that the patients after receiving homeopathic treatment survive their diagnosis for a longer piece of time than in control.

For the following let us stick to the data of patients suffering from pancreatic tumor (PC), because this seems to me the best example to illustrate my points. The cohort of patients with locoregional disease consists of more than 7000 people, so we may take the Kaplan-Meier-Plot (KMP) in Fig. 2 of Boyd's paper as survival curve for PC (and ignore for the time being, that Boyd's patients were much older, mean being 78.1 years instead of a median of 62 years for the PC-patients of Gaertner.).

Patients in the control group were included into the study of Boyd et al. from the day of their diagnoses onward. That means, deaths that occur from day 1 onward are included in the final data there, which finally leads to a median survival time of 6.6 months. Gaertner's PC-patients, however, in the median did join full six months after their diagnoses. Deaths that occur in the PC-patients from the Vienna oncology within these six months are not included in Gaertner's data, these patients simply did not show up in the homeopathic outpatient station and thus were not counted in the survival ratios.

Median survival time is defined as the time 50 % of sample population in the study survive. Statistical chance of survival would be the number of patients alive compared to the total number of patients present at the beginning of the observation.

Let us consider female patient #39 who started her homeopathic treatment 10 months after her diagnosis. This patient already had outlived the expected median survival time of 6.6 months when she joined - but was this a result of her homeopathic treatment? I hope we are of the same opinion here, that this is not the case.

Did she take a profit from her homeopathic treatment? This would burn down to the question if she did live longer with her homeopathic treatment than could be expected? Or better still, what was her risk of death at the time she died 19 months after her diagnosis? The KMP gives a mere 16.2 % chance of survival if the totality of the total cohort is considered.

But what looks like a good result was mostly achieved without homeopathy. Her chance to be alive long enough to show up to her first homeopathic appointment after 10 months was a poor 34.6 % as derived from the KMP. To consider, if she fared better with adjunctive homeopathy than the patients without can only be established by looking at what happened after the effect of this treatment set in. So we have to compare her performance to the patients without homeopathy that have achieved 10

months survival, too.

Median survival time for this subgroup having already survived 10 months could be found in the KMP at the point in time when half of these people will have died, that is only half of 34.6 % of the total number of patients. This gives a time of 18.3 months. The patient in question lived for 19 months which for rounding effects may roughly be the same. Consequence: even if we assume that homeopathy started to be effective immediately after her first session she just outlived medium survival time as was to be expected in her group by a short piece of time only.

But if we assume that homeopathy got effective later, after the second or third session only, this implies that she had lived to this point in time without homeopathy. That is to 12.5 or even 15 months, if, as we take it from Gaertner's paper, the time between sessions was eight to twelve weeks. And if she had lived for 15 months without homeopathic getting effective, then she would have been one of the 22.4 % of survivors out of the totality of patients - and her median expected survival would have exceeded 24 months, where the KPM we have available ends.

Let us consider the annual survival rates.

The KPM gives 28.6 % and 12 % chance of survival after one and two years respectively. But our patient is one of the last 34.6 % only that survived 10 months. The chance of her being alive after 12 months is much higher now once she managed 10 months already than it was at the beginning. 34.6 % from the original cohort of 7027 patients with the locoregional disease gives 2431 patients still alive after 10 months, out of which 2010 will survive 12 months - which amounts to 82.7 % of the patients alive two months before. The same way her chance for survival for two years is 34.7 % - all this under the assumption that her adjunct treatment was effective immediately after her first consultation.

So now please indicate, what and where is the fault in my reasoning and computations. Your statement about the competence of the authors, sorry, I cannot consider it very convincing. I would want to know the exact point where you think that I went wrong.

Recalculation of PC-data

In Table 1 I used the methodology outlined above to recalculate the data for all eight PC-patients included in the Gaertner-paper under the assumption that homeopathy was effective immediately after the first homeopathic session.

Pat. #	Start	S-ratio	1a	2a	E-med	Reached	Delta
37	4	64.2	44.5	18.7	10.8	15	+ 4.2
38	9	38.2	74.8	31.4	16.9	25	+ 8.1
39	10	34.6	82.7	34.7	18.3	19	+ 0.7
40	24	12	--	100	>> 24	26	< 0
41	1	87.6	32.6	13.6	7.7	1	- 6.7
42	?	?	?	?	?	36	> 0 ?
43	6	52	55.0	23.0	13.3	14	+ 0.7
44	2	77.8	36.7	15.4	9.2	20	+ 10.8

Table 1: Recalculation of PC-data

Explanation:

Start: time from diagnoses to first homeopathic session as in Gaertner's paper

S-ratio.: ratio of survival at time of first homeopathic session, KMP Fig. 2 of Boyd's paper

1a: Chance to survive one year after diagnosis for this patient, based on 28.6 % chance of survival after one year as given in KMP Fig. 2 of Boyd's paper

2a: Chance to survive two years after diagnosis for this patient, based on 12 % chance of survival after two years as given in KMP Fig. 2 of Boyd's paper

E-med: Medium expected survival time for this patient, KMP Fig. 2 of Boyd's paper

Reached: achieved survival time of this patient as given in Gaertner's paper

Delta: difference between reached and expected medium survival + patient lived longer

From this table we can take that median expected survival time is 13.3 months (patient #43) and median exceeding of survival time is a mere 0.7 months (patient #43).

