

PhD degree in Foundations of the Life Sciences and their Ethical
Consequences

European School of Molecular Medicine (SEMM) and University of Milan

Settore disciplinare: M-FIL/02

**Cancer during pregnancy: a framework for
ethical care**

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Anno accademico 2015-2016

Abstract

Cancer affects about 1 in 1000 pregnancies, which is estimated to account for approximately 5000 pregnancies in Europe each year. Despite affluent availability of clinical practice guidelines for cancer management in the course of pregnancy, there is very little ethical guidance consolidated for everyday use. Therefore, the aim of this work is to construct a framework, which would serve healthcare professionals as a reference tool when addressing ethical issues in cancer care during pregnancy.

The framework is constructed around *relational approach* to respect for patient's autonomy and *ethics of care*. It combines classical biomedical ethics principles and relational approaches to patient care. It emphasizes the importance of recognising the patient as another human being with her views on life, relationships and wishes, as well as forming a relationship between the patient and healthcare team, which is known as *relational ethics*.

However, respect for individual autonomy is not discarded entirely. First and foremost, evidence-based information disclosure is essential to personalised patient care. The latter invites to integrate technical aspects of personalised medicine with relational approach to patient care. Furthermore, protection of the vulnerable also serves as a safeguard ensuring that patient is not compelled to choices that are not her own.

Overall, this framework is expected to serve as a tool supporting ethical decision-making in cancer care during pregnancy. It can also be utilised by a variety of patient counselling services.

For those facing difficult decisions

Olga (35) lives in a remote area of the country with her husband Giulio (39) and their 5-year-old daughter Eliza. Their attempts to have a second child were marked with few miscarriages. Currently Olga is 20 weeks pregnant and her last scan revealed that they are expecting a boy. Delight and excitement, however, is overshadowed by a recent diagnosis of Olga's locally advanced, HER 2 positive breast cancer. She was offered three therapeutic options in order to treat her disease: 1) standard treatment which is not compatible with pregnancy; 2) surgery followed by adapted chemotherapy which is compatible with foetal development but has lower response rate to treatment; 3) just surgery, postponing all other treatments until after the delivery of the baby.

Giulio is categorically against any choices which could compromise Olga's chances of complete recovery and survival. He would rather have one child with a mother than raise two children as a widower. Giulio's parents and extended family share the same view and encourage Olga to fight her disease and stay alive for Eliza.

Meanwhile, Olga's treating physician Dr. Silvia feels that Olga is being compelled by her husband's family into having her current pregnancy terminated. Dr. Silvia believes that based on currently available evidence, Olga could continue her pregnancy to term while also receiving treatment for her breast cancer. Hence Olga seems to be inclined to submit to her husband's view because if she dies, Giulio will have to bring up the children on his own. Dr. Silvia feels that the developing baby also has a right to live and finds it difficult to accept Olga's reasoning. Dr. Silvia is tempted to refer Olga to another hospital with a hope that additional hurdles in accessing pregnancy termination will make Olga to reconsider her choice.

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Acknowledgements

Embracing in this work has been an extraordinary journey both professionally and personally. It was made possible by a big team of people who kindly guided me through this intellectual endeavour, helped me to overcome everyday challenges and supported me in many different ways.

I could have never succeeded to complete it without intellectual support of my supervisors who challenged and encouraged me in the course of my PhD work. I am very grateful to Prof.dr. Giovanni Boniolo, Prof.dr. Matteo Mameli and Prof. dr. Maria Rescigno for believing in my potential and directing my learning. I also owe special thanks to my internal advisor Fedro A Peccatori MD, PhD and decisional counsellor Leonora Chiavari at the European Institute of Oncology (IEO), who introduced me to the realities of cancer treatment during pregnancy, and my external advisor Prof.dr. Kris Dierickx at K.U. Leuven for methodological research guidance.

I would also like to express my gratitude to the *European Institute of Oncology* (IEO) for providing facilities and inspiring environment to work; the Graduate Office at the *European School of Molecular Medicine* (SEMM) for their devotion in helping to resolve bureaucratic puzzles; *Umberto Veronesi Foundation* (FUV) for supporting my research; supervisors, faculty and visiting scholars at the *Foundations of the Life Sciences and their Ethical Consequences* (FOLSATEC) PhD programme for helping their students flourish.

My past and present colleagues at the FOLSATEC programme also played a major role in developing my project through formal activities and informal discussions. I highly benefited from the mentoring offered by Virginia Sanchini PhD and advice shared by

Marco Annoni PhD PhD. Dorit Barlevy from the University of Basel and Mahsa Shabani from K.U.Leuven kindly shared inspiring intellectual and bibliography resources. I also benefited from the meetings and collaboration with Prof.dr. Maria Rescigno's research group.

Last but not least, none of this work would have ever reached a final stage without generous support and sacrifices made by my family. First and foremost I am indebted to my partner Albert for encouragement to embrace in this work, continue it despite numerous challenges and hurdles. His support, critique and advice while tackling philosophical puzzles and real life challenges was the driving force for me to go forward while Albert spent many months alone with our baby daughter thousands of miles away from Milan. Further, I thank my parents and other family members for their contesting but supportive approach to my work. I owe a very special thanks to my three sisters, all healthcare professionals, who were always there to give a helping hand even if being miles away.

There were many others who contributed to my success in completing this work and I am very grateful to everyone who shared this journey with me!

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Abbreviations

Due to an interdisciplinary nature of this work the extensive use of abbreviations is avoided and they are explained as they occur. Footnotes are used to explain the terms and concepts which are specific to one particular discipline. This is done to assist the readers who might not be familiar with discipline specific concepts.

Introduction

Cancer is usually considered a disease of older adults. It is not very common that it affects children, adolescents or women and men in reproductive age. Lifetime risk of developing cancer for people below 65 years of age is around 50%, which means that over half of the people will be affected by cancer at some point of their lives (Ahmad, Ormiston-Smith, and Sasieni 2015). Developing cancer under the age of 40 is still a rare event in the general population of women (Cardoso et al. 2012)(Andersson et al. 2015) as more than half of all cancer cases are diagnosed in individuals who are 70 years old or older¹. However, the Center for Disease Control in the US reports that cancer is the second most common cause of death in women between the ages of 25-34, while in women aged 35-65 cancer is the leading cause of death². Moreover, increasingly concerns are raised that cancer incidence is becoming more prevalent in all age groups around the world (Fitzmaurice et al. 2015)(Global Burden of Disease Study 2013 Collaborators 2015)(Ward et al. 2014).

The biggest coordinated attempt to advance research, train clinicians and provide care and support to cancer patients regarding fertility issues is the Oncofertility

¹ Cancer incidence by age, Cancer Research UK, <http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age> [accessed 2016-04-04].

² Leading causes of death by age group, all females-United States 2013, The Center for Disease Control (CDC) http://www.cdc.gov/women/lcod/2013/womenall_2013.pdf [accessed 2016-04-04].

Consortium³ in Chicago, USA. This is where multi-disciplinary attempts to launch a new field of oncofertility were started.

Oncofertility is perceived as “*an interdisciplinary field that bridges biomedical and social sciences and examines issues regarding an individual’s fertility concerns, options, and choices in light of cancer diagnosis, treatment, and survivorship*” (Snyder 2007). It uses expertise from different fields of research to offer state of the art services for cancer patients, their families, healthcare professionals and other support service providers. Oncofertility does not necessarily claim the status of a new independent discipline; it is rather a field where multidisciplinary expertise is merged together to *train clinicians* (Coutifaris 2012) and provide *counselling support to patients* (Jungheim, Carson, and Brown 2010).

Being a young field, it mainly focuses on fertility preservation⁴ and, in addition to practical clinical approaches, also offers some theoretical considerations on the ethical, social, legal as well as medical implications that fertility preservation practices might have in the future. Cancer care during pregnancy is not in the mainstream oncofertility debate but has its place under this wide umbrella (Wang 2012), as well as work already done in the areas surrounding fertility preservation can offer in-depth insights to ethical problems arising when caring for pregnant patients diagnosed with cancer.

For example, the last few years witnessed a release of numerous clinical practice guidelines concerning cancer management in reproductive age patients. All of them

³ The Oncofertility Consortium® is a national, interdisciplinary initiative designed to explore the reproductive future of cancer survivors <https://oncofertility.northwestern.edu/>

⁴ Fertility preservation options available for reproductive age women are embryo cryopreservation, oocyte cryopreservation (established) and ovarian tissue cryopreservation (experimental); for reproductive age men sperm and also embryo cryopreservation is available (established); only experimental ovarian and testicular tissue cryopreservation methods are available for pre-pubertal children.

unanimously suggest that fertility issues should be discussed with all cancer patients of reproductive age. Summary of these guidelines⁵ is provided in Appendix A.

Therefore, distinction has to be noted between fertility preservation for cancer patients and cancer care during pregnancy, which usually does not include fertility preserving interventions. I will start with some key findings concerning fertility preservation but my main focus through entire thesis will be on care of pregnant cancer patients.

Returning to the mainstream oncofertility findings, it is known that despite available recommendations, nearly half of reproductive age cancer patients are not given enough information about cancer treatment effect on their future fertility (Linkeviciute et al. 2014). Other studies report that cancer patients have a strong desire to be informed about fertility preservation options available to them even if they do not chose to proceed with fertility preservation for themselves (Penrose et al. 2012)(Geue et al. 2014). Moreover, fertility concerns are not limited to young and childless patients who are in a relationship (Yee et al. 2012). While patient's age, relationship status, sexual orientation, religion and/or a number of existing children should not be an indication to withhold fertility consultation, it appears to influence physicians' decision to address patient's fertility concerns (Linkeviciute et al. 2014). Unfortunately, numerous studies exploring physicians' attitudes towards fertility consultations with cancer patients report that some physicians are misled by their personal biases and do not always inform their patients about cancer treatment effect on their future fertility (Linkeviciute et al. 2014).

Discussion, however, remains open, if reservations towards fertility preservation are determined by the lack of medical knowledge, conservative attitude towards pregnancy

⁵ This summary is not a systematic review and originally was presented in Cancer Treatments Review journal (Linkeviciute et al. 2014) and was expanded based on a systematic review, which appeared in Asian Pacific Journal of Cancer Prevention (Haddadi et al. 2015).

after cancer or genuine survival fears by physicians and patients alike (Lambertini et al. 2013)(Linkeviciute et al. 2014). It has to be acknowledged that fertility preservation techniques (e.g. oocyte freezing) remain highly ineffective in some cases (von Wolff, Germeyer, and Nawroth 2015) and, in addition to therapeutic solutions they offer to cancer patients, some unintended implications also emerge⁶ (Linkeviciute et al. 2015). For example, oocyte cryopreservation for non-medical reasons might result in more women delaying pregnancy for later age, which by itself increases the risks to the mother and her foetus. Pregnancy in the advanced maternal age is also known to carry increased medical risks to the mother and the foetus due to already existing chronic conditions such as hypertension (Dietl et al. 2015), more frequent occurrences of pregnancy induced diabetes, preeclampsia (von Wolff, Germeyer, and Nawroth 2015) and placentation defects (Jackson et al. 2015).

This is especially relevant for women who are due to take hormonal therapy (e.g. tamoxifen) following their cancer treatment. Such therapies have to be taken for 5 or even 10 years following their cancer treatment and are contraindicated during pregnancy (Lambertini, Peccatori, and Azim 2015). Therefore, cancer survivors either have to wait until they finish their therapy and by that time they might already be of advanced maternal age, or interrupt their therapy, risking higher chances of cancer reoccurrence (Davies et al. 2013). One study suggests that a third of reproductive age women, who are on hormonal therapy, are willing to compromise their chances of survival by discontinuing the therapy in order to have a baby (Llarena et al. 2015) and another study reveals that similar numbers would be willing to take part in clinical trials investigating the effects of tamoxifen therapy interruption due to attempts to conceive (Pagani et al. 2015).

⁶ Declaring oocyte cryopreservation as an established procedure for fertility preservation in cancer patients (Loren et al. 2013) resulted in fast commercialization of oocyte cryopreservation for non-medical purposes (Linkeviciute et al. 2015) which raises numerous ethical, social and legal problems (Petropanagos et al. 2015).

Despite established fertility preservation methods for cancer patients and numerous recommendations to make fertility preservation consultation an integral part of cancer management, some reservations are still held based on bad or uncertain prognosis and varying effectiveness of fertility preservation procedures (Linkeviciute et al. 2014). Since some fertility preservation methods are expensive⁷ and may not be covered by public healthcare funds or an individual patient's insurance, it is reasonable to resort to it if successful pregnancy and healthy live birth can be expected to occur. For example, not all cancer survivors are going to be cured or regain good enough health to carry the pregnancy and look after the resulting children⁸. Common critiques of pregnancy attempts by cancer survivors refer to the shorter parental lifespan (Pennings and Mertes 2012), greater health problems these patients face, unrelated to cancer (Córdoba et al. 2013) and their frequent admissions to the hospital (Richardson et al. 2015) as well as potentially having less energy for looking after the children (Schover 2005). Despite the above criticisms, the debate surrounding parenthood after cancer quite often focuses on parental rights and interests to have a “completed family” (Wenzel 2005)(Niemasik et al. 2012) even if other forms of parenting are recognised as viable options for people affected by cancer (Rodriguez et al. 2013).

Despite the above concerns and reservations, cancer occurrence in the course of pregnancy is a relatively rare event. Professional societies, as the European Society of Medical Oncology (ESMO), offer an estimation that 1 out of 1000 pregnancies is complicated by cancer (Pentheroudakis et al. 2010)(Peccatori et al. 2013) which is diagnosed either during the course of pregnancy (Cardonick, Usmani, and Ghaffar 2009) or

⁷ Oocyte cryopreservation might cost up to USD 18 000 at <https://www.fertilityauthority.com/egg-freezing/cost> [accessed 2015-11-17] and slightly less in Europe: GBP 4000-5000 in the UK (Hawkes 2014), CHF 3000-5300 in Switzerland (Wunder 2013), EUR 3000 in Germany (Geue et al. 2014).

⁸ Those who want genetically related children might use surrogacy but that is an ethically, socially and legally problematic practice in itself which is not elaborated on in this work.

up to two years post-partum (Murphy et al. 2012)(Andersson et al. 2015). These numbers, however, may vary depending on the type of malignancy and the age of a pregnant woman. Research group from Catholic University of Leuven (K.U.Leuven) estimates that in Europe there might be up to 5000 women diagnosed with cancer during pregnancy every year⁹.

The most common malignancies occurring in the course of pregnancy are breast, thyroid, cervical, ovarian cancers and melanoma (Moran et al. 2007)(Pentheroudakis et al. 2010) but currently available data is limited mainly to the regions in Western/Central Europe and North America (Loibl et al. 2012)(Córdoba et al. 2013). Some recent reports suggest that other types of cancers might be more prevalent in pregnant women in specific regions such as more cases of melanoma in Scandinavia (Andersson et al. 2015) and more frequent occurrences of gastrointestinal cancer in Asia (Shim et al. 2016).

Moreover, it is plausible that these figures are going to rise as a consequence of social trend to delay motherhood for an older age (Oduncu et al. 2003)(Pereg, Koren, and Lishner 2008)(Rizack et al. 2009)¹⁰. The older maternal age is associated with an increased number of benign (Stagnaro-Green et al. 2011) and malignant tumours (Schedin 2006) as well as with various maternal and foetal health risks not necessarily related to cancer (von Wolff, Germeyer, and Nawroth 2015). Older women's attempts to take the last chance for motherhood are well document in mass media describing women in their late thirties or early forties desperately seeking assisted reproduction services with a hope for motherhood

⁹ Cancer in Pregnancy (CIP) study <https://www.uzleuven.be/en/cancer-in-pregnancy/research-project>, http://www.uzleuven.be/sites/default/files/Kanker_tijdens_zwangerschap/Poster%20CIP%20versie%20EN%20leken.pdf [accessed 2016-04-04].

¹⁰Reports show that maternal age at the birth of the first child is reaching or even exceeding 30 years of age in some developed countries (Laopaiboon et al. 2014)(Sauer 2015), including the increased number of women having their children in a very advanced maternal age, which is currently considered to be 45 years and above (Carolan 2013).

(Burrell 2014)(Kennedy 2015) with the consequence that some countries are making the attempts to introduce age limits for accessing IVF and related services at public expense (Berg Brigham, Cadier, and Chevreul 2013)¹¹ as well as due to moral concerns regarding some recent news headlines reporting women in their sixties and seventies having children with the help of assisted reproduction technologies¹².

A trend to pursue motherhood later in life is influenced by various factors as women delay childbearing for different reasons¹³ (Statista 2014). Current technologies make motherhood possible in the late forties or even after menopause, using either self-stored oocytes that have been frozen early in life, or donated oocytes. The former procedure is known as *social egg freezing* (Linkeviciute et al. 2015). The procedure is still under scrutiny by ethicists, policy makers and healthcare providers. None of the professional bodies such as American Society for Medical Oncology (ASCO), American Society for Reproductive Medicine (ASRM), European Society for Medical Oncology (ESMO), European Society for Human Reproduction and Embryology (ESHRE)

¹¹Hence some countries as for example Sweden exercise rather liberal policies offering the state funded IVF including single women (Savage 2016). Moreover, continuous attempts to create artificial gametes might change how artificial reproduction is viewed and its services organised (Cyranski 2016).

¹² Such stories are Annegret Raunigk, who at 65 gave birth to quadruplets:

<http://www.dailymail.co.uk/news/article-3200884/This-not-egotism-selfishness-like-children-65-year-old-gave-birth-QUADS-gets-ready-babies-home.html> [accessed 2016-05-19]; Indian couple in their seventies celebrate the birth of their first child: <http://www.theguardian.com/world/2016/may/12/indian-doctors-ivf-woman-70s-gives-birth-fertility-treatment-daljinder-kaur> [accessed 2016-05-19].

¹³ Even though a lot of attention is given to gender disparities in the employment market and possible exploitation of female employees by ‘forcing’ them to delay childbearing, empirical research data suggest that even bigger problem for educated career women is finding a committed partner to have family with. In popular media it is referred to as ‘finding Mr. Ready’, which invites further debates on how people view reproductive choices and what meanings they ascribe to their relationships with romantic partners.

endorsed¹⁴ it for the use by healthy patients while in 2013 it has been approved as non-experimental procedure for fertility preservation in female cancer patients by ASCO¹⁵ (Loren et al. 2013)(Linkeviciute et al. 2015). Meanwhile, success stories are reported concerning fertility preservation in cancer patients and the later use of reproductive materials for conception, such as cryopreserved embryos (Luke et al. 2016), oocytes (Perrin et al. 2016), and ovarian tissue, which remains an experimental fertility preservation technique (Demeestere et al. 2015). One recent review suggests that oocyte cryopreservation is an “established procedure” but it mainly focuses on the procedure itself and its acceptability among the patients rather than pregnancy and long-term outcomes for the children conceived from frozen oocytes (Argyle, Harper, and Davies 2016).

Facing a potentially lethal disease and expecting a baby at the same time can be challenging not only for the patient but also for her relatives, friends and healthcare team. Therefore, the knowledge about cancer effect on the course of pregnancy and pregnancy effect of the progression of cancer is of crucial importance for successful treatment of the

¹⁴ The Human Fertilisation and Embryology Authority (HFEA) in the UK, however, expresses rather flexible position stating that reproductive age women, who are concerned about their fertility decline due to age and are not in the position currently to have a baby might want to discuss oocyte cryopreservation options with their clinic. “Freezing and storing eggs” at <http://www.hfea.gov.uk/46.html> [Accessed 2016-03-16, last updated 2015-06-15]

¹⁵ Even though such fertility preservation procedure is not recommended to the healthy women as a family planning method and some countries even restricted it (e.g. China (“BBC News” 2015)), the interest has been recorded (Tan et al. 2014)(Stoop, Nekkebroeck, and Devroey 2011) and positive attitudes towards the procedure documented (Nekkebroeck, Stoop, and Devroey 2010)(Stoop et al. 2015). A possibility to preserve fertility leads to two types of future implications. Firstly, it allows cancer survivors to achieve pregnancy after fertility impairing treatment. Secondly, it allows healthy women to delay childbearing until the age when cancer becomes more common. Both scenarios raise complex ethical concerns which are intertwined with medical aspects surrounding pregnancy after cancer and/or at increased maternal age, social attitudes and expectations towards women, personal wishes and family influences on the patient’s decisions.

mother and favourable outcome for the foetus (Morice, Uzan, and Uzan 2012). Evidence-based knowledge is also essential for running patient counselling services. However, such knowledge is still being consolidated, mostly in a patchwork manner since controlled clinical trials are not always possible due to the rarity and diversity of the condition. Moreover, even evidence-based knowledge can be presented to the patients in a biased manner due to personal views held by healthcare team.

Furthermore, pregnancy occurring at advanced maternal age is associated with an increased medical risk for the mother and for the foetus (Jackson et al. 2015) but it is not always clear which risks arise due to increased maternal age and which occur as a result of using assisted reproduction technologies (Linkeviciute et al. 2015). It is known, however, that risk of cancer increases with age and women carrying pregnancies in advanced age face higher risk of cancer diagnosis due to their age. Hence, pregnancy in itself, if occurring in advanced age has not been identified as a risk factor for maternal cancer.

Meanwhile, currently available data suggests that pregnancy and maternal cancer treatment could be compatible (Amant, Vandembroucke, et al. 2015)(Cardonick et al. 2015) but there are also calls for caution when interpreting and using this data (Greene and Longo 2015)(Reichman, Eldar-Gava, and Paltiel 2016). Moreover, most studies focus on outcomes for the children born after gestational exposure to cancer treatments (Peccatori, Corrado, and Fumagalli 2015) while maternal outcomes are surrounded by much more uncertainty and potential bias¹⁶ (Royal College of Obstetricians and Gynaecologists 2011)(Andersson et al. 2015).

In general, it is accepted that cancer and its treatment can be compatible with pregnancy. However, opinions concerning maternal prognosis and children's health after cancer treatment during pregnancy are still divided. Currently available evidence can only offer some provisional guidance and decisions, concerning cancer management during pregnancy, and treatment decisions have to be taken under numerous uncertainties.

¹⁶ For example, healthy mother effect.

Moreover, careful considerations of much broader aspects than just clinical knowledge have to be considered in cancer during pregnancy care. This includes but is not limited to patient's values, preferences and impact that the decision will have on different parties¹⁷. Ethical dimensions of each case could extend far over and above the requirements of sound medical knowledge, evidence-based data and good clinical practice, neither solution could be reduced to solely consequentialist or exceptionally duty based thinking.

In this work I will show that ethical concerns are deemed to be important by clinical practice guidelines and give in depth overview of existing theoretical and practical approaches, which could offer potential solutions to ethical conflicts arising in cancer care during pregnancy. Hence, at the same time, it has to be recognised that only limited ethical guidance is available to healthcare professionals who have to manage ethical problems while caring for pregnant cancer patients and finding the solutions which best fit individual situations.

Therefore, I developed a *framework for ethical care of pregnant cancer patients*. *Firstly, I strive to assist the healthcare professionals by providing a conceptual guidance for addressing ethical issues in cancer care during pregnancy. My framework could serve as a reference tool when searching for ethically sound solutions in problematic cases. Secondly, I would like to show how theoretical concepts found in biomedical ethics¹⁸ can be incorporated in the structures of everyday clinical practice and help to deliver a higher quality care for pregnant cancer patients.*

¹⁷ Here I mean those who might be directly affected by pregnant cancer patient's treatment decisions.

Primarily these parties are pregnant woman's partner, the fetus and in some case other dependants of a pregnant woman.

¹⁸ I consistently use the term "biomedical ethics" in reference to the principles of biomedical ethics (Beauchamp and Childress 2013) and also to avoid any potential confusion concerning the diversity of the terms such as medical ethics, clinical ethics, healthcare ethics, etc. My take is that they all fit under the umbrella of *biomedical ethics*, or *bioethics*, which I perceive as a multidisciplinary field where knowledge

The material for my work is gathered by employing the classical sources and tools used in biomedical ethics. I use the principles of biomedical ethics and feminist contributions to bioethics to lay a foundational background for addressing ethical conflicts in cancer care during pregnancy. I refer to the *ethics of care*¹⁹ and *relational ethics* as feminist contributions crucial to my work. Both have been developed in the context of nursing care urging for compassion, recognition and empathy when attending to the physical needs of the patient. That closely coincides with patient-centred personalised care and personal philosophy of pregnant cancer patient. Therefore, incorporating contributions from feminist scholarship to principlism based thinking helps me to show the importance of relational approaches to patient care.

The conceptual part of the framework I build on *relational approach* to respect for patient's *autonomy* (relational autonomy) and also use three additional concepts to support my relational proposal. The supporting concepts, which I use, are the following: *evidence-based information disclosure*, *personalised patient care* and *protection of the vulnerable*. After exploring and scrutinising currently available evidence, practices and solutions for cancer care during pregnancy, I construct a framework for ethical care and discuss remaining limitations.

and expertise from different fields is merged together in order to reach sustainable solutions in ethically challenging situations in a field of biomedical sciences and medicine.

¹⁹ Ethics of care (or care ethics) forms a cluster of normative ethical theories which emphasise the importance of relationships, interaction and response criticising the application of universal standards and principles. It began with attention given to care provided by women in their own homes by pleading for redistribution of chores (van Heijst 2011). Carol Gilligan can be considered as one of the founders of care ethics as her book 'In a Different Voice' (1982) marks a landmark in understanding that male and female view morality in different terms. Other important contributions to care ethics are made by Joan Tronto, Sara Ruddick, Chris Gastmans, Michael Slote, to name just a few, whose work I found inspiring.

In order to be relevant to the actual clinical world, I took the effort and made every attempt to stay informed by available empirical evidence in clinical, biomedical and social sciences research. This includes an entire chapter devoted to an overview of clinical complexity of cancer management during pregnancy (Chapter 1), ethical concerns arising in cancer care during pregnancy, including a deep analysis of choices available to a pregnant woman, who is diagnosed with cancer (Chapter 2), physicians' and patients' perspectives towards cancer treatment and other critical conditions in the course of pregnancy as well as challenges of facing cancer and fulfilling parental commitments (Chapter 3), a systematic review of clinical practice guidelines concerning cancer treatment in the course of pregnancy (Chapter 4) and ethics support services available to healthcare professionals and patients in order to address pressing ethical problems (Chapter 5).

