SUPPLEMENTARY MATERIAL

Appendix 1: Elicitation exercise on residual disease at primary surgery for advanced ovarian cancer sent to BGCS members

Job title

Please specify your job title

1. Sub-Specialist Consultant
2. Consultant gynae oncologist
3. Consultant gynaecologist –Unit Lead
4. Consultant gynaecologist –Other
5. Consultant Clinical Oncologist
6. Consultant Medical Oncologist
7. Consultant Histopathologist
8. Consultant Cytopathologist
9. Consultant Radiologist
10. Staff or Associate Specialist –Gynaecological Oncology
11. Staff or Associate Specialist –Other
12. Subspecialty Trainee Gynaecological Oncology
13. Specialty Registrar or Clinical/Research Fellow –O&G
14. Specialty Registrar or Clinical/Research Fellow –Clinical/Medical Oncology
15. Specialty Registrar or Clinical/Research Fellow -Radiology
16. Specialty Registrar or Clinical/Research Fellow –Palliative Care
17. Specialty Registrar or Clinical/Research Fellow –Other

Introduction

Participant Information Sheet

Bryant A, *et al*. *BMJ Open* 2022; 12:e060183. doi: 10.1136/bmjopen-2021-060183

Invitation

This is an invitation to complete a complex survey on residual disease at primary surgery for advanced ovarian cancer that will take up to 30 minutes, but as BGCS members you might consider the altruistic value of contributing towards an area of uncertainty within your field.

The nature of expert elicitation surveys are that they typically only need completion from relatively few experts but it is important that respondents have the necessary expertise and interest in the area. Elicitation surveys are often the only way of resolving issues of uncertainty.

The survey has been designed in consultation with several gynae-oncologists and that is the main reason for the detailed level of explanation given with visual examples so it is clear what is being asked of the respondent.

**Please use a computer or laptop to complete the survey as it is not mobile-friendly.*

Introduction to research problem

Residual disease at surgery for advanced ovarian cancer is one of the factors that influences survival. However, there is a lack of randomised controlled trials (RCTs) in upfront surgery for advanced ovarian cancer. This may be because some clinicians believe that tumour biology plays a greater role in predicting patient survival, undermining the importance of making every possible effort to obtain complete cytoreduction.

Available studies are retrospective in nature, looking at residual disease at surgery and patient survival after upfront surgery and chemotherapy. There is also huge variation in reporting and definitions. One consequence of this is the potential for publication bias due to selective or nonreporting of studies.

This presents challenges when conducting systematic reviews and meta-analyses. To overcome some of the challenges, we can think about what sort of studies have been conducted but not published. One way to do this is to ask for the opinions of experts such as yourself and incorporate your beliefs into our analyses. To do this we would like your opinions about a number of different scenarios describing the likelihood of different studies not being published.

Impact of this survey

Meaningful and reliable conclusions will be drawn from this survey and it is the views from experts that is crucial to get informative, reliable and representative results. The adjustments for publication bias based on the survey results can potentially be transferred into other areas of Oncology so the survey will be extremely informative moving forward.

The results of the survey will be confidentially shared with all contributors and you will of course be acknowledged for your efforts. The results of the survey will be part of a publication on residual disease threshold after primary surgical treatment for advanced epithelial ovarian cancer (EOC), using your expert views to adjust for potential publication bias. This publication will be sent to BGCS members as soon as it is published.

How the survey works

The next sections describe the overall objective of the research this survey will inform, and a short summary of the methods used to address this. You will then be presented with the expert elicitation exercise, which will have three main parts. Expert elicitation is essentially a scientific consensus methodology. It allows for parametrisation (using your highly 'educated guesses'), for the respective questions and scenarios under consideration. The main purpose of this elicitation exercise is to quantify uncertainty.

Objectives

Objective of the type of research this survey will inform

1. *To evaluate the effects of residual disease on survival after primary cytoreductive surgery for women with advanced epithelial ovarian cancer (stages III and IV).*

To address this objective the following methods, briefly summarised next, will be used.

Please take some time to familiarise yourself with the methods.

