Ten-year experience of a national multidisciplinary tumour board for cancer and pregnancy in the Netherlands

Dutch Advisory Board for Cancer during Pregnancy; Heimovaara, Joosje H.; Boere, Ingrid A.; de Haan, Jorine; van Calsteren, Kristel; Amant, F.; van Zuylen, Lia; Lok, Christine A.R.

Published in:
European Journal of Cancer

DOI:
10.1016/j.ejca.2022.04.040

Publication date:
2022

European Journal of Cancer 171 (2022) 13–21

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Ten-year experience of a national multidisciplinary tumour board for cancer and pregnancy in the Netherlands

Joosje H. Heimovaara [a,b,*], Ingrid A. Boere [c], Jorine de Haan [d], Kristel van Calsteren [e], Frédéric Amant [a,b,f], Lia van Zuylen [g], Christine A.R. Lok [b,f] on behalf ofthe Dutch Advisory Board for Cancer during Pregnancy[1]

[a] *Department of Oncology, KU Leuven, Leuven, Belgium*
[b] *Department of Gynecology, Antoni van Leeuwenhoek – Netherlands Cancer Institute, Amsterdam, the Netherlands*
[c] *Department of Medical Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, the Netherlands*
[d] *Department of Obstetrics and Gynecology, Reproduction and Development Research Institute, Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands*
[e] *Department of Obstetrics and Gynecology, University Hospitals Leuven, Leuven and Department of Development and Regeneration, KU Leuven, Leuven, Belgium*
[f] *Center for Gynecological Oncology Amsterdam (CGOA), Antoni van Leeuwenhoek – Netherlands Cancer Institute, Amsterdam, the Netherlands*
[g] *Department of Medical Oncology, Amsterdam University Medical Centers, Cancer Center Amsterdam, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands*

Received 9 March 2022; received in revised form 19 April 2022; accepted 29 April 2022

KEYWORDS
Multidisciplinary tumour board;
Cancer;
Pregnancy

Abstract ***Background:*** Most physicians encounter pregnant women with cancer incidentally, leading to a lack of expertise or confidence to inform and treat these patients based on the most recent guidelines and expert opinions. In the Netherlands, a national multidisciplinary tumour board for cancer, infertility and pregnancy (CIP-MDT) was founded in December 2012, including 35 specialists from a variety of disciplines. This study evaluates the frequency of consultation of the CIP-MDT, the types of questions asked and the satisfaction of consulting physicians with its existence.

Methodology: Of all requests to the CIP-MDT between December 2012 and June 2021, tumour type, stage, gestational age at diagnosis and recommendations were collected and

* *Corresponding author*: Department of Gynaecologic Oncology, Antoni van Leeuwenhoek – Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands.
E-mail address: j.heimovaara@nki.nl (J.H. Heimovaara).
[1] Members Dutch advisory board for cancer in pregnancy June 2021.

https://doi.org/10.1016/j.ejca.2022.04.040

analysed. For evaluating the methods of the CIP-MDT, a survey with questions regarding experiences with the CIP-MDT and its impact on treatment decisions was sent out to physicians that consulted the CIP-MDT.
Results: Recommendations (n = 213) concerned preferred and safest options for imaging, treatment options during pregnancy, possible effects on the child and fertility preserving options. Most frequently discussed malignancies were breast cancer (n = 66), cervical cancer (n = 34), haematological malignancies (n = 32) and melanoma (n = 21). The questionnaire was completed by 54% of the physicians (n = 50). Satisfaction with the recommendations of the CIP-MDT was high, and 94% of the physicians informed their patients about consulting the CIP-MDT and felt supported by the received recommendations.
Discussion: The national Dutch CIP-MDT contributes to a high level of satisfaction among physicians requesting advice. Further research should be executed to confirm that a CIP-MDT improves the outcomes for pregnant women and their children.

1. Introduction

Although cancer in pregnancy affects more than 2000–4000 women in Europe each year, individual physicians encounter this situation infrequently [1]. Therefore, many physicians lack the expertise and confidence to treat pregnant women with cancer, according to the most recent insights. Pooling, reviewing and analyzing cases of multiple patients with cancer during pregnancy will increase the expertise. This leads to suboptimal care, both oncological and obstetrical [2]. A national multidisciplinary tumour board (MDT) for cancer, infertility and pregnancy (CIP-MDT) could contribute to improved care for these patients.