In terms of terminology, I tend to use “pregnancy termination” rather than “abortion” as my focus is on a very narrow set of circumstances where pregnancy termination could be considered as one of available options. I also use “interests” rather than “rights” when referring to maternal and foetal welfare claims (Chapter 2) as this work is not meant to be a legal study. Interests are also used with an intention to stay neutral concerning wider debates on pregnancy termination. In addition, evaluating foetal welfare-related interests, especially those relating to welfare of a future child often requires making judgements about parental capacities to take care of the child. The later is often limited to the scrutiny of such capacities of the mother but not others who might also be playing a role in care of the future child.

Therefore, in this work I focus more on maternal cancer and its implications on the developing foetus, such as prenatal harm and future health related welfare, but only touch a few key points from pregnancy termination debate as this is a very broad and inconclusive field in itself (Chapter 2). Furthermore, I do not harbour the ambition to make a substantial contribution to the debate concerning pregnancy termination in general. Hence, I do

explore the concept of *foetal patienthood* and spend some time discussing the role that foetal viability plays in decision-making concerning maternal cancer treatment.

It is important to note that empirical data concerning medical aspects as well as physicians and patients' attitudes and experiences are limited and should be interpreted with caution. Therefore, ***clinical practice guidelines first and foremost are aimed at guiding clinical management of cancer during pregnancy and not ethical decision-making. This signifies the importance of my work as I aim to fill this gap by laying a solid foundation for future development of a guideline focusing on ethical aspects of cancer care during pregnancy, which is thoroughly informed by evidence offered by clinical and social science research.***

For some parts of this work I used systematic review methods which are known as *empirical turn in Bioethics* and have been extensively developed by some Belgian scholars (Borry, Schotsmans, and Dierickx 2005). Depending on research questions there can be different types of systematic reviews. Initially they have been modelled mirroring the reviews of medical literature, suggesting that reviews identifying and evaluating arguments in normative ethics literature can serve as a formal tool for clinicians (McCullough, Coverdale, and Chervenak 2004).

Being systematic and recording search strategy is widely agreed to be an important feature of bioethics research (McCullough, Coverdale, and Chervenak 2004)(Strech, Synofzik, and Marckmann 2008)(Strech and Sofaer 2012)(McDougall 2015), especially following the critique that methods used by bioethicists are very diverse among and within themselves (Walker and Morrissey 2014). Diverse approaches to bioethics research reflect the multidisciplinary nature of the field but at the same time can create confusion when discoveries are compared among themselves or have to be applied practically. As a result evidence-based ethics mirroring evidence-based medicine has not been welcomed

enthusiastically (Goldenberg 2005) but it seems to provide empirical content for informed deliberation towards normative implications (e.g. guideline drafting, policy formation).

Therefore, precisely for the later reason I took an advantage of systematic review approach to ensure that relevant previous works are taken into consideration, empirical bioethics findings noted and different normative stand points presented and evaluated. I believe that systematic approach to existing literature helps avoiding biases and allows informed discussion. It also hopefully serves as a safeguard preventing cherry-picked examples and ideas used to support the author's views and safeguards objectivity.

Systematic approach is employed in numerous parts of this work when exploring existing guidelines, writing medical overview of particularities surrounding cancer treatment during pregnancy, gathering empirical data on attitudes, experiences and practices towards these unfortunate cases. Depending on the question I used different types of systematic reviews. In some cases I used systematic reviews of empirical bioethics (Strech, Synofzik, and Marckmann 2008), systematic reviews of normative bioethics literature providing arguments (McCullough, Coverdale, and Chervenak 2004) and/or reasons (Strech and Sofaer 2012) and critical interpretative literature reviews (McDougall 2015) for my background research and later refined the contents for this work through critical narrowing down. Sometimes I blend these approaches together as my primary goal was not always limited to information gathering but also interpretation and critical evaluation of existing data and ideas. Systematic review tools mainly served me as a springboard for further intellectual endeavour.

Concerning the practical applicability of my conceptual work, I show how my conceptual proposal fits in a wide variety of patient counselling services aimed at supporting decision-making processes. Approaches to patient counselling and decisional support are very diverse and practice itself is still being developed. Two mainstream approaches can be distinguished in this heterogeneous field. The first one is predominant in

the USA and Canada. It exercises an effort to resolve the conflicts and aims to offer an ethically justified solution to the problem it addresses (Tarzian 2013). The second approach found in the Western Europe and partly in the Nordic countries focuses on facilitating an ethical reflection, offering advice and support but not a resolution for troubling clinical cases (Gaucher, Lantos, and Payot 2013)(Stolper, Molewijk, and Widdershoven 2015)(Silén et al. 2015). One more model, specifically developed for Obstetrics and Gynaecology domain is known as *preventive ethics* (McCullough and Chervenak 1994). Preventive ethics model advocates for informed consent as the main clinical strategy for preventing ethical conflicts. It seeks to prevent dehumanization of the patient and dehumanization of clinician by treating female patient and pregnant patient as a unique individual with her own needs for information and desired level of participation in medical decision-making process. It is pictured as an ongoing dialogue between the patient and physician, sometimes involving negotiation and respectful persuasion (McCullough and Chervenak 1994).

The main argument I develop through the entire work is that in order to deliver ethically minded care to the patients, who are diagnosed with cancer in the course of their pregnancies, a biomedical ethics principle known as *respect for patient's autonomy* needs to be refined by recognising its socially embedded nature. The position I hold is that decisions concerning cancer treatment are not made in isolation and might have significant implications on the parties other than pregnant cancer patient herself. Therefore, a framework for ethical care is constructed around relational approach to respect for patient's autonomy and ethics of care. This does not mean that pregnant woman's autonomy regarding her medical care should be diminished or abolished. On the contrary, to empower a pregnant cancer patient to make decisions that are in-line with her values, expectations and correspond to her particular circumstances, her relationships have to be recognised and she should not be forced to ignore or abandon

them. Therefore, accommodating the respect for patient's relational autonomy I view through the prism of ethics of care which emphasises the importance of compassion, recognition and empathy from healthcare professionals. I build this on the basis offered by clinical practice guidelines (Chapter 4) informed by extensive background research concerning ethical issues arising in cancer care during pregnancy (Chapter 2 and Chapter 3). Hence, I also recognise the dangers of relational approach to pregnant woman's individuality, autonomy and personal philosophy (Chapter 6).

Therefore, I do not view maternal-fetal relationship as a fight between the two, nor subscribe to one single model of motherhood such as self-sacrifice or self-defence (McDonagh 2002). I construct my framework under the premise that most patients who are diagnosed with cancer during pregnancy have welcoming²⁰ attitudes towards their pregnancies and cancer diagnosis is compromising their protective and nurturing maternal role. Furthermore, I accept that foetuses have certain health and welfare related interests which could (and possibly should) be granted some level of protection. However, I recognise that such protection can be a two-edged sword and discuss this in more detail by examining the implications the establishment of *foetal patienthood* might have on maternal interests (Chapter 2).

Moreover, I also recognise that under some circumstances *maternal-foetal conflict* does exist and some compromises have to be made. Therefore, I analyse different positions and arguments concerning maternal and foetal interests with a significant focus on

²⁰ I chose to use 'welcomed pregnancy' rather than *planned, wanted or voluntary* to respect the previous choices patients made disregarding the circumstances of conception. Using the above term I mean that a woman accepted her pregnancy and is willing to experience some discomforts associated with carrying her pregnancy to term. Hence I recognise that there might be numerous social and political determinants of woman's choice to be in a situation where she might fall pregnant, attempt to get pregnant and remain pregnant (Torres and De Vries 2009).

justifications offered to the permissibility of *prenatal harm* (McMahan 2006) to the future child when the pregnant woman has to be treated for a disease that might endanger her own life (Chapter 2).

Such treatment decisions closely relates to a *personalised care*, where patient's values, preferences and particular ways of seeing life play an important role in medical decision-making. I use a broad definition of personalised care, taking into account patient's psychological needs, religious beliefs, cultural inclinations and ethical views (Cornetta and Brown 2013). It strongly corresponds to patient's personal philosophy, which in this work is perceived as "...a coherent and justified set of beliefs, assumptions, principles, and values each individual possesses. ...[it] characterises individual in the way [...] she sees, understands, and approaches the world, life, and death" (Linkeviciute et al. 2015). Therefore, the framework which I put together offers conceptual background built on respect for patient's relational autonomy in the context of ethics of care and relational ethics. Since my main aim is to assist healthcare professionals to address ethical issues arising in cancer care during pregnancy, I also show how it could be used by ethics support services such as ethics consultation and counselling, if and when they are deemed to be needed.

A framework I propose for ethical care (Chapter 6) focuses on the situations where a pregnant woman is diagnosed with cancer. It does not reject the principlist approach which is widely used in Western Judeo-Christian biomedical ethics (especially in the North America) but rather *delivers a balanced specification of respect for patient's autonomy principle recognising its relational segments when a pregnant woman is facing cancer diagnosis and treatment decisions such as whether to continue with pregnancy, delay treatment until after the delivery of the baby or have treatment while pregnant*. This is further elaborated through the lens of ethics of care and relational ethics. I also show how theoretical concepts can enrich patient counselling services and contribute

to a higher standard of patient care by being more patient focussed, compassionate, recognising and empathetic.

To date most more or less established ethics support services are mainly healthcare professional focused (Gaucher, Lantos, and Payot 2013)(Linkeviciute and Sanchini 2016) while ethics support for patients come in many different forms often blended with other forms of patient support (Feary 2003)(Chiavari et al. 2015)(Lawson et al. 2015)(Boniolo and Sanchini 2016). ***In this work I support the idea that patients should be recognised as active participants and, in some cases, independent ethics support service users.***

In summary, the framework for ethical care of pregnant cancer patients can be used as a reference tool when addressing ethical conflicts, it can also serve as a base for further research on clinical practices, patient experiences and attitudes as well as experiences of other stakeholders. Together with theoretical concepts which I present in this work it can be used for drafting a clinical practice guideline focusing predominantly on ethics as currently the importance of ethics is recognised but only scarcely addressed in clinical practice guidelines for cancer management during pregnancy.

Chapter 1. Cancer during pregnancy: clinical background

1.1. A complex condition

Cancers diagnosed during pregnancy are not different from those affecting non-pregnant women. However, in some cases (e.g. thyroid cancer, melanoma) pregnancy might be related to a worsened outcome (Vannucchi et al. 2010)(Khosrotehrani et al. 2011) while in other malignancies (e.g. breast cancer) pregnancy can suppress or promote the progression of neoplastic development (Schedin 2006). To date, there is no consolidated clinical opinion if pregnancy can induce the occurrence or re-occurrence of cancer and how, if at all, it correlates with maternal age²¹ other than the statistical data indicating that older people are more likely to be affected by cancer. Some studies speculate that women with preclinical malignant disease are less likely to conceive due to physiological changes induced by malignancy (Andersson et al. 2015) and might have to rely on assisted reproduction services in order to achieve pregnancy. Interventions used in artificial reproduction (Storegen et al. 2012) and the use of hormonal contraception (Cibula et al. 2010) have been also associated with an increased cancer risk but data is still lacking for drawing concrete conclusions. Moreover, the modern reproductive patterns, such as a younger age at menarche, older age at the birth of the first child and fewer pregnancies leading to increased number of menstrual cycles, are reported to contribute to the increased risk of oestrogen positive breast cancer (Aktipis et al. 2015)²².

²¹ The term ‘pregnancy-associated cancer’ is sometimes used but it usually refers to cancers occurring in the course of pregnancy or in the post-partum period indicating the correlation in time but not necessarily a causation (Ibrahim et al. 2000)(Martires et al. 2015).

²² In this work I have not explored the effect which pregnancy termination after cancer diagnosis could have on tumour development.

Expert estimations suggest that approximately 1 in 1000 pregnancies is complicated by cancer (Pereg, Koren, and Lishner 2008)(G. Koren et al. 2013). However, not all registries contain the information on how many pregnancies were terminated because of cancer diagnosis, recording just those pregnant cancer patients who decided to continue their pregnancies (Andersson et al. 2015). Such recording practices are subject to numerous biases and require caution when interpreting the numbers.

1.1.1. Clinical challenges in cancer care during pregnancy

Despite high hopes and reassuring observational data that cancer and pregnancy can be compatible with each other, some challenges still remain. One of them is *timely diagnosis* of maternal malignancy because cancer symptoms can be easily mistaken for normal physiological changes related to pregnancy. For example, enlarged breasts, constipation, aching joints, general tiredness or nausea are usual symptoms that most pregnant women experience at some point of gestation. However, there are numerous case reports confirming that the same symptoms can also be an indication of malignant disease (Jaspers, Gillessen, and Quakernack 1999)(Moran et al. 2007)(Pentheroudakis et al. 2010)(Stensheim et al. 2015). Fortunately, constant development of diagnostic tools and regular antenatal care can help to detect even asymptomatic cancers in pregnant women. For example, ultrasound scans might detect pelvic tumours (e.g. ovarian), vaginal examination might reveal potential malignant cervical changes, routine blood tests could lead to detecting thyroid abnormalities and screening for foetal trisomy is also reported to detect tumour DNA in maternal plasma samples (Amant, Verheecke, et al. 2015). All these tests are of great importance for maintaining a healthy pregnancy and detecting cancer before it progresses to an advanced stage. Such findings, however, are usually regarded as incidental findings and should be communicated to the patient with extreme caution

avoiding unnecessarily stressing the patient²³. Moreover, it is also important to consider the possibility of overdiagnosis which can lead to stress, anxiety, unnecessary testing and treatment²⁴ (Ferretti, Linkeviciute, and Boniolo 2016).

The second challenge arises when *optimal doses of therapeutic agents* need to be determined for a pregnant cancer patient. There is only scarce body of knowledge available about effectiveness of different treatment regimens when patient is pregnant. Common recommendation is that pregnant cancer patients should be treated as closely as possible to non-pregnant patients (Amant et al. 2010) but it is still unclear, what impact pregnancy specific physiological changes (e.g. hormonal balance, gut microbiota, immunotolerance towards the foetus) have on pharmacokinetics of chemotherapeutic agents. Therefore, adjusting the optimal doses of chemotherapy for pregnant patients still requires further research (van Hasselt et al. 2014). Targeted therapies are similarly under investigation with additional concerns surrounding placental crossing (Jovelet et al. 2015) and effect on the developing foetus (Lambertini, Peccatori, and Azim 2015). Decrease in maternal drug exposure due to pregnancy has been reported, but establishing dose adaptations requires further studies of pregnancy effects on pharmacokinetics of therapeutic agents used to treat cancer (van Hasselt et al. 2014).

²³This is important not only as a human factor but also as potential teratogenic exposure. Stress is shown to have a teratogenic effect on fetal development (Hansen, Lou, and Olsen 2000)(Mulder et al. 2002).

²⁴This is especially relevant to the older women who are routinely offered enrolment in cancer screening programmes and might be missing their appointments during the course of pregnancy. Hence, it is important to distinguish *preventive* (used for colorectal and cervical cancer screening) and *early detection* methods (used for breast, prostate and lung cancer screening). Preventive methods help to reduce the mortality from cancer while early detection sometimes only results in more cancer cases diagnosed in an early stage but overall mortality from screened disease remains the same (Croswell, Ransohoff, and Kramer 2010)(Wegwarth and Gigerenzer 2013).

Furthermore, alterations in maternal microbiota²⁵ during pregnancy are observed (O. Koren et al. 2012)(Rautava et al. 2012)(Mueller et al. 2015), which presupposes that response to cancer therapies can also be affected. It is thought that gut changes related to pregnancy can affect maternal response to cancer treatment as gut microbiota is shown to influence the response to chemotherapy and immunotherapy (Viaud et al. 2013)(Vetizou et al. 2015).

The third challenge complicating cancer management during pregnancy is the occurrence of *advanced maternal cancer*. This imposes two problems: 1) managing the metastatic spread of cancer and 2) prolonging mother's life to allow foetal maturity, which might include heavy sedation and in some cases keeping the pregnant cancer patient on life support.

Metastases to the placenta are rarely reported and mainly occur in advanced cancers such as bronchial carcinoma (Kochman et al. 2001), gastric cancer (Miller et al. 2012)(Chen et al. 2014), pancreatic cancer (Al-Adnani, Kiho, and Scheimberg 2007), colorectal cancer with metastases to liver (Robson et al. 2015), melanoma, metastatic lung cancer, and haematological malignancies (Al-Adnani, Kiho, and Scheimberg 2007). Even though melanoma is not the most common malignancy²⁶ occurring during pregnancy, it accounts for about a third of all the cases involving placental or foetal metastases (Valenzano Menada et al. 2010). It is a standard good clinical practice to send the placenta for histological examination after the delivery, if mother was affected by cancer during the gestation (Loibl et al. 2006)(Pentheroudakis, Pavlidis, and Castiglione 2008)(Amant et al. 2009). Foetal metastases from maternal malignancies are known to be fatal in most cases (Alexander et al. 2003). However, there are some cases reporting spontaneous regression

²⁵ Microbiota is the community of microorganisms living in symbiosis with our body.

²⁶ It appears that melanoma is the most common cancer diagnosed during pregnancy in the Nordic regions, e.g. Sweden (Andersson et al. 2015).

of foetal metastases and infants reaching a complete remission (Valenzano Menada et al. 2010) but any infant born to the mother with placental metastases has a higher risk of developing tumours and should be considered at high-risk (Alexander et al. 2003).

1.1.2. Maternal-foetal microchimerism and cancer

Pregnancy could be a potential model for further understanding how a single malignant cell could proliferate and metastasize. For example, in normal human pregnancy the development of placenta invades the uterus, and a semiallogeneic²⁷ foetus escapes the rejection from maternal immune system which is an example of immunologic tolerance (Holtan et al. 2009). Furthermore, presence of foetal cells in maternal blood and tissues, also known as *foetal cell microchimerism*, can be linked to the induction of immunological tolerance towards the foetus and also the development of autoimmune diseases (Fugazzola, Cirello, and Beck-Peccoz 2010). Interestingly, some reports suggest that foetal cells, which enter maternal circulation during pregnancy and engraft in a variety of maternal tissues, can induce the formation of blood and lymphatic vessels (Nguyen Huu et al. 2009) which play a role in maternal tumour formation. Further research suggests that in some cancers (e.g. melanoma) pregnancy induced *lymphangiogenesis* contributes to the subsequent metastases (Khosrotehrani et al. 2011). Disagreement still exists, however, if currently available evidence allows to conclude that pregnancy has an effect on the progression of melanoma (Martires et al. 2015) or the prognosis for any other types of cancer (Crivellari and Militello 2013)(Peccatori et al. 2013). In a light of differing hypothesis on foetal microchimerism and its role, some researchers take a different approach trying to understand the therapeutic uses of maternal-foetal microchimerism. As a result, suggestions are made that it is not necessarily associated with a rise in the incidence of malignant disease (Koopmans et al. 2008) but on the contrary could potentially be used to

²⁷Semiallogeneic means that two organisms share some but not all of their genes.

treat maternal tumours by using infusions of microchimeric foetal cells (Fugazzola, Cirello, and Beck-Peccoz 2010).

Furthermore, microchimerism is also shown to be a two-way process and is not limited to the presence of foetal cells in the maternal organism as maternal cells can also be transferred to the fetal tissues and remain present in neonatal organs (Srivatsa et al. 2003). It is speculated that such phenomenon might be quite common (Srivatsa et al. 2003). However, it can also have a detrimental effect on the foetus. There are two reports describing a malignant cells transfer from cancer affected mother to the foetus. They include infantile acute monocytic leukaemia, which was caused by transmission of maternal leukemic cells, and transplacental transmission of aggressive natural killer cell lymphoma (Fugazzola, Cirello, and Beck-Peccoz 2010). Fortunately, such cases of maternal cancer transfer to the foetus are extremely rare, but despite reassuring data, the interaction of pregnancy, maternal cancer and its treatment can be difficult to predict, control and manage due to multiple factors which still have to be explored, investigated and understood.

1.2. Approaches to treatment

The typical modes of cancer treatment include surgery, chemotherapy, radiotherapy and targeted therapies (summarised in Table 1.2.) The latter three can be used as curative or neoadjuvant therapies, which are usually given following or preceding the surgical removal of the malignant tumour.

Surgery is generally considered safe during the course of pregnancy. Some recommend to postpone surgery until after the 12th gestational week due to higher risk of spontaneous abortion in the first trimester, especially if surgery site is close to the pregnant uterus (Mlynarsky and Lishner 2011). Other modes of treatment initially were deferred

until after the delivery (Molho et al. 2008)(Lishner and Osadchy 2011) but growing amount of evidence suggests that standard treatment can be given to pregnant patients without adverse consequences to the foetus. Moreover, staging initially thought to be potentially harmful to the foetus, now is considered to have an added value when detecting distant metastases in pregnant cancer patients (Montagna et al. 2014).

Chemotherapy works by stopping the rapid division of malignant cells but, while this is an intention in the case for cancer, it also affects normal functioning of bone marrow, gastrointestinal tract and growth of hair follicles leading to complications such as anaemia, various infections and hair loss. Therefore, for a long time it has been thought that administering chemotherapy during pregnancy would have a detrimental effect on the developing foetus as rapidly dividing cells characterise foetal development. The breakthrough occurred after the observation that placenta plays a key role in protecting the foetus from toxic effects of chemotherapeutic agents (Dekrem, Van Calsteren, and Amant 2013). Small reports of long longitudinal studies suggest that in haematological malignancies chemotherapy can also be given in the first trimester without adverse effects to the foetus and with significant survival benefit to the mother, even if data are still scarce (Avilés, Neri, and Nambo 2012). Hence, concerns remain about the effect of chemotherapeutic agents which are accumulated in the placenta (Abellar et al. 2009)(Jovelet et al. 2015). There are not many reports on maternal adverse effects specific to pregnancy in the course or as a result of chemotherapy. As such preeclampsia was reported once (Massey Skatulla et al. 2012) with reservation that this was just an accidental occurrence. Moreover, as already mentioned, pregnancy, especially in the older women, can have some maternal health related complications not necessarily directly related to cancer (Loibl et al. 2012)(Carolan 2013)(Jackson et al. 2015)(Dietl et al. 2015).

Ionizing radiation is used in *radiotherapy* which aims to control the division of malignant cells. Generally pregnant women are advised to delay radiotherapy until after

the delivery but some argue that such recommendation is not supported by scientific evidence and can be given safely with proper shielding of pregnant uterus. The gestational radiation exposure of 0,1-0,2 Gy²⁸ and above is used as a threshold leading to mental retardation and organ malformation. It is not usually reached during the course of treatment during pregnancy (Kal and Struikmans 2005), particularly when the target is far from the uterus. A review of more than 100 cases suggests that radiotherapy could be associated with adverse outcomes to the foetus but it also cautions that not all adverse effects occurring after radiation exposure are necessarily caused by it (Luis et al. 2009). Some reports of using heavy doses of radiotherapy to control brain tumour metastasis during pregnancy suggest good outcome for the foetus (Tachibana et al. 2015). There appears to be very little data reporting long-term outcomes after gestational exposure to radiotherapy. Despite the small numbers, findings seem to be consistent and it is suggested that upper body radiation before the third trimester with a shielding of pregnancy is not harmful for a foetus (Amant, Han, et al. 2015)(Amant, Vandenbroucke, et al. 2015).

Targeted therapies are a general term for a wide range of therapies used in cancer treatment such as hormonal therapy, immunotherapy, antibody therapy, etc. The common feature they all share is that they work by aiming at a particular receptor to block one particular pathway which is responsible for malignancy inducing molecular activities. Widely held expectation is that targeted therapies might be more effective in treating certain cancers (e.g. HER2-positive breast cancer) and produce less side-effects because of specific action as compared to systemic effect of chemotherapy. Still a good number of

²⁸ There are four different but interrelated units for measuring radiation: radioactivity, exposure, absorbed dose and dose equivalent/effective dose. Radiotherapies for cancer refer to radiation absorbed dose (rad) by the patient's body which is the amount of energy that radioactive source depositing in the materials (patient's body tissues) through which they pass. One gray (Gy) is the international system of units (SI) equivalent of 100 rads, which is equal to an absorbed dose of 1 Joule/kilogram. An absorbed dose of 0,01 Gy means that 1 gram of material absorbed 100 ergs of energy (United States Nuclear Regulatory Commission 2014).

targeted agents are contraindicated in pregnancy due to the lack of clinical data about their effect on the foetus (Lambertini, Peccatori, and Azim 2015). Agents used as targeted therapies are diverse, and while some can be compared to chemotherapy because of small molecules (e.g. tyrosine kinase inhibitors - TKI); others require active transport across placenta to reach the foetus (e.g. monoclonal antibodies). TKIs raise particular concerns due to worrying preclinical and clinical data showing a potential to interfere with vital physiological functions of foetal development (Apperley 2009) but some case reports suggest normal foetal development and neonatal outcome under gestational exposure to imatinib, which is a TKI used to treat some forms of haematological malignancies and gastrointestinal tumours (Goel et al. 2013). Nevertheless, some leading experts suggest that using targeted agents during pregnancy might be possible and not all of them should be avoided completely during pregnancy (Lambertini, Peccatori, and Azim 2015)(Lishner et al. 2016). Hence, the use of targeted therapies during pregnancy cannot be presented to the patients as an established practice and each case has to be assessed individually. The adverse effects, when targeted agents are used include foetal renal insufficiency, which was reported following trastuzumab (monoclonal antibody) treatment (Gottschalk et al. 2011) and numerous other agents show embryo-toxicity, teratogenicity and might induce spontaneous abortions (Lambertini, Peccatori, and Azim 2015).

Hormonal therapies are used to manipulate the endocrine system. Steroid hormones (e.g. antiestrogens, aromatase inhibitors) can regulate gene expression in some cancer cells. Therefore, it has a potential to stop tumour growth and make it shrink. Generally it is contraindicated in pregnancy. Tamoxifen is the standard hormonal agent used in treating pre-menopausal women with endocrine-responsive breast cancer (e.g. HER2-positive, endocrine (oestrogen and progesterone) receptor positive, triple (HER2 and endocrine receptors) positive breast cancer) but due to reported congenital

abnormalities is advised not to be used during pregnancy (Azim, Peccatori, and Pavlidis 2010b).

