European Journal of Cancer xxx (xxxx) xxx–xxx

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Current perspective

Duty to recontact in genomic cancer care: A tool helping to assess the professional's responsibility

Martine C. Ploem [a,b], Noor A.A. Giesbertz [c,d], Annelien L. Bredenoord [c,e], Valesca P. Retèl [f,g,*,1], Wim H. van Harten [f,h,1]

[a] *Amsterdam University Medical Center, University of Amsterdam, Amsterdam, the Netherlands*
[b] *Faculty of Law, University of Amsterdam, Amsterdam, the Netherlands*
[c] *Department of Genetics, University Medical Center Utrecht, the Netherlands*
[d] *Department of Clinical Genetics, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands*
[e] *Erasmus School of Philosophy, Erasmus University Rotterdam, Rotterdam, the Netherlands*
[f] *Department of Psychosocial Research and Epidemiology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands*
[g] *Erasmus School of Health Policy and Management, Erasmus University Rotterdam, Rotterdam, the Netherlands*
[h] *Department of Health Technology and Services Research, University Twente, Enschede, the Netherlands*

Received 22 January 2023; Received in revised form 3 March 2023; Accepted 3 March 2023
Available online xxxx

KEYWORDS
Duty to recontact;
Ethics;
Legislation;
Responsibility;
Genomic testing;
Whole genome sequencing

Abstract Tumour DNA and germline testing, based on DNA-wide sequencing analysis, are becoming more and more routine in clinical-oncology practice. A promising step in medicine, but at the same time leading to challenging ethicolegal questions. An important one is under what conditions individuals (patients and their relatives, research participants) should be recontacted with new information, even if many years have passed since the last contact. Based on legal- and ethical study, we developed a tool to help professionals to decide whether or not to recontact an individual in specific cases. It is based on four assessment criteria: (1) professional relationship (2) clinical impact (3) individual's preferences and (4) feasibility. The tool could also serve as a framework for guidelines on the topic.

1. Introduction

An increasing number of studies and related publications in oncology fuel the promise of genome-driven, personalised treatment. A better understanding of

* *Correspondence to*: Department of Clinical Genetics, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, Amsterdam 1066 CX, the Netherlands.
[1] These authors contributed equally

https://doi.org/10.1016/j.ejca.2023.03.004
0959-8049/

genome-related cancer characteristics can lead to offering treatments and preventive strategies that are tailored to the individual genetic nature of the disease, thereby reducing overtreatment and improving treatment outcomes [1,2]. Considering the rapid developments in genomic cancer research, it will not take too long until tumour DNA and germline testing, based on DNA-wide sequencing analysis, will be broadly applied in oncology practice [1,2].

These developments lead on their turn to new questions in the ethicolegal field. An important one is whether a professional – a physician or medical researcher – carries a duty to 'recontact' individuals when previously obtained genetic results gain new meaning over time. Equally, scientific research or re-analysis of already available genomic (tumour) data, may result in novel information shedding a different light on applied treatments, prognosis or additional preventive or treatment options [3,4]. To put it concretely: to what extent it may be expected of professionals that they (re)contact an individual—a patient, a research participant or a relative—if new information becomes available [5]?

Below we first summarise the main lines of the ethical and legal framework on recontact. Then we present criteria and a corresponding 'decision support tool' to assist professionals in taking reasonable and well-founded decisions with regard to recontacting. Although the tool is meant primarily to function as an instrument for responsible decision-making in individual cases, it could also be useful, as a framework, for guideline development in this field. In conclusion, we mention topics related to recontacting that need further study.

2. Ethical and legal framework

Being informed about newly discovered (genetic) health information, can enable individuals to undergo additional treatment or screening or it can influence important life choices. However, it can also cause distress or conflict with their wish not to receive further updates. Ethical values such as respect for autonomy and the principle of beneficence are arguments in favour of recontacting individuals, while the principle of not causing harm (non-maleficence) and respecting an individual's wish not to be recontacted, are possible arguments against it. Furthermore, practical circumstances, such as limited healthcare resources, can be an argument to refrain from recontacting. In light of these potentially conflicting values, the existence of an ethical duty to recontact very much depends on the specific circumstances of a case [6].

On the basis of human rights, such as Article 10 of the Biomedicine Convention ensuring the right to be informed about available health information, similar starting points can be deduced. Recontacting may, under obvious circumstances, be the professional's responsibility; however, individuals cannot claim an absolute right on recontact and further information should they wish to receive it. In that direction also points the fact that a right to recontact as such is not being a part of national legal systems. The legal standard can—roughly—be described as that professionals need to do what, in light of the specific circumstances, can be reasonably expected from them [7]. For example, when recontacting an individual requires disproportional efforts (and costs) from professionals recontacting could not easily be considered their duty.