Bryant A, *et al*. *BMJ Open* 2022; 12:e060183. doi: 10.1136/bmjopen-2021-060183

Types of studies
Data from randomised controlled trials (RCTs), prospective and retrospective cohort studies, and unselected case series of 100 or more patients that included concurrent comparison of different residual disease (RD) thresholds after primary surgical intervention.

Any data collected from RCTs were retrospective and taken from trials that randomised groups of women to various chemotherapy protocols after primary surgery and the surgical outcome was categorised as complete (microscopic or no visible disease), optimal, and suboptimal based on the maximum size of postoperative residual disease.

Case-control studies, studies that did not have concurrent comparison groups, and case series of fewer than 100 patients were excluded.

In order to minimise selection bias, we included only studies that used statistical adjustment for baseline case mix using multivariable analyses (for example age, stage, grade, extent of disease).

Types of participants
Adult women (over 18 years of age) with surgically staged advanced epithelial ovarian cancer (FIGO stage III/IV) who had confirmed histological diagnoses. Women with other concurrent malignancies were excluded.

Types of interventions
Intervention: primary optimal cytoreductive surgery followed by adjuvant platinum-based chemotherapy. We only included studies that defined optimal cytoreduction as surgery leading to residual tumours with a maximum diameter of any threshold up to 2 cm. Patients who received chemotherapy prior to surgery were excluded.

Comparison: women who had primary surgery resulting in residual disease which did not meet the criteria specified in the study as optimal, followed by adjuvant platinum-based chemotherapy.

Outcome
Overall survival was the outcome of interest and was defined as survival until death from all causes.

Searches
Electronic databases indicating the Cochrane Gynaecological Cancer Collaborative Review Group Trials Register, CENTRAL, MEDLINE and EMBASE were searched from 1950 up to January 2020. A comprehensive search of the grey literature was performed and extensive hand searches were carried out in pertinent areas. There were no language restrictions.

Expert elicitation

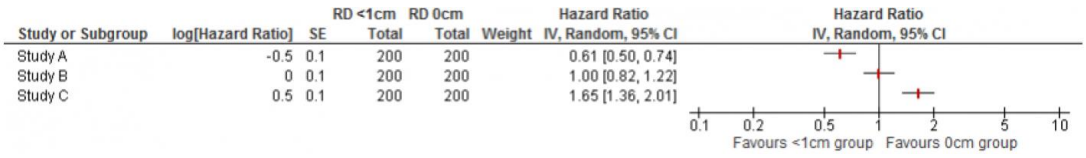
The expert elicitation exercise has three parts: A-C. Please answer these parts in order.

Before you do this please read the following text:

In subsequent tasks in the survey, you will be presented with statistics commonly reported in studies using survival models e.g., hazard ratios (HR). To help you familiarise with these statistics, kindly take a moment to consider the forest plot below for three studies A, B, and C and the associated interpretations in bullet points. *Do not worry about having to memorise the results, they are merely for illustrative purposes.*

- Study A shows statistically significant prolonged survival in the RD <1 cm threshold (or more risk of death in the RD 0cm threshold) than when residual disease was completely cytoreduced to 0cm.
- Study B shows no statistically significant difference in the risk of death between RD <1 cm and RD 0cm thresholds.
- Study C shows statistically significant prolonged survival in the 0cm threshold (or more risk of death in the RD <1cm threshold) than in the RD <1cm threshold.

Although it is possible for studies favouring RD <1cm (or other RD thresholds) over complete cytoreduction (0cm) to be published, it seems less likely because of the greater likelihood of reporting bias amongst studies reporting no statistical significance or ones favouring RD <1cm over RD of 0cm. This will be interpreted in light of any adjustment made.



Part A

Question 1

This section requires you to please provide estimates of the chance (probability) a study of a given sample size, for a certain comparison, is published.

The table below shows residual disease (RD) thresholds and sample sizes, which are all compared to the reference microscopic disease (RD 0cm). The studies mimic the inclusion criteria as outlined in the introduction. Please complete what in your opinion would be the chance that a study of a certain sample size comparing a specific RD threshold versus RD 0cm is published. Kindly do this for each of the 16 options below.

Kindly enter the percentage chance of being published for studies of given sample size and residual disease thresholds compared to microscopic disease (0cm). Kindly enter a value between 0 (no chance of publication) and 100 (certainly published).

