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What oncologists tell patients about survival benefits of palliative chemotherapy and implications for informed consent: qualitative study

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EDITORIAL by Munday and Maher

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ABSTRACT

Objective To examine how much oncologists tell patients about the survival benefit of palliative chemotherapy during consultations at which decisions about treatment are made.

Design Qualitative study in which consultations were observed and digitally recorded.

Setting Teaching hospital and district general hospital in south west England.

Participants 37 patients with advanced non-small cell lung cancer (n=12), pancreatic cancer (n=13), and colorectal cancer (n=12); and nine oncologists, including four consultants and five registrars.

Main outcome measures All recordings were transcribed completely, anonymised, and electronically coded with ATLAS.ti. Constant comparison was used to identify themes and patterns. The framework method of data management, in which data were charted, was used to aid transparency of interpretation.

Results During the consultations, information given to patients about survival benefit included numerical data ("about four weeks"), an idea of timescales ("a few months extra"), vague references ("buy you some time"), or no mention at all. In most consultations (26/37) discussion of survival benefit was vague or non-existent.

Conclusions Most patients were not given clear information about the survival gain of palliative chemotherapy. To aid decision making and informed consent, we recommend that oncologists sensitively describe the benefits and limitations of this treatment, including survival gain.

INTRODUCTION

Every year in the United Kingdom many thousands of patients are told they have incurable cancer and are offered palliative chemotherapy. Because of the considerable toxicity and the modest survival benefits, decisions about treatment can be extremely difficult. Many patients want more information about their disease and treatment options,[1 2] and this is important if they are to exercise informed consent. For patients with advanced cancer, however, there is wide variation in the amount of information given, and decision making aids are scarce.[3]

If survival benefit of palliative chemotherapy is not discussed when treatment decisions are being made, there can be a considerable gap between patients' hopes and what can usually be achieved. At the advanced stages of cancer, survival gain from palliative chemotherapy tends to be months rather than years. Statistics relating to survival benefit can be contested, prompting concerns among clinicians about how patients can make informed decisions if experts do not agree among themselves.[4] Furthermore, there are concerns that the "intrusiveness of unfavourable numbers" can undermine healthcare relationships and destroy hope.[5]

We focused on qualitative data from oncology consultations during a study of patients' experiences of treatments (ASPECTS) and examined the extent to which survival gain was discussed when patients were offered palliative chemotherapy.

METHODS

Study design and setting

The ASPECTS study used qualitative research methods to describe patients' experiences of palliative chemotherapy and to explore how the decision making process might be improved in the light of those experiences (see bmj.com for full details). Three common cancers were chosen: colorectal, non-small cell lung, and pancreatic cancer.

Recruitment

Clinical members of the research team identified patients according to cancer site. Patients had locally advanced or metastatic disease, had been given a diagnosis, and had been offered an appointment to see an oncologist. They were informed about the study and asked if they would be willing to participate. Those who expressed an interest were given an information leaflet and contacted by the qualitative researcher. At a subsequent meeting, the researcher explained the study again and the patient signed the consent form. At each stage it was made clear to patients that their medical care would be unaffected whether or not they took part.

Forty five patients with advanced cancer were recruited to the main study, 15 with each type of cancer (see bmj.com). We provided an information leaflet, letter of invitation, and consent form for 33 recruited partners and carers.

Process

The consultations were digitally recorded, and we undertook non-participant observation to capture non-verbal communication. The researcher did not take notes during consultations as this was likely to be distracting for participants and might have prompted concerns about what was being noted and why but he/she completed a reflective diary as soon as possible after the consultation. All the recordings were fully transcribed and anonymised to protect confidentiality, and field notes were inserted in the text of transcripts to highlight contextual issues where appropriate.

Analysis

During analysis we used the method of constant comparison derived from grounded theory.[67] Full details of the process are on bmj.com. During the process, variations in the discussion of survival gain emerged which we categorised as "numerical," "idea of timescales," "vague," and "not discussed." Further reading and analysis, identified triggers and barriers to discussion of survival gain.

Participants

We observed and digitally recorded 37 oncology consultations. The nine oncologists who saw the patients were mixed in terms of age, experience, and sex; and included four consultants and five registrars.

RESULTS

Purpose of treatment

Towards the beginning of the consultation all the patients were informed that their cancer could not be cured. The oncologists explained the main purpose of chemotherapy either in terms of shrinking, slowing down, controlling, or stabilising the tumour; improving symptoms such as pain and weight loss; and/or improving quality of life—for example, enabling patients to feel "as well as possible for as long as possible."

Patients who were offered chemotherapy were given the names of relevant drugs; information about the treatment regimen; and details of common side effects. Those who accepted chemotherapy signed consent forms to enable the oncologists to order drug treatment. Patients were told that this did not commit them to having the treatment if they subsequently decided against it, and that the nurses responsible for administering chemotherapy would explain the treatment again and answer further questions. None of the patients who consented at the initial oncology consultation subsequently refused treatment.