Please note, these data would look much less favorable still if we assume the homeopathic treatment to be effective at a later point in time. Five months later, after another two homeopathic sessions as the inclusion criteria of Gaertner et al. imply, median expected survival time would be 18.3 months (mean of patient #37 and #43 as patient #40 cannot be evaluated), which the patients failed to reach in the median by 4.3 months.

Now we could discuss the impact of the much more advanced age of the patients (mean 78.1 years) in the control group compared to (median) 62 years in the homeopathy group. But, as I do not have any deeper medical knowledge, you may be in a far better position to do this.

Reviewing the data of Gaertner's PC-patients, I cannot but help to make some further comments.

Patients #38, 39 and 40, starting homeopathy 9, 10 and 24 months after their diagnoses are attributed with an expected survival time of 8, 8 and 22 months respectively. That is one or two months shorter than they had already lived. Sorry, Sir, but this is ridiculous. The patient applied to the homeopath and is rated that he was to be expected to have died some weeks earlier. (Okay, I see the improvement, no longer treating corpses but only people that should be corpses by now :-)) And even, if this prognoses were true, then it could not have been homeopathy that made these people survive it.

For the other indications, the approach is pretty much the same, if the data are available. That is some consistency between the time of the start of treatment, Kaplan-Meier-Plot and survival data. I guess, it is not my task to perform all this work.

Presentation of results

Yes, taking your words literally, the data presented in Tab. 4 and Fig 2 of the Gaertner paper are not wrong. Sticking to the PC-data again, the median survival given in literature is 6.6 months and the patients have had a median survival of 17.5 months. Both figures are as valid as they can get, no discussion about it. But the way you present them implies that the comparison of these two figures could have some meaning. In Fig. 2 they are presented as columns side by side. But this implication is wrong as long as you cannot point out where my approach is at fault. It is like I would set side by side the age of Emil von Behring when he was awarded his first Nobel-Prize (48) and your own (you know yourself) - both figures are absolutely correct and independent from each other, but together they may convey some implication. Unjustified of course, but still ...

You in person presented the data in Berlin. I cannot tell if you really said that homeopathy DOES help cancer patients or not. There are no - and I fear there will never be - minutes of meeting or conference-proceedings or any other printed reference to what was said and done there. But this was not a meeting of scientists but it was training session for homeopathic practitioners and it is what they will carry with them in their minds what makes it. There was a very impressing chart of blue and red columns indicating that people that received additive homeopathic treatment had up to three times longer survival time than those without. Do you really believe that anyone of your listeners - except the one skeptic in there of course - understands or even cares to find out what may have been the reason for this data in reality? They all got the impression what powerful a tool homeopathy is, and your presentation just adds the 'and it even can keep cancer at bay for some considerable amount of time' notion to this impression. Well, it can't be helped, but this is the implication that Fig. 2 and Tab. 4 of Gaertner's paper present - or at least offer themselves to anybody who cares to use them as a tool to convince his audience to this avail - as I have witnessed in Freiburg with a homeopathic practitioner

specialized in the treatment of cancer trying to convince his audience and future patients.

Okay, this writing is long enough now, so I do not want to argue your point about skeptics taking to (in their eyes) quackery if in need nor the reasoning why so many studies exist in pilot-stage only. The lack of funding might be the reason for this situation - but I am discussing the conclusions that the evidence of a pilot paper is not valid evidence, which seems rather not affected by what caused the deplorable situation, lack of funding, publication bias or whatever else.

Just one point occurs to me. I do not know how to assess your point, that some of the cancer patients may still be alive, have at least outlived the observation time. It comes to me as a surprise, that a paper dealing with survival times contains any sizable amount of patients that are still alive. That might even be alive full seven years after the observation period ended. In fact how is this to be understood? Complete remission after a metastatic situation? Comparison to full remissions from patients not treated with homeopathy? Quality of the rating as fatal? Well, we will see what you make of it.

And there may be other paragraphs that I did not address, but I thought it more important to enlarge on the proper deployment of the control-data at hand - not convinced, that I am wrong.

May 5, 2015

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Doctor of mechanical engineering, specialist in fluid dynamics and thermodynamics, R&D-manager, QM-manager, patent holder, homeopathy critic, hobby statistician, hobby physicist, hobby mathematician, skeptic - and by no means anything medical.