



The Health Report: 18 April 2005 - Chemotherapy

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Norman Swan: Good morning Fran and welcome to the program. This morning on the Health Report globalisation writ small. Why go down the road for your surgery when you can avoid the waiting lists, get it cut price in another country and have a holiday with the money you've saved? A personal story involving new knees coming up.

And, has cancer chemotherapy, the use of drugs to treat malignancies been oversold? That's the clear implication of a paper published by some Australian cancer specialists, two of whom, perhaps non-coincidentally are radiation oncologists – radiotherapists.

Anyway in this summary of evidence, the assertion is that chemo has only added about 2% to cancer survival. The lead author is Association Professor Graeme Morgan who's at Royal North Shore Hospital in Sydney. Is this, I wondered, an in house battle, the revenge of the radiotherapists?

Graeme Morgan: Well one could cynically say that but the reason I did it was that we were sick and tired of hearing about these new drugs and it wasn't really cementing into anything. And the reason for my doing the paper was to really show that there hasn't been any improvement in survival, or the improvement has been very, very modest despite all these new drugs and new combinations and bone marrow transplants.

Norman Swan: So what did you do in this study?

Graeme Morgan: Well what I did was that I took the major cancers and got their incidence from the Australian data sets and also got the breakdown of those cancers into their stages and also then compared that with the data from America.

Norman Swan: So you knew how many people were coming down with cancer per 100,000 of the population or whatever?

Graeme Morgan: Yes, we knew the exact number who were diagnosed in I think the years were 1998 and we then broke it down into the various stages and we looked at those stages what impact chemotherapy would have on a particular stage and a particular cancer.

Norman Swan: And where did you get that information from?

Graeme Morgan: We searched the literature – what we looked at was meta-analyses on a particular cancer.

Norman Swan: These were reviews of studies bringing together the available evidence on a certain form of chemotherapy for a certain cancer. So it wasn't just one study, they'd amalgamated several studies. And did you do it for all cancers?

Graeme Morgan: We did for 85% of the cancers, we didn't do it for leukaemias and the reason we didn't do it for leukaemia is that in acute leukaemia it's very difficult to differentiate between adults and children and the numbers are fairly small. And in chronic leukaemias, particularly in chronic lymphatic leukaemia which is basically a disease of the elderly, it's an indolent disease and the median survival is way over ten years. And we also excluded smaller cancers.

Norman Swan: So there might be a slight bias against chemotherapy because you've eliminated the leukaemias which can be quite chemo sensitive.

Graeme Morgan: Well yes, but the other reason that I eliminated those because they are mostly looked after by haematologists rather than medical oncologists. So this was really looking at the impact of medical oncology.

Norman Swan: And medical oncologists are basically physicians who specialise in cancer and use drugs.

Graeme Morgan: Yes, correct.

Norman Swan: Whereas you as a radiation oncologist do it through radiotherapy?

Graeme Morgan: Correct, yes.

Norman Swan: What were your findings?

Graeme Morgan: Well the findings were that in Australia that the five year survival due to chemotherapy was 2.1% of the total cancers.

Norman Swan: You mean the additional survival benefit?

Graeme Morgan: Yeah, from the chemotherapy. So in other words if there was no chemotherapy in Australia, the survival of all patients with cancer would drop from 62% to 60%.

Norman Swan: You say you allowed for a stage of diagnosis because the trend in Australia has been to earlier and earlier diagnosis which makes 5 year survival somewhat of an iffy figure because when you diagnose it earlier people may survive longer.

Graeme Morgan: No not necessarily. This is the way patients present. The other thing was that I have been a member of a number of committees looking into radiotherapy services in Australia and as you may not be aware, only 35% of newly diagnosed cancer patients in NSW receive radio therapy. And that's been flat for the last 10 years.

Norman Swan: And what should be the figure?

Graeme Morgan: The figure has always been around 50%.

Norman Swan: That's the percentage of people according to the best evidence who should be having it but aren't.

Graeme Morgan: Yeah.

Norman Swan: What would the figure be if you did a meta-analysis for radiotherapy? Is that that much better than chemo?

Graeme Morgan: There happened to be two papers that I've got and they are both fairly recent. One is here from Prince Alfred here in Sydney and the other's from Westmead also in Sydney. The one from Westmead shows that there is a survival gain with radiotherapy of 16.1%. But getting back to these reports is that one of the things that people always mention to us is well, people can have chemotherapy and the inference was that chemotherapy was an equal treatment. It's obviously not.

Norman Swan: One of the criticisms of this study is that you pooled all cancers and not all cancers are the same. Some have much better response rates to chemotherapy than others and if you divided it up you would actually get a very different picture. You've mixed it up, averaged, when you can't really average when for example if you've got Hodgkin's Lymphoma the cure rate can be up to 90% and chemo contributes significantly to that. Whereas solid tumours are pretty low, the tumours of the lining – why didn't you segregate by individual tumours?

