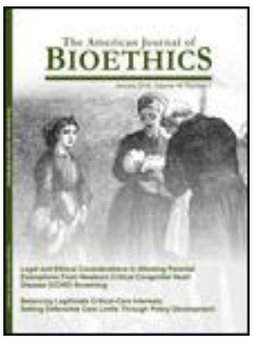

The American Journal of Bioethics

ISSN: 1526-5161 (Print) 1536-0075 (Online) Journal homepage: http://www.tandfonline.com/loi/uajb20

Relative Risk and Relatives' Risks in Genomic Medicine

Angela Fenwick, Shiri Shkedi-Rafid & Anneke Lucassen

To cite this article: Angela Fenwick, Shiri Shkedi-Rafid & Anneke Lucassen (2016) Relative Risk and Relatives' Risks in Genomic Medicine, The American Journal of Bioethics, 16:2, 25-27, DOI: 10.1080/15265161.2015.1120809

To link to this article: http://dx.doi.org/10.1080/15265161.2015.1120809

Published online: 01 Feb 2016.

REFERENCES

Arora, K. S., and V. Blake. 2013. The 2013 review of the Children's Health Insurance Program Reauthorization Act: A call to action. *Obstetrics and Gynecology* 121(6): 1313–17.

D'Alton, M. E. 2010. Where is the "M" in maternal–fetal medicine. *Obstetrics and Gynecology* 116(6): 1401–4.

El-Mohandes, A., A. A. Herman, M. Nabil El-Khorazaty, P. S. Katta, D. White, and L. Grylack. 2003. Prenatal care reduces the impact of illicit drug use on perinatal outcomes. *Journal of Perinatology* 23(5): 354–60.

Figdor, E., and L. Kaeser. 1998. Concerns mount over punitive approaches to substance abuse among pregnant women. Available at: http://www.guttmacher.org/pubs/tgr/01/5/gr010503.html (accessed October 26, 2015).

Kremer, M. E., and K. S. Arora. 2015. Clinical, ethical, and legal considerations in pregnant women with opioid abuse. *Obstetrics and Gynecology* 126(3): 474–78.

Lyerly, A. D., M. O. Little, and R. Faden. 2008. The second wave: Toward responsible inclusion of pregnant women in research. *International Journal of Feminist Approaches to Bioethics* 1(2): 5–22.

Maternal decision making, ethics, and the law. 2005. ACOG Committee Opinion No. 321. American College of Obstetricians and Gynecologists. *Obstetrics and Gynecology* 106:1127–37.

McDonough, K. 2014. Tennessee just became the first state that will jail women for their pregnancy outcomes. Available at: http://www.salon.com/2014/04/30/tennessee_just_became_the_first_state_that_will_jail_women_for_their_pregnancy_outcomes (accessed October 26, 2015).

Minkoff, H., and M. F. Marshall. 2016. Fetal risks, relative risks, and relatives' risks. *American Journal of Bioethics* 16(2): 3–11.

Paltrow, L. M. 1990. When becoming pregnant is a crime. *Criminal Justice Ethics* 9:41–48.

Roberts, S. C. M., and A. Nuru-Jeter. 2010. Women's perspectives on screening for alcohol and drug use in prenatal care. *Women's Health Issues* 20:193–200.

Relative Risk and Relatives' Risks in Genomic Medicine

Angela Fenwick, Medicine at the University of Southampton
Shiri Shkedi-Rafid, Medicine at the University of Southampton
Anneke Lucassen, Medicine at the University of Southampton and University Hospital Southampton NHS Foundation Trust

Minkoff and Marshall's (2016) exploration of the concept of risk, revisiting a *Lancet* (2010) editorial statement that women "do not have the right to put their baby at risk," is important, although incorrectly attributed to Kingma. The original article advised that hospital births "should be the preferred method of delivery for high risk pregnancies" because of the higher risks associated with home births. Minkoff and Marshall point out that the risk being referred to relates to the fetus rather than to a child. Kingma (2011), in fact, had assertively criticized the editorial, pointing out that the woman's voice is missing. Here we also focus on the fetus and discuss how novel genomic tests that uncover a multitude of different risks further complicate the issue of risk interpretation.