Survival benefit

Although there was consistency in informing patients that a cure was not being sought, the amount of information given about survival benefit varied considerably (table). This ranged from giving numerical data, to vague references, to not being mentioned at all. During the recorded consultations, only six of the 37 patients were given numerical data about the survival benefit of treatment. These included three of the 23 patients who accepted palliative chemotherapy. In most consultations (26/37) the discussion of survival benefit was either vague or non-existent.

We found no patterns in relation to the sex or age of the patient, hospital site, cancer site, treatment decision, or the actual survival of the patient. Individual oncologists did not adopt a consistent approach with all patients in relation to the amount of information given about survival benefit. Registrars seemed less likely to discuss the issue, but the numbers are too small to draw any firm conclusions.

Triggers and barriers

We identified some triggers and barriers to discussion of survival benefit.

Triggers

A few patients, or their relatives, specifically asked for details. For example:

> Son: And what's the best you would expect with that?
> Oncologist 104: It may improve it by two to three months.
> Patient 335: Mm.
> Oncologist 104: [to wife who was distressed] Is that what you thought?
> Wife: No, I'm afraid I didn't give it much thought, not in actual months.
> Son: I'm sorry I had to ask that mum, because it's an

Treatment decisions and discussion of survival benefit in oncology consultations

Information about survival benefit	Total	Treatment decision			
		Chemotherapy offered and accepted	Chemotherapy offered and refused	Chemotherapy not offered	Further appointment
Numerical data	6	3	2	1	0
Idea of timescales	5	5	0	0	0
Vague	18	14	1	2	1
Not discussed	8	1	2	3	2
Total	37	23	5	6	3

important part of making the decision isn't it?
Wife: Yes, of course. I know that, yes.
Son: If you're going to go through lots of pain and problems.
Patient 335: Oh yes. Em, I em, I would have asked it anyway if my son hadn't.

Chemotherapy was offered and accepted; the patient died two months later.

Sometimes the oncologist volunteered the information to give a realistic expectation of what the treatment could achieve:

Oncologist 101: Now if somebody has chemotherapy we're, we're not unfortunately talking about people living years longer, we're talking about months on the whole. Some lucky people may live some years longer, but that's not the average expectation.

Chemotherapy was offered and accepted; patient 309 died five months later.

Discussion of survival benefit seemed to be helpful for some patients who decided that they did not want chemotherapy and enabled them to justify their decision, especially to family members who wanted them to "fight" the disease:

Patient 315: Off the record, do you think there's any benefit for me to have treatment?
Oncologist 103: The problem is I only know that after the event.
Patient 315: After the event, yes.
Oncologist 103: My problem is I see it both sides.
Patient 315: Yeah.
Oncologist 103: I've got some patients who've done very well with these treatments and have lived for much longer than frankly I would have expected.
Patient 315: Hmm mm.
Oncologist 103: I have other patients who either have a lot of side effects with the treatment and no benefit, or clearly go through it all and shortly after it's playing up and what would be really helpful is if I could tell you which of those two folk there you were going to be and the whole problem in this situation is that I can't.
Patient 315: My worse nightmare would probably be to have some treatment and end up back in hospital with another ailment.

Later in the consultation:

Patient's wife: You're going to fight it. You said you would.
Patient 315: Yeah but it doesn't mean to say it's only going to be nine months I mean it might be 12, it might be 15, it might be.
Oncologist 103: Averages are dangerous statistics.
Patient 315: Yeah, you never know. I said to you before I'd sooner have a short amount of time with a bit of bonus to it, a bit of benefit. If I had to go into hospital for five weeks every day and, and not benefit from it and even catch something worse and end up back in hospital for the rest of me life basically, then I'd have to top myself.

Chemotherapy was offered and refused; the patient died three months later.

When clinicians judged that patients were too ill to tolerate the treatment they could point to the statistics on low survival benefit to show that they were not withholding valuable treatment:

Oncologist 102: And even if it does work, it can prolong life, but only by about four weeks. So it's not the answer, we know that, but it can be a dangerous thing, and shouldn't just be thrown about.

Chemotherapy was not prescribed; patient died two weeks later.

Barriers

Some of these apparent triggers could also be barriers to the discussion of survival benefit. If patients made it clear from the outset that they did not want chemotherapy, then the treatment might not be discussed in any detail:

Patient 327: Chemotherapy that is completely out. I don't want that at all.
Oncologist 104: OK, right.
Patient 327: If I'm offered the opportunity of radio . . .
Oncologist 104: Yeah.
Patient 327: Em, and that would ease the pain . . .
Oncologist 104: Yeah.
Patient 327: I'm quite happy to have that.

Patient refused chemotherapy and received radiotherapy; died three months later.

If oncologists judged patients to be too unwell for chemotherapy, the conversation might be steered away from the survival benefit of chemotherapy towards recommending other medication:

Oncologist 103: I don't think your general condition now would tolerate chemotherapy quite honestly.

Triggers and barriers to informed consent in oncology consultations

Triggers: survival benefit discussed

Patient
- Asking direct question*
- Justifying refusal

Oncologist
- Responding (numerical data/idea of timescales)
- Justifying no active treatment
- Volunteering information (realistic expectations)

Barriers: survival benefit not discussed or information is vague

Patient
- Is patient assuming lengthy survival?
- Not wanting treatment
- Blocking*

Oncologist
- Focusing on other benefits (symptom relief)
- Is patient aware of potential benefits?
- Responsibility to (sensitively) inform

*Or by partner/carer, with patient's agreement.