A percentage of 0% indicates that you think there is no chance at all of publication and 100% means it is certain to be published. The value you should put for each option should lie between 0 and 100% likelihood of being published. Tossing an unbiased coin and getting a head would have 50% chance. There is no correct answer; your judgements for each option are your own personal opinions and reflect your experience in this area, but it is with these we hope to use in our analyses.

RD threshold (versus microscopic disease (RD 0cm)	Sample size (n) in comparison with microscopic disease (RD 0cm)	% chance of being published [value between 0 (no chance) and 100 (certain)]	n in comparison with RD 0cm	% chance of being published [value between 0 (no chance) and 100 (certain)]
LESS THAN 1 cm	100		1000	
GREATER THAN 0cm	100		625	
BETWEEN 1cm and 2cm	100		210	
LESS THAN 2cm	100		250	
GREATER THAN 1cm	100		1000	
GREATER THAN 2cm	100		250	
BETWEEN 1cm and 5cm	100		250	
GREATER THAN 5cm	100		250	

Part B

In lay terms, there is large literature suggesting a strong association with complete cytoreduction (0cm) and prolonged survival. However, due to the nature of studies looking at the association between complete cytoreduction and survival, whether there is selective reporting of studies is open to debate.

As experts in this area, it is assumed you will be very familiar with the literature and be aware of publications in ovarian cancer debulking journals on a regular basis. It is the studies that MAY have been conducted but not published in journals that you will not be aware of and we want you to consider how many of these there are likely to be.

In this part of the survey, we would like you to provide us with responses to questions that allows us to adjust the overall effect estimate when data from unobserved studies are added to the final analysis.

Question 2

2. Near optimal RD<1cm versus complete cytoreduction (0cm)

In this section, we would like you to provide us with responses to questions that allows us to adjust the overall effect estimate when data from unobserved studies are added to the final analysis. This adjustment will account for an absence (or not) of studies favouring near optimal RD <1cm or ones showing no statistically significant difference between RD <1cm and RD 0cm, based upon your own opinion and clinical experience in this area.

How likely is it that relevant studies reporting adequately sized analyses that did not favour complete cytoreduction (RD to 0cm) when compared to RD <1cm would not have been identified from the literature searches and therefore omitted from the meta-analysis? By this we mean how likely is it that studies that either favoured RD <1cm or studies that found no statistically significant difference (p>0.05) in survival between RD 0cm and RD <1cm) would not be published?

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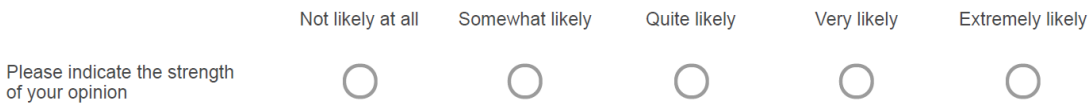
- Studies reporting statistically significant prolonged survival in favour of RD LESS THAN 1cm (that is the effect size in the form of a hazard ratio is less than 1 and the upper 95% confidence interval does not cross 1)

OR

- Studies that reported no statistically significant difference in survival between RD LESS THAN 1cm and 0cm (that is the 95% confidence interval, reporting lower and upper estimates of hazard ratio, crosses 1)



Thinking about your response the question above and giving a realistic answer based on your own experience and awareness of previous analyses in this area, how many studies in total do you think will have been missed that should have been included?

Please give a brief reason for your answer

Please indicate in the table below where you think the number of studies you gave will be distributed. You're not expected to fill in all rows and columns and you may include multiple studies of the same size and magnitude. Assume for this scenario that the missing studies have an assumed 5 year survival of 36%

Assumed 5 year survival: 36%		RD <1cm and 0cm are the same i.e. HR = 1	10% less chance of mortality favouring RD <1cm i.e. HR = 0.9	20% less chance of mortality favouring RD <1cm i.e. HR = 0.8	30% less chance of mortality favouring RD <1cm i.e. HR = 0.7	40% less chance of mortality favouring RD <1cm i.e. HR = 0.6	>=50% less chance of mortality favouring RD <1cm i.e. i.e. HR ≤ 0.5
Size of studies missed that could have been included in the analysis	n=100						
	n=200						
	n=300						
	n=400						
	n=500						
	n>500						

Question 3

3. Sub-optimal RD>1cm versus complete cytoreduction (0cm)

In this section, we would like you to provide us with responses to questions that allows us to adjust the overall effect estimate when data from unobserved studies are added to the final analysis. This adjustment will account for an absence (or not) of studies favouring suboptimal RD >1cm or ones showing no statistically significant difference between RD >1cm and RD 0cm, based upon your own opinion and clinical experience in this area.

