Summary points

Rationing decisions are currently based on the cost of the average gain from a treatment

Some patients may not want certain treatments because they weigh the side effects more than the gains

Patients who would decline treatment should not be included in assessment of average gain

Excluding these patients increases the cost effectiveness of a treatment

AS has published extensively on health needs assessment. AG, MM, AA, and DB have interests in statistics and modelling and AG is sponsored by MATCH to develop novel approaches to modelling. RL conceived the idea for this paper in discussion with MM and DB. RL, AG, and AS wrote the manuscript, AA assisted with some calculations. RL is the guarantor.

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Ethics

One-time general consent for research on biological samples

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It is now recognised that people should give informed consent for use of their biological samples in research. The literature on individuals' views supports one-time general consent as the best approach for this purpose

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Clinicians and clinical researchers routinely obtain human biological samples and store them for future research. Previously, samples were often stored and used without informed consent. Most investigators thought that the protections in place for research with human participants were not needed for research with human samples.

Recent commentators recognise the importance of informed consent for research with biological samples, but they disagree about when it is required and what types of consent should be obtained. Some argue that people should provide consent for each new study, at the time the study is proposed. Others support prospective consent, but they endorse different sets of options regarding the storage of samples, which investigators can use the samples, and what types of research can be performed.

This profusion of guidance has led to divergent practices,[1 2] with one study finding that institutional review boards in the United States recommend "various consent options, all of which are different."[3] Such variation may undermine the scientific value of patients' contributed samples and greatly increase the costs of such research. Assessing whether people's views support one of the recommended options for consent could provide a solution to these problems.

Methods

I searched PubMed (see appendix 1 on bmj.com) for studies published in English that reported the views of individuals on consent for research with human biological samples. This search identified 30 eligible studies.

Results

Individual willingness

The 30 studies provide data on the views of more than 33 000 people (table).[4–32] The studies assessed the views of patients, research participants, family members, religious leaders, and the public. The studies yield consistent findings, despite being conducted around the world, over a 10 year period, in different groups, using different methods. Most respondents want to decide whether their samples are used for research purposes.

Of the 20 studies that assessed willingness to donate, 17 found that at least 80% of respondents would donate a sample if asked. Respondents who

Appendices showing the search terms used and the consent process for research with human biological samples are on bmj.com

Studies of views on consent for research with biological samples

First author (year)	No of participants; country	Response rate (%)	% Willing to provide sample for research	% Willing to allow study of other diseases	Comments
Subject donors*:					
Matsui (2005)[4]	5361; Japan	98	>90	NA	Willingness to provide sample for genetic research 5-9% lower
Hoeyer (2005)[5]	1200; Sweden	81	NA	NA	49% wanted results; 36% not aware they gave a sample
Chen (2005)[6]†	1670; US	100	91	87	7% refused all research
Wendler (2005)[7]‡	347; Uganda	98	95	85	54% wanted results; 4% thought samples might be used for non-research purposes
McQuillan (2003)[8]§	3680; US	80	85	85	84% agreed to genetics research; minorities slightly less willing
Stegmayr (2002)[9]	1409; Sweden	95	93	NA	3% opposed industrial research; 22% wanted renewed contact for new projects
Malone (2002)[10]	7565; US	100	94	87	4% lower consent rate with less detailed consent form
Wendler (2002)[11]¶	814; US	94 (subject donors)/ 47 (patient non-donors)	NA	92	88% wanted results; consent more important for clinical samples
Nakayama (1999)[12]	120; Japan	88	99**	NA	92% remembered donating; 61% thought it was for clinical care
Patient donors:					
Jack (2003)[13]	3140; UK	100	99	NA	Only 2 individuals concerned about commercial research
Moutel (2001)[14]	170; France	30	100	NA	None agreed that DNA "storage duration should be limited"
Hamagima (1998)[15]	583; Japan	96	95	NA	Some decliners concerned about spreading their disease
Public donors:					
Womack (2003)[16]††	106; UK	71	100	NA	5% stated family or deceased opposed tissue donation
Kozlowski (2002)[17]	3383; US	70	18	NA	Study solicited genetic samples by mail from random individuals
Patient non-donors:					
Start (1996)[18]	450; UK	91	83‡‡	NA	Some concerned with spreading their disease
Goodson (2004)[19]	100; UK	100	82§§	NA	35% wanted results; 75% "not happy" to contribute to cloning
Public non-donors:					
Roberts (2005)[20]	63; US	NA	NA	NA	Support genetic research; concern about children or prisoners
DeCosta (2004)[21]	59; India	97	86	NA	14% fewer willing to provide sample of child's blood
Hoeyer (2004)[22]	1000; Sweden	60	NA	NA	48% "feel respected" if get results
Wong (2004)[23]	708; Singapore	70	49	NA	38% unwilling to donate owing to fear of needles/injections
Ashcroft (2003) (personal communication)	155; UK¶¶	NA	100	NA	Wanted control; opposed cloning; wanted new consent for new tests
PSP (2002)[24]***	16 focus groups; UK	NA	NA	NA	Supported research; willing to contribute biological samples
Stolt (2002)[25]	21; Sweden	NA	NA	NA	Supported research on other diseases; some wanted results
Asai (2002)[26]	21; Japan	NA	NA	NA	Supported research; concerned about risks; some wanted results
Schwartz (2001)[27]	1383 US (Jewish Americans)	20	>80	>80	Endorsed consent for each study, but not offered general consent
Wang (2001)[28]	3130; US	84	79	79	21% not willing to donate or store blood for genetic research
Welcome Trust (2000)[29]	16 focus groups; UK	NA	NA	NA	Most would provide sample; preferred research on specific diseases
NBAC (2000)[30]	7 hearings; US	NA	NA	NA	Supported research, including for profit; endorsed one-time consent; concerned about confidentiality
Merz (1996)[31]	99; US	10-20	60	87	26% wanted results; 30% would restrict drug company access
Phan (1995)[32]	21 US†††	49	NA	NA	91% supported genetic research; concerned about confidentiality