MDTs are part of standard oncological care, assuring multidisciplinary treatment according to the best available evidence or multidisciplinary consensus [3]. The establishment of CIP-MDTs in every hospital providing oncological care is not realistic due to low patient numbers. Geographical and logistic barriers can hinder the referral of these patients to hospitals with dedicated CIP-MDTs. Finding alternative ways to provide the most optimal care to these patients is therefore highly relevant.

In the Netherlands, a national CIP-MDT, 'Adviesgroep Kanker en Zwangerschap', was founded in December 2012 to support Dutch physicians with treatment decisions regarding their pregnant patients with cancer. This CIP-MDT consists of specialists of varying disciplines (Table 1). Physicians requesting advice are asked to send a (anonymous) summary of the obstetrical and oncological medical history of their patient together with their routine cancer treatment proposal for a non-pregnant patient. The CIP-MDT formulates written recommendations on how and if standard treatment is possible in relation to the pregnancy, with any obstetrical adjustments or precautions.

This study evaluates how often a CIP-MDT is consulted, whether this has changed over the years, the recommendations given, the feedback on the working methods of the MDT and the satisfaction of the physician requesting advice.

2. Material and methods

2.1. Summary of cases

All patients discussed in the CIP-MDT were anonymously registered in a database. The recommendation letters were gathered. Data on tumour type and stage, trimester at diagnosis, type of request and final recommendations were extracted. Data were retrieved from August 2013 until June 2021. In some cases, the documented recommendation was not available since the requests required immediate response by mail or phone due to the urgency of the request. Fig. 1 shows the routine handling of requests by the CIP-MDT.

2.2. Questionnaire

In October 2020, a questionnaire was sent out to 93 Dutch physicians, who requested one or more recommendations from the CIP-MDT between August 2013 and October 2020, even when no formal recommendation

Table 1
Disciplines represented by the CIP-MDT.

Medical specialists
Anaesthesiologist
Clinical pharmacologist
Ethical advisor
Fertility specialist
Gynaecologic oncologist
Haematologist
Medical oncologist
Obstetrician
Medical physicist
Pediatric oncologist
Radiation oncologist
Radiologist
Surgical oncologist