How likely is it that relevant studies reporting adequately sized analyses that did not favour complete cytoreduction (RD to 0cm) when compared to RD >1cm would not have been identified from the searches and therefore omitted from the meta-analysis? By this we mean how likely is it that studies that either favoured RD >1cm or studies that found no statistically significant difference (p>0.05) in survival between RD 0cm and RD >1cm) would not be published?

- Studies reporting statistically significant prolonged survival in favour of RD GREATER THAN 1cm (that is the effect size in the form of a hazard ratio is less than 1 and the upper 95% confidence interval does not cross 1)

OR

- Studies that reported no statistically significant difference in survival between RD GREATER THAN 1cm and 0cm (that is the 95% confidence interval, reporting lower and upper estimates of hazard ratio, crosses 1)

	Not likely at all	Somewhat likely	Quite likely	Very likely	Extremely likely
Please indicate the strength of your opinion	○	○	○	○	○

Thinking about your response the question above and giving a realistic answer based on your own experience and awareness of previous analyses in this area, how many studies in total do you think will have been missed that should have been included?

Please give a brief reason for your answer

Please indicate in the table below where you think the number of studies you gave will be distributed. You're not expected to fill in all rows and columns and you may include multiple studies of the same size and magnitude. Assume for this scenario that the missing studies have an assumed 5 year survival of 36%

Assumed 5 year survival: 36%		RD >1cm and 0cm are the same i.e. HR = 1	10% less chance of mortality favouring RD >1cm i.e. HR = 0.9	20% less chance of mortality favouring RD >1cm i.e. HR = 0.8	30% less chance of mortality favouring RD >1cm i.e. HR = 0.7	40% less chance of mortality favouring RD >1cm i.e. HR = 0.6	>=50% less chance of mortality favouring RD >1cm i.e. HR ≤ 0.5
Size of studies missed that could have been included in the analysis	n=100						
	n=200						
	n=300						
	n=400						
	n=500						
	n>500						

Question 4

4. Sub-optimal RD>2cm versus complete cytoreduction (0cm)

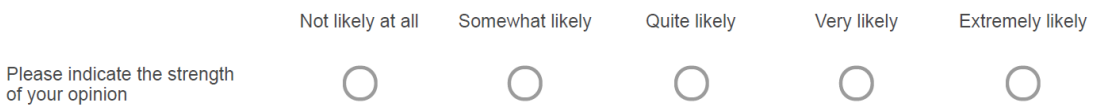
In this section, we would like you to provide us with responses to questions that allows us to adjust the overall effect estimate when data from unobserved studies are added to the final analysis. This adjustment will account for an absence (or not) of studies favouring suboptimal RD >2cm or ones showing no statistically significant difference between RD >1cm and RD 0cm, based upon your own opinion and clinical experience in this area.

How likely is it that relevant studies reporting adequately sized analyses that did not favour complete cytoreduction (RD to 0cm) when compared to RD >2cm would not have been identified from the searches and therefore omitted from the meta-analysis? By this we mean how likely is it that studies that either favoured RD >2cm or studies that found no statistically significant difference (p>0.05) in survival between RD 0cm and RD >2cm) would not be published?

- Studies reporting statistically significant prolonged survival in favour of RD GREATER THAN 2cm (that is the effect size in the form of a hazard ratio is less than 1 and the upper 95% confidence interval does not cross 1)

OR

- Studies that reported no statistically significant difference in survival between RD GREATER THAN 2cm and 0cm (that is the 95% confidence interval, reporting lower and upper estimates of hazard ratio, crosses 1)



Thinking about your response the question above and giving a realistic answer based on your own experience and awareness of previous analyses in this area, how many studies in total do you think will have been missed that should have been included?