Graeme Morgan: I did include cancers where chemotherapy doesn't have any impact because this was looking at the overall contribution of chemotherapy.

Norman Swan: If someone is listening to this, they've just been diagnosed with cancer and they've been told they need chemotherapy and radiotherapy. Do they walk away and say to the doctor well look I'll just have radiotherapy

now, don't bother with chemo?

Graeme Morgan: No, it's not saying that radiotherapy is more appropriate. What it's saying is that chemotherapy is oversold. I've asked people what they thought the percentage was and most of them have said

Norman Swan: You've done a straw poll?

Graeme Morgan: Yeah, a straw poll and most of them have said oh 5%, some have said 10% and 15% but then when you ask them about the individual cancer that's when the real differences emerge because most people when you ask them about breast cancer they say oh, 10% and 15% and of course it's 1.5%. And it's 1.5% because most women don't benefit from chemotherapy in breast cancer.

Norman Swan: In other words you've got to treat quite a lot of woman for one person to survive?

Graeme Morgan: Well that's right but you see there's no data in women over 70 for the effect of chemotherapy. Now that's about one third of the total population of breast cancer women.

Norman Swan: Why has it been oversold? Are you suggesting that medical oncologists in Australia are just sort of marketing shysters or what?

Graeme Morgan: Well, that's what happened when chemotherapy first came to this country. In the 1970s that I think the first chemotherapy

Norman Swan: But Australia's not alone in this, I mean chemotherapy's if you look at the journals, chemotherapy is a prominent treatment.

Graeme Morgan: Yes, that's right.

Norman Swan: So why has it come to that?

Graeme Morgan: Well I'm not really sure but it has been oversold. Well the benefit has been sold in the incorrect way because it's reduction of risk of relapse, it's not absolute survival benefit.

Norman Swan: What you're saying is that it isn't a proven survival for some women but a fair number of women have got to be treated to get that improvement in survival.

Graeme Morgan: Yes, that's right yeah. And the other thing as a radiation oncologist what I've seen is that there are no real guide lines for palliative chemotherapy and you often see patients referred to you who have had a number of drugs given when in fact none of them have done any good - in the pious hope that something's going to happen, that the survival is going to be increased by two months and I think that's part of the over-selling.

Norman Swan: How is the consumer to respond to this message?

Graeme Morgan: Well I think the consumer has to really evaluate the information they're given.

Norman Swan: Well let's just test you on this. I know you didn't do the paper on radiotherapy, but let's just see whether you're that much better. I mean what do you normally say to a woman who's got breast cancer and it's reasonably early, there's maybe only one lymph node involved, you've got a reasonable expectation of long term survival and she's been offered radiotherapy and chemo. OK, let's leave chemo to one side, what's the informed consent for radio therapy here?

Graeme Morgan: The informed consent with someone who's had the lumpectomy is that the radiotherapy will reduce the likelihood of recurrence from an absolute risk of 25% at ten years to less than 5% at ten years.

Norman Swan: You're saying that one out of four women will have a recurrence without radiotherapy and that will go down to one in twenty.

Graeme Morgan: Yes, that's right.

Norman Swan: And how many women have to have radiotherapy to get that benefit?

Graeme Morgan: Well 80% of them don't need it do they? 75% of them don't need it.

Norman Swan: But you don't know which 75%.

Graeme Morgan: That's right and that's the problem.

Norman Swan: Where do we go from here?

Graeme Morgan: The interest I've had in this paper from overseas has been in service provision and so that this calls for a re-evaluation of the amount of money that spend on chemotherapy and whether we're getting a bang for our dollar.

Norman Swan: Somebody I showed this paper to who's reasonably expert in meta-analysis reckons you've done this rather crudely and that if you were to have done this in a journal which is more used to meta-analysis they might have actually criticised your technique. And when she did a back of the envelope calculation just looking at it in a slightly different way she got 6% rather than 2%. How confident are you in those results?

Graeme Morgan: We think that this is a maximum because it includes all patients who were eligible to have the treatment.

Norman Swan: Dr Graeme Morgan who is in charge of Radiotherapy at Royal North Shore Hospital in Sydney. And you're listening to the Health Report here on ABC Radio National.

Norman Swan: Needless to say medical oncologists, the specialists who dole out chemo aren't taking this criticism lying down. Here's Associate Professor Michael Boyer, Head of Medical Oncology at the Sydney Cancer Centre at Royal Prince Alfred Hospital.