We agree that the pernicious criminalization of pregnant women may be fueled by such statements. By examining both relative risk (the expression of risk in relation to a baseline) and relatives' risks (risks to the interests of the collective family) in their article, Minkoff and Marshall expose some of the complexities of decision making during pregnancy. This complexity increases with advances in available technologies not only with regard to the actual delivery of the fetus, but also in the choices that women, and their partners, are able to make during pregnancy, or even before embarking on a pregnancy. One area that deserves attention is how advances in genomics can predict risks to the future child in a way that then further impacts on the Minkoff and Marshall debate. Advanced genomic tests use broad yet highly sensitive techniques to examine the fetal genome and are increasingly offered as risk predictors in pregnancy. Whilst prenatal genetic testing in the past could also offer broad testing in the form of chromosome examination, the sensitivity of this testing was only a tiny fraction of what current techniques can offer. In the past, any detailed approach to genome analysis was targeted to specific sections of the genomic code by signs, symptoms, family history, or, for example, maternal age. New genomic technologies in effect "trawl" the whole

Address correspondence to Angela Fenwick, Clinical Ethics and Law, Faculty of Medicine, University of Southampton, Room 4001, Building 85, Highfield Campus, University Road, Southampton, SO17 1BJ, United Kingdom. E-mail: a.j.fenwick@soton.ac.uk

genome, rather than "fish" for specific portions of the genetic code that have a high a priori risk of abnormality. The output of such "trawling" is a vast array of risk information that needs interpreting (Fenwick et al. 2015).

Minkoff and Marshall rightly highlight that the language of risk is often misunderstood by both patients and health care professionals. In genomic tests the possibility of finding variants where the magnitude of the effect on health risk is uncertain is far greater than in the past. Furthermore, where health risks are not anticipated through family history or signs and symptoms, communication and understanding become even more challenging. We have previously written about inappropriate amounts of predictive powers being ascribed to genetic findings and the pervasive climate of genetic determinism (Fenwick et al. 2015): Genetic relative risks may be interpreted and communicated as more definite—as absolute and therefore more worrying—than they actually are. Even if risk information is communicated well, it is often difficult to know how to incorporate it into any decision making. For example, suppose a woman is told that her fetus has a relative risk of schizophrenia of about 2; this translates to an approximately 100% greater chance of developing schizophrenia than for someone without that genetic variant. Presented like this the risk sounds quite dramatic, but given that the background population risk of schizophrenia is roughly 1% these relative risks translate to a roughly 2% lifetime chance of developing schizophrenia, with a corresponding >98% chance they will not. A 100% greater chance is thus very different from a 100% chance, highlighting the importance of understanding what the risk information actually means (Joint Committee on Genomics in Medicine [JCMG] 2015). We agree that absolute risk is less opaque than relative risk, but other factors also come into play: A high absolute risk of a treatable condition in adulthood is very different from a high absolute risk of an untreatable one in infancy. Furthermore, many common conditions are multifactorial, where a risk from one gene variant will depend on the interaction between it and other variants, or variables, resulting in predictions with wide confidence intervals. Minkoff and Marshall show that people interpret risk depending on their attitude to risk—adverse or tolerant—and their approach to reasoning. An added dimension is that misunderstandings of the risk involved are particularly difficult in pregnancy since the decision-making window is finite, so decisions to continue with or terminate a pregnancy may need to be made more quickly than is ideal for complex decisions.

While relative risks need to be carefully communicated, the higher they are—or more importantly, the higher the absolute risk is—the more this information may be relevant not only to the future child but also to family members who might benefit from this information: relatives' risks. Thus, in the genetic context, the notion of relatives' risks takes on different meanings. The mother may have to interpret risk information in relation not only to her fetus but also to herself and, together with the clinician, have to consider who else this information may pertain to—for example, the parents, existing and future siblings, or other family members. A whole-genome test on a male fetus may reveal, for example, an inherited BRCA1 mutation that carries no known health implications for the future child (since it predisposes to adult-onset disease) or even the adult (as risks in males are very low compared to females). However, since BRCA1 mutations confer a high risk of breast and ovarian cancer to women, such information is potentially useful information to other family members, who may benefit from screening or treatment (Lucassen et al. 2014). This then raises the question of whether the fetal finding should be communicated to others. If it should, who has an obligation to ensure that this is done, and what, when, and how (Dheensa et al. 2015)? When does a relative risk also become a risk that relatives should know about?

Although genetic tests have always raised these issues, the rapid increase in the use of genetic technologies will mean that such considerations will be more widespread and will need to become part of the discourse surrounding risk. Their use in pregnancy means that clinical conversations may take place under considerable time pressures, especially when decisions about continuation of pregnancy are to be made. *The Lancet*'s editorial assertion that women have no right to put their babies at risk is even more problematic in the era of testing that measures multiple risks and for which confidence intervals are still often very broad. Moreover, we should be mindful of where such reasoning and interference in women's life choices and decision making might lead us: Suppose a woman knows (from family history or perhaps from previous testing) that her own or her partner's genome composition means that they are at increased risk of having—or indeed will have—a baby with a genetic condition. Does she have a right to embark upon a pregnancy that will clearly put her baby at higher than average risk? If she has a right, does she have a responsibility to do something about it during her pregnancy (Inside the Ethics Committee 2009)? How much risk would be "too great" and who would decide? ■

REFERENCES

Dheensa, S., A. Fenwick, S. Shkedi-Rafid, G. Crawford, and A. Lucassen. 2015. Health-care professionals' responsibility to patients' relatives in genetic medicine: A systematic review and synthesis of empirical research. *Genetics in Medicine*. doi:10.1038/gim.2015.72

Fenwick, A., S. Dheensa, G. Crawford, S. Shkedi-Rafid, and A. Lucassen. 2015. Rescue obligations and collective approaches: Complexities in genomics. *American Journal of Bioethics* 15(2): 23–25.