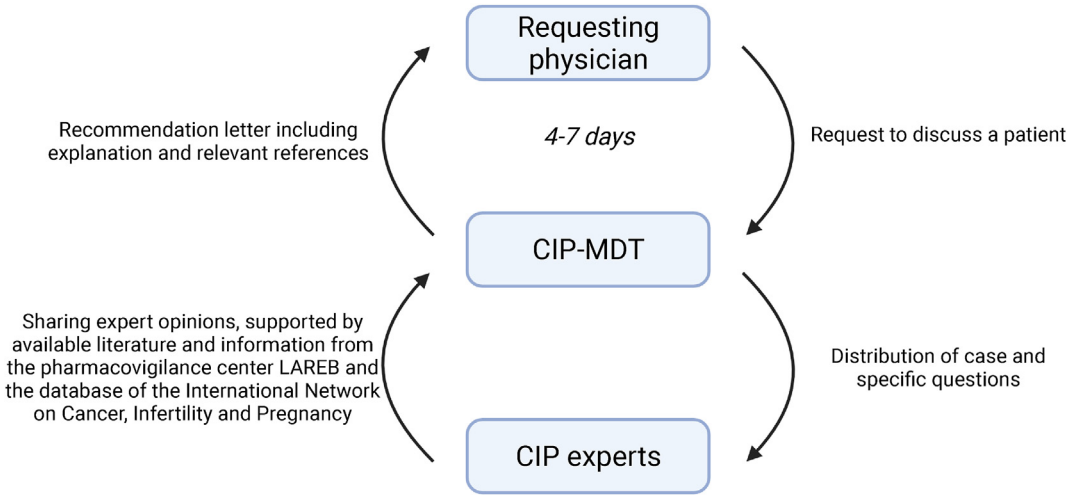

Fig. 1. **Workflow of the CIP-MDT**. Requests to discuss a patient in the CIP-MDT and to formulate a recommendation were received by e-mail. Patient data were anonymized and distributed by e-mail in standardized format among all members of the CIP-MDT along with specific questions of the treating physician. All medical experts of the CIP-MDT contributed to the conversation by mail in their area of expertise. The discussion continued until a uniform, tailor made recommendation letter could be formulated. Beside expert opinion, the recommendations were supported by available literature, by data from the Dutch pharmacovigilance center LAREB and by additional data of similar patients in the database of the International Network on Cancer, Infertility and Pregnancy (INCIP). [35] The letter containing the formulated recommendation including the explanation and relevant references, was sent to the requesting physician usually within four to seven days after the request was received. When needed, urgent on-demand recommendations can be provided.

letter was available. SurveyMonkey (www.surveymonkey.com) was used for the distribution of questionnaires and collection of data. Reminders were sent three and five weeks after the first invitation. The questionnaire contained 28 questions regarding accessibility of the CIP-MDT, recommendations received and their impact on treatment decisions (Appendix). There were 17 multiple-choice questions, seven 1 to 10 scale questions (from 'strongly disagree' to 'strongly agree') and four open-end questions. Informed consent was obtained from all participating physicians. Since this is not an interventional study according to Dutch law, formal ethical approval was waived by the Ethical review board of the Netherlands Cancer Institute.

Data were analysed in IBM SPSS Statistics (version 25). Standardised descriptive analyses were used with medians, percentages and ranges (0–10). Subgroups of different tumour types were analysed for stage, the subtype of cancer and the type of initial treatment. Gestational age was categorised into weeks and trimesters. An independent samples t-test was performed to compare the number of times that different types of requests were asked of the advisory board in the first five years compared to the last five years.

3. Results

From August 2013 until June 2021, 213 recommendation letters were formulated for 119 requesting physicians from 42 different hospitals (Supplementary Fig. 1). The number of requests increased from two in 2013 to 44 in 2020 (Fig. 2). The questions concerned cancer during and after pregnancy or were related to fertility (Table 2). The vast majority regarded breast cancer (n = 65, 30.5%), followed by cervical cancer (n = 35, 16.4%), haematological malignancies (n = 32, 15.0%) or melanoma (n = 21, 9.9%). 141 (81.1%) of all pregnant patients were in their 2nd or 3rd trimester of pregnancy at the time of advice request. The content of recommendations is summarised in Fig. 3. When comparing the types of requests asked in the first five years of existence compared to the last five years overall, a decrease in percentages was seen for all types of requests except treatment during delivery and timing or modus of delivery (Table 3). Of all percentages of types of requests that decreased, four were significantly lower between 2017 and 2021, as shown in Table 3.

3.1. Breast cancer

Of 65 breast cancer patients, 53 (81.5%) had their diagnosis during pregnancy, nine (13.8%) wished to conceive after cancer (treatment), and three (4.6%) were pregnant shortly after cancer (treatment). Stages of disease varied. Of 50 patients with a registered hormone receptor status, breast cancer was triple negative in 20 (40%), ER and/or PR positive and HER2NEU negative in 16 (32%) and triple positive in 10 (20%) patients. The content of the requests is outlined in Fig. 3.

Information on starting and/or sequence of therapy mostly concerned questions on whether to start with surgery or neoadjuvant chemotherapy. The CIP-MDT