Please give a brief reason for your answer

Please indicate in the table below where you think the number of studies you gave will be distributed. You're not expected to fill in all rows and columns and you may include multiple studies of the same size and magnitude. Assume for this scenario that the missing studies have an assumed 5 year survival of 36%

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Assumed 5 year survival: 36%		RD >2cm and 0cm are the same i.e. HR = 1	10% less chance of mortality favouring RD >2cm i.e. HR = 0.9	20% less chance of mortality favouring RD >2cm i.e. HR = 0.8	30% less chance of mortality favouring RD >2cm i.e. HR = 0.7	40% less chance of mortality favouring RD >2cm i.e. HR = 0.6	>=50% less chance of mortality favouring RD >2cm i.e. HR ≤ 0.5
Size of studies missed that could have been included in the analysis	n=100						
	n=200						
	n=300						
	n=400						
	n=500						
	n>500						

Part C

Question 5

In a meta-analysis including non-randomised studies, often only univariate results are reported with no attempt made to adjust for potentially important baseline imbalances. This risks making the results biased.

On a scale of 0-100, to what extent do you think that the reason study authors only report univariate analyses is to maximise the magnitude in effect estimates to favour either an experimental or comparator group?

Question 6

In your opinion, how many attempted submissions should you make to journals to publish the results of your study?

Question 7

In your opinion, how many attempted submissions should you make to journals to publish the results of your study if it is not statistically significant (p>0.05)?

Question 8

What is lowest impact factor in a journal that you would consider submission of your work, regardless of the significance of your results?

	<1 e.g. Turkish Journal of Medical Sciences	1-5 e.g. BJOG	6-10 e.g. BMC Medicine	11-14 e.g PLoS Medicine	15-19 e.g. Annals of Internal Medicine	20-24 e.g. BMJ	25+ e.g. Lancet Oncology
Lowest impact factor	○	○	○	○	○	○	○

Question 9

To what extent do you think it is important to publish the results of a study even if the impact factor of the accepting journal is perceived to be very low?

Not important at all — Vitally important

0 10 20 30 40 50 60 70 80 90 100

Acknowledgment

(Optional) If you would like to be acknowledged for your contribution to the survey, kindly leave your name.

You may choose to provide your full name (e.g., Sam Smith) or an abbreviation (e.g., S Smith).

Data on your name will be kept separate from the data file containing the survey results so that your personal information cannot be traced back to your responses. Your name will only be used for purposes of acknowledgment and will not be used in analysis.

Which of the following mediums do you consent to being acknowledged in? You may choose all that apply.

- ☐ Journal publication
- ☐ Conference poster/oral presentation
- ☐ BGCS internal dissemination (e.g., newsletter)

Appendix 2: Statistical considerations and analysis

Part A

The scenario in part A of the elicitation exercise assumed that there is a population of studies which have been conducted assessing OS in RD thresholds after primary surgery for EOC. Then, it assumed that there are a finite number of published studies that have reported an estimated effect, with precision around that estimate (measured using standard error). In the presence of publication bias these studies are a non-random sample of all studies that have been conducted in this area. It is assumed that very large studies have a probability of being published very close to one, as journals tend to trust larger studies. Conversely, small studies have a diminished chance of publication. An additional consideration is that if effect size is correlated with the probability of a study being published, then this will introduce additional bias.(1)

Part B

The results of section B are a particularly novel aspect of this research, specifically as they could be used as prior information to inform adjustment of meta-analyses for publication bias. Here, we outline how this could be achieved.

First, we require that all calculations should give each expert responder the same weight, such that they contribute equally to the prior formation. The average study size for each effect size (HR) point estimate is then calculated; the sample size is dictated by the number of studies selected by each individual expert, with the average then calculated giving equal weight to each respondent. A normal prior is then formed for each HR, before these are combined in a weighted manner to a single elicited prior suitable for adjusting for publication bias.