Patient 334: Well no, I thought it might buy me some time, but I mean . . .
Oncologist 103: And I think the problem is that because you've become so weak with it and lost so much weight. . .
Patient 334: And you don't want to eat.
Oncologist 103: Absolutely, and that's one of the commonest symptoms that the get-up-and-go gets up and goes, and one just doesn't want to.
Patient 334: Yes, and my get-up-and-go's gone.
Oncologist 103: Have you tried steroids or anything like that?
Patient 334: No, I, no.
Oncologist 103: Right. Well I think that will be a worthwhile thing to do, is for you to have some steroids and something to stop them upsetting your stomach.

Steroids were prescribed; the patient died six weeks later.

Emphasising the other benefits of chemotherapy could also divert the conversation away from survival benefit. This patient asked about life expectancy and survival benefit, saying he was quite happy to be given figures:

Oncologist 112: OK. So we, in some people, in some cases it can actually really help with their cancers but in a lot of patients it can help with the symptoms.
Wife: Yes.
Oncologist 112: And this is why we give it.
Patient 339: Right

The oncologist did not give figures for life expectancy or survival benefit. Chemotherapy was offered and accepted; the patient was alive six months after consultation.

Patients and their partners sometimes blocked the discussion:

Oncologist 103: Do you want me to tell you what the statistics are?
Husband: Not particularly, do you?
Patient 303: No.
Husband: No.
Oncologist 103: The problem with statistics is they don't tell you which, which side, and it comes down to, Is it worth it, going through this treatment? Is there something that's worthwhile going through all this treatment, that I want to live longer or. . .
Husband: I think we have to make that decision as well. I don't think we want to go into the statistics.
Patient 303: Yeah.

Chemotherapy was offered and accepted; the patient was alive 18 months after consultation.

DISCUSSION

For patients with advanced cancer to make informed decisions about palliative chemotherapy, oncologists need to describe the benefits and limitations of this treatment, including survival benefit. The oncology consultations studied here were the first consultations with an oncologist after patients had been told their cancer was advanced and a cure was not being sought; at which patients expected to receive information from the oncologist about further treatment options; and when most patients consented to receive palliative chemotherapy. We examined whether the information provided at this stage was "enough information to make a decision" and whether it included "the benefits they [the oncologists] hope will result" and "the chances of getting such benefits," according to the recommendations from the Department of Health guidance.[8]

Impact on decision making

Study of the triggers and barriers to a discussion of survival benefit during the consultations showed clear implications for informed consent. In some oncology consultations the decision making process included giving patients information about the limited survival benefit of treatment (box).

We identified barriers to the discussion of survival benefit that might undermine informed consent. If the oncologist focuses on the benefits of palliative chemotherapy in terms of control of symptoms and quality of life, but omits information about survival benefit, the patient might assume much greater potential to prolong life than is likely to be the case. Conversely, when patients decline the offer of palliative chemotherapy without a discussion of the potential benefits, including survival gain, they might be basing their decision on incomplete or inaccurate information. Perhaps most difficult of all is when a patient, or their partner or carer, makes it clear that they do not want to receive any more bad news. Talking about life expectancy can seem cruel at this point.

Do patients want to know?

Giving comprehensible and appropriate information about survival benefit is extremely difficult, and reluctance to inform patients of the limited survival gain of palliative chemotherapy might be motivated by a desire to "protect" patients from bad news. During the ASPECTS study, although patients and their partners sometimes indicated that they did not want to discuss prognosis at this stage, there was no clear evidence that they did not want information about survival gain, and so it cannot be argued that clinicians were simply responding to patients' preferences.

Strengths and limitations

We did not have a large number of participants. Yet the range of patients and oncologists involved, and the inclusion of three cancer sites and two hospitals, suggest that the findings could be transferable to other settings. A further strength is the examination of data from consultations as they occurred, rather than

WHAT IS ALREADY KNOWN ON THIS TOPIC

Survival benefit is often a primary outcome measure in clinical research in palliative chemotherapy and is an important concern to patients

The survival benefits of palliative chemotherapy are modest

Current UK health policy places emphasis on the importance of informed consent

WHAT THIS STUDY ADDS

Most patients are not given clear information about the survival benefit of palliative chemotherapy, with consequent implications for decision making and informed consent

Training for oncologists should include guidance on how to inform patients about the survival benefit of palliative chemotherapy

Consideration should be given as to whether, and how, NICE should include this important information in its guidance leaflets for the public

retrospective interviews with patients or their oncologists.

The sample of patients comprised a higher proportion of men than might be expected but was in line with the wider ASPECTS sample, suggesting that the recruitment process was not biased. There was no evidence that sex affected the discussion of survival benefit.

The presence of a researcher who observed and recorded the consultations might have changed the content of discussions, although it might have encouraged oncologists to be more thorough and to provide patients with more, rather than less, information.