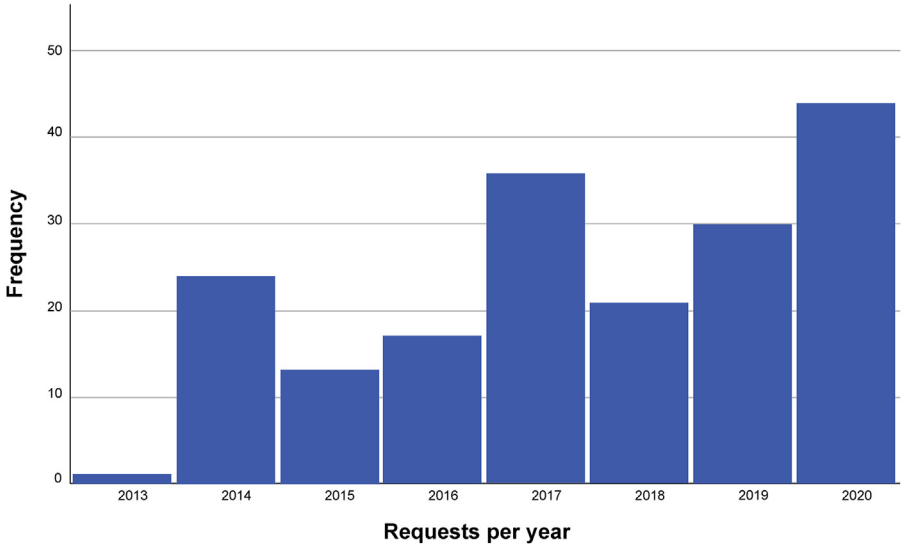

Fig. 2. Amount of requests discussed by the CIP-MDT per year (2013–2020).

Table 2
Overview of cases discussed in the CIP-MDT.

Total number of patients	213
Cancer type	
Breast cancer	66 (31.0%)
Cervical cancer	34 (16.0%)
Haematological Cancer	32 (15.0%)
Melanoma	21 (9.9%)
Ovarian cancer	11 (5.2%)
Sarcoma	9 (4.2%)
Brain tumour	8 (3.8%)
Thyroid cancer	4 (1.9%)
Urothelial cell carcinoma	3 (1.4%)
Gastric cancer	3 (1.4%)
Colon carcinoma	3 (1.4%)
Neuro-endocrine tumour	2 (0.9%)
Lung cancer	2 (0.9%)
Rectal carcinoma	2 (0.9%)
Vulvar carcinoma	2 (0.9%)
Other	11 (5.2%)
Type of request	
Cancer during pregnancy	174 (81.7%)
Preconception	23 (10.8%)
Pregnancy after cancer (treatment)	13 (6.1%)
Postpartum cancer diagnosis	1 (0.5%)
Cancer of the fetus	1 (0.5%)
Cancer treatment of father during conception	1 (0.5%)
Trimester at time of request	174
1st	33 (19.0%)
2nd	80 (46.0%)
3rd	61 (35.1%)
Metastatic disease	20 (9.4%)
Recurrent disease	14 (6.6%)
Only pain relief and supportive care during pregnancy	4 (1.9%)

considered chemotherapy as optimal therapy during pregnancy in 31 (67.4%) patients, after at least 12 weeks of gestation, ending before 36 weeks of pregnancy [4,5]. Surgery during pregnancy was recommended for 20 (43.5%) patients [6]. When a sentinel node procedure was part of the proposed treatment plan, it was recommended to perform this without blue dye due to the possibility of an anaphylactic reaction of the mother [7]. For nine pregnant patients (20.5%), radiation therapy was part of the proposed treatment plan. Of the 37 documented recommendations regarding treatment during pregnancy, 12 (32.4%) did not follow standard protocols for non-pregnant patients, mostly because the CIP-MDT advised against hormonal and HER2NEU targeted therapy in pregnancy. Six patients were diagnosed with distant metastases, including four with a recurrence. For these patients, recommendations were requested regarding options for pain relief and radiation therapy for metastatic lesions or delivery options in the presence of vertebral or pelvic metastases. For patients with early pregnancies and/or poor prognosis, termination of pregnancy was considered. It was only recommended in the pregnancy was discovered after diagnostic imaging and/or adjuvant radiation therapy, resulting in a very high fetal radiation dose, leading to a significant risk of congenital abnormalities. Requests regarding women with active intention to conceive mostly concerned premature interruption of hormonal therapy and preconception questions in patients with poor prognosis.

3.2. Cervical cancer

Recommendations were requested for 34 patients with cervical cancer. Of 26 patients with the known stage of disease, 12 (46.2%) were diagnosed with FIGO stage IB during pregnancy, six (23.1%) with stage IIB, three (11.1%) with stage IA1, two (7.7%) with stage III, two (7.7%) with stage IV and one with stage IIA (3.8%).