We note that this is only one potential way to form a prior based on this elicited data and that a sensitivity analysis should certainly be conducted and potentially also other approaches considered. In our elicitation exercise, the choice of the number of missing

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studies was left open ended as to not lead experts to a choice and bias the results. Consequently, a sensitivity analysis could be conducted removing high estimates of unpublished studies if it was judged that unrealistic entries were unduly inflating an average.

Given an assumed 5 year survival rate of 36% (2-4) and a minimum sample size of n=100 to meet the criteria for inclusion in the network meta-analysis (NMA), then a minimum 64 events (deaths, d) would be required with 36 participants being alive and censored at the end of the study:

$$(d = 100\{1 - 0.36\})$$

Generalising this result, we assume that d can be related to n in general through the following formula.

$$n = \frac{d}{1 - (\text{5 year suvival rate})} = \frac{d}{0.64}.$$

The standard error of the log hazard ratio (SElogHR) can then be related to n by rearranging the following.

$$d = \frac{4}{\text{SE}(\log HR)^2},$$

$$\Rightarrow \text{SE}(\log HR) = \sqrt{\frac{4}{d}} = \sqrt{\frac{4}{0.64n}} = \sqrt{\frac{6.25}{n}}.$$

Next, we denote by m_{cij} the number of missing studies according to expert responder $c = 1, \dots, C$, with a HR of HR_j and a sample size of n_i, where:

$$n_1 = 100, n_2 = 200, n_3 = 300, n_4 = 400, n_5 = 500, n_6 = 625,$$

$$HR_1 = 1, HR_2 = 0.9, HR_3 = 0.8, HR_4 = 0.7, HR_5 = 0.6, HR_6 = 0.5.$$

We compute the average number of missing studies of type ij, across the responders, as:

$$m_{ij} = \frac{1}{C}\sum_{c=1}^{C} m_{cij}.$$

We use this to form an average sample size of missing studies with a HR of HR_j through:

$$m_j = \frac{\sum_i n_i m_{ij}}{\sum_i m_{ij}}.$$

With this, we assume that information from missing studies with a HR of HR_j can be categorised through the following distribution:

$$P_j \sim N\left(\log HR_j, \frac{6.25}{m_j}\right).$$

The P_j can then be combined in a weighted manner, giving more weight to those values of j with a larger value of m_j, via conflation. This gives a single elicited prior of:

$$P \sim N\left(\frac{\sum_j \frac{m_j \log HR_j}{6.25}}{\sum_j \frac{m_j}{6.25}}, \frac{1}{\sum_j \frac{m_j}{6.25}}\right) = N\left(\frac{\sum_j m_j \log HR_j}{\sum_j m_j}, \frac{6.25}{\sum_j m_j}\right).$$

This elicited estimate can then be used as prior information and be applied in a Bayesian analysis(5-7) that reflects the results of the expert opinion in the elicitation exercise.(1, 8).

Appendix 3: Breakdown of distribution of size and magnitude of elicited unpublished studies of sub-optimal RD >1cm versus complete cytoreduction (0cm)

N=154 (n=8.6)		**Estimated effect size**					
Assumed 5 year survival: 36%		**HR=1**	**HR=0.9**	**HR=0.8**	**HR=0.7**	**HR=0.6**	**HR≤0.5**
		RD <1cm and 0cm are the same	**10% less chance of mortality favouring RD <1cm**	**20% less chance of mortality favouring RD <1cm**	**30% less chance of mortality favouring RD <1cm**	**40% less chance of mortality favouring RD <1cm**	**>=50% less chance of mortality favouring RD <1cm**
Size of studies missed that could have been included in the analysis	**Sample size**						
	n<100	STUDY EXCLUDED					
	n=100	29.5	7.67	3.17	2.8	0.1	1.43
	n=200	14.5	6.67	3.17	2.8	0.1	1.43
	n=300	5	1.67	0	1.67	0	1.33
	n=400	9.66	8.33	8.33	8.33	8.33	9.66
	n=500	2.66	0	0	0	0	1.33
	n>500	6	2	0	0	0	6.33
Total studies[a] (mean)		67.3 (3.7)	26.3 (1.5)	14.7 (0.8)	15.6 (0.9)	8.5 (0.5)	21.5 (1.2)
Effective n[b] (mean)		16294 (905)	7184 (399)	4283 (238)	4673 (260)	3362 (187)	9313 (517)
Effective d[c] (mean)		10428 (579)	4598 (255)	2741 (152)	2991 (166)	2152 (120)	5960 (331)
SElogHR (√(4/d))[d]		0.083	0.125	0.162	0.155	0.183	0.110
95% CI for HR[e]		0.85-1.18	0.71-1.15	0.58-1.10	0.52-0.95	0.42-0.86	0.40-0.62
Elicited estimate[f]		HR=0.77 (95% CI 0.70 to 0.85), logHR=-0.26 SElogHR=0.05 (n=2500, d=1600)					