Implications for practice

Oncologists reinforced the diagnosis of advanced cancer and explained that, in prescribing chemotherapy at this stage, a cure was not being sought. But current guidance also places emphasis on informed decision making. Oncologists attempt to meet this obligation by giving details of the potential side effects of chemotherapy with much less time given to discussing the possible benefits of treatment. Nevertheless, most patients accepted treatment, in line with the argument that patients will risk negative impacts on quality of life for survival gain.[9] It is particularly important that patients with advanced cancer are made aware of the limitations of that survival gain during the decision making process. While it seems unlikely that this will change the treatment decision for many patients, it will contribute to narrowing the gap between what oncologists can currently offer and what some patients hope for.

Patients' understanding of survival gain is also pertinent to the debate about access to drugs through the National Health Service. While data about survival gain are included in National Institute for Health and Clinical Excellence (NICE) guidance for healthcare professionals, they are omitted from the "information for the public."[10-14] Though the intent might be to reduce distress, this can reinforce the gap between patients' hopes and what can usually be achieved. It might also heighten concerns that valuable lifesaving treatments are being withheld for purely economic reasons. We recommend, therefore, that oncologists receive support and training in how to communicate relevant information about survival benefit to their patients.

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Role of blood pressure in development of early retinopathy in adolescents with type 1 diabetes: prospective cohort study

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ABSTRACT

Objective To examine the relation between blood pressure and the development of early retinopathy in adolescents with childhood onset type 1 diabetes.

Design Prospective cohort study.

Setting Diabetes Complications Assessment Service at the Children's Hospital at Westmead, Sydney, Australia.

Participants 1869 patients with type 1 diabetes (54% female) screened for retinopathy with baseline median age 13.4 (interquartile range 12.0-15.2) years, duration 4.9 (3.1-7.0) years, and albumin excretion rate of 4.4 (3.1-6.8) µg/min plus a subgroup of 1093 patients retinopathy-free at baseline and followed for a median 4.1 (2.4-6.6) years.

Main outcome measures Early background retinopathy; blood pressure.

Results Overall, retinopathy developed in 673 (36%) participants at any time point. In the retinopathy-free group, higher systolic blood pressure (odds ratio 1.01, 95% confidence interval 1.003 to 1.02) and diastolic blood pressure (1.01, 1.002 to 1.03) were predictors of retinopathy, after adjustment for albumin excretion rate (1.27, 1.13 to 1.42), haemoglobin A_{1c} (1.08, 1.02 to 1.15), duration of diabetes (1.16, 1.13 to 1.19), age (1.13, 1.08 to 1.17), and height (0.98, 0.97 to 0.99). In a subgroup of 1025 patients with albumin excretion rate below 7.5 µg/min, the cumulative risk of retinopathy at 10 years' duration of diabetes was higher for those with systolic blood pressure on or above the 90th centile compared with those below the 90th centile (58% *v* 35%, P=0.03). The risk was also higher for patients with diastolic blood pressure on or above the 90th centile compared with those below the 90th centile (57% *v* 35%, P=0.005).

Conclusions Both systolic and diastolic blood pressure are predictors of retinopathy and increase the probability of early retinopathy independently of incipient nephropathy in young patients with type 1 diabetes.

INTRODUCTION

Retinopathy is common in young patients with diabetes: in a population based study from Australia, 24% of children and adolescents with type 1 diabetes had early background retinopathy after only six years' duration of diabetes,[1] and retinopathy was present in 27% of Swedish patients after 13 years' duration.[2] Adolescents with diabetes are an ideal group in which to study the effect of blood pressure on the very early development of retinopathy, because of the absence of coexistent disease, smoking, and treatment with other drugs in most patients. We hypothesised that blood pressure as a continuous variable is a predictor of early development of retinopathy and that this relation is present even in the absence of incipient nephropathy.

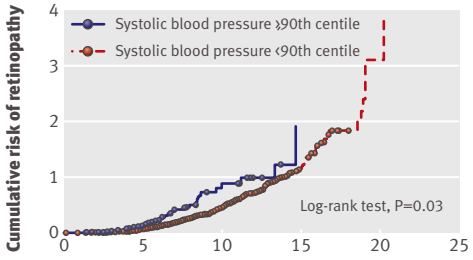
METHODS

This study included 1869 adolescents aged under 15 (54% female) with a clinical diagnosis of type 1 diabetes who had retinal screening at the Diabetes Complications Assessment Service at the Children's Hospital at Westmead (Sydney, New South Wales, Australia) between 1989 and 2007.

Screening for complications of diabetes

We screened adolescents for complications of diabetes according to established guidelines.[3] We assessed retinopathy by fundal photography after dilatation of the pupils with cyclopentolate 1% and phenylephrine 2.5%. One experienced paediatric ophthalmologist (SH) graded the photographs.[4] We defined retinopathy as the presence of at least one microaneurysm or one haemorrhage (grade 21).