In light of future technological developments, such as personal health records and ways in which individuals can electronically communicate with professionals, it does not seem unlikely that the responsibilities described above will gradually develop into a more clearly defined professional task to re-establish contact with individuals if this follows from their preferences and health interests.

3. Tool for assessing recontact responsibility

When new information becomes available, it will not be an easy task for clinicians and other professionals to assess whether it is their responsibility to recontact an individual or not, since this highly depends on contextual factors and circumstances. Such situations easily lead to moral distress and uncertainty about eventual liability among the professionals involved [8]. Based on the ethical [6] and legal [7] framework on the duty to recontact, as summarised above, as well as an empirical analysis [8], we established 'assessment criteria' that support professionals in responsible decision-making about recontacting individuals. Applying these criteria produces a 'score' that indicates whether recontact is: 'recommended'; 'not recommended'; or 'should be discussed in a multidisciplinary team or ethics committee' (Fig. 1).

3.1. Individual's preference-criterion

Three situations regarding the individual's preference are possible: 1) the individual explicitly stated a desire to be recontacted; 2) the individual explicitly objected against recontact; and 3) the individual did not articulate a preference. A duty to recontact is stronger when it is known that a patient or research participant explicitly wants to receive new information whereas a free choice of a well-informed individual not to be contacted by a physician weakens the duty considerably [9]. A dilemma may arise when new information is of great clinical benefit while the individual made a clear choice not willing to be approached again. For example, if a breast cancer patient has previously indicated that she does not want to receive new information, but a promising drug with a considerable chance of longer survival has become available (Textbox 1)