Treatment of cervical cancer during pregnancy is difficult since standard treatment is often not compatible

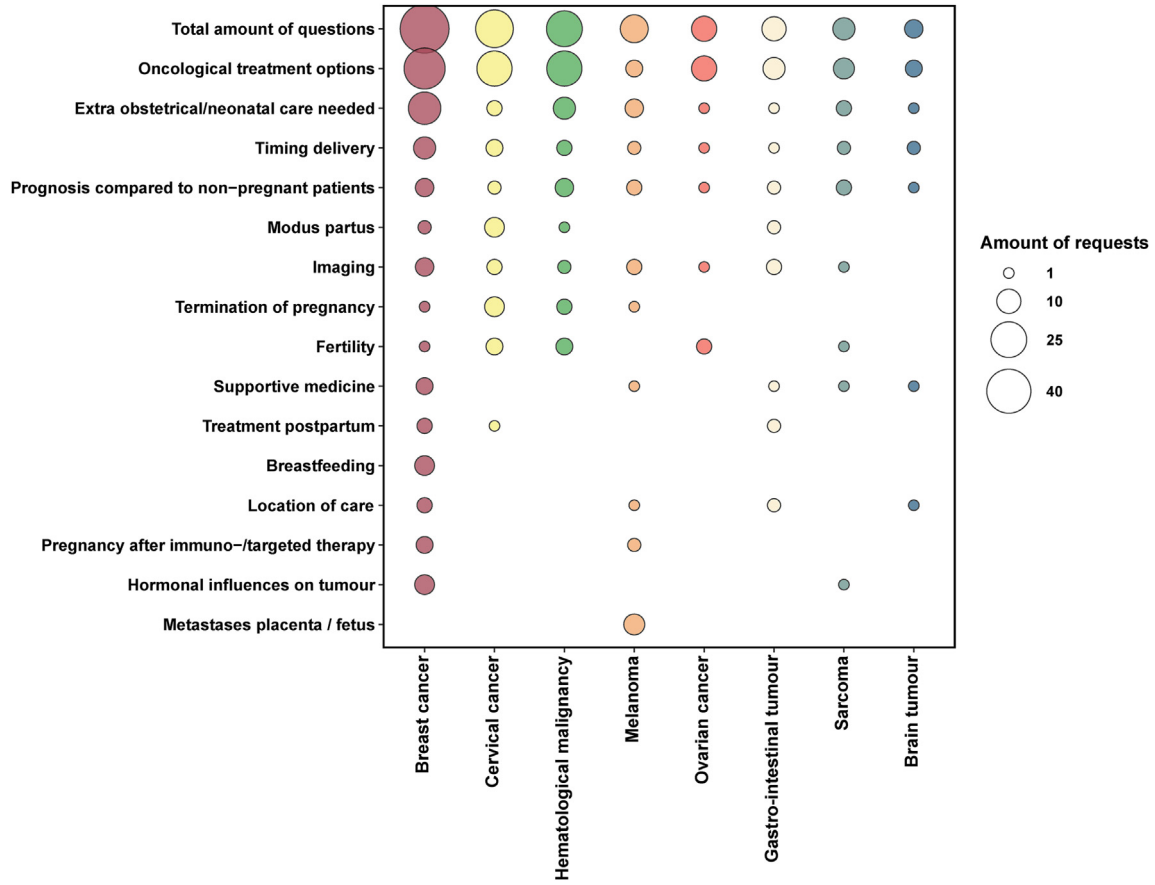

Fig. 3. **Types of requests asked per tumour type**. Bubble chart shows the amount of times different types of requests were asked per tumour type. First row shows maximum amount of times requests were asked. Some requests concerned several questions, these are all scored separately.

with ongoing pregnancy. For seven patients (25.8%) with early stage disease, conisation and/or lymphadenectomy (during early pregnancy) was recommended [8]. For higher stages, the majority of requests concerned the possibility of preserving the pregnancy, the possibility of postponing definitive treatment until after

Table 3
Types of requests asked per time frame.