We determined albumin excretion rate from three consecutive timed overnight urine specimens. We defined microalbuminuria as albumin excretion rate ≥20 and <200 µg/min in two out of three samples. We



No remaining:						
›90th centile	94	58	12	1	0	0
‹90th centile	931	648	189	33	1	0

Fig 1 | Cumulative probability of first event of retinopathy for each year since onset of diabetes in patients with albumin excretion rate always below 7.5 µg/min (n=1025). Patients were grouped according to systolic blood pressure below or on/above 90th centile

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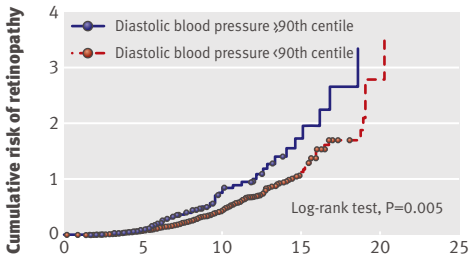

No remaining:						
≥90th centile	132	94	21	4	0	0
<90th centile	893	615	181	30	1	0

Fig 2 | Cumulative probability of first event of retinopathy for each year since onset of diabetes in patients with albumin excretion rate always below 7.5 µg/min (n=1025). Patients were grouped according to diastolic blood pressure below or on/above 90th centile

defined normoalbuminuria as mean albumin excretion rate <7.5 µg/min in all urine samples.

At each complications assessment, we assessed glycaemic control by measuring glycated haemoglobin colorimetrically[5] before February 1994 and subsequently by haemoglobin A_{1c} with high performance liquid chromatography. We converted glycated haemoglobin values to haemoglobin A_{1c} (see bmj.com).

Blood pressure and other measurements

We used auscultation with a conventional mercury sphygmomanometer device and appropriate cuff sizes to measure systolic and diastolic blood pressure twice in the seated position after five minutes' rest (see bmj.com).

Statistical analysis

We present descriptive statistics as mean and standard deviation for normally distributed data or median and interquartile range when distributions were skewed. We used the χ^2 test to compare groups for categorical variables. We evaluated differences between independent samples by using Student's *t* test if variables were normally distributed or Mann-Whitney U test for skewed data.

We used Cox proportional hazards regression to examine predictors of the first retinopathy event in all participants (n=1869), with duration of diabetes as the time variable. To exclude the effect of early elevation of albumin excretion on the development of retinopathy, we used Kaplan-Meier survival curves to estimate the probability of developing the first retinopathy event in participants who had albumin excretion rate <7.5 µg/min (n=1025). We used high-normal cut off for systolic and diastolic blood pressure, defined as blood pressure on or above the 90th centile,[6] as factors and used the log-rank test to compare survival times.

We did longitudinal analysis in participants who were retinopathy-free at baseline and followed prospectively, by using generalised estimating equations so that correlations between repeated measures for a given patient could be taken into account.[7] In this model, we examined different covariates as predictors of the outcome variable, presence or absence of retinopathy at any time (see bmj.com).

Table 1 | Results of Cox proportional hazards regression for development of first event of retinopathy, with duration of diabetes as time variable, in young patients with type 1 diabetes mellitus (n=1869)

Covariates	Hazard ratio (95% CI)	P value
Systolic blood pressure (mm Hg)	1.02 (1.01 to 1.03)	<0.001
Female sex	1.29 (1.10 to 1.51)	0.002
Age (years)	0.83 (0.81 to 0.85)	<0.001
Haemoglobin A_{1c}	1.06 (1.01 to 1.12)	0.02
Body mass index >95th centile	1.34 (1.01 to 1.78)	0.04

RESULTS

Clinical characteristics

For the whole group (n=1869, 54% female), median age was 13.4 years (interquartile range 12.0-15.2), duration of diabetes was 4.9 (3.1-7.0) years, albumin excretion rate was 4.4 (3.1-6.8) µg/min, and haemoglobin A_{1c} was 8.4% (7.7-9.3%) at first assessment. Overall, 673 (36%) participants developed retinopathy at any time during the follow-up. We compared participants who never developed retinopathy with those who developed retinopathy at any stage during the follow-up and found no difference in baseline age, albumin excretion rate, or prevalence of microalbuminuria. However, systolic blood pressure, diastolic blood pressure, duration of diabetes, and haemoglobin A_{1c} were higher in patients who developed retinopathy.

In all, 1231 (66%) participants had more than one visit, with median follow-up of 4.1 (3.1-7.2) years and a median number of visits of 3 (2-5). The incidence of retinopathy was 14.5 per 100 person years of follow-up. In this group, 138 participants had retinopathy at baseline, of whom 50 (36%) regressed, 56 (41%) were unchanged, and 32 (23%) progressed during follow-up.

Cox proportional hazard regression

In Cox proportional hazard regression (n=1869), systolic blood pressure, female sex, haemoglobin A_{1c}, age, and body mass index above the 95th centile were significantly associated with a higher cumulative risk of retinopathy (table 1). The quadratic term for blood pressure was not significant, suggesting a linear effect.

Among participants with albumin excretion rate <7.5 µg/min (n=1025), the cumulative risk of retinopathy at 10 years' duration of diabetes was higher for those with systolic blood pressure on or above the 90th centile than for those below the 90th centile (58% *v* 35%, P=0.03) (fig 1). Similarly, diastolic blood pressure on or above the 90th centile conferred a higher risk compared with those below the 90th centile (57% *v* 35%, p=0.005) (fig 2).

