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A narrative review of the psychosocial impact on, and understanding of genetic testing and personalized medicine in adolescents with cancer or at risk of cancer: Current state of evidence and recommendations

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Abstract (97/100)

Genetic testing is becoming increasingly available for adolescents who are undergoing cancer treatment or at risk of cancer predisposition syndromes. With this narrative review, we aimed to synthesize the evidence on psychosocial outcomes and adolescents' understanding of genetic testing – thus far, an under-researched topic. Both psychological benefits and harms of predictive testing were reported in adolescents from high-risk families. Harms were mainly related to cancer-specific distress and increased worries. Findings on genetic understanding were sparse. Future studies should focus on psychosocial outcomes and adolescents' understanding undergoing genetic testing and enabling access to genetic counselling pre- and post-testing.

Introduction

Genetic testing and screening for cancer predisposition syndromes can be effective in reducing cancer morbidity and mortality in adolescents¹ However, adolescent and young adult cancers may differ from paediatric and adult cancers biologically and genetically.²⁻⁴ An adolescent with a pathogenic APC variant (which causes familial .improves survival and quality of life.⁵ Other adolescents have a cancer suggesting a rare broader cancer predisposition syndrome such as Li Fraumeni syndrome, which has implications for their treatment and cancer risk for their relatives.⁶ Other traditionally ‘adult’ cancers such as Lynch syndrome or breast and/or ovarian cancer syndromes are not normally tested for in adolescence but can rarely occur in adolescents in high risk families.²

Whole genome sequencing or exome sequencing, and interest in genetic testing and personalized medicine for adolescents is growing.⁷ Increasing awareness of genetic syndromes, may be of value to adolescents in different contexts, including 1) enabling adolescent cancer patients to explore more treatment options 2) highlighting risks to adolescent survivors of childhood cancers, and 3) alerting adolescents who do not have cancer of their future cancer risk.

First, for adolescents who do not respond favourably to standard cancer treatments, identifying a germline or somatic mutation may allow clinicians to offer treatment regimens, personalized to their genetic profile.⁴ Personalized medicine is also becoming more common in this age group even at diagnosis. Second, genetic testing for adolescents may also be important during follow-up care of childhood cancer survivors⁸ depending on their family history, medical history and tumour type.⁸ The uptake of a genetic test is likely dependant on the possible treatment options and therefore future testing should be a function of disease

penetrance regardless of age.⁹ Finally, at risk adolescents who have not had cancer could benefit from predictive testing to clarify their risk and allow creation of a tailored surveillance plan.^{10,11} Genetic testing in this context may be valuable however, guidelines, recommended surveillance protocols and available preventative actions differ for different genes. Typically, genetic testing is recommended if the disease is likely to manifest during adolescence and effective screening and intervention programs have the potential to reduce morbidity and mortality.¹² In the context of BRCA1 and 2 mutations, interventions such as prophylactic surgery or chemoprevention are usually not recommended before the age of 25 years, making genetic testing in adolescence less clinically relevant.^{13,14} However, testing in adolescents might still be salient as parents discuss cancer risk with their adolescent offspring, which might influence their child's concerns. Offering genetic testing and personalized medicine to adolescents raises a number of psychosocial, ethical and legal issues. These include concerns around adolescents' ability to understand complex genetic concepts and anticipate the often lifetime consequences of their decisions to enable fully informed consent.^{14,15} Further issues regarding adolescents' age include how best to involve the adolescent to their full capacity while respecting that parents may need to have input into the consent and shared decision making processes⁶. As adolescents' maturity levels vary widely some adolescents want to make their own decisions but are legally not able to while others, even though legally able, rely more on their parents.¹⁶

A recent systematic review on the psychological impact of acquiring genetic knowledge in childhood and early adolescence indicated that while no major psychological distress was reported, there were feelings of discrimination and guilt/regret, and in some cases intra-familial distress.¹⁷ In adults undergoing predictive genetic testing, several factors appeared to influence testees' psychological health. Feelings of uncertainty, distress and worry before undergoing testing and feelings of relief, reassurance or guilt after receiving a

negative test result were also common.¹⁸ It is clear though that genetic testing impacts are variable across groups, for example, patients with different types of cancer can have differing responses, perhaps reflecting variable risk management options.⁹