Application of *immunotherapies* to cancer treatment is a relatively new approach. It refers to a number of treatment approaches which either activate the immune system in order to fight the malignancy or provide it with some of the components needed to boost the immune response. Not all immunotherapeutic agents share the same mechanism of action and not all of them are considered targeted therapies. Sometimes a term of *biological therapies* is used instead to better describe them. This, for example applies, to vaccines and bacteria, which are used to stimulate bodily reaction against cancer cells. Initially, the most focus was put on vaccines as studies showed that they can initiate or amplify a host organism response against evolving tumours (Siguo Hao, Moyana, and Xiang 2007). Various vaccine components activate resting dendritic cells²⁹, which migrate to a local lymph node where they display fragments of proteins in the form of small peptides, also known as antigens, to T naive lymphocytes. After this presentation, T lymphocytes become cytotoxic T lymphocytes (CTLs), which are specific and able to kill the target. More recent approaches are centred around blocking the immune checkpoint molecules with monoclonal antibodies (Drake, Lipson, and Brahmer 2013) which are artificially made immune system proteins designed to target very specific part of cancer cell. One such mechanism involves cell-surface expression of molecules that limit T cell proliferation and their killing capacity (Pardoll 2012). Molecules which show the ability to block the activity of T cells are referred to as *immune check points* (Drake, Lipson, and Brahmer 2013). Many of them are initiated by ligand-receptor interactions and can be

²⁹ The main function of dendritic cells is to act as a messenger between innate and adaptive immune system. They do this by processing antigen material and transporting it to the surface of T cells (Reis e Sousa 2004; Malissen, Tamoutounour, and Henri 2014).

blocked by antibodies or modulated by recombinant forms of ligands or receptors (Pardoll 2012).

One more option is delaying treatment until after the delivery of a baby. This is possible because not all cancer cases, especially in early stages (e.g. breast cancer), require immediate intervention, but in other cases it can lead to worse prognosis (e.g. acute leukaemia) (Shapira-Rotenberg and Lishner 2011). Therapeutic abortion or preterm delivery before initiation of maternal cancer treatment has not shown to improve prognosis (Peccatori et al. 2013).

General approach to managing cancer during pregnancy is to apply the same treatment as to non-pregnant patients as closely as possible (Helewa et al. 2002)(Cardoso et al. 2012)(Peccatori et al. 2013)(Galofré, Riesco-Eizaguirre, and Álvarez-Escolá 2014)(Ali et al. 2015) and to allow foetus to mature as closely as possible to term (Amant et al. 2010)(Loibl, Han, and Amant 2012)(Peccatori et al. 2013)(Amant et al. 2014). It is also generally accepted that pregnancy does not seem to compromise maternal survival as compared to non-pregnant cancer patients (Pentheroudakis, Pavlidis, and Castiglione 2008)(Amant et al. 2014)(Eyre et al. 2015). The latter, however, is still debated and subject of further studies.

Table 1.2. Summary of cancer therapies

Therapeutic intervention	Expected benefits	General challenges	Pregnancy specific challenges
Surgery	Removes the tumour from its locality in the body	Some cancer cells or small metastases might be left behind.	Might increase the risk of miscarriage in 1 st trimester,

		Therefore, following chemotherapy or radiotherapy treatment might be required.	especially if close to the pregnant uterus.
Chemotherapy	Acts systemically by destroying all tumour cells irrespectively from their location in the body	It has an adverse effect on other rapidly dividing cells in the body (e.g. bone marrow) which results in infections, anaemia, hair loss, subsequent infertility.	Placenta plays a key role in protecting the foetus. Gestational exposure might result in lower birth weight, preterm delivery and IUGR.
Radiotherapy	Can be targeted locally following the surgery or before it	Might result in sore skin, anaemia and tiredness, nausea, loss of appetite, subsequent infertility, and secondary cancer caused by radiation exposure.	Could cause miscarriage in early stages of pregnancy, fetal organ malformation and mental retardation. Contraindicated in third trimester as limiting fetal growth.
Targeted	Targets the tumour	Can cause rash (<i>EGFR</i>	Could cause

therapies	cells directly through their mechanism of action	<i>inhibitors</i>), high blood pressure, bleeding and slow wound healing (<i>angiogenesis inhibitors</i>), heart damage (<i>HER2 inhibitors</i>), autoimmune reactions (<i>immune checkpoint inhibitors</i>).	miscarriage, major malformations, data is still lacking for most agents.
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1.3. Maternal and foetal outcomes

Data on maternal survival and prognosis remain controversial. Despite reassuring data for some cancers (e.g. breast cancer), experts recognise that it is too early to draw concrete conclusions (Loibl, Han, and Amant 2012)(Peccatori et al. 2013)(Reichman, Eldar-Gava, and Paltiel 2016). Case reports of less frequently occurring cancers suggest that pregnant women might have a very poor prognosis in case of colorectal cancer (Jeppesen and Østerlind 2011)(Araujo Júnior et al. 2012)(Toosi et al. 2014), bronchial carcinoma (Kochman et al. 2001) and gastric cancer (Yoshida, Matsuda, and Furuya 2009) due to delayed diagnosis and also rapid progression which theoretically could be induced by pregnancy. Moreover, some malignancies (e.g. ovarian cancer) diagnosed and treated during pregnancy might be prone to reoccurrence (He et al. 2012) and also are known to have poor outcomes if diagnosis is delayed (Serkies, Węgrzynowicz, and Jassem 2011).

One more point of a concern is that women diagnosed with cancer in the first year post-partum have worse chances of survival³⁰ (Bladström, Anderson, and Olsson 2003)

³⁰ This could also be related to immunology changes induced by post-partum depression but while it is known that cancer patients who experience depression have worse treatment and survival outcomes (Kanani

and recent birth is considered to be an adverse prognostic factor among young women diagnosed with breast cancer (Whiteman et al. 2004). A study from Spain including 25 breast cancer patients, who were diagnosed in the course of their pregnancies, reports that these patients, developed numerous complications unrelated to cancer treatment (Córdoba et al. 2013). It is of a concern because it might compromise general wellbeing of these women and their foetuses and also have an effect on their ability to take care of themselves and their children.

Overall, despite high cure rates, long-term cancer survivors have an increased mortality rate (Follows et al. 2014), are hospitalized more often (Richardson et al. 2015) and young survivors (e.g. breast cancer) have poorer prognosis than older women (Whiteman et al. 2004). In addition, it is known that pregnancy rates are about 40% lower among cancer survivors as compared to general population (Peccatori et al. 2013) including the 44% higher rates of abortion among the survivors (Lambertini et al. 2013), which suggests that even if prognosis is good, the reality that patients have to face might be slightly harsher.

During the course of maternal cancer treatment no specific interventions exist to protect the foetus from the adverse effects. One exception is pelvic area shielding in case of radiotherapy, which protects the foetus from external scattered radiation but internal scatter cannot be prevented (Sylene N Han 2015).

The most recent studies investigating the foetal, neonatal and paediatric outcomes after gestational exposure to chemotherapy are very much reassuring (Cardonick et al. 2015)(Amant, Vandenbroucke, et al. 2015)(Peccatori, Corrado, and Fumagalli 2015) unanimously suggesting that children, born to mothers with cancer who have undergone chemotherapy, are developing without any major health problems which could be

et al. 2015; Vodermaier et al. 2014), it is not known what role post-partum depression plays in relation to post-partum cancer occurrence and diagnosis.

attributed to maternal cancer treatment. Hence, despite reassuring data that a good number of cancer treatments can be given to pregnant women without causing detrimental effects for the foetus, it is expected that babies born after exposure to chemotherapy are of lower birth weight, might experience intrauterine growth restriction (IUGR), and premature birth (Rizack et al. 2009)(Peccatori et al. 2013)(Amant, Vandembroucke, et al. 2015) which might have unfavourable health-related consequences later in life. Not all studies yield the same results. For example, one study found that congenital anomalies, preterm delivery, and growth restriction were not increased when exposure to chemotherapy occurred after the first trimester (Cardonick, Usmani, and Ghaffar 2009).

Gestational exposure to chemotherapy needs to be carefully planned, however. The optimal delivery timing is three weeks after the last round of chemotherapy due to expected foetal bone marrow depression, potential bleeding and increased risk of infections (Walfisch 2011). Some remaining concerns on potential foetal complications, even if they do not seem to be occurring regularly, are the possibility of impaired cognition (Nulman, Tobias, and Uleryk 2011)(Amant et al. 2012), cardiac toxicity (Gziri, Amant, et al. 2012)(Gziri, Debiève, et al. 2012), renal toxicity³¹ (Gottschalk et al. 2011), future infertility (Hahn et al. 2006), premature menopause in female offspring³² (Stefansdottir et al. 2016) and hearing loss³³(Shuai Hao et al. 2011). As already mentioned, it has to be noted that current state of knowledge suggests that these complications are rather

³¹It was reported after exposure to trastuzumab. Therefore, after accidental exposure close monitoring of the foetus with particular attention to amniotic fluid and the foetal bladder volume is recommended as they reflect foetal renal function. Low volumes of amniotic fluid could lead to foetal pulmonary problems.

³² This was observed in mice when using chemotherapy drug etoposide; mice foetuses exposed to a study drug before follicle formation reportedly had 90 percent reduction in a number of follicles. However, exposure to the same drug after foetal follicles were formed did not seem to affect future fertility of the offspring.

³³ This has only been observed in guinea-pigs when using cisplatin.

theoretical than evidence-based but caution is still warranted (Reichman, Eldar-Gava, and Paltiel 2016). Overall, experts consider the observational results on foetal outcomes to be reassuring and suggest that gestational exposure to cancer treatments is not associated with increased risk of congenital abnormalities, cognitive or cardiac impairments when adjusted and compared to healthy controls (Cardonick et al. 2015)(Peccatori, Corrado, and Fumagalli 2015)(Amant, Vandembroucke, et al. 2015).

As already noted, caution when interpreting the above results is warranted, mainly due to the rarity and diversity of the condition. Currently available data still has some limitations such as small sample sizes, data being collected from various registries with lack of valid controls, which is often done retrospectively, without rigorous systematic approaches and sometimes with methodological deficiencies (Greene and Longo 2015)(Reichman, Eldar-Gava, and Paltiel 2016). It is important to note, however, that cancer therapies are constantly changing as new are being developed. Therefore, this makes it difficult to have a long-term data on new therapies. For the time being the most knowledge on cancer treatment during pregnancy comes from retrospective studies which use cancer registries to study birth outcomes (Cardonick, Usmani, and Ghaffar 2009)(Loibl, Han, and Amant 2012), maternal survival and prognosis (Amant et al. 2013), and long-term outcomes for children who had gestational exposure to chemotherapy (Amant, Vandembroucke, et al. 2015). Some attempts to conduct systematic prospective studies on foetal cardiac function after exposure to chemotherapy are reported as well (Gziri, Debiève, et al. 2012).

Overall, there are still uncertainties remaining about cancer treatment effect on maternal cancer, its prognosis and risks it is posing to the developing foetus. There is also only limited data available on the effect that a subsequent pregnancy might have on cancer reoccurrence in cancer survivors. Concerning less frequently occurring cancers the evidence remains scarce and in some cases treating pregnant women with cancer still

might be regarded more as a research than a consolidated medical practice. In addition, not all cancer treatment regimens have been researched explicitly for cancer during pregnancy context and a significant body of knowledge still comes from animal studies such as baboon (Van Calsteren et al. 2010) and mice models (Van Calsteren et al. 2011). Moreover, the largest studies on maternal and foetal outcomes have been conducted with patients affected by the most common cancers which are breast (Loibl et al. 2012)(Amant et al. 2013) and gynaecologic malignancies (Amant et al. 2014). Therefore, it is not immediately apparent, what are the outcomes when different cancers and treatment regimens are compared.

1.4. Special circumstances

Foetuses developing the congenital tumours independently from maternal tumour status are also rare occurrences. Most common are foetal brain tumours, neuroblastomas (Reif et al. 2014), teratomas and gliomas (Vibert-Guigue et al. 2008)(Milani 2015). In the majority of cases prognosis is poor, recommended treatment includes neurosurgical tumour resection and chemotherapy (Milani 2015). Malignancies of foetal origin which metastasise to the placenta or maternal body organs are extremely rare. There have only been a few cases reported in the literature which involved tumour transmission from the foetus to the maternal part of the placenta or maternal organs (Reif et al. 2014).

Prolonging maternal life for the benefit of the foetus is a very challenging situation from numerous perspectives. The goal when putting a critically ill pregnant woman on a life support by allowing her somatic functioning to continue is to deliver a viable and healthy infant with a beneficial long-term outcome (Esmailzadeh et al. 2010). One of the largest systematic reviews on the management of pregnant brain-dead women found that out of 30 cases reported between 1982 and 2010, 12 viable infants were born and survived a neonatal period (Esmailzadeh et al. 2010). To date most reports come from patients who

experienced a fatal injury but otherwise had healthy pregnancies. Common medical problems occurring in brain-dead pregnant women include adrenal insufficiency which could lead to hypotension causing foetal hypoxia. It is also very important to maintain maternal body temperature as hypothermia might lead to intrauterine growth restriction (IUGR) and take all precautions to prevent infection (Said et al. 2013). Clinical recommendations suggest that there are no clearly indicated lower limits for gestational age which would restrict the medical efforts to support brain-dead mother and her foetus (Esmaeilzadeh et al. 2010).

1.5. Summary

Overall, currently available studies give an optimistic message, suggesting that chemotherapy (and some other treatments) can be safely given to the pregnant patients in the second and third trimesters, pregnancy termination does not improve maternal survival and that children who experienced gestational exposure to chemotherapy are developing fine (Cardonick et al. 2015)(Amant, Vandenbroucke, et al. 2015). Radiotherapy is also thought to be possible in the second trimester with some limitations due to the radiation field without compromising healthy foetal development (De Sanctis et al. 2012)(Syleny N Han 2015) while there is very little data on the use of targeted therapies.

The remaining challenges include timely diagnosis of maternal disease, choice of optimal treatment and management of advanced maternal cancer during the course of pregnancy. Speculations are still made that pregnant women have worse survival outcomes for some cancers (e.g. colorectal cancer, thyroid cancer, melanoma). Moreover, cancer survivors in general are known to have higher hospitalization rates and more health problems not necessarily related to cancer and/or its treatment. In addition, some studies report that pregnancy rates among cancer survivors are about 40% lower as compared to

the general population (Peccatori et al. 2013) and that up to 44% of breast cancer survivors who get pregnant, choose to terminate their pregnancies (Lambertini et al. 2013).

Furthermore, maternal tumour spreading to the placenta or the foetus are rare events, just as it is very rare that independently developed foetal tumours would spread to the placenta and maternal organs. There are also case reports suggesting that brain dead pregnant women could be kept on life support in order to allow foetal maturity (Esmailzadeh et al. 2010).

Chapter 2. Cancer care during pregnancy: ethical issues

2.1. Maternal-foetal conflict³⁴

2.1.1. Definition of the conflict

Looking from a clinical perspective this type of conflict occurs when optimal treatment for a pregnant woman is not compatible with a healthy development of her foetus. Historically, in the oncology context one of the most common problems was the uncertainty about maternal treatment effect on the developing foetus and future child the foetus will become. Sometimes it was presented as a choice between life and death or choice between two lives. In clinical and ethics literature it is referred to as a *maternal-foetal conflict* (Weisz, Schiff, and Lishner 2001)(Moran et al. 2007)(Patni et al. 2007) due to a potential harm that maternal treatment can cause to the developing foetus.

One of the most widely discussed conflicts is that appropriate and timely treatment for the cancer affected mother can pose high risk for the developing foetus (Weisz, Schiff, and Lishner 2001)(Backes, Moorehead, and Nelin 2011)(Del Pup et al. 2012)(Morice, Uzan, and Uzan 2012). Therefore, traditionally the view was held, that cancer treatment during pregnancy was not compatible with normal foetal development (Backes, Moorehead, and Nelin 2011) leading to either under treating a pregnant cancer patient due to a fear of foetal harm or offering inadequate therapy, which increased foetal morbidity and mortality (Oduncu et al. 2003)(Azim and Peccatori 2011). However, as it was mentioned previously, research data suggest that from a medical point of view a conflict

³⁴ The term “maternal-foetal conflict” is widely used but not everyone agrees with such usage and propose another formulation “ethical dilemmas that arise in the care of pregnant women” (Flagler, Baylis, and Rodgers 1997). Referring to maternal-foetal conflict I mean a conflict between the pregnant woman’s autonomy and/or beneficence and the best interest of the foetus.

concerning cancer treatment and pregnancy is not so severe anymore and it might be considered a *compromise* rather than a *choice* between life and death. There is a growing body of evidence suggesting that in many cases of early cancer, the treatment in the course of pregnancy is possible without adverse effects on the foetus and compromised survival of the mother (Amant, Vandenbroucke, et al. 2015). This, however, is an ideal general scenario while in reality there can be numerous factors affecting maternal and foetal outcomes in individual cases as well as future implications such as for example more frequent hospitalisations of cancer survivors (Richardson et al. 2015). The *compromise solution* when pregnant woman is critically ill is also recognised by ethics scholars suggesting that perimortem decisions should take into consideration the *wishes of the pregnant woman, foetal viability, health status of the foetus, and the views of her partner and family* (van Bogaert and Dhai 2008).

It has to be acknowledged that maternal treatment usually does not have any direct or active health-related benefit to the foetus other than increasing the maternal chances of survival. Hence, in some cases prolonging mother's life is of crucial importance to foetal development and survival, but under some other circumstances the optimal solution for the foetus would be postponing maternal cancer treatment until after the full-term delivery. Generally experts aim to save two lives by urging to seek compromise and favourable treatment solution for a pregnant woman affected by cancer and her foetus. However, if such compromise is not possible, some favour maternal health-related benefit (G. Koren et al. 2013)(Follows et al. 2014)(Amant et al. 2014) while just a few express restrictive position on pregnancy termination in case of maternal cancer (Papini et al. 2010)(De Haan, Verheecke, and Amant 2015)³⁵. The results of a systematic review of clinical practice

³⁵One of the leading researchers in Europe F. Amant, in an interviews with Cancer World expresses the position that cancer should not be seen as a reason to terminate the pregnancy and developing baby has a right to live arguing that this ethical position is based solely on clinical evidence without any influence of his

guidelines concerning cancer management during pregnancy reveal that ethical views embedded in such guidelines are diverse but leaning to giving preference to maternal beneficence (Chapter 3).

Maternal-foetal conflict can also occur in circumstances where disagreements arise between a pregnant woman and her treating physician, entire healthcare team or some of the relatives. In such situations pregnant woman's interests, as defined by her, might clash with the interests of her developing foetus, as defined by her treating physician (Fasouliotis and Schenker 2000) or other parties involved. On one hand, it can be a maternal-foetal conflict in a light of disagreement towards medical treatment options but on the other, it could also be a conflict between a pregnant patient and her physician and/or relatives, when defining and balancing maternal and foetal benefits not necessarily limited to health-related benefits. In such circumstances some scholars suggest to make a distinction between clinical and ethical decision-making (Boniolo and Sanchini 2016). Such decisions extend further and above health related decisions and might include the welfare of the future child the foetus will become, welfare of pregnant woman's family members and/or other relatives who might not be in a position to take care of the future child if the patient dies after the baby is born (Linkeviciute and Peccatori 2016). Furthermore, it can be argued that becoming an orphan at an early age could also compromise child's welfare. Hence, such concerns are not solely specific to cancer and losing one's parent or parents due to a disease does not necessarily constitute a life which is not worth living for an orphaned child.

Such disagreements might also be loaded with heavy emotions, which can be influenced by social expectations, cultural and religious beliefs. In addition, it is important to note that the pregnant cancer patient and her care providers might be facing *ethical*

personal religious beliefs: "Frederic Amant: Building the evidence base for saving mother and child" by Mark Beishon in July-August 2015. No 67. http://issuu.com/cancerworld/docs/cw67_complete_issue [accessed 2015-09-24].

*dilemmas*³⁶ which are not necessarily the same (Morice, Uzan, and Uzan 2012). Emotions and feelings are known to play an important role in our moral life. They also play a crucial role in moral judgments we make. However, relying on emotions might not be the most efficient way to reaching satisfying solutions to ethical problems. Therefore, it is argued that recognition of emotions together with reason-giving could serve better in deciding which course of action best conforms with one's goals, beliefs and values (Annoni 2016), which in this work is understood as *personal philosophy*, which implies that patient's views and beliefs play an important role in decision-making and should be addressed (Linkeviciute et al. 2015)(Boniolo and Sanchini 2016).

2.1.2. Models of pregnancy

The relationship between pregnant woman and her developing foetus is unique. Explicit understanding of maternal-foetal conflict requires explanation on how pregnant and non-pregnant women are similar and also different, and how foetuses are unique entities, which are potential human beings, but as of yet not independent. Therefore, in order to address ethical, social and legal issues arising when medical interventions are required during the course of pregnancy calls for clarification on how physical and metaphysical relationship between pregnant women and their foetuses is understood and used in medical and ethical decision-making processes.

³⁶ Ethical dilemma arises in the situation where moral principles and personal values are compromised because the agent is expected to do each of two (or more) actions but can only do one which presupposes that no matter what choice the agent makes, she will fail to do something what she ought to do (Stanford Encyclopedia of Philosophy) <http://stanford.library.usyd.edu.au/entries/moral-dilemmas/> [accessed 2016-03-25; last updated 2014-06-30]. For example, a doctor might feel obliged to treat maternal cancer and to protect the foetus; pregnant woman might feel that she has to do everything possible to overcome her disease but also avoid harming the foetus.

Pregnant woman's relationship to the foetus is still subject to clarifications due to numerous speculations concerning pregnancy, motherhood and bearing of children in general. Some distinguish *self-sacrifice* and *self-defence* models of motherhood/pregnancy arguing that the first one is a traditional model which limits our insights to an entire debate of pregnancy and pregnancy termination, while the second one is overlooked equally by pro-life and pro-choice proponents (McDonagh 2002). Self-sacrifice model presents a pregnant woman as agreeing to give up some of her interests for the benefit of her foetus while self-defence model suggests that pregnant women should have a right and means to defend themselves from pregnancies which threaten their health and might result in significant injury. Meanwhile, others argue that parental relationship in itself presupposes special responsibility to a child where parents have to be ready to make certain sacrifices, no matter the circumstances (Lee and George 2005) and therefore self-defence model is not valid alternative. Hence, I do not take a stand that pregnant woman and her foetus are in a fight against each other. My view is that in cases of maternal-foetal conflict protective and nurturing role of a would-be-mother is compromised by various circumstances pregnant woman finds herself in, be it malignant disease, financial hardship or certain expectations from her family and/or society. Therefore, disagreement or conflict *per se* is not strictly between a pregnant woman and her foetus, it could extend to a pregnant woman and her environment, particular social circumstances, health condition, and availability of resources.

Solutions to maternal-foetal conflict, however, could strongly depend on the views on pregnancy and maternal-foetal relationship. Moreover, such solutions might be influenced by societal, cultural and religious views but will mainly affect a pregnant woman and her foetus, not the society at large. Two often conflicting positions are centred on maternal autonomy and protection of the foetus (or the unborn child). The maternal autonomy centred approach could be said to be predominant in most legal systems and

ethical debates (Shanner 1998)(Fasouliotis and Schenker 2000)(ACOG Committee on Ethics 2005). Hence, there have been some cases in the USA where pregnant women were found guilty of “foetal abuse” due to their addition to alcohol or illegal substances (e.g. cocaine) while some pro-life thinkers also reject the term “unborn” suggesting to replace it with “pre-born” attributing higher moral value and more protection to the foetuses (Ruth Macklin 2014). Some have also suggested to address *foetus as a patient* (Chervenak et al. 2004)(Chervenak, McCullough, and Brent 2011) establishing a *prematernal duty* to the unborn child, which presupposes that a pregnant woman should care for her unborn child (Yeast 1995) and be ready to make certain sacrifices once she accepted to carry the pregnancy to term³⁷ (Torres and De Vries 2009) while others go even further suggesting that any burden or sacrifice a pregnant woman makes cannot be compared to the harm caused by terminating the pregnancy (Lee and George 2005).

The proponents of foetal patienthood argue that maternal autonomy plays a major role only until foetal viability is reached. Up till then a pregnant woman is free to decide if she wants to present the foetus as a patient to the physician and she can also change her mind and withdraw previously attributed patienthood status all the way until the foetus can be considered viable³⁸. During the time before foetal viability physician has autonomy and beneficence-based obligations to the pregnant woman but not beneficence-based obligation to the foetus if pregnant woman did not present it as patient to the physician. Meanwhile, after viability physician has beneficence-based obligations to the foetus as well as to a pregnant woman and therefore should protect foetal health-related interests when caring

³⁷ This point, however, is only valid for the societies where an individual woman has a freedom to decide when and with whom she has sexual intercourse, access to reliable contraception and pregnancy termination.

³⁸ It remains unclear, however, what are physician’s duties to pre-viable foetal patient when pregnant woman presents her foetus as patient and then changes her mind. Relationship between pre-viable foetal patient and a physician appears to be tentative and does not seem to require protection of the best interest of the foetus if pregnant woman withdraws foetal patient status from her pre-viable foetus.

for a pregnant patient (McCullough and Chervenak 1994)(Fleischman, Chervenak, and McCullough 1998)(Chervenak et al. 2004)(Chervenak, McCullough, and Brent 2011).