Michael Boyer: Well I'm a little puzzled by this paper. I mean on one level it purports to show that chemotherapy adds almost nothing to the cure of patients, on another level it's clear that chemotherapy results in if you just accept this all at face value, at least 1700 being alive at five years who wouldn't otherwise be.

Norman Swan: Based on the Australian figures?

Michael Boyer: Based on the Australian figures, and as a person that treats cancer patients and looks them in the eye every day I mean what we are trying to do as doctors is cure people and so to sort of come up with the idea that this is in some way not worthwhile is a very bizarre approach. But I think actually that you need to look just a little bit deeper than those superficial figures because within this paper the argument that is made that in some way because a modality only adds a little bit to cure....

Norman Swan: Modality being a form of treatment.

Michael Boyer: A form of treatment adds only a little to cure, and it really ignores the way in which the modern treatment is evolving. If you go back two or three decades we used to treat cancer with a single type of treatment, typically surgery. Then the concept that you could do better in terms of survival and control of symptoms by adding additional treatments was evolved and nowadays I think -

Norman Swan: - adjuvant treatment.

Michael Boyer: So called adjuvant treatment, and nowadays I think that most people would agree that the best outcomes for cancer is when you have a team of people each using their own particular treatments in the right patient and the right time to and up with the best results. So I don't see this as an argument of whether chemotherapy adds a little bit, or radiation adds a little bit, or surgery adds a lot. What this really should be about is what is the best treatment, what is the best sequence of treatments, what's the right time to use those treatments.

Norman Swan: So what you just see as a bit of old fashioned turf war between the radiotherapists and the medical

oncologists?

Michael Boyer: I'm a little reluctant to actually say that but to be honest I think that this reads as though a pre-conceived conclusion was arrived at and then the data gathered to sort of support that conclusion rather than saying OK what's the best way to treat these diseases, let's look critically at what each bit adds.

Norman Swan: But I mean a 2% additional survival does not sound impressive.

Michael Boyer: Well it doesn't sound impressive and it's also not correct. It's not correct for a number of reasons. That 2% figure is achieved by including a whole series of diseases in which chemotherapy would never be used. The paper itself actually states that yet they are included as part of the denominator if you like. So if you start taking those things out and saying well OK, how much does chemotherapy add in the people that you might actually use it, the numbers start creeping up. If you pull it altogether that number probably comes up to 5% or 6%, I guess what's important is that it doesn't go up to 50% or 60% but we know that and we know that these treatments are at the margin. I mean we are adding a little bit to survival and that has been the nature of all advances in cancer treatment that you actually add to marginal survival rather than these huge leaps with a couple of exceptions.

The other point about this is that some of the figures that they use I believe don't represent the most accurate and the most up to date figures that we have available.

Norman Swan: Such as?

Michael Boyer: Well such as in head and neck cancer the contribution to chemotherapy as it is currently used, the contribution of chemotherapy is bigger than the 4% that is claimed in the paper. With myeloma the reference that they use and the data they are basing this on in fact is not a paper that compares chemotherapy and no chemotherapy. It's a paper that compares two different sorts of chemotherapy and finds there's no difference between those two sorts of chemotherapy. That's a far cry from saying that chemotherapy versus nothing is ineffective.

Norman Swan: One of Graeme Morgan's points is that there's great hype about new chemotherapy treatments and therefore demand that they go on the market immediately, obviously from desperate families who think that this is going to be answer for their loved one who's dying of cancer. Therefore there's a waste of resources.

Michael Boyer: Well in this country there is a process that drugs go through firstly to be able to be marketed and secondly to get onto the PBS.

Norman Swan: The Pharmaceutical Benefits Scheme.

Michael Boyer: The Pharmaceutical Benefits Scheme, in other words to be subsidised by the public purse. Now this process applies equally to anti-cancer drugs as it does to blood pressure drugs as it does to cholesterol lowering agents. Included in that process to my knowledge is both an evaluation of the effectiveness of the drug and also the cost effectiveness compared to either other similar drugs or compared to nothing if there is no accepted drug. Now if what Dr. Morgan is saying is that that process is wrong or in some way flawed that might be the case and maybe it should be opened up to public debate. But that's not really what this paper is about and so I think the two things are slightly different.

Norman Swan: What about the issue of informed consent? I mean for example if you're a woman with early breast cancer you know you've had a lumpectomy, you've had merely one node, I mean my understanding is give or take is that you do a bit of radiotherapy and the chemotherapy for most women in that situation.

Michael Boyer: Or hormonal therapy depending on the exact nature of the tumour.

Norman Swan: The survival benefit is of the order of what 10% or something like that?