While there have been reviews of the psychosocial impact of genetic testing in childhood¹⁷ and adulthood⁹, the impact of genetic testing during adolescence is understudied. In this narrative review, we explore the available literature, identify gaps and summarize the available recommendations for appropriately managing cancer-related genetic testing and personalized medicine in adolescents. The main focus will be on the psychosocial impact of genetic testing and adolescents' understanding of, and knowledge about, genetics.

Methods

We performed a narrative review based on Economic and Social Research Council guidance.¹⁹ This form of review provides a broad overview of available evidence.²⁰ To search for relevant articles we used three databases (Medline, EMBASE and PsycINFO) and the following search terms: ([adolescens\$ OR "young adult" OR teen\$] AND [oncol\$ OR cancer] AND [personalised medicine OR personalized medicine OR genet\$])." To search for grey literature, we used OpenGrey and Grey Literature Report. The search was limited to English language and human studies which were published between 2001-2017. The initial search was performed in October 2015 and updated in August 2017. For the purpose of this review we only included studies focusing on adolescents aged 10-19 years to capture the unique developmental challenges and legal and ethical issues which differ from their younger and older counterparts. We excluded studies if results for adolescents and young adults were not separately discussed.

Three reviewers identified key articles by title and abstract screening (JF, KM, JV). Additional articles were obtained by searching reference lists of included articles, publications of recognized experts and hand searches on Google Scholar. Three investigators selected articles with the most relevance and potential impact to guide the findings of the review (JV, JF, CW).

Results

We screened 310 titles/abstracts and included a total of 9 articles. Most studies were published in the US, Australia and UK (n=8).

Psychosocial impact of family history and genetic testing in adolescents

There is little information available on the psychosocial impact of predictive genetic testing in adolescents from high-risk families. The largest published study of the psychosocial impact of a positive family history of breast cancer (incl. BRCA) of more than 250 11-19 year old girls reported that psychosocial adjustment did not differ between girls with a strong family history of breast cancer and those without.²¹ Girls with a family history of breast cancer had higher self-esteem than girls without a family history.²¹ However girls from breast cancer families and BRCA1/2 positive families had higher distress than girls who were identified as population risk.²¹ The study showed positive associations for breast cancer-specific distress in girls who perceived a high risk and in mothers who had a higher cancer-related distress.²¹ Another study of 55 daughters (aged on average 15.6 years) of women with breast cancer reported increased worries about their future health and genetic risk for breast cancer compared with the control daughters.²² However, there was no evidence of additional emotional, behavioural or familial impact.²² Girls whose mothers had breast cancer reported

more benefits of undergoing genetic testing, however both groups were equally willing to undergo testing.²²

A small qualitative study reported benefits for nine adolescents (six tested positive for cancer predisposing genes) who actively underwent predictive testing.²³ No psychological harms were reported by the adolescents however distress occurred around the pretesting process.²³

Adolescents' understanding of genetics

Qualitative interviews with adolescent girls from population risk (n=19) and high risk families (n=35) indicated that they had a limited understanding of BRCA1 and 2 genes.²⁴ Although they may not have known the genes, those with a family history of breast cancer perceived themselves to be at increased risk.²⁴ Most appeared to acquire their cancer-related genetics knowledge from their mothers.²⁴ Approximately half of the 54 participating girls believed that breast cancer can develop during the teenage years; these results were consistent between high-risk and population-risk girls.²⁴ Another study with young people aged 12-18 years affected by or at risk for breast cancer reported that boys' perceived risk was minimal likely due to gendered disclosure.²⁵ Another study on predictive testing for FAP demonstrated that young adults who had undergone FAP-testing when aged between 10-17 years had limited understanding of the process and consequences and were often not involved in decision-making, but spoke about their predictive genetic test as a major life event.²⁶