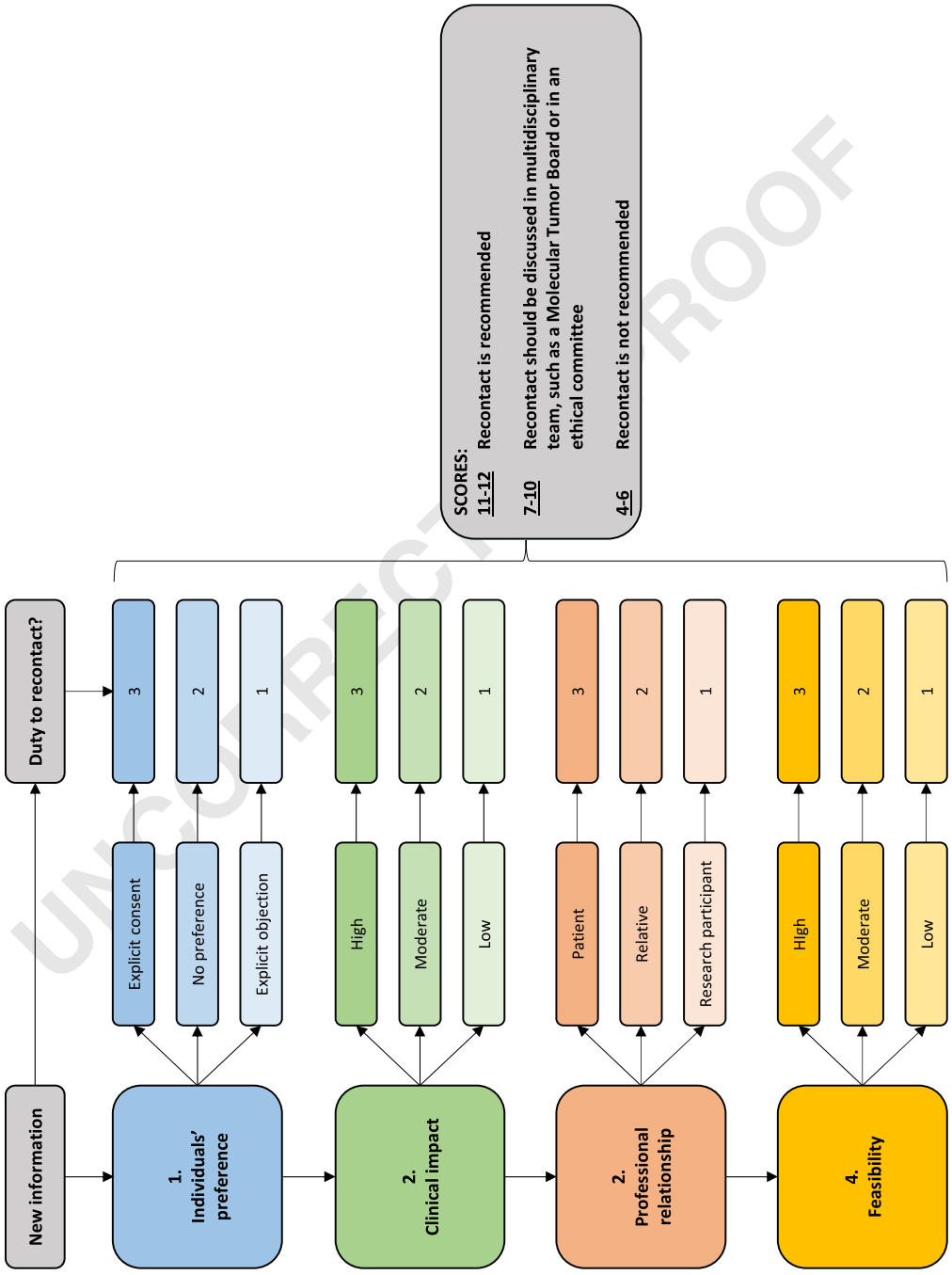

Fig. 1. Decision support tool for responsible decision-making concerning recontacting in personalised oncology.

Textbox 1: applying the decision support tool in a hypothetical case.

Hypothetical case #

An oncogeneticist, involved in DNA-testing of a now 38-year-old female patient, learns that the BRCA1 variant of this patient is reclassified from a class 4 to class 2 variant. There was no discussion with her about recontacting at the time of the initial testing. Since she was a patient 8 years ago, she has changed her address two times.

Evaluating the strength of the duty

Individual's preference:

There is no information on the individuals' preferences about being recontacted or not: 2 points

Clinical impact:

The clinical impact can be considered high; first of all for the patient herself because this will influence decision-making about a prophylactic bilateral salpingo-oophorectomy; there is also clinical relevance for her relatives because this has implications for the predictive DNA testing policy: 3 points

Professional relationship:

There was a care relationship: 3 points

Feasibility:

With considerable effort it is possible to track down the woman's address: 2 points

Conclusion: strong duty to recontact (10 points); recontact is recommended

3.2. Clinical impact criterion

If newly discovered information significantly alters someone's treatment options or outcome, or gives rise to preventive measures for themselves or their relatives, seeking contact is considered most compelling [10]. This holds in particular when survival is expected to improve substantially. By contrast, if, for example, a variant in a specific cancer gene is reclassified from class 2 (likely benign) to class 1 (benign), the impact of the information is marginal, hence recontacting seems to be less meaningful.

3.3. Professional relationship-criterion

The nature of the relationship between professional and individual who may be contacted also strengthens or weakens the duty to recontact. An ongoing and, to a somewhat lesser extent, a former physician–patient relationship put most weight in this respect, as such a relationship is founded on the trust that the physician acts in the patient's best interest. If it concerns not a patient, but his or her relatives, an eventual duty to recontact is weaker; not a (post) contractual obligation is here at stake, but a general 'duty to warn' for medical professionals in case of a significant risk of serious health damage.

We consider the position of research participants as the least strong when it comes down to an eventual professional responsibility regarding recontact, unless these are joining a clinical trial.[7] This holds in particular for the context of large-scale biobank and big data projects that take place on large distance of individuals involved. A responsibility to recontact in the latter context seems therefore only 'reasonable' if the circumstances point clearly in that direction. It should be the participant's preference (or her or his preference should be unknown), it should involve highly relevant clinical information as well as a relatively small effort to reach those involved. The Molecular Tumor Board (MTB) could play a role here in advising the clinical or research team whether to initiate recontact.

3.4. Costs and effort-criterion

Since recontacting individuals and providing further treatment or preventative options implies costs and requires efforts, the strength of a duty also depends on what can be reasonably expected from professionals in light of the health care and financial system in which they work. Therefore, when establishing guidelines on recontacting, the costs and efforts to recontact individuals should also be taken into consideration [9].

4. Importance of guideline development

As personalised cancer care, based on genome-wide analysis, becomes more common in oncology practice, it is likely that the duty to recontact individuals will gradually evolve into a clearly defined professional responsibility. We expect that, in due time, this will be mirrored in case law and legislation. In this process, the development of professional guidelines must have a high priority. Medical professionals, e.g., professionals who have experience in a Molecular Tumor Board (MTB), should take the lead, in close consultation with patient organisations and other stakeholder parties, should take the lead as they are best placed to assess what they can reasonably do for patients, their relatives and research participants in this regard [11,12].