[a] Absolute number of estimated missing studies elicited from responders with mean (simply absolute number divided by 18 (number of responders)) given in parentheses

[b] Absolute number of estimated missing participants elicited based on total studies with mean given in parentheses

[c] Absolute number of deaths estimated from number of participants assuming 5 year survival rate of 36% with mean in ()

[d] Approximation of the standard error (SE) of the log hazard ratio (HR) using formula derived by Parmar(9), namely the square root of 4 divided by mean number of deaths

[e] 95% confidence interval for hazard ratio (HR) calculated using logHR ± 1.96 multiplied by standard error of log HR then transforming back by taking the exponential

[f] Elicited Hazard ratio with 95% confidence interval using mean responses for all aggregated effect sizes

[g] Number of studies given in the breakdown were rescaled in three respondents to correspond to the total number estimated

Appendix 4: Breakdown of distribution of size and magnitude of elicited unpublished studies of sub-optimal RD >2cm versus complete cytoreduction (0cm).

N=112 (6.2)		**Estimated effect size**					
Assumed 5 year survival: 36%		**HR=1**	**HR=0.9**	**HR=0.8**	**HR=0.7**	**HR=0.6**	**HR≤0.5**
		RD <1cm and 0cm are the same	**10% less chance of mortality favouring RD <1cm**	**20% less chance of mortality favouring RD <1cm**	**30% less chance of mortality favouring RD <1cm**	**40% less chance of mortality favouring RD <1cm**	**>=50% less chance of mortality favouring RD <1cm**
Size of studies missed that could have been included in the analysis	**Sample size**						
	n<100	STUDY EXCLUDED					
	n=100	14.67	7	5	0	0	0.67
	n=200	8.67	8	5	0	0	0.67
	n=300	0.67	0	0	0	0	0.67
	n=400	9	8.33	8.33	8.33	8.33	9
	n=500	1.33	0	0	0	0	0.67
	n>500	7	0	0	0	0	0.67
Total studies[a] (mean)		41.3 (2.3)	23.3 (1.3)	18.3 (1)	8.3 (0.5)	8.3 (0.5)	12.3 (0.7)
Effective n[b] (mean)		12042 (669)	5632 (313)	4832 (268)	3332 (185)	3332 (185)	4756 (264)
Effective d[c] (mean)		7707 (428)	3604 (200)	3092 (172)	2132 (118)	2132 (118)	3044 (169)
SElogHR (√(4/d))[d]		0.097	0.141	0.153	0.184	0.184	0.154
95% CI for HR[e]		0.83-1.21	0.68-1.19	0.59-1.08	0.49-1.00	0.42-0.86	0.37-0.68
Elicited estimate[f]		HR=0.79 (95% CI 0.71 to 0.89), logHR=-0.24 SElogHR=0.06 (n=1736, d=1111)					

[a] Absolute number of estimated missing studies elicited from responders with mean (simply absolute number divided by 18 (number of responders)) given in parentheses

[b] Absolute number of estimated missing participants elicited based on total studies with mean given in parentheses

[c] Absolute number of deaths estimated from number of participants assuming 5-year survival rate of 36% with mean in ()

[d] Approximation of the standard error (SE) of the log hazard ratio (HR) using formula derived by Parmar(9), namely the square root of 4 divided by mean number of deaths

[e] 95% confidence interval for hazard ratio (HR) calculated using logHR ± 1.96 multiplied by standard error of log HR then transforming back by taking the exponential

[f] Elicited Hazard ratio with 95% confidence interval using mean responses for all aggregated effect sizes

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