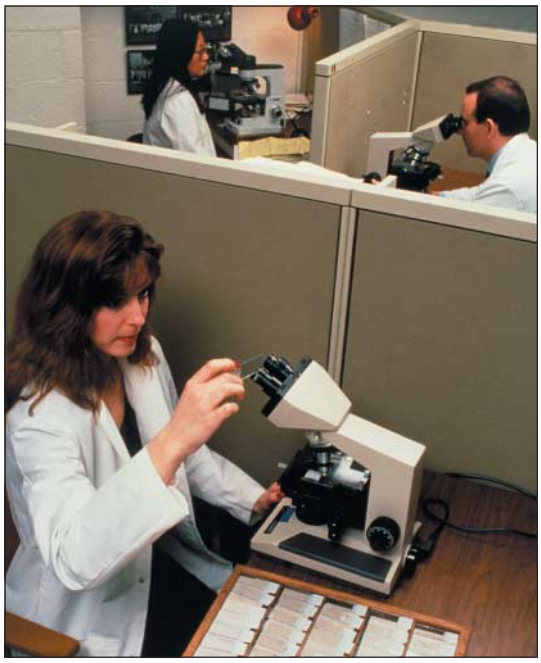
NA=published study does not provide quantitative data on the relevant question.
*Donors had donated a sample for research, non-donors had not donated; subjects were participating in research, patients were receiving medical care, and "public" were participating in random surveys.
†Denominator varies for different questions.
‡Respondents were guardians, in most cases the mothers, who donated children's blood samples.
§Using year 2000 data.
¶Most respondents were subject donors, remainder were public non-donors.
**Of the 96 respondents who participated in the follow-up survey.
††Donated tissue from deceased member of the family.
‡‡Percentage who would agree to their leftover tissue being used for medical research.
§§Percentage who were "happy" for tissue to be used for cancer research.
¶¶35 individuals in focus groups, 120 in individual interviews.
***Also interviewed clinicians, patients, community leaders, and organisation spokespersons.
†††Respondents were religious leaders from the midwest United States.

were unwilling to donate samples tended to be concerned with the method of obtaining samples, not the possible use of the samples for research. In one study 38% of unwilling respondents cited a fear of needles or injections, and in another study many people who were unwilling to donate cited the time required for the consent discussion.[16 23] Similarly, respondents in the study by Kozlowski et al were required to complete a telephone interview, agree to receive and use a sample kit, and mail the sample back to investigators unknown to them.[17]

Consistent with these findings, four of five studies that specifically assessed leftover samples found that most respondents (93-99%) were willing to donate them for research.[9 10 13 15] In the fifth study 83% of patients were willing to donate and 2% were unwilling; the remaining patients were unsure, many because of concerns about spreading their disease.[18]

Individual preferences

Studies investigating different consent options found that most people are willing to provide a sample for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research in general. In the six studies that examined the issue, most people (79-95%) were willing to provide one-time general consent and rely on ethics committees to determine the studies for which their samples would be used.[5 7–10 22] Even studies that assessed research on potentially stigmatising conditions found high rates of willingness to consent.[7 10 19 27] Three studies found that people were marginally less willing to provide a sample for commercial rather than academic research.[9 13 31] Nine studies found that many people would like some information on the projects for which their samples will be used, although the type of information desired was not specified.