Referring to the foetus as a patient suggests that pregnant woman and a foetus can be seen as two separate entities. Separation of maternal-foetal unit is presented as one of the major critiques when addressing foetus as a patient topic (Brown 2008)(Lyerly, Little, and Faden 2008)(Rodrigues, van den Berg, and Düwell 2013). Debates separating pregnant women and their foetuses also tend to concentrate on balancing rights and interests of two parties but some argue that such attempts are deemed to fail as pregnant woman and her foetus cannot be separated from each other (Shanner 1998). Therefore, well known “violinist example” (Thompson 1971) or Thompson’s argument³⁹ is argued to be irrelevant analogy to maternal-foetal relationship (Shanner 1998). Some feminist authors suggest that medicalisation of pregnancy (e.g. ultrasound technology) contributed to the perception that foetus is a separate individual who “unfortunately” is imprisoned in maternal body (Mullin 2005)(Watt 2016). Hence from biological and physiological point of view it is obvious that foetus is dependent on the pregnant woman and it is known that it is in the best health related interest of the foetus to gestate inside of the uterus until full-term is reached. This presupposes that even if the foetus can survive outside of maternal body, its health could be significantly compromised if pre-term delivery is induced.

Furthermore, the foetal patienthood concept has another problem when applied to cancer during pregnancy cases. As the authors of the concept explain, being a patient has

³⁹ In her classical paper “A defence of abortion” Judith Jarvis Thompson invites her reader to imagine that a famous violinist is dying of a rare disease and the only way to save him is to attach his circulatory system to another person for nine months. Furthermore, Thompson speculates that should someone be kidnapped by the Society of Music Lovers and find herself in the hospital hooked up to the violinist in order to provide him with a metabolic support, she has no obligation to remain in a hospital bed next to the famous violinist for the next nine months even if unplugging herself from the violinist’s circulatory system would result in his immediate death (Thompson 1971).

two components: 1) human being is presented to the physician; 2) clinical interventions exist that are reliably expected to clinically benefit that human being (Chervenak, McCullough, and Brent 2011) but in cancer during pregnancy cases the foetus does not necessarily need an intervention for its own health benefit. On the contrary, foetus might benefit (especially concerning health-related benefits) if no medical interventions are carried out on its mother. Therefore, foetus is presented to the physician as a part of pregnant woman who needs treatment, but not as an entity requiring specific intervention for itself. This means that if cancer is diagnosed during pregnancy, it is a pregnant woman who needs treatment and, therefore, is a patient, while foetus has to bear the adverse effects not necessarily getting any kind of benefit other than remaining in a functioning maternal body until the end of its gestation. However, the later aspect is a very important benefit for both viable and pre-viable foetuses as gestating as close as possible to term has been observed to have health benefit (Loibl, Han, and Amant 2012) and could be viewed as a trade-off. Some call the notion of foetus as a patient a *cautionary concept* intended to prevent the injury to the foetuses and to spare families the distress of finding out that treatment choices made in a good faith by unfortunate oversight cause birth defects or other injuries to the future children that foetuses are due to become (Dickens and Cook 2003). The later interpretation, however, does not focus on the way how a patient is presented to the physician or direct interventions designed for the foetal benefit specifically.

Therefore, the pregnancy *embodiment model*⁴⁰ is suggested in order to address potential conflicts better (Shanner 1998). Embodiment model recognises that pregnancy is

⁴⁰ This view is gaining more recognition recently with attempts to clarify the metaphysical relationship between the pregnant woman and her foetus, especially concerning the ‘parthood’ rather than separation of the two. One such project is ‘Taking Pregnancy Seriously in Metaphysics, Ethics and Epistemology’ run by the University of Southampton in the UK

both unity and duality; that mother and foetus are not identical entities but also inseparable. It transcends, which means that a pregnant woman is experiencing a change during which she is becoming something more than her previous self or transcending the usual boundaries of self. According to this model pregnancy is seen as a gradual process where a pregnant woman is herself and another person at the same time but at birth the “other” individual fully emerges and the woman returns to a non-transcendental, non-pregnant state where she returns to being herself alone again. Moreover, pregnancy is seen as an active state (in opposition to passive)⁴¹ which requires a recognition and respect for the commitments, sacrifices, and contributions a pregnant woman undertakes in carrying a pregnancy (Shanner 1998).

As already noted, maternal-foetal conflict does not have to entail a fight for survival between the mother and her foetus. Occurrence of malignant disease in the course of pregnancy can compromise numerous plans, wishes and desires a pregnant woman was cherishing such as to be a parent, take care of one’s children, and provide her children with welfare. Therefore, even if medical aspects concerning cancer treatment during pregnancy allow uncompromised foetal development, there are also other factors to be taken into consideration. For example, financial and childcare arrangements, family situation, care required for pregnant cancer patient and her cancer care after giving birth. There are numerous everyday aspects to be thought about when addressing reproductive issues in oncology (Rodriguez et al. 2013). Hence, the view I am defending in this work is that pregnant cancer patient should not be forced into any kind of the decision while reasonable

http://www.southampton.ac.uk/philosophy/research/projects/taking-pregnancy-seriously.page#project_overview [accessed 2016-03-25; updated: no info; attended workshop: 2015-09-18]

⁴¹ Some feminist philosophers, as for example Catriona Mackenzie, argue that causal responsibility for pregnancy is shared equally by males and females but it cannot be equated to moral responsibility for pregnancy continuation because it is uniquely shouldered by females (Mackenzie 1992).

evidence-based measures are being taken to protect the welfare of her foetus and a future child this foetus will potentially become.

There have been attempts to offer theoretical justification for late and even “after birth abortion” on the grounds that the mother cannot take care of the child and has to give it up for adoption. Giubilini and Minerva argue that concerning maternal welfare it might be better to kill a healthy newborn than give it away for adoption due to stress and guilt the mother will be experiencing because of separation with a child⁴² (Giubilini and Minerva 2013). Such stand would allow waiting and seeing at birth if a newborn has been affected by maternal cancer treatment regiment and could be killed if adverse effect has been significant. Such practices could be permissible under the *Groningen Protocol* which allows performing euthanasia for severely ill infants⁴³. On the other hand, if mother was dying and did not want to leave an orphan child in the world, the child could also be killed after birth to spare the suffering for the mother, who will not be present while a child is growing up and also the suffering a child might experience by to not having a parent present while growing up. Hence such practice would also face legal challenges as in most jurisdictions one acquires legal status at the moment of birth which attributes the right to

⁴² It has to be *stressed* that ***these philosophical speculations are highly theoretical and rather serve as an intellectual exercise than a proposal for any practical solution!*** The proposal by these authors was met by a public outrage in many countries. In response the authors said that their philosophical argument was not meant to be read by lay audiences and was directed only to other bioethicists without any suggestions on what should be done or implemented as a public policy: <http://blogs.bmj.com/medical-ethics/2012/03/02/an-open-letter-from-giubilini-and-minerva/> [accessed 2016-03-29].

⁴³ Reports from the Netherlands suggest that applying the Groningen Protocol did not lead to the ‘slippery slope’ situations and shaped the medical practices towards more prenatal screening and pregnancy termination in case of foetal deformities (Verhagen 2013). However, the Groningen Protocol is still highly criticised claiming that it lacks grounding in firm moral principles (Vizcarrondo 2014).

bring up legal suit on behalf of the newborn where attempts to actively kill it would be treated as an assault.

2.1.3. Maternal death during or shortly after the pregnancy

Some women in advanced stages of malignant disease might be expressing a wish to be left alone and spared from any interventions trying to save the foetus. One of such examples is the case of Angela Carder⁴⁴, where 27 weeks pregnant woman with a terminal cancer refused Caesarean section but was obliged to have it by the court order. This case served as a landmark in establishing the priority which is given to maternal autonomy concerning medical interventions for foetal benefit. It presents a tragic scenario faced by a cancer survivor who achieved a subsequent pregnancy following her recovery but was confronted by cancer reoccurrence before reaching the end of gestation. In this case a terminally ill patient refused any attempts to prolong her life despite previous plan to continue the pregnancy until 28th week in order to reach foetal viability, and requested for palliative care at 27th week of her pregnancy due to her fast deteriorating condition. One of the reasons why hospital administration sought the court order for Caesarean section in Angela's case was that clinical knowledge, available at that time, suggested that premature babies born at the 27th week of gestation had approximately 60% chance of survival. This presupposes that hospital had reasons to believe that 6 out of 10 babies in a similar situation would have survived and therefore, felt obliged to take extended measures to try to give Angela's baby a chance to live. Given the fatal outcome, Angela's family appealed and three years later, the court order was vacated dismissing the claims for the protection

⁴⁴ This case occurred in 1987 in the USA: <http://www.nytimes.com/1990/12/08/opinion/the-fruit-of-angela-carder-s-agony.html> [accessed 2015-08-30; short description of the case]; https://www.nymc.edu/Clubs/quill_and_scope/volume2/murphy.pdf [accessed 2015-08-30; detailed case study]; (Pinkerton and Finnerty 1996)(Dickens and Cook 2003).

of foetal rights. This case became a milestone in establishing a priority that *maternal autonomy* holds in clinical decision-making surrounding pregnancy care.

But let's speculate that Angela's case unfolded in a slightly different way and her baby survived. It would be hard to imagine that Angela's family would have appealed against the enforced surgery decision if the baby lived. It also might be disturbing to think about the court, which would rule that attempts to save the baby under given circumstances were wrong when the baby is alive and developing fine. To add more complexities to the potential narratives of similar cases, we can try to imagine, how we would judge the same case if the premature baby survived but had to live with disability, which required expensive healthcare services and there were no family members, who could afford the time and resources to look after this child. This illustrates, that in addition to clinical knowledge, socio-economic circumstances and emotions also might play a significant role in decision-making process (Kanate, Auber, and Higa 2009)(Azim, Peccatori, and Pavlidis 2010a) which could present further hurdles for reaching a well-reasoned and ethically justified decision.

The case of *Susan Torres*⁴⁵ unfolded in a slightly different way. It happened in 2005 and there was no legal battle involved. Susan survived melanoma, when she was 17, after combating her disease she got married, fell pregnant and gave birth to a healthy boy. Her disease returned 10 years later and struck her at the time of her second pregnancy. Unfortunately, doctors were not able to identify the exact cause of her disease on time and at the 17th week into her pregnancy she collapsed at home and was declared brain-dead

⁴⁵http://usatoday30.usatoday.com/news/nation/2005-06-15-saving-baby-cover_x.htm [accessed 2015-08-30; reports the mother being on life support]; <http://www.lifenews.com/2005/08/03/nat-1507/> [accessed 2015-08-30; celebrates the birth of the baby]; http://www.nbcnews.com/id/9314586/ns/health-womens_health/t/baby-girl-born-brain-dead-woman-dies/#.VeLLGCXtmko [accessed 2015-08-30; reports the death of the baby]; (Gregorian 2010).

upon arrival to the emergency room. Since Susan was pregnant, she was put on the life support in a hope that the foetus could reach viability and survive⁴⁶. The foetus reached 27th weeks of gestation and Caesarean delivery was performed. A premature baby girl required numerous surgeries but died two months later. A two-year old boy was left an orphan, which might raise questions about parental responsibilities towards already existing children, when planning their reproductive lives and proceeding with new pregnancies. There was also a significant amount of money involved⁴⁷ which was later collected by Christian charities to cover the medical care expenses. Susan was kept on life support for 10 weeks while brain-dead in order to try to give her developing foetus a chance to mature.

Increasingly it becomes possible to keep pregnant patients on life support to allow foetal maturity but it also raises numerous ethical issues. Currently in case of post-mortem pregnancy, just as in ethical frameworks recognising the foetus as a patient (Chervenak et al. 2004), *foetal viability* plays a major role in determining the level of protection which the third parties owe to the foetus (Gregorian 2010). Meanwhile, legal scholars argue that pregnant woman's wishes should always be respected whatever the consequences for the foetus because enforcing actions, which are for the benefit of the foetus but in conflict with pregnant woman's wishes would sacrifice the fundamental woman's rights to bodily integrity and self-determination for the benefit of the foetus, who does not have the same moral and legal status as a pregnant woman (Lemmens 2010). However, proponents of maternal autonomy also recognise that attempts should be made to let the foetus to be born alive.

⁴⁶ Some USA states require to provide the pregnant patients with life sustaining treatment as long as they are pregnant, notwithstanding contrary instructions in patient's living will, advance directive or from a surrogate decisions maker (Mayo 2014).

⁴⁷Above mentioned sources quoted USD 400 000.

2.2. Foetal interests in a light of prenatal harm

2.2.1. Approaches to foetal interests

Foetal interests can be considered from various perspectives such as *foetus as a foetus*, *foetus as a potential person*, *foetus as a person in an early developmental stage*, *foetus as a patient*, *foetus as a future child*. In this section my main focus will be on the interests of a future child that the foetus will potentially become. However, not all foetuses, who are *potential future children*, will become *actual future children* (Callhan and Knight 1992). It can be said, however, that any future child, potential or actual, has an interest to be born healthy and have access to a reasonable welfare, which includes availability of food, clothing, safe, caring and stimulating environment. For example, reasonable welfare argument is further elaborated by some oncofertility scholars, who argue that cancer patients should only be required to provide the same level of welfare to their children as it is expected from the general population (Pennings et al. 2006)(Pennings and Mertes 2012). Furthermore, some extensive studies have been carried out exploring ethical, legal and social problems relating to the care of the unborn in the context of maternal-foetal surgery (Health Council of the Netherlands 2009). In current state of affairs it does raise more questions than answers but the very important aspect for this work is that we need to distinguish when we speak about the *foetus as a foetus* and when we refer to the *foetus as a future child*. This closely echoes with the above mentioned notion of potential and actual future children.

Moreover, there are numerous disagreements about the moral status of the foetus. One possible solution is graded moral status which can be presented by using two different models (DeGrazia 2008). The simpler one is *two-tier model* including two classes of beings with full moral status and those with lower level of moral status. The *sliding scale model* allows any number of degrees of moral status. Others, especially proponents of

seeing foetus as a patient, suggest that using the concept of moral status is futile because it does not offer any practically applicable solution and therefore, it should be abandoned (Fleischman, Chervenak, and McCullough 1998).

Whether we accept or reject the applicability of moral status for determining the foetal interests, in any case it could be argued that foetuses have an interest to continue to exist unless their life prospects as future children could be defined as *a life not worth living*⁴⁸. According to this line of reasoning terminating pregnancy because of feared side effects of maternal cancer treatment could almost never be justified unless side effects are so severe that the life of the child born is full of *unbearable suffering*⁴⁹ that it is better for such child not to have existed at all. There can be many speculations concerning the individual interests of existence and non-existence. However, most philosophers and ethicists accept that existence is better than non-existence (Hope 2004). Therefore, the standpoint in this work is that foetuses have health and welfare related interests which deserve some level of protection⁵⁰.

2.2.2. Problems with moral status of the foetus

Creators of a framework based on the concepts of “foetus as a patient” suggest to replace the moral status with the “foetal patient” where practical decisions in maternal-

⁴⁸ This is called non-identity problem, a concept developed by Derek Parfit and commented upon by many other authors <http://plato.stanford.edu/entries/nonidentity-problem/> [accessed 2016-03-25; updated 2015-09-25].

⁴⁹ This concept is mainly used in debates surrounding euthanasia and usually entails terminal illness, severe pain and no prospects of getting better; in reproductive ethics it is used when discussing welfare of children to be but is less defined and subject to the need of further specifications.

⁵⁰ This work does not have an ambition to answer the question if foetuses have a right to live. It seeks to provide a framework which would hopefully serve as guidance in finding an ethically sound balance in most cases.

foetal medicine are concerned (Chervenak et al. 2004)(Chervenak, McCullough, and Brent 2011). They are not alone. Some other scholars also acknowledge the view that focusing on moral status might be blinding to the range of features that are morally relevant in decision-making (Beauchamp and Childress 2013).

There are five main stream theories identified in the bioethics literature which could be used for attributing moral status for beings in question. However, it has to be recognised that none of these theories by themselves can resolve the questions about moral status. Hence, if taken collectively, they can provide a general framework for addressing some of the problems (Beauchamp and Childress 2013).

The first such theory focuses on *biological human properties*, where a necessary and sufficient condition for moral respect is being a living member of *Homo sapiens* species. The second theory puts emphasis on *cognitive properties* that distinguish higher level beings from lower level beings. One of the major problems with this theory is that it does not ensure that vulnerable human beings with cognitive deficiency will be morally protected. The third theory attributes moral status to those who can exercise *moral agency* by demonstrating capacity of making moral judgements on what is right or wrong and possess individual motives, which can also be morally judged. Just as the second theory based on cognitive capacities, this theory leaves those with cognitive deficiencies without the moral status. The fourth theory is based on *having consciousness*, which is understood in the form of feeling pain and pleasure and experiencing the suffering. This view distinguishes consciousness as 1) having capacity to perceive and think and 2) being sentient. From the perspective of this theory, all entities that have capacity to experience pain and suffering are considered to have a moral status because they can be morally wronged when others infringe pain and/or suffering on them. The fifth theory considers *relationships* between parties as a basis for attributing moral status. Primarily it focuses on relationships which establish roles and obligations. For example, it could be argued that human foetuses and newborns come to have a significant moral status through special

social relationships. However, some authors consider that the claim for moral status could be weaker depending on the degree of social relationships (social matrix) that foetus is a part of (Strong and Anderson 1989). Some philosophers elaborating relational theory call it a *modal-relationalism* where a being is considered to have a moral status if it is capable of having a certain causal or intentional connection with another being (Metz 2012). This fifth theory echoes with a view presented by Chervenak and McCullough (Chervenak et al. 2004) where foetal patienthood status can only be determined by a pregnant woman upon her decision to continue her pregnancy. But once foetus is considered to have reached the viability, patient status is granted automatically and pregnant woman cannot withdraw patient status from the foetus at her discretion anymore. Therefore the framework offered by Chervenak and McCullough (Chervenak et al. 2004) seem to employ *relational* (mother and foetus, clinician and foetus) together with *biological and sentience properties*. Even though they claim that the criteria of moral status is not of help in addressing the ethical problems in maternal-foetal medicine (Fleischman, Chervenak, and McCullough 1998), they appear to recognise the grading of moral status, attributing higher moral status and protection for viable foetuses (Chervenak et al. 2004)(Chervenak, McCullough, and Brent 2011).

It seems that foetal patienthood debate echoes closely with the concept of graded moral status in regard to what level of protection to foetal beneficence has to be attributed by the physician. It allows attributing moral status in the degrees increasing it with the stage of development, which is called a “principle of unequal consideration” and referred to as “balancing approach” (Beauchamp and Childress 2013). Based on the balancing approach pregnant women might be considered to have more rights, as well as higher moral status as compared to their foetuses, at least at early stages of foetal development. However, this raises the problem in the situations where foetal interests are compromised in the early stages of the development (e.g. substance abuse, which could result in permanent damage; cancer therapies administered to the mother in the first trimester).

Therefore, some pose very legitimate question of why we only offer protection to the foetuses who reached viability while pre-viable foetuses can also experience harm and in some cases it might even be more severe and life lasting in children into whom pre-viable foetuses will potentially develop (Health Council of the Netherlands 2009). The latter is discussed in more detail below concerning the paradox of prenatal harm and pregnancy termination.

2.2.3. Foetal interests in pregnancy termination debates

Two major accounts defending foetal interests can be distinguished in contemporary philosophy works concerning the termination of pregnancy which results in foetal death.

Time-relative interest account of the wrongness of killing (McMahan 2002) suggests that we need to consider not only the total amount of future value that the victim would be deprived of by death, but also the extent to which the relation of psychological unity would have held between the victim at the time of death and herself at a later time if she had not died. Such interests are determined by two factors: 1) the *total value of the future*, of which one is deprived and 2) the degree of *psychological unity* that would have been obtained between oneself at some later time. According to this account the worst time to die is a young adult while in cases of foetuses there would not be much of psychological unity with their later selves.

Future like ours account holds that abortion deprives the foetus of a valuable future (Marquis 1989). Marquis is seen to believe that the future of “standard foetus” includes a set of experiences, projects, activities, which are identical with the futures of adult human beings and are also identical with the futures of young children. It is because of the *identity relation* that holds between the foetus and the later adult that the foetus now possesses the future like ours. According to this account abortion deprives a foetus of its own future.

Therefore, Marquis contends that the loss of a future of value is a sufficient condition for the presumption that it is wrong to kill a being with such a future.

Some authors think that the fact that abortion prevents foetal future interests from occurring also means that it does not frustrate those interests. Hence both accounts are subject to critique, further developments and clarifications (Nichols 2012). Furthermore, other lines of argumentation extend to attempts to clarify if foetus is a person. On one side of the debate personhood is denied to the foetus because it is not aware of itself due to the lack of higher mental capacities or function; opponents of such view respond that definition if foetus is a person and therefore has a right to live, should not depend on its *developmental stage*, age or place (Lee and George 2005).

One of the major concerns in cancer treatment during pregnancy is the possibility that foetal health-related interests might be compromised. The extent of such harm, however, might not become apparent until foetus becomes a child or even an adult in the future. It is also difficult to predict the concrete outcomes as the probabilities of harm remain undetermined while currently available data offers assurance (Amant, Vandembroucke, et al. 2015)(Cardonick et al. 2015) caution due to remaining uncertainties is warranted (Reichman, Eldar-Gava, and Paltiel 2016).

As it is discussed in Chapter 1, some cancer therapies can be administered to pregnant cancer patients without significant side effects to the children they carry (Amant, Vandembroucke, et al. 2015) but IUGR⁵¹, lower birth weight and preterm labour have been continuously observed (Cardonick, Usmani, and Ghaffar 2009)(Peccatori, Corrado, and Fumagalli 2015). Therefore, the question still remains if terminating the pregnancy is a

⁵¹ Intrauterine growth retardation/restriction is a condition where the foetus is not growing at the normally expected rate inside of the uterus. IUGR is associated with certain health problems during pregnancy, delivery and after birth, including low birth weight, decreased oxygen levels, low resistance to infections, etc.

morally justified way of action for preventing prenatal harm, which maternal cancer treatment can cause to the foetus.

2.2.4. Complexities of prenatal harm

As it has been shown so far, cancer treatment might have an effect on the developing foetus. It does not usually cause severe deformities or impairing health conditions but could be associated with negative effect on future health as for example prematurity is known to correlate with cognitive capacities later in life (Amant et al. 2012). Many people would object the permissibility of causing foetal injury which will affect the health of the future child, even if they would justify pregnancy termination by the appeal to pregnant woman's interests. The later has been presented as a *paradox of abortion and prenatal injury* (McMahan 2006) because if we say that injuring the foetus is wrong then abortion to prevent the injury must be even more objectionable, since killing is usually more seriously objectionable than just causing an injury. Furthermore, some argue that it is justifiable to exclude pregnant women from participation in clinical trials due to a potential harm for their foetuses (Allesee and Gallagher 2011). It appears more difficult to justify a significant prenatal injury than it is to justify abortion because pregnancy termination and prenatal injury compromise *present interests of the foetus* but only prenatal injury compromises *future interests of the child a foetus will become* (McMahan 2006).

Some maternal-foetal conflicts concerning treatment incompatibilities with the best outcome for a mother and healthy development of the foetus can be at least partially resolved applying the *doctrine of double effect* (sometimes referred to as a principle or rule). The doctrine of double effect is used to justify the actions which have one good effect (e.g. saving a woman's life) and one harmful effect (e.g. terminating the pregnancy/causing an injury to the foetus). For a harmful effect to be permissible four conditions have to be satisfied: 1) the nature of the act must be good or neutral; 2) only

good effect must be intended while bad effect can only be foreseen, tolerated or permitted; 3) the bad effect must not be a means for the good effect; 4) there must be a proportionality between the good effect and the bad effect (Boyle 1991). In cancer care during pregnancy foetal deaths could possibly be justified by the proportionately grave reasons for saving the pregnant woman's life but only if foetal death occurs as a side effect of cancer treatment and is not used as a means to treat the mother (Beauchamp and Childress 2013). For example, a miscarriage or a foetal death could be justified if it occurs as a side effect of a treatment given to a mother. This also includes quite often presented case of hysterectomy where cancerous uterus has to be surgically removed from the maternal body therefore preventing the foetus from further development.

Terminating the pregnancy prior maternal cancer treatment initiation cannot be justified by the doctrine of double effect because pregnancy termination serves as a means (which could be seen as bad means) to achieve good ends (treat maternal cancer). The use of this doctrine remains controversial, especially when it comes to determining a practical way for distinguishing the intended effects from those which are merely foreseen (Beauchamp and Childress 2013). Some suggest to use the criterion of desire of bringing about the bad effect which would help to determine the responsibility for the bad effects caused (Chan 2000).

As it is illustrated above the doctrine of double effect does not offer clear cut practical guidance for clinical decisions due to uncertain distinction between intending and foreseeing the bad effect. Hence, it seems to lay a background for justifying the occurrence of prenatal harm as a result of maternal cancer treatment but not pregnancy termination to prevent prenatal injury of occurring. A debate on permissibility of prenatal injury versus pregnancy termination still continues and speculations on possible legal implications are still being made (McMahan 2006). However, the most common normative stand is that even though maternal-foetal relationship attributes certain moral rights to the foetus and

obligations to the expectant woman, such rights should not be equated to legal rights and responsibilities which could be enforced by legal structures (Post 1996).

2.2.5. *Mother and foetus: socially embedded relational unit*

As already discussed, pregnancy can be viewed as an *embodiment*, which also involves some significant costs⁵² for a pregnant woman and (in some cases) to her partner. It entails emotional and intimate relationship between the developing foetus and its parents (Watt 2016). In this light a pregnant woman and her foetus are viewed as a larger *relational unit*, where inter-subjectivity plays a key role for mutually empathetic relationship between a mother and her child to be. Such relationships are not build on individual autonomy of the mother but require the competence to create and sustain a relationship of mutual inter-dependence (Held 1993). Therefore, it can be said that emphasis on individual autonomy carries a risk of disrupting the interpersonal relationships discarding the relational aspect of woman's identity. Hence, a vast amount of potential solutions have been offered in the feminist literature, which could be collected under the umbrella term of *relational autonomy* (Mackenzie and Stoljar 2000). A relational autonomy account is considered a female-friendly account of autonomy involving the possibility to choose and live according to standards and values that could be considered one's "own", which closely relates to the concept of personal philosophy⁵³ (Linkeviciute et al. 2015)(Boniolo and Sanchini 2016).