	Timeframe		Difference	p-values
	2012–2016	2017–2020		
	n = 33	n = 134		
Oncological treatment options	69.7	79.1	+9.4%	0.251
Extra obstetrical/neonatal care needed	54.5	20.1	−34.4	<0.001
Timing delivery	9.1	14.9	+5.8%	0.387
Prognosis compared to non-pregnant patients	21.2	5.2	−16.0%	0.003
Modus partus	6.1	7.5	+1.4%	0.782
Imaging	18.2	9.7	−8.5%	0.171
Termination of pregnancy	12	5.2	−6.8%	0.154
Fertility related questions	9.1	4.5	−4.6%	0.296
Supportive medicine	0	5.2	+5.2%	0.182
Treatment postpartum	6.1	3	−3.1%	0.398
Breastfeeding	12.1	1.5	−10.6%	0.003
Location of care	6.1	3.7	−2.4%	0.553
Pregnancy after immuno/targeted therapy	6.1	3	−3.1%	0.398
Hormonal influences on tumour	27.3	4.5	−22.8%	<0.001
Metastases placenta/fetus	6.1	3.7	−2.4%	0.553

Percentage of times types of requests were asked during the first five years of existence of the advisory board (2012–2016, n = 33) and the second (2017–2020, n = 134).

delivery, and the mode of delivery (Fig. 3). Preservation of pregnancy was possible in 24 patients (80%). Chemotherapy during pregnancy was recommended for 17 patients (54.8%), with possible further treatment postponed until after delivery. To avoid a previable termination in four patients, up to six cycles of chemotherapy were needed. To avoid the slightest possibility of tumour spill during vaginal birth with possible metastasis in a vaginal or perineal tear, episiotomy site or even to the child, the CIP-MDT recommended a caesarean section in all cases [9–11].

For seven (35%) patients with stage IIB or IIIC (FIGO 2018) diagnosed prior to 24 weeks of gestation, termination of pregnancy was recommended to avoid suboptimal treatment [12]. In most of these cases, chemoradiotherapy was proposed, making fetal death inevitable.

3.3. Haematological malignancies

Of 32 patients with haematological malignancies, 27 (84.4%) had a malignancy during pregnancy, three (9.4%) patients were diagnosed postpartum and two (6.3%) wanted to conceive after haematological treatment. Twelve (37.5%) patients had acute myeloid leukaemia, including three acute promyelocytic leukaemia, three (9.4%) had acute lymphoblastic leukaemia, three (9.4%) chronic myeloid leukaemia, eight (25.0%) non-Hodgkin lymphoma and six (18.8%) Hodgkin lymphoma.

Most requests were concerned with advice on haematological treatment options during pregnancy (Fig. 3) due to toxicity of most standard chemotherapy regimens for haematological malignancies and the lack of cancer treatment experience during pregnancy [13–16]. Of 21 cases with documented recommendations regarding treatment during pregnancy, 10 (47.6%) deviated from the standard protocol for non-pregnant patients. The CIP-MDT supported the proposed termination of pregnancy in four (12.5%) cases due to a stem cell transplantation or intensive chemotherapy needed during early pregnancy, both not compatible with a viable fetus.

3.4. Melanoma

Of thirteen requests concerning patients with melanoma during pregnancy, four wished to conceive after melanoma treatment, three were pregnant after previous melanoma treatment, including immunotherapy, and one was diagnosed postpartum.

Recommendations were mostly sought regarding the possibility of placental and fetal metastases and whether extra obstetrical precautions would be necessary (Fig. 3). Information on whether pregnancy would increase the risk of recurrence or consequences of immunotherapy on a future pregnancy was also requested. The CIP-MDT recommended delaying conception to at least six months after treatment, based on biological aspects of the tumour and targeted and immunotherapeutic agents, case reports and available literature [17]. Surgery during pregnancy was recommended for 83.3%, e.g. (re-)excision of the tumour and/or sentinel node procedure (with Technetium-99 and avoiding blue dye) [7]. The CIP-MDT recommended performing a histologic examination of the placentas due to the increased risk of placental metastasis in melanoma patients, especially in the case of metastatic disease [18]. Diagnostic imaging, including fluorine-18-fluorodeoxyglucose positron emission tomography integrated with computed tomography, was considered feasible for three patients when necessary for treatment planning since the radiation dose is far below the threshold for fetal damage [19].