Table 2 | Factors associated with occurrence of retinopathy in adolescents with type 1 diabetes mellitus who were retinopathy-free at baseline: longitudinal analysis using generalised estimating equations (n=1093)

Covariates	Odds ratio (95% CI)	P value
Model 1*		
Systolic blood pressure (mm Hg)	1.01 (1.003 to 1.02)	0.008
Diastolic blood pressure (mm Hg)	1.01 (1.002 to 1.03)	0.02
Age (years)	1.13 (1.08 to 1.17)	<0.001
Duration (years)	1.16 (1.13 to 1.19)	<0.001
Haemoglobin A_{1c}	1.08 (1.02 to 1.15)	0.01
Log albumin excretion rate	1.27 (1.13 to 1.42)	<0.001
Height (cm)	0.98 (0.97 to 0.99)	<0.001
Model 2†		
Diastolic blood pressure (mm Hg)	1.02 (1.01 to 1.04)	0.004
Age (years)	1.12 (1.06 to 1.18)	<0.001
Duration (years)	1.14 (1.09 to 1.18)	<0.001
Haemoglobin A_{1c}	1.14 (1.03 to 1.26)	0.009

*Included systolic and diastolic blood pressure measurements from patients who were retinopathy-free at baseline (n=1093) along with other covariates.
†Included systolic and diastolic blood pressure measurements from patients who were retinopathy-free at baseline and had albumin excretion rate consistently below 7.5 µg/min throughout follow-up (n=594).

Longitudinal analysis

In participants with more than one visit who were retinopathy-free at baseline (n=1093), retinopathy was significantly associated with higher systolic and diastolic blood pressure. Age, duration of diabetes, haemoglobin A_{1c}, height, and log albumin excretion rate were also significant predictors of retinopathy (model 1, table 2). Among 594 participants with more than one visit who were retinopathy-free at baseline and had albumin excretion rate consistently <7.5 µg/min, diastolic blood pressure, in addition to age, duration of diabetes, and haemoglobin A_{1c}, predicted retinopathy (model 2, table 2). In both groups, quadratic terms for systolic and diastolic blood pressure were not significant, suggesting a linear rather than a threshold effect of blood pressure as a predictor for retinopathy.

DISCUSSION

Our study showed that higher blood pressure contributes to the early development of retinopathy in adolescents with type 1 diabetes, independent of other known risk factors. Both systolic and diastolic blood pressure contributed to risk of retinopathy. Not only was the effect independent of glycaemic control but it was independent of early elevation of albumin excretion. This supports the hypothesis that blood pressure acts independently, rather than by association with nephropathy, in the development of retinopathy. In addition, the results suggest that the effect of blood pressure as a predictor for retinopathy is linear rather than a threshold effect (see bmj.com).

We found that higher diastolic blood pressure was still an independent predictor of retinopathy in adolescents with albumin excretion rate consistently below 7.5 µg/min, an earlier marker of incipient renal disease. Conversely, albumin excretion rate also predicted development of retinopathy in the entire cohort. Although antihypertensive agents prevent the progression from normoalbuminuria to microalbuminuria in patients with and without hypertension,[8] whether treatment of normotensive young patients with type 1 diabetes and normoalbuminuria will influence retinopathy risk is not known.

Hypertension has been implicated in the development of diabetic retinopathy, on the basis of data from observational studies. Interventional studies with angiotensin converting enzyme inhibitors have shown a reduction in progression of retinopathy in adults with type 1 diabetes,[9] in the absence of hypertension, and in type 2 diabetes.[10 11] Although this suggests that lowering of high blood pressure influences the risk of retinopathy, these drugs may have benefits on the eye independent of their antihypertensive properties, possibly by affecting local production of angiotensin converting enzyme by retinal vascular endothelial cells.[12]

Conclusions

This study shows that a continuous relation exists between blood pressure and risk of retinopathy. These findings highlight the importance of close blood pressure monitoring by all professionals involved in the management of adolescents with diabetes, regardless of urinary albumin excretion and glycaemic control, and indicate that lowering blood pressure, even in patients without hypertension or microalbuminuria, may improve retinal outcomes in diabetes. However, interventional trials are needed to test the risks and benefits of lowering blood pressure in children and adolescents with type 1 diabetes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

No longitudinal data exist on the effect of blood pressure on the development of retinopathy in children and adolescents with type 1 diabetes

In adults with diabetes, hypertension has emerged as a risk factor for diabetic retinopathy and its progression

WHAT THIS STUDY ADDS

Higher systolic and diastolic blood pressure contribute to the early development of diabetic retinopathy independent of glycaemic control, duration of diabetes, and albumin excretion

Blood pressure had a continuous effect rather than a threshold effect on risk of retinopathy, suggesting that lower blood pressure protects the eye in diabetes

This relation has potential implications for blood pressure lowering treatment for the prevention of diabetic retinopathy in adolescents with type 1 diabetes

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Do overweight children necessarily make overweight adults? Repeated cross sectional annual nationwide survey of Japanese girls and women over nearly six decades

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ABSTRACT

Objective To compare growth curves of body mass index from children to adolescents, and then to young adults, in Japanese girls and women in birth cohorts born from 1930 to 1999.