Discussion and recommendations arising from the literature

Research regarding the impact of and adolescents' understanding about genetic testing and personalized medicine in adolescents is sparse. The identified studies reported that genetic testing can benefit adolescents, but can cause psychological harms such as distress in some young people. Adolescents' understanding appeared limited however this needs to be

confirmed by future studies. Several papers provide clear recommendations for the appropriate management of adolescents considering genetic testing. One key recommendation is to limit analysis to genes of clinical relevance to the adolescents' cancer and cancer treatment rather than analysing all possible genes, because of challenges with incidental findings and uncertainties around clinical significance of some mutations.¹⁵ A recent policy discussion however suggested that reporting incidental findings of genomic testing might be the only way of learning about the family's cancer risk.²⁷ The impact of reporting incidental findings in the setting of adolescents undergoing genetic testing for cancer, needs to be further explored. For adolescents considering genetic testing for adult-onset conditions, the literature recommends that they be encouraged to consider deferring testing until adulthood, due to their more limited capacity for decision-making and the complexity of the information.¹⁵ Exceptions are noted if there are clinical reasons to test, or effective screening or preventative interventions are available as is the case for FAP.^{1,15} Healthcare professionals should provide resources and assist adolescents and their family members weigh the benefits and disadvantages of genetic testing for the adolescent, to help them make an informed decision.¹ Although younger adolescents may be unable to provide full consent for genetic testing, they should be included in giving assent and discussions about the implications of testing.²⁸

As others have noted, genetic counselling and testing of adolescents presents unique challenges related to the patients' developmental stage.²⁹⁻³¹ 'Adolescent friendly care' which involves, amongst other things, communicating in an age-appropriate language and respecting adolescents' autonomy and capacity to engage in discussions about their health,²⁹ may be fostered through a close working partnership with genetic health professionals and experts in adolescent psychology. An 'anticipated regret' model, where health professionals present hypothetical results to the adolescent and asks how they would react to receiving that

result³² is useful in helping adolescents to anticipate difficulties, and consider potential consequences of genetic testing. Further, healthcare professionals should be knowledgeable about the potential psychological impact of genetic testing and personalized medicine on adolescents and their families.^{1,15} Adolescents may benefit from developing a communication plan with their healthcare team, outlining who should be involved in learning genetic results and possible staging of information sharing depending on the maturity of the young person being tested.¹⁵ Healthcare professionals could facilitate access to genetic counselling and specialist genetic services (including a geneticist and psychosocial support) if the healthcare team, the adolescent, or their family, would benefit.¹⁵ This support ideally should be offered both before and after testing.¹ This aligns with the recommendations made in the adult setting, where results should be disclosed in a ‘comfortable setting’ and counselling offered before and after testing.³³ However, genetic counsellors might also be confronted by different challenges in the future with widespread use of personalized medicine intersecting with the known problems such as communication and confidentiality working with adolescents and this needs to be acknowledged.^{15,30,31} Adolescents could be offered the opportunity to discuss genetic testing and personalized medicine without their parents present,²⁹ although parents should be involved where clinically appropriate, such as discussion of secondary findings.¹⁵ The evidence further suggests that it is important to ensure that the adolescent understands the long term implications of genetic testing and personalized medicine (bearing in mind that adolescents may be a population less likely to, or less able to consider long term consequences of their decisions).¹⁵ ²⁹Further, to ensure confidentiality, if siblings are also tested at the same time, results should be shared individually, and testing preferably performed on different days.^{26,29}

Conclusion

The evidence regarding the psychosocial impact of genetic testing and personalized medicine during adolescence is sparse. This is particularly the case for studies with adolescents from high-risk families, and those who are undergoing ‘treatment-focused’ and predictive genetic testing. However, it is important to ensure that age-appropriate educational and psychosocial support is available to adolescents undergoing genetic testing. The implications of genetic testing ideally need to be discussed both with the adolescent alone and together with their family with pre- and post-test counselling whenever possible.

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