Moreover, "socially situated" person can take responsibility for events that extend beyond her individual agency (Lloyd 2000) and can also choose not to exercise autonomy under certain conditions (Mackenzie and Stoljar 2000) because sometimes healthcare decisions are made in a state of confusion, where a patient is influenced by numerous

⁵² Here I mean the costs in a broad sense such as physical, psychological, emotional, financial, etc.

⁵³ The dangers which could compromise the expression of personal preferences in a relational autonomy context and ways to defeat them are discussed in Chapter 6.

internal and external factors such as pain, discomfort, worry, and concern for others (Dodds 2000).

The later also indicates relational features of responsibility a pregnant cancer patient might choose to take. In practice, acknowledgement of relational autonomy requires to expand our perception of respect for patient's autonomy as informed consent which is free from ignorance, coercion and impediments for decision-making capacity (Beauchamp and Childress 2013) by enriching it with social circumstances and power relationships, which might affect the patient's choices (Dodds 2000).

Even though the proposal of foetal patienthood advocates for the protection of foetal interests after the viability (Chervenak et al. 2004), it cannot not be protected as a separate entity independent from the pregnant woman. In addition, pre-viable foetuses are also subject to protection (Health Council of the Netherlands 2009), which can only be achieved if pregnant woman is willing to collaborate. However, it is important to note that when pregnant woman is facing a potentially lethal disease, her relationship with a developing foetus might be compromised by numerous other circumstances such as commitments to other children and/or relatives, stage of the disease, prognosis and available treatments.

2.4. Summary

One of the major conflicts in cancer care during pregnancy is the choice of treatment for a pregnant woman as it can have some adverse effects on the foetal development and therefore the child foetus will become.

In order to frame potential conflicts metaphysical definition of motherhood and pregnancy might be helpful. There have been some attempts to do so by distinguishing self-sacrifice and self-defence models of motherhood while also defending the embodiment model of pregnancy. The later is defined as a dynamic, transcendent and most importantly

active state of being, which requires recognition and respect for the commitments, sacrifices and contributions a pregnant woman undertakes in carrying her pregnancy.

Foetal interests are well pictured by two philosophical accounts: time-relative interest account and future like ours account. Both of them suggests that unless a life of a future child the foetus will potentially become is not worth living because it will be filled with unbearable suffering, it is in the best interest of the foetus to gestate to term and be born, even if in the course of gestation some prenatal harm will occur.

Chapter 3. Cancer and parenthood: views of affected stakeholders

3.1. Moral and social significance of having children

Overall ethical debates surrounding human reproduction seem to presume a right to genetic parenthood (Goold and Savulescu 2009)(Petropanagos 2010) and offering fertility preservation for young children and adults is argued to serve as an open future guardian (Quinn et al. 2012)(Satkoske and Parker 2013). On the contrary, some argue that value of genetic parenthood is often overemphasized in fertility related debates leading to stress, anxiety and inadequate attempts to conceive or maintain the pregnancy by people affected (Sparrow 2014).

Nevertheless, oncofertility scholars explicitly emphasize the importance that pregnancy and motherhood play in many women's perception of identity, which is formed by social expectation that women should bear and rear children (Quinn et al. 2012). They argue that fertility and/or pregnancy loss due to cancer, even if not visible directly like hair loss or surgical breast removal, can affect cancer survivor's sense of self as well as quality of life (Campo-Engelstein 2010)(Quinn et al. 2012). It can be associated with low self-esteem because of a perception that having no children or losing the ability to bear them diminishes the social value of affected women (Penrose et al. 2012).

Meanwhile, some cancer treatments are known to induce spontaneous abortions (Peccatori et al. 2013) and could lead to long lasting regret, guilt and remorse, especially in cases where pregnancy loss occurs due to a malignancy or its treatment and is accompanied by subsequent inability to conceive and bear children. However, social expectation to bear children does not necessarily mean that parenthood should be sought or maintained by any means. Some cases studies suggest that cancer survivors might feel under pressure to pursue parenthood because of social expectation to do so (Sender 2010)

while they might not have even considered having children if they were not affected by cancer. It certainly is a great goal for all cancer patients to be informed about treatment effects on their fertility and fertility preservation options. Hence, it should not be forgotten that some cancer patients and survivors might prioritize survival over ability to have children (Goncalves, Sehovic, and Quinn 2014) and not all place the same value on preserving their reproductive capacities.

Some reports conclude that cancer survivors place a very high value on having a family (Schover 2005) and, in case of pregnancy, protecting the foetus from potential harm which cancer treatment might induce (Hauenstein et al. 2010). In addition, some patients might see a therapeutic value in fertility preservation and the future prospect of becoming a parent (Goncalves, Sehovic, and Quinn 2014). It is argued that fertility preservation helps patients stay optimistic and see the future after cancer treatment but its cost and low effectiveness as well as sometimes poor prognosis indicate that it might lead to false hopes (Pennings and Mertes 2012). Moreover, the hype about fertility preservation sometimes tends to promote the view that alternatives to the genetic parenthood are only second best option (Petropanagos 2010).

Furthermore, the choice and use of contraception is also an important aspect to be discussed with cancer patients and survivors as some of them might presume that cancer treatment left them sterile while this does not necessarily happen to every patient (Sileny N Han et al. 2015). Therefore, patient counselling should include both fertility preservation options, including alternative options to genetic parenthood (e.g. adoption, foster parenting), and a discussion on contraceptive measures to prevent unwanted conception.

3.2. Parenting while facing cancer

While some cancer patients demonstrate enthusiasm (Geue et al. 2014), clinicians are reported to have reservations based on both clinical uncertainty and personal bias

towards fertility preservation procedures (Adams, Hill, and Watson 2013)(Küçük et al. 2013)(Linkeviciute et al. 2014). Despite the positive attitudes to preservation of future fertility, induced abortion rates for pregnancies after breast cancer range as high as 44% (Lambertini et al. 2013), calling for additional patient support and reproductive counselling services in the course of treatment and after cancer has been treated.

Meanwhile, there does not seem to be sufficient data showing that children born to cancer survivors are of poorer health, other than the possibility that they might have a genetic predisposition to cancer⁵⁴. Still some cancer survivors have reservations towards prospective parenthood due to health-related concerns and their future ability to care for their children. This later point is also relevant to patients who have not been affected by cancer directly but have a genetic or familial predisposition to cancer and sometimes are called cancer *previvors* (Shulman and Dungan 2010)(Werner-Lin et al. 2014). In addition, the decision to use fertility preserving biomaterial for proceeding with conception and pregnancy can be surrounded by new uncertainties, such as fear of cancer reoccurrence and implications that an attempt to have a child will have on the partner, family and child to be born (Linkeviciute and Peccatori 2016).

Addressing the needs of existing or potential children that cancer patients feel responsibility to take care of is not usually conceived as a routine cancer care, even though the estimation is that about 24% of cancer patients in treatment have children living at home (Rauch and Muriel 2004). Meanwhile, qualitative studies show that parents with cancer tend to describe their potential death as an *abandonment* of their children (Elmberger et al. 2008) and cancer affected women see it as a breach of moral

⁵⁴This problem can potentially be resolved by resorting to artificial reproduction technologies. Prenatal genetic diagnosis (PGD) can be employed for selecting embryos which are free of gene mutations associated with cancer. Hence, using assisted reproduction technologies are known to have some negative health-related effects on future children such as increase in mental health problems (Svahn et al. 2015) and imprinting disorders (Lazaraviciute et al. 2014).

responsibility in mothering (Elmberger, Bolund, and Lützén 2005). Therefore, there seems to be a growing need to understand how being a parent or expecting to become one affects individual treatment decisions and quality of life assessment. It is especially relevant in order to overcome the barriers (e.g. time constraints and perceived lack of knowledge for relevant recommendations), which clinicians face when addressing parenting concerns by adult oncology patients, (Rauch and Muriel 2004).

Overall, most studies focus on women's experience while facing cancer and juggling parental responsibilities. Experiences and support for partners who share parental responsibilities with a woman affected by cancer are poorly researched with very few studies reported (Corney, Puthussery, and Swinglehurst 2016). Inclusion of the partner appears to be abandoned area in practice as well as research.

3.3. Provisional views of affected stakeholders

3.3.1. Clinicians' perspectives

Just recently high numbers of physicians had reservations about treating cancer during the course of pregnancy (Sileny N Han et al. 2013) and were advising their patients to have an abortion based on fears that treatment might harm the foetus and that pregnancy might compromise maternal outcome (Weisz, Schiff, and Lishner 2001)(Morice, Uzan, and Uzan 2012). Delivery before initiation of maternal treatment was considered an ethical approach when managing cancer during pregnancy cases (Oduncu et al. 2003). Concerns surrounding fetal safety and maternal prognosis are still relevant today but there is also more scientific assurance concerning the outcomes when cancer is treated during the course of pregnancy (Amant, Vandenbroucke, et al. 2015). Common agreement among the leading experts is that pregnancy termination does not have a survival benefit for the mother (Marsden et al. 2010)(G. Koren et al. 2013) but some reservations are still held due

to the “healthy mother effect”⁵⁵ (Royal College of Obstetricians and Gynaecologists 2011)(Andersson et al. 2015).

One study exploring the attitudes and practices of the European oncologists found that out of 142 physicians working in cancer and/or pregnancy care 44% would prefer pregnancy termination if cancer was diagnosed in the first half of pregnancy, 58% would delay maternal treatment and initiate early delivery if cancer was diagnosed in the second half of the pregnancy and 37% would not give chemotherapy or radiotherapy during pregnancy (Sileny N Han et al. 2013).

Few insightful reports can be found in fertility preservation for cancer patients’ studies done by oncofertility scholars. Despite existing guidelines and fertility preservation methods as well as recorded wishes of cancer patients to be informed about fertility preservation options available to them, significant numbers of physicians worldwide still choose not to include discussion about reproduction in their consultation (Linkeviciute et al. 2014). We reviewed physician survey studies from the UK, Japan, Saudi Arabia, Turkey, Iran and the USA, which reported fertility preservation practices and factors influencing physicians’ decision to discuss reproductive issues with cancer patients. Our review found that only British and American physicians include a discussion about patient’s reproductive concerns in their consultation. Moreover, some physicians have numerous biases concerning the initiation of a conversation concerning fertility and cancer. Such biases are based on social issues, patient’s age, gender, race, sexual orientation, marital status, existing children and medical prognosis, and in some cases religion

⁵⁵‘Healthy mother effect’ implies that only those women who feel healthy and are able to cope with a disease continue with pregnancy after cancer diagnosis or seek pregnancy after cancer was cured, agree to be in the registries and participate in follow-up programmes, while those who have health problems are less enthusiastic and get lost in the follow-up. Recent study reports that only 37% of young breast cancer patients were interested in a study of endocrine therapy interruption to allow pregnancy (Pagani et al. 2015).

(Linkeviciute et al. 2014). Overall, general tendency in most studies appears to be that physicians are concerned about patient prognosis and type of cancer which make them reluctant to allow any treatment delays if patient decides to explore fertility preservation options. In addition, the British, Japanese, Turkish and Iranian doctors report that the lack of knowledge about reproductive issues in oncology and consultation time constraints are among the reasons why they do not bring fertility preservation to the patient's attention (Linkeviciute et al. 2014). Similar trends are reported in previously described study exploring physician's attitudes towards cancer treatment during pregnancy by Han and colleagues (Sileny N Han et al. 2013).

Another interesting study from the USA explores physicians' attitudes towards conscientious objection towards medical procedures which are legal but not in line with physician's moral values and beliefs. Out of 1144 American physicians representing different specialties 86% believed that physicians are obliged to present all available treatment options for their patient but only 71% agreed that in case of moral objections the physician should refer the patient to another physician (Curlin et al. 2007). The later suggests that depending on moral convictions which the physician harbours, her patients might not be referred to another physician and the treating physician might consider this to be an ethical practice.

Furthermore, cancer care during pregnancy is complicated by the fact that multidisciplinary team has to be involved. Therefore, perspectives of other specialty doctors are also very important. For example, an Australian study reporting attitudes and beliefs of 336 midwives and doctors conclude that they are inconsistent in their responses concerning pregnant women's right to take a final decision in regard to their care (Kruske et al. 2013). Same study also found that doctors hold different attitudes as compared to midwives concerning the competency to make the final decision, which could possibly be closely related to legal accountability attached to medical decisions. However, some

healthcare providers tend to believe that they are legally and morally responsible for the foetus, which could be used as a justification to override the needs of a pregnant woman (Kruske et al. 2013). Meanwhile, from a legal point of view it has been established that maternal autonomy should prevail concerns about the foetus because until it is born, foetus is not considered a legal entity in most jurisdictions.

3.3.2. *Patients' perspectives*

Unfortunately, to date there are no systematically collected empirical data reporting experiences, attitudes and choices of the patients who experienced cancer and pregnancy at the same time. However, there are two studies conducted in the UK reporting patient experiences from participation in *ORACLE* (Kenyon et al. 2006) and *Magpie Trial* (Smyth, Jacoby, and Elbourne 2012)⁵⁶.

Both studies explored the experiences of pregnant women who took part in randomised clinical trials for the critical conditions, which posed medical risks to themselves and their foetuses. The *ORACLE* investigated the possibility that treatment with broad spectrum antibiotics prolongs labour and improves neonatal outcomes in women who are less than 37 weeks pregnant and experiencing either pre-term labour or premature rupture of membranes (Kenyon et al. 2006). The *Magpie Trial* investigated a prophylactic use of anticonvulsants (magnesium sulphate) for women with severe preeclampsia, which also run the QUOTE (Qualitative Understanding of Trial Experience) Study (Smyth, Jacoby, and Elbourne 2012). After interviewing the *ORACLE* participants, the researchers found that participants attributed a high value to interaction with healthcare professionals and also put a lot of trust on them when making a decision to joining the trial. Moreover, most *ORACLE* participants expected that by joining the trial their babies might

⁵⁶ I am also aware of some ongoing studies exploring experiences and attitudes of pregnant cancer patients, but at the time of thesis submission, none of the findings have been published yet.

benefit and this was a pre-condition for altruistic motivation to benefit others who might be in a similar situation in the future (Kenyon et al. 2006). The second study, which interviewed the participants of a Magpie Trial, found that self-interest was a key motivating factor to participate in clinical trial. Major motivating factors were identified as *self-benefit* (trial might help to treat preeclampsia), *benefit to their child* (treatment might minimise the associated risks of preeclampsia to the unborn baby) and *altruism* (participation might help future women or is for the good of medical science). This study also showed that although some women sought the opinion of family members and friends, they had little involvement or influence on the women's decisions. Partners played a role in providing a second opinion for many women but study participants dismissed the idea that their relatives or friends were in the position to influence their decision (Smyth, Jacoby, and Elbourne 2012).

Two studies offer just a provisional insight to pregnant women's experiences, when they face critical conditions, because both of them were conducted in the same country (the UK) and focused on participation in randomised controlled trials rather than therapeutic treatment decisions. This, however, is very much relevant to cancer management during pregnancy because it might be reasonable to think that women being treated for cancer during pregnancy should be asked to take part in clinical trials and/or enrol in registries, so clinical knowledge about this rare co-occurrence could be better consolidated. Hence, it is also important to note that above discussed studies show that pregnant women's decision to take part in clinical trials are led by the expectation of self benefit which could be considered a therapeutic misconception and require further ethics foresight.

3.4. Summary

Parenthood plays an important role in human life but parenting concerns of cancer patients remain highly unexplored topic. Physicians are reported to give preference to the maternal wellbeing and would also recommend pregnancy termination to avoid prenatal

harm, when cancer has to be treated in the course of pregnancy. Meanwhile, studies of pregnant patients in critical conditions report that they attribute high value to the interaction with healthcare professionals and trust them to guide decision-making process, expect that treatment for their disease will also benefit the developing baby, and interestingly, it appears that family members and friends play a supportive role but have little involvement or influence on decisions pregnant women take. Hence the views, attitudes and experiences from pregnant women who were diagnosed with cancer are still missing and it remains a significant gap in knowledge required for a development of ethical care guidelines.

Chapter 4. Clinical practice guidelines: a review of ethics content

4.1. Methodological background

In this part of work I use a systematic review of clinical practice guidelines concerning cancer management in the course of pregnancy, in order to find out what ethical concepts are mentioned and which ethical standpoints adopted in these documents.

Systematic reviews are common in clinical research but some authors also propose to transfer PICO (Population, Intervention, Comparison, Outcome) model used in biomedical literature to systematic reviews of reasons in bioethics (Sofaer and Strech 2012), where “outcome” is supposed to help to evaluate ethical justifiability of chosen action (Sofaer and Strech 2011). However, evaluating the reasons or arguments provided in normative bioethics literature can be a challenging task because identifying all the relevant literature on a particular topic in bioethics can be very time consuming and not always possible due to high volumes of grey literature⁵⁷.

Therefore, some argue that even though doing the search systematically should be maintained in bioethics research, the type of systematic review will depend on the research question (McDougall 2015). In some cases, identifying all the literature concerning a particular question might not be feasible and even if it is, the time spent will not add significant value to the research (McDougall 2014) as “broad brush” approach can yield the same information. Systematic reviews can provide a greater variety of reasons or arguments but the proponents accept that the review itself does not involve or replace the critical analysis of the materials collected (Sofaer and Strech 2012). That is why some

⁵⁷ The sources referred to as grey literature mainly constitute of books and edited book volumes, which are not indexed in major data bases.

advocate a turn to *critical interpretative reviews* which might better serve bioethics research purposes (McDougall 2015).

I took a combined approach. Clinical practice guidelines can be identified using the search strategy common in biomedical and clinical literature reviews and then I explored the ethics content in these guidelines by adopting a critical interpretative approach.

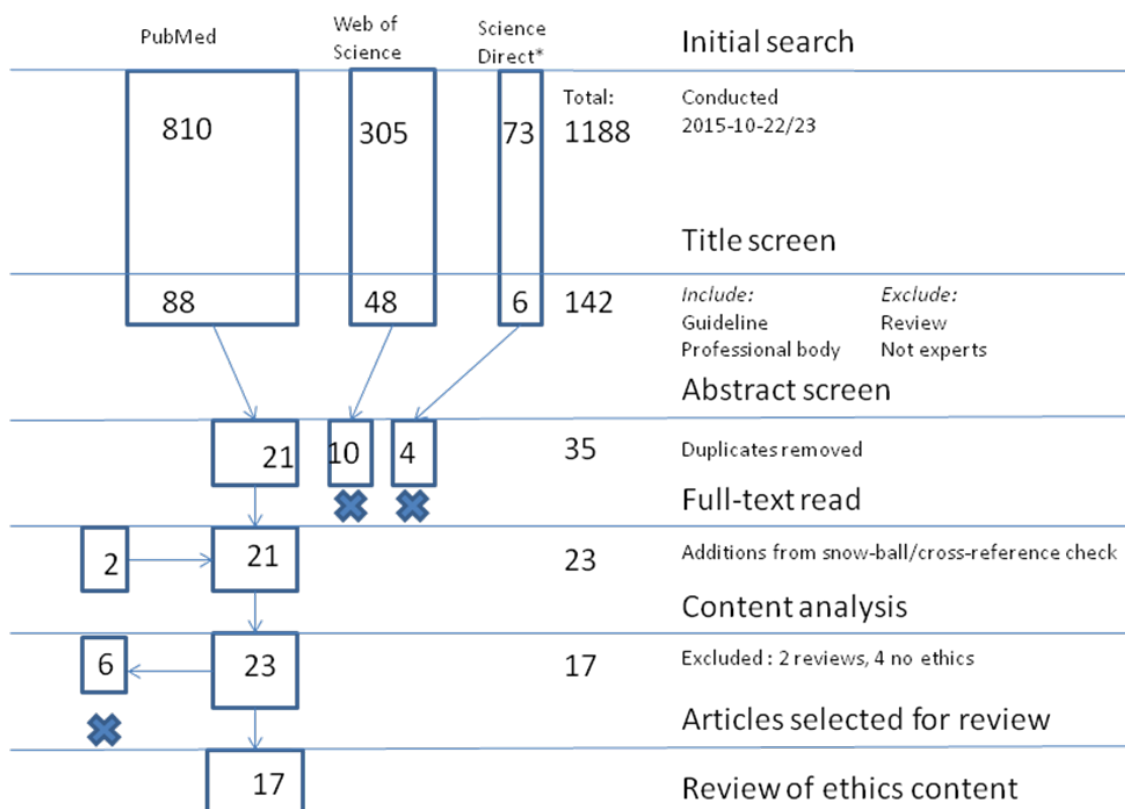
4.2. Identification of relevant documents

A systematic review tools were used in this part of work (McDougall 2014). The *PubMed*, *Web of Science* and *Science Direct* data bases were searched in order to identify the relevant clinical practice guidelines concerning cancer management in the course of pregnancy published in English language without time limits. A string of search terms (pregnancy AND cancer AND guideline*) was chosen to be used with an intention to identify the documents which healthcare professionals would turn into when in search for practical guidance in managing cancer during pregnancy. Therefore, the following inclusion criteria were set up: 1) articles and expert meeting reports which clearly state that they aim to provide clinical practice guidelines or recommendation for cancer management during pregnancy; 2) publications were released, reviewed or endorsed by a professional society representing clinicians practicing in a clinical field relating to oncology.

Reviews stating that their primary objective is to provide guidelines for management of tumours diagnosed during pregnancy but not related to any professional organisation were excluded due to a potential opinion bias, presuming that guidelines relating to professional clinical organisations would present more objective, better researched and balanced view. The last search was performed on October 22-23, 2015. The search strategy is presented in Figure 4.2., which describes the search findings in a flow chart. The initial search in three data bases yielded 1188 articles. Title screen reduced the selection to 142 papers which were selected for abstract read and 35 papers meeting the

inclusion criteria were selected for full-text read. Discarding the duplicates reduced the collection to 21 articles to which 2 articles were added after cross-reference check (snow-balling). Full-text read revealed that 2 papers were reviews without professional organisation affiliation and 4 guidelines did not mention anything what could be considered as ethics content. The final collection constitutes of 17 articles which are released or endorsed by a professional society or a much focused expert group and offers clinical guidelines for cancer management during pregnancy. Summary of these guidelines is presented in Table 4.2.

Figure 4.2. A flow chart of a systematic review



*Full-text search yielded 21 172 results, which was narrowed down by searching only the titles, abstracts and keywords, which represents 73 articles

Table 4.2. Summary of the clinical guidelines for cancer management during pregnancy

Reference;	Guideline	Management recommendatio	Patient support	Ethical content
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Organisation	description	n		
Ali et al. 2015 (Ali et al. 2015); UK-based medical practitioners with expertise in acute myeloid leukaemia (AML) , reviewed by Haemato-oncology Task Force of the British Committee for Standards in Haematology (BCSH), British Society of Haematology (BSH), UK AML National Cancer Research Network (NCRN)	Offers a uniformed consensus which, due to scarcity of the literature, is mainly based on expert opinion than trials for treating AML patients. Includes grade of evidence for all clinical recommendations	Management by multidisciplinary team; Pregnant patients with AML should be treated without delay after full and frank discussion; Beyond 32 weeks gestation it might be reasonable to deliver the foetus before chemotherapy	The women should be fully informed about the diagnosis, treatment of the disease and possible complications ; Reasons for and against elective termination should be discussed with a patient; Offer parents reassurance on baby's health by performing tests and follow-up during infancy	Considerations should be given to the health of both mother and foetus and informed wishes of the patient (<i>enabling patients to take informed decisions, respect for patient's autonomy; balancing maternal and foetal beneficence</i>)
Follows et al 2014 (Follows et al. 2014); UK-based medical experts and patients' representatives; revised by Haemato-oncology Task Force of the British Committee for Standards in Haematology (BCSH)	The guideline for first line management of classical Hodgkin lymphoma	The priority must be the health of the mother and, ideally, management should be in conjunction with an obstetrician experienced in high-risk pregnancies	Patient's personal priorities should be taken into consideration when making treatment decisions	Attention to patient's personal wishes (<i>respect for patient's autonomy</i>); Maternal health and wellbeing should prevail (<i>maternal beneficence</i>)
Amant et al 2014 (Amant et al. 2014); European Society of Gynecological	Provides timely and effective guidance for pregnant women and	To maximize the maternal outcome, cancer treatment	Individualization of the treatment and effective	Maximizing maternal outcome (<i>maternal</i>

<p>Oncology (ESGO) task force "Cancer in Pregnancy" in concert with other international experts</p>	<p>health care providers to optimize maternal treatment and foetal protection and to promote effective management of the mother, foetus, and neonate when administering potentially teratogenic medications in <i>gynaecological malignancies</i></p>	<p>should follow a standard treatment protocol as for non-pregnant patients;</p> <p>Despite limited evidence-based information, cancer treatment during pregnancy can succeed;</p> <p>Iatrogenic prematurity should be avoided;</p> <p>State-of-the-art treatment should be provided for this vulnerable population to preserve maternal and foetal prognosis.</p>	<p>psychological support is imperative to provide throughout the pregnancy period</p>	<p><i>beneficence</i>)</p> <p>Best treatment for vulnerable population [pregnant women with cancer] (<i>protection of the vulnerable</i>)</p>
<p>Peccatori et al. 2013 (Peccatori et al. 2013); European Society of Medical Oncology (ESMO), endorsed by Japanese Society of medical Oncology (JSMO)</p>	<p>Provides Clinical Practice Guidelines for managing patients diagnosed with cancer during pregnancy and provide guidance on fertility considerations for women desiring pregnancy following cancer diagnosis (<i>breast, cervical, lung cancer,</i></p>	<p>Referral to institution with expertise;</p> <p>Multidisciplinary team;</p> <p>Standard chemo might not be feasible in all cases;</p> <p>Target full-term delivery whenever possible;</p> <p>Pregnancy termination strongly discouraged</p>	<p>Involving a partner and family in decision-making process;</p> <p>Multidisciplinary care and counselling</p>	<p>Partner and family involvement in decision-making (<i>respect for relational autonomy</i>)</p>