Inside the Ethics Committee. 2009. BBC Radio 4, July 30. Available at: http://www.bbc.co.uk/programmes/b00lszh4 (accessed October 27, 2015).

Joint Committee on Genomics in Medicine. 2015. Recommendations for the use of chromosome microarray in pregnancy. Available at: http://www.bsgm.org.uk/media/956141/g144_useofcmapregnancy_jun15.pdf (accessed October 27, 2015).

Kingma, E. 2011. *The Lancet*'s risky ideas? Rights, interests and home-birth. *Internal Journal of Clinical Practice* 65 (9):918–920

Lancet. 2010. Home birth—Proceed with caution. *Lancet* 376:303.

Lucassen, A., G. Widdershoven, S. Metselaar, A. Fenwick, and M. Parker. 2014. Genetic testing of children: The need for a family perspective. *American Journal of Bioethics* 14(3): 26–28.

Minkoff, H., and M. F. Marshall. 2016. Fetal risks, relative risks, and relatives' risks. *American Journal of Bioethics* 16(2): 3–11.

Parental Obligations Regarding Fetal Risk: Finding the Appropriate Analogy

Janet Malek, Baylor College of Medicine

Howard Minkoff and Mary Faith Marshall take on important questions at the intersection of maternal decision-making and fetal exposure to risk in their "Fetal Risks, Relative Risks, and Relatives' Risks" (Minkoff and Marshall 2016). Specifically, they seek to refute the claim that pregnant women's behavior may be constrained to prevent fetal risk. Although Minkoff and Marshall's interpretation of this claim may be extreme in that they assume that any activity causing increased risk would be prohibited under such a view, the key arguments in their piece can also be applied to a more moderate interpretation and so merit serious consideration nonetheless.

Minkoff and Marshall deploy various analogies to make their argument that the relationship between a pregnant woman and her fetus does not require a pregnant woman to act (or abstain from acting) in particular ways to avoid incremental fetal risk. However, the way in which these analogies are used is problematic, compromising the soundness of the authors' reasoning.

The authors first consider "duty-to-rescue" scenarios, citing legal precedent from various jurisdictions refuting the existence of such a duty. The reference to such cases presumably is intended to demonstrate that if a person cannot be compelled to rescue an individual in danger of death or serious harm, a person certainly cannot be compelled to make choices to protect an individual from lesser risks. However, rescue contexts are not morally equivalent to standard cases of pregnancy.

Paradigmatic duty-to-rescue cases involve an innocent bystander, put in the position of deciding whether to be a "splendid Samaritan" and offer assistance to a vulnerable individual in a situation she is otherwise unrelated to. In contrast, a pregnant woman is integrally involved with the situation that puts a fetus at risk. By allowing conception and permitting the continued development of a fetus, a pregnant woman makes choices that bring about the fetus's vulnerability to harm. Unlike the defendants in the cases cited by Minkoff and Marshall, she causes the circumstances that put a fetus at risk.

The existence of a causal relationship between one individual and another's risk of harm is clearly morally significant. The key role of this variable is even noted in the judicial opinion in one case cited by the authors, *Yania v. Bigan*, in which the judge stated, "The mere fact that Bigan saw Yania in a position of peril in the water imposed upon him no legal, although a moral, obligation or duty to go to his rescue *unless Bigan was legally responsible, in whole or in part, for placing Yania in the perilous position*" (*Yania v. Bigan* 1959, italics added). It is not ethically or legally controversial to claim that (under normal circumstances) an individual bears responsibility for foreseeable downstream effects of his own voluntary choices but does necessarily bear the same responsibility for the choices of others. Because there is a causal connection between a pregnant woman and the vulnerability of her fetus that is not present between a typical rescuer and victim, there is a morally relevant difference between these two types of cases. As a result, the fact that most jurisdictions do not recognize a duty to rescue is not informative about justifications for constraining maternal behavior to prevent harm to a fetus.

To their credit, Minkoff and Marshall address a second important difference between typical duty-to-rescue scenarios and cases involving pregnant women: the nature of the relationship that exists between a pregnant woman and her fetus. In this discussion, they state that the legal picture may be different when an individual is in a position to rescue her own child rather than a stranger, acknowledging that a duty to rescue or to prevent harm may exist in such cases. Minkoff and Marshall then aim to undermine the use of this parent–child analogy in the maternal–fetal case by questioning whether duties that apply to children apply to fetuses as well.

Address correspondence to Janet Malek, Baylor College of Medicine, Center for Medical Ethics and Health Policy, 1 Baylor Plaza, Houston, TX 77030, USA. E-mail: janet.malek@bcm.edu