Design Retrospective repeated cross sectional annual nationwide surveys (national nutrition survey, Japan) carried out from 1948 to 2005.

Setting Japan.

Participants 76 635 females from 1 to 25 years of age.

Main outcome measure Body mass index.

Results Generally, body mass index decreased in preschool children (2-5 years), increased in children (6-12 years) and adolescents (13-18 years), and slightly decreased in young adults (19-25 years) in these Japanese females. However, the curves differed among birth cohorts. More recent cohorts were more overweight as children but thinner as young women. The increments in body mass index in early childhood were larger in more recent cohorts than in older cohorts. However, the increments in body mass index in adolescents were smaller and the decrease in body mass index in young adults started earlier, with lower peak values in more recent cohorts than in older cohorts. The decrements in body mass index in young adults were similar in all birth cohorts.

Conclusions An overweight birth cohort in childhood does not necessarily continue to be overweight in young adulthood. Not only secular trends in body mass index at fixed ages but also growth curves for wide age ranges by birth cohorts should be considered to study obesity and thinness. Growth curves by birth cohorts were produced by a repeated cross sectional annual survey over nearly six decades.

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INTRODUCTION

Several papers have reported on secular trends in childhood body mass index, compared body mass index values at fixed ages, and described secular trends in the prevalence of obesity and overweight, defined by body mass index.[1-3] Most of these studies have shown increasing body mass index and prevalence of obesity in children.

In Japan, as in most nations, the mean body mass index of girls aged 6-14 years increased between 1976 and 2000, and prevalence increased from 1.2% to 2.9% for obesity and from 10.1% to 17.2% for overweight and obesity (International Obesity Task Force definition[4]).[1 5] However, the mean body mass index of young women aged 15-29 has decreased.[6 7] These results indicate the possibility that a birth cohort that might have been more overweight in childhood became thinner as young adults. We provide the growth curves of body mass index by birth cohorts in Japanese girls and women aged 1-25 years to quantitatively assess differences in growth curves. We focused on females, because the trend of young Japanese women being thinner is striking compared with the opposite trend of most other nations as well as young Japanese men.[6]

METHODS

The national nutrition survey, Japan, has been done annually since 1948 with large random samples of the Japanese population.[8 9] The survey covers approximately 5000 households in 300 randomly selected census units. The data are regarded as representative of the Japanese population. Participants were gathered locally, and height and weight were measured. We used data from the 1948-2005 surveys for females aged 1-25 years who were born from 1930 to 1999. We grouped the birth cohorts by decade, giving seven cohort groups from the 1930s to the 1990s (see bmj.com).

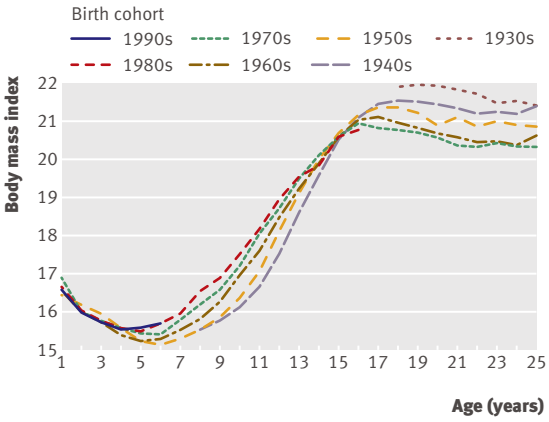

Fig 1 | Growth curves of body mass index by female birth cohorts (1930s to 1990s), from national nutrition survey, Japan, 1948-2005

We calculated the body mass index for each survey year as the mean weight (kg) divided by the square of the mean height (m). We calculated the annual change in body mass index by subtracting the previous year's body mass index from the current one, by birth cohorts. We fitted non-linear curves by cohort group to the annual change data by using cubic smoothing spline curves.

RESULTS

Figure 1 shows the growth curves of the mean body mass index in the seven birth cohort groups. The patterns of growth curves are similar; they decrease in preschool children (2-5 years), then increase in children (6-12 years) and adolescents (13-18 years), and slightly decrease in young adults (19-25 years). However, the mean value of body mass index was higher in more recent cohort groups during childhood (6-12 years) and early adolescence (13-14 years) than in older cohort groups. The growth curves intersect at middle adolescence (15-16 years), and the body mass index value was lower in more recent cohort groups during late adolescence (17-18 years) and young adults (19-25 years).

Figure 2 shows the annual change curves for body mass index. The increment in body mass index was larger in more recent cohort groups during early childhood (6-9 years) than in older cohorts. However, the annual change curves intersect at late childhood (10-12 years), and the increments in body mass index in adolescents (13-18 years) were smaller in more recent cohort groups than in older ones.