	<i>leukaemia</i> and other tumours)			
Koren et al. 2013 (G. Koren et al. 2013); Chemotherapy During Pregnancy Working Group, approved by the Society of Obstetricians and Gynaecologists of Canada (SOGC)	Reflects clinical and scientific advances and offers recommendations concerning chemotherapy use in pregnant women and women if child bearing-age	It is important to balance maternal and foetal risks; Decisions should be made individually for each patient; Multi-disciplinary team, including physicians and social workers, psychologists, spiritual advisors	Discuss the available options with pregnant patient and her family	Partner and family involvement in decision-making (<i>respect for relational autonomy</i>); Maternal health and wellbeing should prevail (<i>maternal beneficence</i>)
Cardoso et al 2012 (Cardoso et al. 2012); European Society of Breast Cancer Specialists (EUSOMA)	Position paper, recommendations for treating young women with breast cancer	Pregnancy after breast cancer should not in principle be discouraged	Issues of body image, sexuality, fertility and lactation must be discussed with young women with breast cancer; Counselling for family planning and contraception; Involve the partner if present	Informing the patient about treatment effects and family planning (<i>enabling patients to take informed decisions; respect for patient's autonomy</i>); Partner involvement in decision-making (<i>respect for relational autonomy</i>)
Dauer et al., 2012 (Dauer et al. 2012); Society of	Intends to assist interventionalists and their	Interventions should be justified with	Pregnant patients should	Provide counselling

<p>Interventional Radiology and the Cardiovascular and Interventional Radiology Society of Europe, endorsed by the Canadian Interventional Radiology Association</p>	<p>staff in managing and counselling pregnant patients who need <i>fluoroscopically or CT-guided interventional</i> procedures</p>	<p>the aim for doing more good than harm;</p> <p>Concern about the possible side effects of ionizing radiation exposure on the conceptus [foetus] should not preclude medically indicated diagnostic or interventional x-ray procedures when the medical benefit for the mother is justifiable;</p> <p>Conceptus doses lower than 100 mGy should not be considered a reason for terminating a pregnancy</p>	<p>be counselled based on sound information about the risks of radiation exposure;</p> <p>If possible pre and post procedure counselling should take place involving the mother and the father</p>	<p>support to patients (<i>enabling patients to take informed decisions</i>);</p> <p>Abortion is an individual decision affected by many factors (<i>respect for patient's autonomy</i>);</p> <p>Partner involvement (<i>respect for relational autonomy [indirect reference]</i>)</p>
<p>De Groot et al 2012(De Groot et al. 2012); Endocrine Society Clinical Practice Guideline (US), reviewed and commented on by members of The Endocrine Society, Asia and Oceania Thyroid Association, and the Latin American Thyroid Society</p>	<p>Updates the guidelines for the management of <i>thyroid dysfunction</i> during pregnancy and postpartum published previously</p>	<p>No clear evidence that pregnancy worsens the survival of pregnant patient</p>	<p>Information for the patient making the decision about breastfeeding</p>	<p>Provide information for the patient(<i>enabling patients to take informed decisions; respect for patient's autonomy [indirect reference]</i>)</p>
<p>Royal College of</p>	<p>Provides</p>	<p>Suggests</p>	<p>People with</p>	<p>Informing the</p>

<p>Ob/Gyn, 2011(Royal College of Obstetricians and Gynaecologists 2011); Royal College of Obstetricians & Gynaecologists</p>	<p>clinical guidance to health professionals caring for women of childbearing age with a diagnosis or history of breast cancer. Green-top guideline No.12</p>	<p>auditing the referrals and outcomes</p>	<p>cancer should be fully informed of potential gonadotoxicity before treatment, and specialist psychological support and counselling should be available; Involve a partner in a discussion with a multidisciplinary team</p>	<p>patient about treatment effects (<i>respect for patient's autonomy</i>); Partner and family involvement in decision-making (<i>respect for relational autonomy</i>)</p>
<p>Amant et al., 2010(Amant et al. 2010); an international expert Panel</p>	<p>Provides guidance for clinicians about the diagnosis, staging and treatment of breast cancer occurring during an otherwise uncomplicated pregnancy</p>	<p>Serious consideration should be given to continuing of pregnancy whilst treating cancer; Delivery should not be induced before 37 weeks as morbidity mainly associated with prematurity; Treatment should adhere as closely as possible to standard protocols; Breastfeeding shortly after chemotherapy not recommended</p>	<p>Multidisciplinary team should provide patient with clear explanation of treatment options</p>	<p>Seriously consider continuing of pregnancy whilst treating cancer (<i>balancing maternal and foetal beneficence, protection of the vulnerable [indirect reference]</i>); Provide information for the patient(<i>enabling patients to take informed decisions</i>)</p>

<p>Marsden et al 2010(Marsden et al. 2010); endorsed or had an input from U.K. Melanoma Study Group, the British Association of Dermatologists, the British Association of Plastic, Reconstructive and Aesthetic Surgeons, the Royal College of Physicians, London, the Association of Cancer Physicians, the Royal College of Radiologists, London, the Royal College of Surgeons of England, the Royal College of Pathologists (pathology section only), the Royal College of General Practitioners, London, and the Department of Health</p>	<p>Guideline for management of <i>cutaneous melanoma</i> presents evidence-based guidance for treatment, with identification of the strength of evidence available at the time of preparation of the guidelines, and a brief overview of epidemiology, diagnosis, investigation and follow up.</p>	<p>Chemotherapy does not have survival benefit in IV stage;</p> <p>Melanoma can metastasize to the placenta and foetus more frequently which has poor prognosis for the mother and the baby</p>	<p>Social and family effects of developing recurrent melanoma during pregnancy or after birth are great. Counselling recommended.</p>	<p>Provide support, information and education to patients (<i>enabling patients to take informed decisions; respect for patient's autonomy</i>)</p>
<p>Papini et al 2010(Papini et al. 2010); Joint statement for clinical practice by Italian associations on thyroid cancer</p>	<p>Provides guidance to thyroid nodule and differentiated <i>thyroid cancer</i> management in pregnancy</p>	<p>Most tumours are slow growing and surgery after the delivery will not change the prognosis;</p> <p>Pregnancy should never be interrupted</p>	<p>Assurance about prognosis should be given to the affected patients</p>	<p>Never interrupting the pregnancy (<i>foetal beneficence but also care and support for the expectant mother</i>)</p>

<p>Pentheroudakis et al. 2010(Pentheroudakis et al. 2010); European Society of Medical Oncology (ESMO)</p>	<p>Provides a guide with scientific levels of evidence for management of <i>breast and cervical cancers, and melanoma</i></p>	<p>The optimal therapeutic strategy should be jointly chosen by the medical team, patient and family and will depend on gestational age, nature and stage of cancer, treatment options and patient wishes</p>	<p>All patients at risk of infertility who have not completed childbearing should discuss germ-line storage options with a medical team</p>	<p>Partner and family involvement in decision-making <i>(respect for relational autonomy)</i></p>
<p>Amant et al., 2009 (Amant et al. 2009); international experts in the field</p>	<p>Suggests models for treatment of <i>gynaecologic cancer</i> in pregnancy</p>	<p>Randomised trials and prospective studies on cancer treatment during pregnancy are lacking;</p> <p>Multidisciplinary expertise should be available;</p> <p>It is advisable to engage the expertise of other members of the healthcare team such as psychologists, social and pastoral workers</p>	<p>Counselling both parents on the maternal prognosis and foetal risk is needed</p>	<p>The parents should be informed about the different treatment options and the possible consequences for the patient and the foetus(<i>enabling patients to take informed decisions; respect for relational autonomy [indirect reference]</i>);</p> <p>The prognosis, treatment modalities, gestational age, and patients preference are pivotal in the decision making process on treatment</p>

				during pregnancy or termination of pregnancy (<i>balancing maternal and foetal beneficence [indirect reference]; respect for patient's autonomy</i>)
Pentheroudakis et al., 2008 (Pentheroudakis, Pavlidis, and Castiglione 2008); European society of Medical Oncology (ESMO)	Provides recommendations for <i>diagnosis, treatment and follow-up</i> surrounding cancer treatment, fertility preservation and cancer during pregnancy	Pregnancy termination is advised in the case of chemotherapy or radiotherapy administration during the first trimester, need for radical gynaecologic surgery, poor maternal life expectancy	The optimal therapeutic strategy should be jointly chosen by the medical team, patient and family and will depend on gestational age, nature and stage of cancer, treatment options and patient wishes.	Inclusion of patient and family in decision-making (<i>respect for relational autonomy [indirect reference]</i>); considering patient's wishes (<i>respect for patient's autonomy</i>)
Loibl et al., 2006 (Loibl et al. 2006); Internal expert meeting	Offers guidelines on how to diagnose and treat women with <i>breast carcinoma during pregnancy</i>	Multidisciplinary approach is recommended including psychologist, social workers, and a chaplain; Ongoing psychological support during treatment and delivery should be available for the patient and her family	A supportive patient-physician relationship is required, as is close collaboration and feedback of all disciplines involved in the patient's care, aiming to assist the patient and her partner towards	Informing the patient about the options(<i>enabling patients to take informed decisions</i>); involving partner in consultations (<i>respect for relational autonomy</i>)

			achieving a true informed consent and commitment to treatment	
Helewa et al., 2002 (Helewa et al. 2002); Breast Disease Committee and Executive Committee and Council, Society of Obstetricians and Gynaecologists of Canada	Provides physicians with up-to-date, accurate information and recommendations regarding pregnancy and lactation impact on cancer risk, prognosis, risk of reoccurrence and feasibility of breastfeeding in women affected by breast cancer ; and also offers counselling recommendations	Multidisciplinary approach should be taken; Patients should be counselled regarding the effect of proposed on the foetus and on overall maternal prognosis; Termination of pregnancy should be discussed, but patient should be counselled that prognosis is not altered by termination of pregnancy	Counselling support for breast cancer patients is advocated	Informing the patient about the options (<i>enabling patients to take informed decisions</i>)

The USA National Cancer Care Network (NCCN) guidelines were not identified by the searches in the data bases. Therefore, they were searched manually on NCCN official website on 2015-10-24 www.nccn.org with keyword ‘pregnancy’ but no relevant guidelines were located. These search results correspond to a previous review comparing NCCN and European Society of Medical Oncology (ESMO) guidelines for breast cancer care which found that the NCCN guidelines did not fully address pregnancy issues but in general supports pregnancy after breast cancer (Zagouri et al. 2015).

4.3. Analysis of ethics content

This work does not focus on judging the ethics content present in analysed guidelines. On the contrary, it seeks to understand the standpoints and approaches to ethical issues surrounding cancer care during pregnancy through clinical practice guidelines. Careful analysis of ethics content in 17 guidelines suggests that three main themes can be identified in their texts. That is *respect for autonomy*, *beneficence* and *protection of the vulnerable*. The first two are found in classical biomedical ethics texts and are known as *moral principles* (Beauchamp and Childress 2013) while the third one is also claiming the status of a principle, especially in the European bioethics (Rendtorff 1998)(Rendtorff 2002). Hence, it's conceptualisation, definition and recognition has been slow (Sass 2001)(Tavaglione et al. 2013). Just recently it has been suggested to develop the concept of vulnerability as a *principle of protection of the vulnerable* (Hurst 2008) and also as a *principle of respect for human vulnerability* (Ten Have 2015).

In biomedical ethics *autonomy* is defined as a “principle of patient’s autonomy”⁵⁸ which implies that physicians should empower patients to make informed decisions about their treatment which are of paramount importance in patient care (Blank 2002). It is also known as a “principle of respect for autonomy” which involves acknowledging the value and decision-making rights of patients by enabling them to make decisions about their treatment (Beauchamp and Childress 2013). For the purpose of this work, autonomy is perceived as involving the patient in a decision-making process by informing her about the

⁵⁸ It appears that clinicians tend to refer to the *principle of autonomy* more often than the *principle of respect for autonomy*. While both of them foster very much the same value attributed to patient’s autonomy, the first one is very much clinical practice oriented and was presented by the Medical Professionalism Project as the Physician’s Charter (Blank 2002). The respect for autonomy is usually referred to in biomedical ethics literature as it has been continuously developed by applied ethics scholars (Beauchamp and Childress 2013).

treatment options and taking patient's wishes into account when determining the disease management plan.

The developers of principles of biomedical ethics emphasise the importance of informed consent and argue that it could not be equated to shared (or joint) medical decision-making (Beauchamp and Childress 2013). They argue that shared decision-making could be misleading by merely allowing patients to participate in information exchanges but continuing the legacy of medical paternalism by ignoring patient's rights to approve or reject proposed procedures (Beauchamp and Childress 2013).

Proponents of *preventive ethics* seem to adopt such paternalist approach where informed consent is understood as an ongoing dialogue with a patient followed by negotiation and respectful persuasion if disagreement occurs (McCullough and Chervenak 1994). They seem to give higher preferential value to clinically defined foetal and maternal beneficence, especially after foetal viability is reached (Chervenak et al. 2004). Whereas the fathers of biomedical ethics insist that that "*respect for autonomy in health care relationships requires much more than avoiding deception and coercion. It requires an attempt to instill relevant understanding, to avoid forms of manipulation, and to respect persons' rights*" (Beauchamp and Childress 2013).

However, the later sometimes does clash with what is clinically perceived as the most beneficial intervention concerning the best interest of the patient and her foetus. In biomedical ethics literature it is known as a *principle of beneficence*, which implies that there is a moral obligation to act for the benefit of others. It corresponds with principle of utility and principle of non-maleficence (Beauchamp and Childress 2013) as well as principle of primacy of patient's welfare which is based on serving the interest of the patient (Blank 2002). The relevance of this principle is that cancer treatment during pregnancy might require a compromise between maternal and foetal health, therefore a choice has to be made on whose health-related benefits should prevail. In addition to that

patient might have her own ideas and understanding of what constitutes the best interest of her own and that of her foetus. It is important to note that again in biomedical ethics obligation to do no harm is usually more stringent than obligation to benefit. Therefore, even if best utilitarian outcome could be reached by acting beneficently the duty to do no harm would override the requirements of beneficence (Beauchamp and Childress 2013). That corresponds to the *doctrine of double effect* as discussed in Chapter 2.

Vulnerability can be perceived as a state which is shared by entire humanity because we all are subject to disease and death (Ten Have 2015) but for the purpose of this work it is more relevant to consider vulnerability of the specific groups such as pregnant women, cancer patients, children, who might have reduced capacity, power and control in order to protect and defend their interests as compared to others (Mackenzie, Rogers, and Dodds 2014). In clinical setting, and especially clinical research, vulnerability can be detected in different forms: cognitive, juridical, deferential, allocation and infrastructural (Kipnis 2001)(Kipnis 2003). Some proposals were made to consider vulnerability as a principle of European Bioethics contrasting it to American principlism ethics (Rendtorff 1998)(Rendtorff 2002) but this was not met with much of enthusiasm (Sass 2001). Another proposal suggested to consider it as a “principle of protection of the vulnerable” (Hurst 2008). In this work the concept of “protection of the vulnerable” is used under the definition which includes providing care and support for those who might be under-represented, have limited or restricted capacities to represent their interests or not able to defend their position, which in case of participation in clinical trials is referred to as “poor bargaining position” (Kipnis 2001)(Sheppard 2015). This could include pregnant women, cancer patients, foetuses, neonates, and potential future children and existing children.

The first two concepts can be specified further. In case of respect for patient’s autonomy it can be specified as *enabling patients to take informed decisions, respect for patient’s autonomy, respect for relational autonomy*. In case of beneficence the following

specifications can be applied: *balancing maternal and foetal beneficence, favouring maternal beneficence and favouring foetal beneficence*. It is important to note that such wording, specific for medical ethics literature, is not usually used in the texts of clinical practice guidelines. Table 4.2. illustrates how original wording from the guidelines translates to “ethics language”. For example, “attention to patient’s personal wishes” (Follows et al. 2014), “abortion is a personal decision” (Dauer et al. 2012) is interpreted as respect for patient’s autonomy while “considerations should be given to the health of both mother and foetus” (Ali et al. 2015) is regarded as balancing maternal and foetal beneficence but “maximizing maternal outcome” (Amant et al. 2014) is translated as preference to maternal beneficence. Explanations on what ethical concepts mean and which guidelines contain them are given in Table 4.3.

Enabling patients to take informed decisions and respect for patient’s autonomy were distinguished because informed decisions can be limited to providing information about the treatments and just asking the patient if she accepts or rejects the intervention based on the information provided⁵⁹. While respect for patient’s autonomy goes one step further and in addition to providing patient with information, involves patient in decision-making process making her an active participant where treatment plans can be modified and adjusted to patient’s preferences and wishes. This distinction is not very clearly elaborated by the creators of the guidelines (just as in biomedical ethics literature) but distinction is important as it has been shown that concerning cancer and reproductive issues some clinicians can be reluctant to provide patients with all relevant information

⁵⁹ According to Beauchamp and Childress, a key aspect in ethical patient care is allowing her to approve and authorise the interventions while information exchanges and communication through which patient elects the intervention is medical advice, which could be highly paternalist (Beauchamp and Childress 2013). My approach to this is that patient should not be left alone to take the decision about medical options available to her and in addition to evidence-based medical information, she should also be given space to reflect on available alternatives and use counselling services, if required.

about their options (Linkeviciute et al. 2014) and also significant numbers harbour conservative attitudes towards cancer and pregnancy compatibility (Sileny N Han et al. 2013). Furthermore, even if some scholars like McCullough and Chervenak (Chervenak et al. 2004) suggest that directive counselling based on scientific evidence, otherwise known as respectful persuasion (McCullough and Chervenak 1994) should be allowed in medical practice, paternalist approach to patient care is highly criticised practice (Beauchamp and Childress 2013). In general there is wide agreement in clinical ethics literature that it is a pregnant woman who decides what interventions can be performed on her for the benefit of her foetus and herself (Pinkerton and Finnerty 1996)(Shanner 1998)(Fasouliotis and Schenker 2000)(Dickens and Cook 2003)(ACOG Committee on Ethics 2005). This has become especially evident in medical and ethics literature after the US Supreme Court ruling in Angela Carder's case (Chapter 2).

The later is also clearly reflected in the reviewed guidelines. They appear to endorse the respect for patient's autonomy by stating explicitly that wishes of the patient should always be taken into consideration and even advancing it further by promoting relational approach to autonomy such as *respect for relational autonomy*, where pregnant patient's partner and/or family are included in the decision-making process. This approach is especially relevant in pregnancy care. However, even if some guidelines recognise relational aspects of patient care, they do not mention how conflicts between the patient and her family should be addressed. Such situations, even if rare, can pose some dangers on individual autonomy of pregnant cancer patient if her family members have preferences conflicting to hers. Hence limited empirical data suggests that this might not necessarily be a relevant concern in practice (Kenyon et al. 2006)(Smyth, Jacoby, and Elbourne 2012).

Most guidelines suggest that maternal cancer treatment and healthy development of the foetus are compatible and, therefore, advocate for encouraging and supporting the patient to continue with pregnancy by *balancing maternal and foetal beneficence*. Some

emphasize very explicitly that pregnancy termination is strongly discouraged (Peccatori et al. 2013), serious consideration should be given to continuing the pregnancy (Amant et al. 2010) or that pregnancy should never be interrupted (Papini et al. 2010). It is clear that compromising the maternal outcome by withholding the treatment is not justified and *maternal beneficence* is advocated. Therefore, in cases when optimal balance for both mother and foetus is not possible, maternal health is given more consideration (Follows et al. 2014)(Amant et al. 2014)(G. Koren et al. 2013) but even very categorical views of never interrupting the pregnancy showing preference to *foetal beneficence* advocate for care and support for a pregnant woman (Papini et al. 2010). Moreover, it seems reasonable to think that guidelines, which explicitly state that pregnancy termination in case of maternal cancer is discouraged, do so based on scientific evidence suggesting the compatibility of cancer and pregnancy.

Protection of the vulnerable is only mentioned by one group of experts in two subsequent guidelines (Amant et al. 2010)(Amant et al. 2014) and it is difficult to speculate who is considered as vulnerable. One of the mentioned guidelines also supports the mother focused beneficence and advocates for providing the best treatment for the vulnerable population of pregnant women with breast cancer (Amant et al. 2014) while the other one has only indirect reference encouraging pregnancy continuation by saving the foetus and treating maternal cancer (Amant et al. 2010). Just as in the case of beneficence, the concept of vulnerability seems to be treated in a light of scientific evidence, protecting the women and their foetuses from scientifically unjustified treatment options which might cause harm to both of them.

The major *limitations* of this systematic review are that data for professional guidelines is available from case studies, case study reviews and various registries, which are known to have the numerous downsides concerning the level of evidence. This implies that sometimes recommendations are based on considered expert opinion rather than on the

evidence-based data. It also has to be stressed that clinical guidelines are not expected to offer in-depth ethical analyses of clinical conditions they are addressing but including ethics components could potentially improve patient care⁶⁰ and reduce moral distress among the healthcare team.

Table 4.3. Main ethical concepts identified in the guidelines

Concept	Explanation of its meaning	Guidelines mentioning this concept
Autonomy		
Enabling patients to take informed decisions	Providing patients with the information about available treatment options, including risks and benefits for the mother and the foetus	(Ali et al. 2015)(Cardoso et al. 2012)(Dauer et al. 2012)(De Groot et al. 2012)(Amant et al. 2010)(Marsden et al. 2010)(Amant et al. 2009)(Loibl et al. 2006)(Helewa et al. 2002)
Respect for patient's autonomy	Involving the patient in a decision-making process by informing her about the options and taking patient's wishes into account when determining the disease management plan. That is a classical principle in biomedical ethics	(Ali et al. 2015)(Follows et al. 2014)(Cardoso et al. 2012)(Dauer et al. 2012)(De Groot et al. 2012)(Royal College of Obstetricians and Gynaecologists 2011)(Marsden et al. 2010)(Amant et al. 2009)(Pentheroudakis, Pavlidis, and Castiglione 2008)
Acknowledging the respect for relational autonomy	Involving the patient and her partner/family in a decision-making process by informing about the options and taking patient wishes into account when determining the	(Peccatori et al. 2013)(G. Koren et al. 2013)(Dauer et al. 2012)(Royal College of Obstetricians and

⁶⁰ The research of patients' perspectives on their care is still in its infancy, especially concerning cancer care during pregnancy and ethics support services. Therefore, I do not explore in depth the criteria to be used in order to evaluate patient care.

	disease management plan	Gynaecologists 2011)(Pentheroudakis et al. 2010)(Amant et al. 2009)(Pentheroudakis, Pavlidis, and Castiglione 2008)(Loibl et al. 2006)
Beneficence		
Balancing maternal and foetal beneficence	Considering maternal health outcomes and foetal risks when determining the disease management plan	(Ali et al. 2015)(Amant et al. 2010)(Amant et al. 2009)
Maternal beneficence	Giving preference to maternal health outcomes over foetal risks, if optimal balance for both is not possible	(Follows et al. 2014)(Amant et al. 2014)(G. Koren et al. 2013)
Foetal beneficence	Giving more weight for protecting the foetus and allowing pregnancy to continue but offering support for the pregnant patient	(Papini et al. 2010)
Vulnerability		
Protection of the vulnerable	Providing care and support for those who might be under-represented or not able to defend their position. Could include pregnant women, cancer patients, unborn children/foetuses, neonates, children	(Amant et al. 2014)(Amant et al. 2010)

4.4. Key recommendations for ethical care

The findings of clinical practice guidelines review reveal that three ethical concepts dominate the reviewed guidelines with the most elaboration on respect for patient's autonomy, followed by balanced approach to maternal and foetal beneficence and also introducing less often addressed concept surrounding protection of the vulnerable. The later concept might serve better for practical ethics approach in cancer during pregnancy care as compared to *foetus as a patient* concept.

Overall the reviewed guidelines urge to give consideration to the health of pregnant woman and her foetus, promote maternal health and wellbeing, inform the patient about available options and offer counselling and support in the process of decision-making. It is common to involve the pregnant woman's partner and/or family in counselling and decision-making process. Majority of the guidelines suggest that a multidisciplinary care team is formed for determining treatment plans and managing the condition. Furthermore, protection of the foetus is also given due attention.

4.5. Summary

Clinical practice guidelines for cancer management in the course of pregnancy focus on three concepts found in biomedical ethics literature. These are respect for patient's autonomy, beneficence and protection of the vulnerable. In addition some guidelines recognise the significance of relationships pregnant cancer patient might be inclined to consider when making her treatment choices. Furthermore, experts advocate for a multidisciplinary approach to cancer treatment during pregnancy and counselling services for patients.

Chapter 5. Ethics support services for patients and healthcare professionals

5.1. Methodological diversity

5.1.1. *The landscape*

There are two main stream approaches to ethics support which can be distinguished in clinical ethics (Linkeviciute and Sanchini 2016). The first one is known as *healthcare ethics consultation*⁶¹ and is predominantly practiced in the USA (Tarzian 2013). The second one can be broadly referred to as *moral case deliberation* and is more prominent in Western Europe (Dauwerse et al. 2014)(Stolper, Molewijk, and Widdershoven 2015). Healthcare ethics consultation (HCEC) is characterised by the effort to solve conflicts through a dialogue between all the stakeholders involved and is expected to conclude with a “principled ethical resolution” (Aulisio, Arnold, and Youngner 2000)(Gaucher, Lantos, and Payot 2013)(Tarzian 2013). Meanwhile, in the context of moral case deliberation (MCD) more emphasis is put on the conceptualization of and reflection on the problem rather than on the problem-solving dimension. The MCD is often perceived as a space where healthcare professionals can discuss and share their ideas on troubling ethical problems arising in their practice (Dauwerse et al. 2014). Hence some methods, as for example the Nijmegen method (Steinkamp and Gordijn 2003) and Karolinska model for ethical analysis (Bartholdson, Pergert, and Helgesson 2014), allow space for exploring the possible solutions and their justification.

Furthermore, differences between American and European approaches were also partly determined by legal system differences in two continents. A historical moment marking a milestone in the development of HCEC services was the “Quinlan case” in 1976 where a legal dispute took place in order to determine if Ann Karen Quinlan’s life

⁶¹ Previously it has been known as “clinical ethics consultation” and the term is still in use (Linkeviciute and Sanchini 2016).

supporting ventilator could be switched off. The Supreme Court of New Jersey ruled that ventilator can be removed, and urged the hospitals to form ethics committees which would help to resolve similar problems in the future (Tapper 2013). Following this case, the U.S. President's Commission suggested that consultations with ethics committees could be used as means to approach ethical disputes in clinical setting (Aulisio, Arnold, and Youngner 2000). Therefore, the American approach to ethics consultation has a nudge from a legal system to act as a guardian, so that ethical decisions can be reached within the hospital without resorting to the courts.