Discussion

The ethical requirements to respect the autonomy and values of individuals and protect them from serious risks are consistent with several approaches to consent for research on biological samples. For example, respect for autonomy does not determine whether people should provide one-time general consent or should specify which diseases may be studied using their samples. In this context, data on the views of individuals can help identify a best approach among the available options.

Current data provide consistent and strong evidence that people want to control whether their samples are used for research and that most are willing to contribute samples. The data also show that most people prefer one-time general consent, on the understanding that an ethics committee will review and approve future projects. These data provide compelling evidence that one-time general consent is the best option (see appendix 2 on bmj.com).

One-time general consent respects the wishes of people to control the use of their samples without mandating that they decide the specific projects for which the samples are used. Widespread support for this approach indicates that it would be socially acceptable and should lead to high rates of donation.

The data also show that one-time general consent is supported by the "reasonable person" standard. This standard directs investigators to offer participants the choices that reasonable people want to make, given their interests, concerns, and goals. The finding that most people endorse one-time general consent is consistent across more than a decade, for thousands of people living in countries around the world. These data are also consistent across many different groups, including religious leaders, participants in past and present research, and the general public. This consistent and widespread support indicates that one-time general consent offers people the choice(s) reasonable people want to make when deciding whether to donate samples for research.

Individual opinions, even when widely held, sometimes reflect confusion and bias, not the views of reasonable people. Granting this possibility, the preference for one-time general consent, in addition to being consistent with relevant values and principles, seems reasonable. One-time general consent allows people to control whether their samples are used for research. Although it does not allow people to control the projects for which their samples are used, there is no reason to think that they want to make such decisions. One-time general consent protects people from serious risks, provided an ethics committee finds that future projects are acceptable and pose no more than minimal risks.

Finally, one-time general consent has practical advantages. It increases the scientific and social value of donated samples and lowers the costs of conducting research on them, eliminating the need to track the choices for each sample. One-time consent also allows people to avoid being repeatedly contacted and asked for consent, possibly for decades.

Limitations

Survey research can be affected by many aspects of a given study, including framing effects and the possibility that individuals did not understand some questions. Nevertheless, these data are consistent across many studies, which surveyed various groups in different countries over a decade, using different questions and different methodologies. Secondly, one-time general consent may not be consistent with the values of some groups. Future research should evaluate its acceptability for groups, such as Native Americans, and areas of the world, such as Latin America, that are not included in the present data. Thirdly, the existing studies focus on blood samples; people may have different views on research with other types of samples, such as semen and placenta.

Implementation

The consistency of these data suggests the default option of one-time general consent should be modified in compelling cases only. To implement one-time general consent, the consent form and process should contain at least the following six elements: request to obtain samples for future research; risks, if any; absence of direct benefits; information, if any, to be provided by individuals; reliance on ethics committees to review and approve future research provided it finds the research is ethical and poses no greater than mini-

Summary points

It is now recognised that people should give informed consent for the use of their biological samples in research

The types of consent needed and when consent should be obtained have not been defined

Studies have collected data on the views of more than 33 000 people on this issue

These data support one-time general consent

mal risk; solicitation of individual questions. Additional elements should be included as appropriate for individual studies (see appendix 2 on bmj.com).

The data do not indicate whether people want information on the research goals of future studies, pooled results, individual results, or a combination of these types of information. The data also do not address the possibility that some information might cause anxiety or that retaining identifiers precludes anonymising samples. Hence, recommendations for a uniform approach to providing information on future studies must await further research. To help investigators and ethics committees determine when personal identifiers should be retained, research should assess how people balance being able to receive future information against the added protection that comes with anonymising samples.

Conclusion

Several approaches to informed consent for research with human biological samples are consistent with the general requirements of respecting the autonomy and values of individuals and protecting them from serious risks. However, the use of different approaches could undermine the social and scientific value of these samples and increase the costs of conducting research on them. Empirical data can help to identify which of the ethically acceptable approaches is most consistent with the views and preferences of individuals. Data from more than 33 000 people around the world support offering individuals a simple choice of whether or not their samples can be used for research purposes, with the stipulation that an ethics committee will decide the studies for which their samples are used. This approach offers a method that could be adopted across institutions and around the world.

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