DISCUSSION

More recent Japanese female cohorts were relatively more overweight in childhood than older cohorts, but they grew to be relatively thin as young adults. Early obesity is considered to result in obesity in later life, as well as a high prevalence of obesity related disorders.[10] However, our result provides a counter-example at the population level; that is, an overweight birth cohort in childhood does not necessarily continue to be overweight in adulthood. This should not be taken as rejecting the possible relation between early obesity and obesity in later life at the individual level. To our knowledge, this is the first report to show the growth curves of body mass index from childhood to young adulthood by birth cohort.

In the national nutrition survey, Japan, in 2002, more than half of women aged 15-29 regarded themselves as being overweight or slightly overweight.[11] This percentage was higher than that in 1979, although the body mass index was lower. The major reason behind this self perception as being overweight was "comparison with other people."[11] The survey data showed that 64% of women aged 15-19 and 54% of those aged 20-29 were attempting to lose weight.[11] The practice of excessive dieting to become slim is seen among teenage girls in Japan.[12] The effects of behaviour to lose weight may appear earlier in annual changes and then be seen in the mean body mass index later. Because body mass index changes dynamically in childhood, secular trends should be interpreted carefully. Annual changes provide complementary information.

The weakness of a repeated cross sectional survey, compared with a longitudinal study, is that all inferences are described in terms of population averages, and the variability of growth curves among individuals and the effects of covariates cannot be inferred. Furthermore, when the curve is non-linear, individual growth curves can differ greatly from that of the population average. The shapes of the growth curve for height and weight obtained by following a single person longitudinally and that obtained by population average are well known to be different because the timing of the growth spurt, the sharp increase in growth, varies greatly between individual people.[13] A repeated cross sectional survey and a longitudinal study should be considered as being complementary.

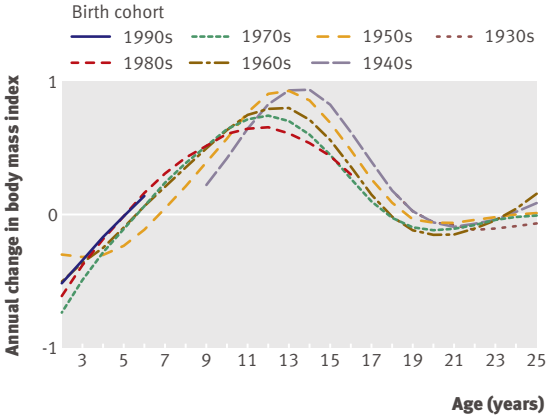

Fig 2 | Annual change in body mass index by female birth cohorts (1930s to 1990s), from national nutrition survey, Japan, 1948-2005

WHAT IS ALREADY KNOWN ON THIS TOPIC

A growing global epidemic of childhood obesity is occurring

The mean body mass index in Japanese females has increased in childhood in recent decades but decreased in young adulthood; the effect of birth cohorts on this phenomenon is unclear

WHAT THIS STUDY ADDS

Growth curves by birth cohorts were produced by a repeated cross sectional annual survey over nearly six decades

More recent cohorts of Japanese females were more overweight in childhood but thinner in young adulthood

Growth curves for a wide age range by birth cohort should be considered in studying obesity and thinness

Recently, the International Obesity Task Force proposed sex and age specific international body mass index cut offs for overweight, obesity, and thinness in childhood and adolescence, from 2 to 18 years.[4 14] These cut offs were developed to help provide internationally comparable prevalences in children and are based on nationally representative datasets from six countries gathered from 1963 to 1993. This means that the current definitions of overweight, obesity, and thinness are based on the distribution of body mass index in past birth cohorts at fixed ages. If the pattern of growth curves has changed with generations, it should affect the prevalence of obesity and thinness. If the timing of growth is accelerated, the prevalence of obesity should increase in childhood, as our results suggest in Japanese girls. We need careful monitoring of the prevalence at later ages for recent cohorts. When long term health promotions are planned or assessed, policy makers need to look at changes in birth cohorts.

Young Japanese women tended to be thinner despite a higher body mass index in childhood. Whether this phenomenon is specific to Japanese women or holds true for other nations is not known. In fact, the intersect of the growth curve at middle adolescence is not seen in Japanese males from the same dataset, although the rate of recent increase in body mass index was smaller in young adults than in children. General patterns of body mass index after about 17 years of age differed between men and women. The body mass index of young women slightly decreased in all cohort groups, whereas that of young men increased. Whether this slight decrease in young women in each cohort is seen in other nations is also unknown. The body mass index in young Korean women is as low as that of Japanese women and also shows the decrease during the ages of 20-25 for cross sectional data; however, this decrease is not seen in each birth cohort.[15] Currently, growth curves of mean body mass index or prevalence by birth cohorts in each nation for a wide range of ages, childhood to old age, are unclear and need further study.

Conclusions

We have shown that an overweight birth cohort in childhood does not necessarily continue to be overweight as young adults. Monitoring growth curves by birth cohort is important in studying obesity and thinness for public health. Values of body mass index from childhood to later life by birth cohort should be examined. For this purpose, a repeated cross sectional survey is suitable. Values of body mass index and annual changes in body mass index are important because body mass index changes dynamically during childhood and adolescence.

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