However, there seems to be a growing interest in using the *mediation* approaches in healthcare ethics consultation (Fiester 2013)(Morreim 2015)(Howe 2016), arguing that mediator's job is to avoid making a recommendation and imposing the solution. Instead ethics consultants are invited to engage the conflicting parties in such a way that resolution emerges from those in conflict and is not imposed by recommending what has to be done (Fiester 2013)(Morreim 2015). Despite the calls to segregate ethics consultation and mediation services (Morreim 2015) and widely unanimous agreement that mediation skills are essential for ethics consultants (Viafora 1999)(Steinkamp and Gordijn 2003)(Neitzke 2009)(Larcher, Slowther, and Watson 2010)(Tarzian 2013), it still remains unclear what exactly is the end product of ethics consultation. Proposals were made to restructure the ethics consultation delivery process by paying more attention to the *closure* which would extend beyond the recommendation or one time solution by calling for more attention to the moral distress and negative emotions associated with a conflict (Fiester 2015). Further suggestions are made to assign greater moral weight to the feelings individual patients and their families experience (Howe 2016).

The European take on ethics consultation is slightly different. While ethics consultants in the American setting are expected to participate in a "principled ethical resolution" to resolve conflicts and avoid turning into courts, British ethics committees,

under recommendation of the Royal College of Physicians, are pictured as offering “ethics support and advice” (Gaucher, Lantos, and Payot 2013). French have so called *Espaces de reflexion éthique*, which are not meant to offer decision-making recommendations. Instead physicians are advised to pursue ethical reflection regarding troubling issues with the help of the ethics committees, but any initiative of sharing decision-making responsibility among ethics committees and physicians is discouraged (Gaucher, Lantos, and Payot 2013). Moreover, MCD is not subject to regulation or standardization and is perceived as “learning by doing enterprise” (Stolper, Molewijk, and Widdershoven 2015) being one of the resources healthcare professionals could use when faced with difficult decisions. Hence it does not share the decisional responsibility with healthcare professionals. However, the most data comes from the Netherlands where MCD is the most widely practiced, Scandinavian countries, Germany, the UK also have clinical ethics support services but they are not unified in structure, goals and delivery methods (Bartholdson et al. 2015)(Dorries et al. 2014)(Larcher, Slowther, and Watson 2010). Ethics committees in the Baltic States (Lithuania, Latvia, Estonia) mainly focus on research ethics and do not offer ethics support services in a form of reflection or consultation (Gefenas et al. 2010)(Dranseika 2011).

5.1.2. Methodological approaches to ethics support in healthcare

The methods used in both approaches to ethics consultation usually have a protocol that lists a number of questions to be answered and steps to be followed. The classical way to start the ethics consultation is by presenting the case and related problem(s) (Steinkamp and Gordijn 2003). This is followed by the gathering of relevant facts and identification of the stakeholders involved. Then, it proceeds with the comprehension of the nature of the problem, the determination of the values compromised, as well as the arguments in favour and against the potential solutions. Depending on the methodology, the concluding part can

arrive at a solution, a recommendation, or a list of possible alternatives leaving the final decision for those who will be affected by it (Linkeviciute and Sanchini 2016).

In the American context the *four principles* of biomedical ethics (*respect for patient's autonomy, nonmaleficence, beneficence and justice*) are used widely as a point of reference for ethical decisions (Beauchamp and Childress 2013). Other attempts to develop practically applicable theories for ethical decision making have also been made. For example, *unified theory* where morality is perceived as a public system has been suggested to be used as a reference for ethical decision-making (Gert, Culver, and Clouser 2006). The concept of common morality is also used by Beauchamp and Childress arguing that four principles might be universally applicable (Beauchamp and Childress 2013).

Some European scholars suggest that a particular method for ethics consultation might be best chosen when we know what case we have to approach and depending if consultation is done retrospectively or prospectively (Steinkamp and Gordijn 2003). There have also been some attempts to propose a list of ethical principles reflecting the European ideas and values. These principles include *respect for autonomy, integrity, dignity and vulnerability* (Rendtorff 2002). Dignity and vulnerability remain highly criticized concepts (Kottow 2004)(R Macklin 2003) but despite the critique referring to the usefulness and relevance of the European bioethics principles (Sass 2001), vulnerability seems to be gaining some recognition in medical ethics literature (Sheppard 2015) and the concept of respect for human vulnerability is being explored as a potentially new principle in bioethics (Ten Have 2015)(Matthews and Tobin 2016).

One of the first attempts aimed at proposing structured tool for carrying out ethics consultation in a clinical setting occurred in 1980. The *Four Boxes Method* in a form of a pocket guide was created with an intention to be used when addressing ethical issues in the clinic. This method focuses on *medical indications, patient preferences, quality of life and other contingencies* as well as incorporates four principles of biomedical ethics (Jonsen, Siegler, and Winslade 2010). The four elements constituting this method are the following:

1) medical indications concern the evidence supporting therapeutic and diagnostic interventions; 2) patient preferences indicate the choices expressed by the patient, based both on personal experience, beliefs, values and on the information provided by the physician; 3) quality of life describes the features of patient's life before and after the treatment, focusing on a degree of satisfaction that they experience and on the values regarding their life and their health; 4) other contingencies refer to the contextual features such as familial, social, institutional, financial, legal setting within which the medical decision has to be taken (Jonsen, Siegler, and Winslade 2010). This method was developed with the aim to help solving practical dilemmas in the clinic, starting with problem-identification and concluding with possible strategies to manage the problem. This method also stresses the importance of using model cases as guides, which could serve as an educational resource (Linkeviciute and Sanchini 2016). Another slightly different methodology called CASES was developed by the Integrated Ethics project at the U.S. Department of Veterans Affairs. The CASES method constitutes of the following steps 1) clarify the consultation request, 2) assemble relevant information, 3) synthesize information, 4) explain the synthesis, 5) support the consultation process.⁶²

Most methods are primarily directed to healthcare professionals even if some of them allow space for patient participation. Similarly also some European methods are first and foremost designed to help clinicians to address and reflect on ethical problems. For example, such are the *Nijmegen Method* (Steinkamp and Gordijn 2003) and the *Lanza Foundation Protocol* (Viafora 1999). Moreover, a Swedish model known as *Karolinska model for ethical analysis* which has been redesigned specifically for oncology setting reject patient participation in ethics consultations motivating that such experience might be too stressful for the patient (Bartholdson, Pergert, and Helgesson 2014). However, other Scandinavian countries report different experiences and positions, for example, users of the

⁶² The guide specifying further questions and offering further guidance for ethics consultants can be found at <http://www.ethics.va.gov/integratedethics/> [accessed 2016-03-19].

Norwegian clinical ethics committee model advocate for patient involvement in order to achieve better outcomes (Forde and Hansen 2009). Furthermore, a comparative study from France, Norway, Germany, Italy and the UK concludes that less patient participation in clinical ethics consultation lays better grounding for protecting patient's confidentiality and allows more objectivity for decision-making while more patient involvement would yield enhanced respect for patient's autonomy and best interest but could lead to unbalanced conclusions favouring the patient's views rather than ethics norms (Fournier et al. 2009).

5.1.3. *Patient focused ethics support methodologies*

Methodologies focusing on patients and offering ethics support to patients are less frequently mentioned in clinical ethics literature⁶³. Two such examples are *Philosophical counselling* (PC) (Matchett 2015) and *Decisional counselling* (DeCo) (Chiavari et al. 2015). It is important to note that traditionally clinical ethics committees dealt with ethical issues surrounding end of life or scarce resource allocation (Linkeviciute and Sanchini 2016) but increasingly there are different types of ethical problems arising in healthcare setting and different approaches to potential solutions are needed (Chiavari et al. 2015)(Boniolo and Sanchini 2016). This is especially relevant in the healthcare areas involving genetic testing, various screening programmes, and use of assisted reproduction technologies, which are all common in the oncology and oncofertility settings. Therefore, two above mentioned methods are precisely focused on an individual facing troubling ethical issue rather than a team of healthcare professionals. They are used to support an individual patient (and in some cases her relatives) in decision-making process.

⁶³ Attempts to address ethical issues occur in psychological counselling services for cancer patients (Lawson et al. 2015) and increasingly the calls are made to establish closer collaboration between bioethics and social work (Brazg, Dotolo, and Blacksher 2015).

Philosophical counselling can be defined as a specific kind of dialogical activity where a consultant (or a counsellor) helps a counselee (or a client) to reflect upon his/her life troubles by using philosophical concepts, theories and techniques⁶⁴. Philosophical counselling has been gaining a growing acknowledgement in the clinical ethics field as an alternative to dispute resolution because it potentially offers a better “closure” of the case. The proponents argue that conflict resolution is not sufficient for a high quality ethics consultation and more attention to patient’s perspectives is required. Therefore, a very much welcomed feature of philosophical counselling is the space, which this method offers for looking more carefully at the specific concepts and patterns of reasoning, which are shaping the counselee’s perspective (Matchett 2015). However, the practice of philosophical counselling has been subject to extensive critique questioning its place within psychological and psychotherapeutic approaches to patient care, whether it is therapeutic in its nature and if it qualifies as contemplation or critical thinking activity (Šulavikova 2012). Some authors express concerns about theoretical and empirical validity of philosophical counselling. For example, Lydia B. Amir raises concerns that philosophical counselling might even compromise patient’s wellbeing by the lack of agreement how patient’s autonomy should be supported. Further downsides are named as blurry boundary between philosophical and psychological counselling and the lack of reliable tools for evaluating the effectiveness and preventing potential risks associated with this practice (e.g. frustration, confusion, bewilderment, fear, discouragement) (Amir 2004).

Decisional counselling is a method which focuses on patient’s personal values and importance that she attributes to the potential benefits, harms and scientific uncertainties

⁶⁴ It was introduced by a German philosopher, G. Achenbach, who, in 1984, published a book containing some lectures he gave on what he defined as a new way of doing philosophy, according to which philosophy has to be interpreted as a practical tool to cope with life and its difficulties (Achenbach 1984). It was further developed by a Canadian scholar Peter B. Raabe (Raabe 2001), who continues to work actively in a field of philosophical counselling <http://www.peterraabe.ca/what.html> [accessed 2016-05-26].

surrounding her condition, available treatments and choices at hand (Chiavari et al. 2015). It focuses on helping patients to think about their choices by presenting which choices exist, describing what each of them entails, deliberating about potential options and forecasting how they might feel about potential implication and outcomes of the choices made. Patient support directed to enhancing their decision-making process can have different focus and be directed to value clarification, improving patient experience or empowering more disadvantaged groups (Stacey et al. 2012). Decisional counselling process is directed by a trained facilitator, who provides the patient with individualised, nondirective information but remains neutral concerning the choice on which patient has to make a decision. Decision counsellor prepares the patient for the consultation with a physician, so patient is better equipped with information concerning her condition, value preferences and uncertainties, which can be further discussed and clarified during the consultation with physician (Chiavari et al. 2015)

Ethical counselling (EC) is developed to fit under the umbrella of philosophical counselling and offers two distinct methodologies for addressing ethical issues in healthcare setting. One methodology is designed for clinicians and serves as space to reflect in order to help clinicians to understand patient's preferences better. The second methodology is aimed to serve the patients directly (Boniolo and Sanchini 2016). However, in both methodologies a patient is seen as a privileged decision-maker concerning the ethical issues occurring in a situation at question, recognising the importance of communication, emotions, understanding of probabilities and attributing high value to respect for patient's autonomy (Boniolo and Sanchini 2016). EC is conceived as a non-directive method, which serves as an orienteering tool for patients and clinicians when thinking about the choices surrounded with ethical questions and uncertainties. Its structure is meant to assist a guided reflection process where ethical arguments supporting and rejecting each available option can be clarified and evaluated. This method takes patient's personal values and beliefs into particular consideration in order to explore and

understand the reasons behind patient's wishes but does not intend to offer justification for one choice over another (Linkeviciute et al. 2015). The developers of EC relate it with the MCD approach to ethics consultation as it highlights the importance of clarifying and conceptualising the problem rather than offering a solution. Just as HCEC model it considers the parties involved recognising the importance of respecting their autonomies but it also discards the idea that consensus-building completes ethical reflection. The latter is the shared common ground with above mentioned tradition of the Philosophical counselling (Linkeviciute and Sanchini 2016)(Boniolo and Sanchini 2016).

5.2. Standardisation and evaluation attempts

5.2.1. Regulation

The American Society for Bioethics and Humanities (ASBH) has been a leading institution in making the continuous attempts to promote the professionalization, institutionalization and quality assurance of ethics consultation services in the USA. It works towards setting up a HCEC service practice standards which includes ensuring that all stakeholders can access HCEC services and receive response in a timely manner, transparent service documentation system, established evaluation procedure and institutional policy, providing details how all these standards are met (Tarzian 2013).

This organisation has also introduced the first code of core ethical responsibilities for individuals performing healthcare ethics consultation which first and foremost was a solid step towards professionalization of ethics consultation practice in the USA (Tarzian and Wocial 2015). Elaboration of an ethics code for healthcare ethics consultants also serves as a protection of the consultants should their recommendations be challenged in court. However, despite establishing the practice standards such as being competent, avoiding conflict of interests, respecting privacy of the patients, communicating responsibly and promoting just healthcare, the code of ethics for healthcare ethics consultants remains highly aspirational (Tarzian and Wocial 2015). Hence, it remains

unclear what professional obligations ethics consultants should adopt as their practice is so diverse. Some suggest that instead of individual responsibility, ethics consultants should share their professional responsibility with an entire healthcare team (Schwab 2016).

The ASBH is playing directive and regulatory role on how HCEC service delivery should be organized in the USA, while its European counterparts such as the UK Clinical Ethics Network (UKCEN) and the European Clinical Ethics Network (ECEN) picture themselves as supporting and guiding, rather than establishing concrete and binding practice requirements for its members or issuing practice licences to individual ethics consultants. Therefore, the European organisations play more passive role as compared to their North American counterpart. European bodies tend to build their activities around offering education, support and space for reflection but not regulation or strict recommendations (Linkeviciute and Sanchini 2016).

5.2.2. Expectations from ethics consultants

Common agreement between European and North American organisations is that in order to provide meaningful ethics consultations, ethics consultants are expected to possess a number of skills (Linkeviciute and Sanchini 2016). The ASBH offers list of core competences, which include the capacities to identify and analyse the disagreements; retrieve the relevant ethics literature, policies, guidelines and other documents; collaborate with institutional structures; organise formal and informal meetings; report the activities and establish follow up processes; communicate and train; represent the views of different parties; recognise and find solutions to communication barriers (Larcher, Slowther, and Watson 2010)(Tarzian 2013). Furthermore, some cultural competencies are also expected, as is the knowledge of moral reasoning, ethical theories and concepts, healthcare systems, institutions and clinical contexts, policies, beliefs and perspectives of patients and staff, relevant codes of ethics, professional conduct, guidelines and health law relevant to ethics consultation (Aulisio, Arnold, and Youngner 2000)(Tarzian 2013).

In Britain, the UKCEN has also released a document providing the summary of skills and competences required when offering ethics consultation services. The major difference is that the UKCEN seems to pay more attention to clinical ethics committees and, therefore, its requirements are specifically aimed to the members of such committees (Larcher, Slowther, and Watson 2010) while the ASBH puts more emphasis on the skills possessed by an individual ethics consultant (Tarzian 2013)(Linkeviciute and Sanchini 2016).

It is interesting to note that both the ASBH and the UKCEN emphasise the importance of character traits and personal qualities of ethics consultants. An ethics consultant is expected to demonstrate tolerance, patience, compassion, honesty, forthrightness, self-knowledge, courage, prudence, humility, and integrity (Aulisio, Arnold, and Youngner 2000)(Larcher, Slowther, and Watson 2010).

The code of ethics for ethics consultants released by the ASBH specifies the core responsibilities that ethics consultants should aspire to cultivate in their work. It includes maintaining the competence and integrity, managing conflicts of interest and respecting privacy, contributing to the field, making public statements responsibly and promoting justice in healthcare (Tarzian and Wocial 2015). Hence as it has already been mentioned these requirements remain aspirational as there are no solid means to enforce them. This particular code has also been criticised as lacking clarity and failing to define role specific responsibilities of ethics consultants (Schwab 2016).

The ways to acquire knowledge and skills for doing ethics consultation are still debated. The ASBH is increasingly suggesting examination and licensing, while the UKCEN also acknowledges self-directed learning (Linkeviciute and Sanchini 2016). The later also applies to the MCD which is even named as “learning by doing enterprise” (Stolper, Molewijk, and Widdershoven 2015).

In the American setting the ethics consultant have two tasks. Firstly, they should help to identify and analyse the nature of the problem. Secondly, the consultant should

facilitate the building of a “principled ethical resolution” (Aulisio, Arnold, and Youngner 2000)(Gaucher, Lantos, and Payot 2013)(Linkeviciute and Sanchini 2016). This means *“ensuring that all involved parties’ voices are heard, assisting them to clarify their own values, facilitating understanding of factual information and recognition of shared values, identifying and supporting the ethically appropriate decision maker(s), and ensuring that identified options comport with relevant bioethics, medical, and scholarly literature, and with laws, pertinent institutional policies and current practice standards”* (Tarzian 2013).

Concerning the MCD the requirements for the ethics consultants (also called facilitators) are not so explicitly defined. Facilitators do not necessarily have to be the ethicists as their major role is to moderate the dialogic process (Linkeviciute and Sanchini 2016). Since Dutch healthcare has a growing interest in MCD, training programmes for health care professionals are being developed to enable them to run MCD sessions themselves without necessarily depending on (external) ethicists. Teaching programmes for MCD include providing the trainees with basic knowledge about ethics, profound knowledge about conversation methods, attitude and skills for easing dialogue and analytical reasoning. However, each trainee is encouraged to find his or her own style of MCD (Stolper, Molewijk, and Widdershoven 2015).

Therefore, certification or attestation of ethics consultants remains a grey area despite the increasing rigour that professionalization of the practice is to be developed. Hence, initially the ASBH held the position which rejected the certification of ethics consultants or even accreditation of programmes which prepare ethics consultants (Aulisio, Arnold, and Youngner 2000). Recently, however, attempts have been made to develop some practical tools for assessing and attesting the individual consultants ability to perform clinical ethics consultation (Fins et al. 2016). In addition, assessments tools for retrospective evaluation of already performed ethics consultations are being developed (Pearlman et al. 2016).

5.2.3. Evaluation of ethics consultation practice

Evaluation of decisional and/or ethics support interventions is complicated by the fact that in many cases there is no singular “best” choice which could be supported by the concrete evidence that certain screening, testing or treatment option is better than other alternative available (Chiavari et al. 2015). However, the ASBH continuously recommends to evaluate HCEC practices (Aulisio, Arnold, and Youngner 2000)(Tarzian 2013) and some attempts to develop the evaluation tools have already been made. One example is a conceptual framework developed in the USA (Pearlman et al. 2016) for assessing ethics consultation quality. This particular framework is perceived as a systematic process promoting a shared understanding of ethics consultation services and their quality. The evaluation process is presented as “Ethics Consultation Quality Assessment Tool” (ECQAT) and, although it is primarily designed to assess the quality of ethics consultation services, it also has an aim to promote the accountability of ethics consultation service providers. The key elements of ECQAT are *ethics question, consultation-specific information, ethical analysis* and *conclusions and/or recommendations* (Pearlman et al. 2016)

Pearlman and colleagues (2016) suggest that ethical analysis might provide the justification for drawing some decisional conclusions and/or recommendations, when adequately structured. However, the choice of the tools for the ethical analysis can be biased by some particular world views which could also affect the conclusions and potentially serve better for supporting specific solution in line with preferred moral conviction (Linkeviciute et al. 2016).

There are just a few empirical studies reporting the data from attempts to actually evaluate the outcomes of ethics consultation. A recent study from Sweden, which employed exploratory and descriptive qualitative approach and interviewed 11 healthcare professionals, found that ethics rounds as a way of supporting healthcare professionals is

seen as a positive intervention to their daily work which helps to see things from different perspectives and gain insights into ethical issues (Silen et al. 2016). However, the same study reports that healthcare professionals who participated in ethics rounds did not experience any changes in their daily work or thinking due to organisational hurdles. A bigger survey study from the USA collected responses from 123 clinicians about their views on healthcare ethics consultation (Wocial, Molnar, and Ott 2015) and found that 60% of respondents thought that ethics consultations helped to clarify the values of the patient and/or their families and also assisted in clarifying their own values. Moreover, 75% of American respondents said that their confidence in patient's care plan increased as a result of ethics consultation. The later resonates with the view that ethics consultation sometimes is perceived as peer-review for the decisions clinicians are making (Neitzke 2009). Not all studies yield the same results, one more study from Sweden found that ethics rounds do not improve the handling of ethical issues and suggests that the outcomes of ethics rounds might be directed to the patient outcomes rather than clinicians working environment (Silén et al. 2015). This remains a significant limitation of the above studies (Wocial, Molnar, and Ott 2015)(Silen et al. 2016) as they do not include patient/family perspectives, nor evaluate patient outcomes as a result of ethics consultation.

5.2.4. Remaining questions for successful evaluation

As myself and colleagues have already argued elsewhere (Linkeviciute et al. 2016) there are three questions which require clarification in order to establish functioning evaluation system for ethics consultation.

Firstly, we have to *appreciate the diversity* in which ethics consultation is practiced. In order to understand what could and should be evaluated in ethics consultations, we might need to draw a clear distinction between varying approaches to the practice of ethics consultation (Linkeviciute and Sanchini 2016) with emphasis

distinguishing those which offer a space to pursue ethical reflection, conceptualize ethical questions and clarify conflicting ethical positions (Gaucher, Lantos, and Payot 2013)(Dauwerse et al. 2014)(Boniolo and Sanchini 2016) and those which seek to provide principled ethical resolution and offer a recommendation (Aulisio, Arnold, and Youngner 2000). In this way we could have a more precise idea if the aim is to evaluate the process of ethics consultation, its outcomes or both.

Secondly, even though we know that ethics consultation in European context cannot be equated to healthcare ethics consultation models in North America (Gaucher, Lantos, and Payot 2013)(Linkeviciute and Sanchini 2016), methods used for actual consultations by both approaches are still very heterogeneous and some standardisation might be required before evaluation is possible (Linkeviciute et al. 2016). The attempts to offer evaluation tools for the European methods might need to *focus more on the process* rather than conclusions reached or recommendations made in case of troubling case or situation. However, as discussed above, even the North American approach to healthcare ethics consultation is not homogenous and increasingly its outputs and impact is being questioned and alterations⁶⁵ to the existing “conflict resolution” approach suggested (Morreim 2015).

Thirdly, we still have to define what kind of accountability we expect from ethics consultants before we can evaluate what they do. The level of accountability would differ if consultants are expected to give a concrete recommendation or just moderate a discussion (Linkeviciute et al. 2016). Furthermore, there are varying proposals on the most

⁶⁵ The most broadly discussed alteration is presented as “bioethics mediation”, which is supposed to extend beyond recommendation/conflict resolution by taking into account feelings and emotions associated with the troublesome situation (Fiester 2015) and also reducing the distress experienced by the parties involved by building patients trust and avoiding hostility to resolutions produced by experts rather than those who will actually be affected by the decision (Howe 2016).

appropriate model for defining ethics consultant's responsibility varying from shared responsibility among the healthcare team (Anderson-Shaw 2014) to distinguishing role-based and activity-based models of accountability (Finder and Bliton 2014).

Therefore, we previously concluded that *“depending on the scope, goals and methodologies used in ethics consultation, we might need different evaluation criteria to make sure that we are judging them adequately. European approaches to ethics consultation have less decisive power; do not seek equal status with clinical consultation and by virtue offer a space for reflection and advice rather than conflict resolution or principled recommendation. This suggests that assessment tools can only partially mirror North American experiences and require further developments to be applicable for the European context”* (Linkeviciute et al. 2016).

5.3. Summary

Ethics support services for healthcare professionals and patients take different forms and approaches. They can be divided into the North American healthcare ethics consultation approach and deliberative approach (e.g. moral case deliberation), which is more common in Europe. There is growing interest to professionalise ethics consultation practice and evaluate its services. Ethics support aimed at healthcare professionals remains a predominant practice while patient focussed ethics support methods are only starting to emerge (e.g. decisional counselling, ethical counselling, philosophical counselling) but ethical concerns are also addressed in the course of other types of patient counselling such as psychological counselling. Meanwhile, there are still many open questions concerning the professionalization, standardisation and evaluation of ethics support services. These questions could be answered upon the agreement on the role ethics support plays in clinical practices. The latter is very much relevant in many European countries.

Chapter 6. Framework for ethical care of pregnant cancer patients

6.1. Relational approach to patient care

6.1.1. Patient in a relational context

This section considers the relationships between a patient and the people around her whom she finds important to take into account when making decisions about her cancer treatment and pregnancy care. It also considers healthcare team in regard to accommodating pregnant cancer patient's wishes aligned with the wishes of her partner and/or family.

Caring for a pregnant woman with cancer usually requires a multidisciplinary team and personalized treatment plan, which usually involves physicians of different specialties. It also often requires support from patient's family members in order to attend appointments with specialists, hospital visits for treatment, preparing for the arrival of the baby, taking care of a newborn while continuing cancer treatment, etc. Therefore, all parties affected by pregnant patient's disease could have different interests or might delegate themselves to represent the interests of the party or parties that are restricted in representing themselves (e.g. foetuses, young children and even pregnant women) and therefore, the involvement of various healthcare providers and family members could inevitably lead to disagreements (Moore, Engel, and Prentice 2014). Some of the affected people might not feel comfortable with the choices of a pregnant cancer patient and attempt to influence her decisions. This could come from a family as well as from a healthcare team and as it has already been mentioned (Chapter 2 and Chapter 3), the ethical questions, which are raised by the healthcare team and patients and/or their families, are not always the same.