5. Topics for further research

Especially from the perspective of Health Technology Assessment several issues concerning recontacting require further scrutiny; there is, for instance, still little insight in the cost-effectiveness of recontact practices [10]. Such knowledge is crucial in guideline development and to negotiate with the government and insurance companies. Another highly relevant topic is how technology can enhance patient autonomy regarding recontacting. Although currently, most often the individual's viewpoint about recontacting will be either unclear or unknown, this will certainly change in the future, resulting in a new practice in which patients are routinely asked about their preferences [13]. One can think of 'integrated digital infrastructures' facilitating the communication with patients and other persons; these seem particularly promising because they can provide maximum room for managing personal health information by individuals while, at the same time, they can keep the costs low.

Funding statement

This study was performed as a part of the "Technology Assessment of Next Generation Sequencing in Personalized Oncology (TANGO)" project, funded by ZonMW, (The Netherlands Organisation for Health Research and Development) #846001002.

CRediT authorship contribution statement

MP, NG, VR have contributed to the original draft, MP, NG, AB, VR, WvH have all contributed to the conceptualisation, analysis, visualisation, and review & editing of the manuscript.

Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The authors have nothing to disclose for the work under consideration for publication. Prof. dr. van Harten reported non-restricted grants from Novartis, Intuitive Surgical and Agendia all ending over three years ago, Dr. Retèl reported non-restricted grants from Intuitive and Agendia outside the submitted work all ending over 3 years ago. The other authors have nothing to declare.

Acknowledgements

We acknowledge Prof. Dr. S.C. Linn for reading through the manuscript and providing us with valuable input. This study was performed as a part of the "Technology Assessment of Next Generation Sequencing in Personalized Oncology (TANGO)" project, funded by ZonMW, (The Netherlands Organisation for Health Research and Development) #846001002.

References

[1] Priestley P, Baber J, Lolkema MP, et al. Pan-cancer whole-genome analyses of metastatic solid tumours. Nature 2019;575:210–6.
[2] Mateo J, Steuten L, Aftimos P, et al. Delivering precision oncology to patients with cancer. Nat Med 2022;28(4):658–65.
[3] Pyeritz RE. The coming explosion in genetic testing–is there a duty to recontact? N Engl J Med 2022;365:1367–9.
[4] Hampel H, Yurgelun MB. Point/Counterpoint: is it time for universal germline genetic testing for all GI cancers? J Clin Oncol 2022;40:2681–92.
[5] Otten E, Plantinga M, Birnie E, et al. Is there a duty to recontact in light of new genetic technologies? A systematic review of the literature. Genet Med 2015;17:668–78.
[6] Giesbertz NAA, van Harten WH, Bredenoord AL. A duty to recontact in genetics: context matters. Nat Rev Genet 2019;20:371–2.
[7] Ploem C, Mitchell C, van Harten WH, et al. A duty to recontact in the context of genetics: futuristic or realistic? Eur J Health Law 2018;25:537–53.
[8] Mitchell C, Ploem C, Retel V, et al. Experts reflecting on the duty to recontact patients and research participants; why professionals should take the lead in developing guidelines. Eur J Med Genet 2020;63:103642.
[9] Wolf SM, Annas GJ, Elias S. Point-counterpoint. Patient autonomy and incidental findings in clinical genomics. Science 2013;340:1049–50.
[10] Carrieri D, Dheensa S, Doheny S, et al. Recontacting in clinical practice: an investigation of the views of healthcare professionals and clinical scientists in the United Kingdom. Eur J Hum Genet 2017;25:275–9.
[11] Marx MF, Ataguba JE, de Vries J, et al. Systematic review of the economic evaluation of returning incidental findings in genomic research. Front Public Health 2021;9:697381.
[12] Stoeklé HC, Mamzer-Bruneel MF, Frouart CH, Le Tourneau C, Laurent-Puig P, Vogt G, Hervé C. Molecular tumor boards: ethical issues in the new era of data medicine. Sci Eng Ethics 2018;24(1):307–22.
[13] Ploug T, Holm S. Clinical genome sequencing and population preferences for information about 'incidental' findings—From medically actionable genes (MAGs) to patient actionable genes (PAGs). PLoS One 2017;12:e0179935. https://doi.org/10.1371/journal.pone.0179935.