Michael Boyer: It varies and without going into the details one of the other problems of this paper is it uses absolute benefits rather than relative benefits. So the relative benefit is about a one third reduction in your risk of death. The absolute benefit of that

Norman Swan: But for you as an individual

Michael Boyer: Depends on how big your risk of death was to start with. In other words, if all the things you had before you get to the chemotherapy stage have basically cured you can't cure more than 100%. If your risk of dying is very high, in other words your chance of having been cured is only 20% then clearly the absolute benefit to you is larger. I should add that that varies for almost every permutation of tumour size, number of lymph glands and a whole lot of other features of the tumour.

Norman Swan: But on average how many women with early breast cancer are you having to treat with chemo for one life to be saved, or one person to survive five or ten years? And is that a kind of routine thing you would say to people?

Michael Boyer: We probably wouldn't put it quite in those terms but the answer to the question is probably in the order of 20 or 25. This is not a situation where every person you treat will clearly be cured. Equally it's not true to say that because you have to 20 or 25 people to benefit one, it's not true to say that nobody benefits. So it's somewhere in between. The terms in which you put it to a patient has been actually the subject of a good deal of research and research actually carried out in this department looking at different ways of expressing it. And you can express this as if we treated a 100 people like you, ten of them would benefit from treatment or five of them or whatever the number is. You can express it as at 5 years the number that would be alive with treatment is x percent, and with treatment it is x plus y percent. You can express it as a reduction in your risk of dying of the disease. Typically I think patients prefer the if we treated 100 people just like you type scenario but having said that there is a good deal of variability and for different people they like a different example of it.

Norman Swan: What about the poor second cousin kind of thing that seems to pervade radiotherapy, they feel that they've been boxed into a corner with the public thinking they are just for palliation, an end of the road treatment?

Michael Boyer: Certainly in our cancer centre here we, the medical oncologists don't regard radiation oncology in that way. I mean it's an absolutely integral part and one of the major parts in fact of treating patients whether that be with the intention of curing a patient, or with the intention of palliating or improving symptoms. As I said at the outset you can't really separate all this out, it's not a situation where you either have chemotherapy or you have radiation therapy. It's a situation where there are good ways of treating these diseases that often encompass several different types of treatment.

Norman Swan: And a corollary of that is do you believe that chemotherapy has been over-hyped which is really probably one of the drivers of this paper?

Michael Boyer: Again hype is a difficult word.

Norman Swan: You may have a better public relations company.

Michael Boyer: Well I may not but certainly the pharmaceutical industry has no shortage of public relations people and I think one has to be realistic. The pharmaceutical industry has a vested interest obviously in selling drugs whether they be anti cancer drugs or any other kind of drugs and one way is to make the target audience aware of their existence. The other issue with this paper is that by lumping all the diseases together I think it obscures some of the detail. The fact is that from a patient's perspective they are not really interested in how much chemotherapy contributes to the cure of all patients, what they are interested in is how much it will contribute to their particular disease and their stage of their disease. And that number ranges from zero in some cases up to almost 100% in other cases. So I don't think this paper helps from a patient's perspective. Similarly from a public funding, or public policy point of view, lumping everything together is not a terribly helpful way, at least in Australia where most drugs that are now approved and reimbursed are really approved and reimbursed for very specific indications. So there are lung cancer drugs that can only be prescribed to patients that have a particular gene mutation. There are anti-cancer drugs for breast cancer that can only be prescribed where other drugs have failed. And that reflects the way those drugs were tested in clinical trials and it really narrows the drugs down to be used in situations in which they are most likely to be effective. And this approach in this paper of lumping everything together really masks that fact.

Norman Swan: And just finally, moving away from this debate altogether, critics in general of the cancer treatment community say look, overall it's been a disappointment, that things are a bit better than they used to be but there are

isolated islands and for all the money we're spending on cancer research, we haven't really cracked it yet?

Michael Boyer: I mean there is some truth in that criticism although I think sort of behind that truth is the stark fact that if you develop cancer, any kind of cancer in Australia today your chances of being cured are in excess of 60% and that certainly was not the case two decades ago. Now why is that? Well some of it is because we're better at picking disease up earlier. Some of it is because we have better ways of ensuring that people get operations that they need and don't have bad problems during or after an operation. Some of it is because we use chemotherapy, some of it is because we use radiation therapy. On the other hand I guess the expectation of the community is not that 60% of people should be cured but that 100% of people should be cured and so I sense why there's a feeling there's a disappointment.

However, as each year goes the by the number creeps up and it is the nature of most modern medicine that we don't have the sort of breakthrough that journalists and the media like to talk about. What we have are incremental gains and when you add up 10 years of incremental gain suddenly you find that your survival has gone from 50% to 60%.

Norman Swan: Michael Boyer who's head of Medical Oncology and the Sydney Cancer Centre.

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Guests on this program:

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