Respect for patient's autonomy being a core principle in modern medical ethics (Beauchamp and Childress 2013) requires due attention to the individual patient's views and wishes, as well as their participation in decision-making and being the main decision-maker in the choice of treatment (Beauchamp and Childress 2013) and ethically troubling situations (Boniolo and Sanchini 2016). However, patients do not live in isolation and their choices might affect other stakeholders involved, just as their choices can be affected by other people or situational and relational factors. Some feminist writers argue that suggesting women to exercise autonomy in its individualistic form is against the female nature and could only lead to disrupted relationships (Mackenzie and Stoljar 2000). Caring for a pregnant cancer patient requires to consider multiple relationships, which this patient has, including her perceived relationship with a foetus, her partner, other children (if present), parents and other family members, in some cases members of the communities pregnant cancer patient identifies with and ethno-socio-cultural and political environment.

A review of clinical practice guidelines for cancer management during pregnancy also reveals that clinicians are encouraged to pay attention to individual patient and her family's wishes. Moreover, these guidelines also call for a careful balancing between maternal and foetal beneficence when administering cancer treatment and protecting the vulnerable actors in cancer treatment process (Chapter 4).

In this section I mainly focus on patient wishes in the context of her relationships, which is also known as *narrative identity* leading to self-creation, which is not limited to having a self-narrative and knowing who we are because we also want our inner story to unfold in a certain way by being or becoming a certain kind of person (DeGrazia 2005) and/or fulfilling the obligations and meeting the expectations of those significant to one's life. That includes but is not limited to life partner, parents, existing and potential future children (Linkeviciute et al. 2015)(Linkeviciute and Peccatori 2016).

Narrative identity could be seen as a connection between pregnant woman's story and stories of people around her (e.g. relationships with a life partner, children, closest friends, neighbours, colleagues, religious community members, etc.), even though these individuals do not literally form a part of a patient, they might certainly be a part of her identity and to some extent their interests are also her interests. Overlapping interests indicate that their wellbeing constitutes a part of patient's wellbeing because if her partner and children flourish, she is also better off (DeGrazia 2005)(Goncalves, Sehovic, and Quinn 2014).

As David DeGrazia explains, a large part of who we are is determined by our interpersonal relationships, some of which are central to our identity (DeGrazia 2005). Therefore, the ideal that a patient is in charge of her life and at liberty to make her own choices, as some feminist authors suggest (Feary 2003), is further complicated by multiple identities of pregnant cancer patients and their social embeddedness. Socially constituted individuals might also identify themselves through their social roles (e.g. partner, mother, friend) and choose to exercise their autonomy in a light of their past experiences, expectations and relationships, which they see as part of their narrative identity (Mackenzie and Stoljar 2000)(Mullin 2005)(DeGrazia 2005).

The later exposes individuals to vulnerability to co-creation such as being dependent on others to develop and maintain skills of putting together a life narrative autonomously (McConnell 2016). While on the other hand, personal identity is mirrored through the relationships with others (DeGrazia 2005) which eventually is reflected in the choices, values and even identity a woman adopts (Mackenzie and Stoljar 2000)(Donchin 2001).

The above indicates that accommodating the need to involve the partner and other family members into information, decision-making and cancer care process of a pregnant cancer patient might enhance her ability to exercise the relational autonomy rather than

restrict it or deprive the patient from making the choices in-line with her wishes, values and ways she sees life (personal philosophy). Hence, some safeguards would be necessary in order to respect the supremacy of pregnant cancer patient as an individual with her genuine personal wishes.

Therefore, even though I argue that in cancer care during pregnancy a different take on respect for patient's autonomy is necessary in order to address the needs of the patients and their closest relations, this does not mean that respect for individual autonomy should be abolished all together. On the contrary, recognising the importance of the relationships would help to empower the patients to exercise their wishes concerning their cancer care in a broader context. Relational approach to such care would help to see and recognise the patient as socially embedded human being who holds individual views on life.

However, respecting and involving others in discussions, decision-making and care of pregnant cancer patients could be very intense, emotional and otherwise difficult task. It might also require change of attitudes towards the relationship between a patient and the healthcare team. While medical paternalism where "doctor knows best" is highly criticised approach in modern biomedical ethics (Beauchamp and Childress 2013), under some circumstances newly emerging concept of medical maternalism⁶⁶ might come in helpful (Specker Sullivan 2016). Furthermore, such change in attitude towards the patient could also be supported by *ethics of care*, which is built on compassion, presence, empathy and recognition of the patient as a fellow human being (van Heijst 2011).

6.1.2. Relational ethics

The focus of this section is on the relationships between healthcare professionals and a patient, requiring cancer care in the course of pregnancy. Relational ethics situates ethical action in relationships where acting ethically "*involves more than resolving ethical*

⁶⁶ This concept echoes with medical paternalism but clinicians, while taking decisions for their patients, give particular consideration to patient's wishes, preferences and values.

dilemmas through good moral reasoning, it demands attentiveness to our commitments, to one another, to the earth, and to all living things. Ethics is about interdependency as well as freedom, our emotions as well as our reason, and our unique situation as well as our human commonalities. It involves finding the fitting responses to our ethical questions” (Austin 2008). Ethics of care is developed further by specifying that compassion, presence, empathy and recognition of a *patient as a fellow human being* play a significant role in relationship between healthcare professionals and their patients (van Heijst 2011).

This approach has been mainly developed in a context of nursing care which could be very intense in both oncology and gynaecology/obstetrics settings. Historically nurses have been known to care for the patients while doctors just prescribed treatment but would not be actively involved in administering it. Currently it is still reported that specialty doctors do not always have enough time and sometimes the latest knowledge, expertise and resources to involve their patients in informative discussion about treatment options available to them, especially concerning fertility preservation for cancer patients (Linkeviciute et al. 2014) and cancer treatment during pregnancy (Sileny N Han et al. 2013).

Guidelines for cancer management during pregnancy (Chapter 4) unanimously suggest that cancer care during pregnancy should be provided by multidisciplinary teams. Hence the guidance is mainly aimed at physicians, just briefly mentioning the involvement and role of nursing staff. However, majority of guidelines suggest that pregnant cancer patients should be offered counselling in the course of decision-making and also during the treatment. Oncology nurses in particular often encounter ethical issues due to complex patient care needs requiring expertise from multidisciplinary teams (Moore, Engel, and Prentice 2014)(Pollard 2015) and could play a significant role in directing patients to or even delivering initial counselling for patients affected by cancer while pregnant.

As I already mentioned at the beginning of this chapter, good caring is not reducible to respect for autonomy (Feary 2003) as it also includes *recognition, compassion, presence and empathy* (van Heijst and Leget 2011). Indeed it is further argued that by overvaluing autonomy, healthcare professionals risk rejecting the patient's need to be loved and belong to others (van Heijst 2011). Therefore, a relational context is considered to be a basic premise of relational ethics in relationship between a patient and healthcare professionals with core tenets of mutual respect, engagement, embodied knowledge, environment and uncertainty (Pollard 2015).

Despite primarily focus to care approach coming from the nurses, care approach is also increasingly recognised among the practicing physicians⁶⁷ with some calling it *professional loving care*. According to the developers of the concept "*the idea of professional loving care rests on the assumption that professionals have the space, time, and ability to react to care-receivers in a way that demonstrates the best possible care*" (van Heijst 2011). Compassion, recognition and presence are argued to be the key features in ethics of care (van Heijst and Leget 2011) and *care* itself is considered to be a value in care ethics (Vanlaere and Gastmans 2011). Care can be perceived as an attitude and also as an activity supported by *theory of presence* (Vosman and Baart 2011), where strong accent is put on developing a relationship between the ones who give care and those who receive it (van Heijst 2011).

In the field of oncology this could even extended to *medical maternalism*, approach where decisions for another person are based on reasonable understanding of that person's own preferences (Specker Sullivan 2016) which would be very relevant for cases where

⁶⁷ "Fedro Peccatori: teaching the world to care" by Daniela Ovadia in Cancer World, January-February 2016: 22-26. <http://www.cancerworld.org/Articles/Issues/70/January-February-2016/Profile/753/Fedro-Peccatori-teaching-the-world-to-care-.html> [accessed 2016-06-23].

pregnant cancer patient is dying and/or being kept on life support for the benefit of the foetus. However, there are concerns that healthcare professionals demonstrate poor understanding of their own legal accountability in regard to the rights of pregnant women and her foetus (Kruske et al. 2013) and also sometimes fail to notice that things have gone wrong for the patient by following the policies to the letter (van Heijst 2011). Therefore, using relational ethics approach to patient care does not make decision-making easier but possibly more considered and fitting to the situation because it helps to see patients as interdependent and connected by challenging the traditional notions of autonomy, equality, and the self as an independent entity (Pollard 2015).

6.2. Protecting individual autonomy in a relational context

6.2.1. Evidence-based information disclosure

Allocating time for informing the patient about her treatment options plays a key role when enabling the patient to take informed decisions about her cancer care and treatment. Some patients might require time to understand the information and consider how options available to them fit to their life narrative and expectations, how it aligns with their social roles, relationships their value and personal philosophy they are keen to cherish.

Considering the time limitations which physicians face in everyday practice, additional patient support services (e.g. counselling) could be beneficial⁶⁸ to patients who are diagnosed with cancer during pregnancy. Such counselling could be offered in different modes and types with unifying feature of helping patient to understand all relevant information, cancer treatment and pregnancy care options at hand, crystallising her own preferences, expectations and perceptions on what would count as a desirable outcome in

⁶⁸ Creating effective evaluation tools for counselling services is still in early infancy and some most current problems are reflected on in Chapter 5.

her individual situation. Decisional counselling is an excellent example of how cancer patients could be helped to understand the complexity of the information about their condition and treatment options as well as implications of choosing one over another and feelings related to the potential consequences of the choice (Chiavari et al. 2015). Hence, patients are different and their needs for counselling vary. Therefore for some, other types of counselling might be better suited to their individual situation such as psychological counselling (Lawson et al. 2015), ethical counselling (Linkeviciute et al. 2015)(Boniolo and Sanchini 2016), other types of ethics support services (Gaucher, Lantos, and Payot 2013)(Linkeviciute and Sanchini 2016) and various other groups of patient support. The latter might not necessarily take counselling as their primary mode of operation and put more focus on experience and idea sharing, practical advice and shared causes (e.g. charity work, fundraising for research, etc.). Hence, it should be recognised and also emphasised that some patients genuinely do not want to be active actors in medical decision-making process.

Meanwhile, assisting patients with informed decision making process and counselling needs would require physicians to be informed about latest evidence on cancer treatment during pregnancy, maternal and foetal outcomes, and remaining uncertainties, especially concerning the long term paediatric and maternal outcomes (Chapter 1). It would also be bound to close interdisciplinary collaboration not limited to multidisciplinary clinical team but expanding it with inclusion of psychologists, decisional, ethical and faith counsellors, social workers and patient navigators to name just a few.

6.2.2. Personalised patient care

Caring for a patient involves an attempt to understand the reality this patient lives in, such as her way of seeing life, personal needs, expectations, commitments, desires and dreams (Feary 2003). This approach to caring corresponds closely with key features found

in ethics of care where patient's wellbeing is promoted by providing good care in a broader sense. That means that care is not limited to a physical level but has to include psychological, relational, social, moral, and spiritual levels (Vanlaere and Gastmans 2011). To excel in this attention to the patient's personal philosophy could be very useful (Boniolo and Sanchini 2016) as it helps getting to know not only the disease but also a person who is fighting it.

Personalised patient care is argued to be an abandoned topic in currently popular personalised and also precision medicine⁶⁹ debate where main focus is on tailoring medical treatment in accordance to genetic and epigenetic characteristics of the patient, including prevention, diagnosis, treatment and follow-up but missing out on noting the patient's needs and preferences during all stages of her care (van Heijst 2011)(Cornetta and Brown 2013)(Boniolo and Sanchini 2016). Overall, both in Europe and the USA personalised approaches to medical care are structured around the aim to provide the right treatment at the right dose, to the right patient at the right time⁷⁰.

Some argue that despite the importance, novelty and promise to improve health, personalised medicine is much more appreciated by the researchers and clinicians rather than patients, who are receivers of such care (Cornetta and Brown 2013). One possible explanation is that patients place more value on care which is perceived much broader than

⁶⁹ The distinction between the two is till debated but while approaches in personalised medicine are centred around an individual patient, precision medicine seems to focus on patient groups who share some common characteristics.

⁷⁰European Science Foundation (ESF) Forward Look. Personalised Medicine for the European Citizen: towards more precise medicine for the diagnosis, treatment and prevention of disease. October 2012. http://www.esf.org/uploads/media/Personalised_Medicine.pdf [accessed 2016-06-30]; U.S. Food and Drug Administration (FDA). Paving the way for personalised medicine: FDA's role in a new era of medicinal product development. October 2013. Report. <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PersonalizedMedicine/UCM372421.pdf> [accessed 2016-06-30]

treating a disease in a strictly technical sense (van Heijst 2011) and taking care of a patient as a whole human being with compassion (van Heijst and Leget 2011) and recognition of her personal philosophy (Boniolo and Sanchini 2016).

6.2.3. Protection of the vulnerable

Relational ethics approach assumes that general principles in bioethics are insufficient means for recognising the particularity of personal situations and personal narratives (Pollard 2015). Therefore, just a referral to four classical principles in biomedical ethics, which are respect for patient's autonomy, nonmaleficence, beneficence and justice, cannot overcome the vulnerability posed to the patient by her individual circumstances. Such vulnerabilities can be potential as well as already materialised (Ferrarese 2011).

As I already mentioned, social connectedness and dependence could subject a pregnant cancer patient to various vulnerabilities. One of such vulnerabilities is known as co-creation, otherwise known as co-authoring, of narrative identity (McConnell 2016). Although everyone is potentially vulnerable and some propose to recognise this concept as respect for human vulnerability (Ten Have 2015), some persons and/or groups can be especially vulnerable due to diminished capacity to protect themselves and their interests, power imbalances and lack of control in given situation (Mackenzie, Rogers, and Dodds 2014), which is also referred to as "poor bargaining position" (Kipnis 2003).

Potential vulnerability of ill pregnant women is rather widely recognised (Allesee and Gallagher 2011)(Sheppard 2015) but it is not to say that pregnant women should be secured in a bubble depriving them of cancer treatment interventions or of making their own choices. Recognition that pregnant woman facing potentially lethal disease could be vulnerable to numerous factors enables the creation of protection mechanisms (e.g. safety

net) to make sure that she is taking her treatment decisions in line with her wishes, exercising free will and has all relevant information to make an informed choice (Sheppard 2015).

Some also talk about an obligation to promote resilience to vulnerability by helping to sustain autonomy (Lotz 2016). This, however, can be done in many different ways. If we follow the notion of respect for relational autonomy and creation of narrative identity in regard to our relationships then we have to acknowledge that all people are vulnerable to having their self-concepts shaped by others (McConnell 2016). If we accept the possibility of narrative self-constitution, then we also have to accept that people depend on others to develop and maintain skills of self-narration which makes them vulnerable to having the content of their self-narratives co-authored by others (Matthews and Tobin 2016).

On the other hand, however, co-authoring could be seen as an essential component for developing a self-narrative (DeGrazia 2005)(McConnell 2016). For example, if others do not treat a pregnant cancer patient as an autonomous agent, she might doubt her own capacity to tell her own story and become dependent on her co-authors to provide much of the material for her personal story and look out for reassurance on which narration is the best for her (McConnell 2016). Hence, another possible scenario is that pregnant cancer patient might not want to consider just her own interests and be willing to make sacrifices for the benefit of those who might be affected by her decision (Chapter 2). Self-narration also implies that one is responsible to others for her choices. Answerability (or self-authorization) includes being responsive to requests for explanation and providing reasons for one's beliefs, plans and choices (Westlund 2009). The agent must be willing to defend or revise her narrative in a light of critical questioning by others (DeGrazia 2005)(McConnell 2016). Therefore, incorporating the element of reason giving into patient

counseling (Annoni 2016) could be a useful approach for identifying patient vulnerabilities and helping them to build resilience to it.

6.3. Patient-focussed counselling approaches

As some philosophical counselling proponents suggest, counselling is not mere application of theory to practice but allows testing the theory against personal experience: *“counselling sessions with women must involve an exploration of women’s life problems with the hope of broadening our concepts, expanding the reasons we give in support of our behaviour, illuminating the ways in which relationships have been conceived, and enriching our theories”* (Feary 2003). This is echoed by the voices of relational ethics advocating for the need to have a connection with a *patient as a person* in order to enable the nurses (and also physicians and other healthcare professionals) to understand what is important to the patient and what would serve best for her interests (van Heijst and Leget 2011)(Pollard 2015).

Patient-focussed counselling could also help the patient to think in terms of self-narrative or inner story, which is coloured by a sense of one’s own beliefs, desires, values, and character because continuing one’s own story could be a way of continuing to exist as a person (DeGrazia 2005). Therefore, recognising the importance of patient’s personal philosophy, involving her significant others in the counselling process and offering the opportunity to acquire all the information necessary for informed decision-making could help to provide state-of-the-art care tailored for each individual patient as well as this unique patient group who experience cancer in the course of their pregnancies.

6.4. Remaining limitations and future directions

Discussion concerning ethics of cancer care during pregnancy remains highly theoretical while clinical approach mainly concerns physical care and technical

interventions giving just a brief concern for ethical issues which could arise in the clinical practice. Emerging data about cancer treatment and pregnancy compatibility seems to present the phenomenon as any other type of illness, which technically could be managed from a clinical point of view. Hence, the aspects concerning emotional, psychological, ethical, social and relational concerns experienced by those affected remain a highly unexplored territory.

The emerging evidence, that cancer treatment can be given to a pregnant woman without significant adverse effects on a developing foetus and a future child, seem to overshadow the importance of holistic approach to patient care. Hence guidelines review suggests that patient counselling is important and should be offered to the patients and their partners/family members.

However, voices of affected patients and their partners/family members are still missing from the mainstream debate as there are only very few studies exploring the experiences of cancer patients who are also parents (Elmberger, Bolund, and Lützén 2005) and pregnant patients who experience critical health conditions (Kenyon et al. 2006)(Smyth, Jacoby, and Elbourne 2012). This knowledge gap is also recognised by Oncofertility scholars (Shen and Badr 2014).

There is only one study exploring the practices and clinicians' attitudes towards cancer treatment in the course of pregnancy (Sileny N Han et al. 2013). More in depth understanding of experiences, attitudes and approaches held by different stakeholders to cancer care during pregnancy would help to form a comprehensive ethics guideline for healthcare professionals. Having such guideline would serve as an ethical reference tool for physicians, nurses, careers, counsellors and other professionals involved in pregnant cancer patients care.

Current framework remains highly theoretical and would need to be developed further in line with advances in medicine and information collected by using social research methods. In order to proceed to the development of a guideline it would require better understanding of practices and views held by healthcare professionals as well as attitudes and experiences of patients and their families. Such work would require interdisciplinary collaboration between physicians, nurses and other healthcare professionals as well as social scientists, psychologists, ethicists and patient representatives.

6.5. Summary

This chapter consolidates the knowledge and ideas gathered in preceding chapters of this work. I present a framework for ethical care of pregnant cancer patients based on recognition that relationships between pregnant cancer patient, her family and healthcare professionals play a very important role. I suggest that respect for patient's autonomy should be re-specified as respect for relational autonomy in this context because doing so helps to understand patient's personal philosophy better and take her personal views into account when assisting her with decisions concerning her cancer treatment and pregnancy care. I recognise that such approach might have some down-sides such as exposing the patient to influences by other parties (co-creation of her narrative identity). However, offering counselling services to pregnant cancer patients and their family members could help to identify their vulnerabilities and build resilience to them.

Furthermore, I expect that having this in-depth theoretical study of concepts found in ethics and informed by evidence-based research in medicine as well as social sciences, will serve as a solid background for reference when facing difficult choices in cancer care during pregnancy, as well as for working further in order to develop an ethics guideline to assist in addressing ethical uncertainties.

Conclusion

In this work I explored the ethical issues surrounding cancer care during pregnancy. In order to stay relevant to clinical practice and offer some reference for real life solutions I took every effort to research and understand the clinical background of the condition, use social science data on experiences and attitudes of affected stakeholders and systematically reviewed clinical practice guidelines for cancer care during pregnancy.

In regards to ethical issues, I examined the theoretical background looking to understand the background of maternal-foetal conflict and foetal interests in the light of prenatal harm. My approach to ethical problems arising in cancer care during pregnancy is that cancer diagnosis compromises the nurturing role a pregnant cancer patient has towards her foetus. This, however, is not to say that I support one particular choice of available care such as treating maternal cancer and continuing pregnancy, delaying treatment until the delivery or terminating the pregnancy.

I focus more on the process how such care could be delivered to the patient and, in some cases, her partner and/or family. Therefore, I suggest that relational context should be taken into account by recognising the patient as another human being with compassion and empathy, acknowledging her personal philosophy and offering personalised care while at the same time indentifying potential vulnerabilities the patient might have.

Clinical practice guidelines review revealed that these documents emphasize the importance of respect for pregnant patient's autonomy but also take relational aspects into account. Moreover, they also recognise the importance of balancing maternal and foetal beneficence as well as protecting the vulnerable. In order to develop a framework for ethical care I build further on guidelines review by specifying what relational autonomy entails and identifying some safeguards to protect the individual patient to make well informed and considered choices

I suggest that it is not only the relationships between the patient and her partner and/or family that are important but also relationships which arise between the patient and her healthcare team, which is known as relational ethics. Therefore, healthcare team also has a responsibility to establish a caring relationship with a patient.

Furthermore, I recognise the dangerous effects which relational approach to patient's autonomy could have on an individual patient. Therefore, I suggest that the following concepts could serve as safeguards of individual autonomy when cancer care is delivered to pregnant patients. They are evidence-based information disclosure, personalised patient care and protection of the vulnerable. All of them could be incorporated in clinical care as well as other patient support services such as counselling.

I also support the idea that patients should be recognised as active participants and, in some cases, independent users of ethics support services. Hence, in this work I only explore the diversity of methods and approaches to such services without prioritising one method or approach over another. What I want to emphasise is that, should patients require ethics support, there should be some means available for delivering it.

Overall, I expect that my work will be a meaningful contribution to continuous development and delivery of ethical care for pregnant cancer patients. In a long-term perspective I hope that my work would serve as a foundational background for further research, point of reference for ethically minded solutions and further evolution of ethics guidance for healthcare professionals attending to pregnant patients with cancer.

Supplementary material

Appendix A: Guidelines for fertility preservation in cancer patients

Releasing body; year	Scope	Main statements regarding toxicity of cancer therapy, fertility preservation (FP) and future procreation
European expert panel consisting of physicians with expertise in the field of fertility preservation in cancer patients (Lambertini et al. 2016)	All cancer patients	<p>Pregnancy in cancer survivors should not be discouraged.</p> <p>All patients with potential interest in fertility preservation should be referred to fertility unit.</p>
National Comprehensive Cancer Network – NCCN, USA; 2014 (Coccia et al. 2014)	Adolescents and Young Adult (15-39)	<p>Fertility preservation should be an integral part of cancer management.</p> <p>The use of contraception should be discussed with all women before initiation of treatment.</p> <p>Women diagnosed with cancer during pregnancy require individualised treatment by multidisciplinary team.</p> <p>All patients should have access to age-appropriate supportive care and medical subspecialty services.</p>
American Society for Reproductive Medicine – ASRM; 2013 (American Society for Reproductive Medicine 2013)	All cancer patients	<p>Clinicians should inform patients about FP options and future reproduction before gonadotoxic treatment begins.</p> <p>Concerns about welfare of resulting offspring are not sufficient reasons to deny assistance in reproduction.</p> <p>Parents may act to preserve fertility for minors (assent and likeliness to provide future benefit).</p> <p>PGD to avoid offspring inheriting high risk of cancer is acceptable.</p> <p>Patients should have access to mental health, genetic and financial counsellors.</p>
American Society of Clinical Oncology – ASCO; 2013 (Loren et al. 2013)	All cancer patients	<p>Discuss FP with all patients of reproductive age (with parents or guardians of children and adolescents).</p> <p>Refer interested (and ambivalent) patients to fertility specialist.</p> <p>Address FP before treatment starts.</p>

		<p>Document FP discussion in medical records.</p> <p>Answer basic questions about FP and its impact on cancer treatment.</p> <p>Refer patients to psychosocial providers if patients experience distress.</p> <p>Encourage patients to participate in registries and clinical studies.</p>
European Society of Medical Oncology – ESMO (endorsed by Japanese Society of Medical Oncology – JSMO); 2013 (Peccatori et al. 2013)	Cancer patients in reproductive age	<p>Male: sperm banking should be planned before treatment initiation.</p> <p>Female: Young women desiring future fertility should be counselled on available fertility preservation options before starting anti-cancer treatment.</p>
European Society of Breast Cancer Specialists – EUSOMA; 2012 (Cardoso et al. 2012)	Young women (under 40)	<p>Fertility issues should always be discussed before the start of any breast cancer therapy.</p> <p>Discussion should allow time for reflection and involve partner, if present.</p> <p>Early referral to reproductive endocrinologist is warranted.</p>
International Society for Fertility Preservation – ISFP; 2012 (Jadoul and Kim 2012)(Kim et al. 2012)(Klemp and Kim 2012)(Schmidt and Andersen 2012)	Cancer patients of reproductive age	<p>All patients who desire to preserve fertility should be counselled and informed about available options.</p> <p>Recommendations should be individualised and not violate ethical principles.</p> <p>FP is strongly recommended if the chance of losing fertility is over 30%.</p>
Fertility preservation network FertiPROTEKT; 2011 (von Wolff et al. 2011)	Reproductive age women (14-40)	<p>All reproductive age women due to receive chemotherapy should be counselled on FP methods.</p> <p>All applicable methods should be mentioned.</p> <p>FP techniques must not affect the efficacy of oncological treatment.</p>
Expert consensus meeting in St Gallen; 2009 (Goldhirsch et al. 2009)	Breast cancer patients	<p>Pregnancy after breast cancer has not been shown to negatively affect prognosis.</p> <p>Women should be counselled about the options for FP.</p>

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