3.5. Rare cancers

Based on the rare disease definition of the European RARECARE project (less than six per 100 000 per year), 52 of all requests (24.4%) concerned rare cancers [20]. Most requests regarded patients with sarcoma (n = 9) and brain tumours (n = 7) (Table 2). The CIP-MDT advised caution with temozolomide administration during pregnancy for brain tumour cases because of unknown effects on the fetus and increased risk of severe thrombocytopenia [21–23]. Cerebral radiation therapy during pregnancy was considered to be safe since the distance from the uterus to the irradiation area remains large enough throughout the whole pregnancy [21].

3.6. Additional recommendations

Furthermore, for all cases discussed, not only the consequences of the primary oncological medication itself were considered, but also issues such as supportive drugs, location of care and obstetrical precautions during surgery or labour and delivery (Fig. 3). Based on these frequently asked questions the CIP-MDT received, default texts were formulated. The CIP-MDT always recommended monitoring fetal growth by ultrasound biometry when systemic therapy is administered and attached supplementary information on obstetrical care to the recommendation letter. Also, it pointed out to focus on the psychological support for pregnant women with cancer and their family and recommended follow-up of the children after birth [24].

3.7. Questionnaire

The questionnaire was answered by 50 physicians (54%). Two-thirds of all responding physicians worked in an academic hospital or oncology centre and one third in a general hospital. Most respondents were gynecologist (n = 28, 56%). The average number of requests per physician was 2, 12 and 27 respondents (56%) contacted the CIP-MTD multiple times, with the maximum of six

times by four respondents. Recommendations were received within a week in 96% of the cases. Overall satisfaction with the recommendations and way of communication was high, with a mean of 8.29 on a scale from 1 to 10 (SD = 2.064), leading to a large number of physicians basing their final treatment plan on the recommendations (M = 8.85, SD = 1.946) (Supplementary Fig. 2). Almost all physicians (94%) informed their patients about consulting the CIP-MDT, felt supported by the received recommendations and would recommend the CIP-MDT to their colleagues.

4. Discussion

This study shows that a national CIP-MDT for cancer during pregnancy is regularly consulted, and the number of requests increases with time. The CIP-MDT is highly appreciated by physicians, and repeat consultation often occurs. However, the percentage of patients discussed in the CIP-MDT is only a fraction of the total number of pregnant women affected by a diagnosis of cancer and the physicians who may be treating them. The incidence of cancer during pregnancy is estimated to be 1 in 1000–2000 live births. With approximately 170 000 live births annually in the Netherlands, close to 170 pregnant women are diagnosed with cancer annually [25–28]. The increase in requests over the years suggests the first.

The change in percentages for the different types of questions in the last 5 years could indicate that more treatment is started during pregnancy leading to more questions on treatment options and timing of delivery and less questions on termination of pregnancy. This trend in more treatment during pregnancy can be a sign of increased knowledge on the often similar prognosis during pregnancy and the obstetrical and neonatal care that is necessary. Another explanation would be that more women are referred to physicians with experience in providing obstetrical care for the patient population, but further documentation of advice requests and recommendations in the figure could show whether this change in percentages is only incidental or remains.

The malignancies discussed in the CIP-MDT reflect the expected incidence in pregnancy [29]. When taking into account all types of malignancies occurring at different gestational ages, most physicians lack the opportunity to acquire enough experience with pregnancy-related malignancies. Exposure of a medical specialist to a rare health problem is related to knowledge and quality of care and is of great importance for the outcome of the patient [30]. A nationwide CIP-MDT increases exposure and thus the experience of members, building sufficient knowledge and supporting colleagues throughout the country to treat and care for mother and child as close to home as possible. Board members of the CIP-MDT have gained experience in determining the feasible treatment options during pregnancy but also the safest way of treatment for mother and child in the absence of evidence-based guidelines. This experience is based on the review and pooled analysis of the outcomes of a larger number of patients with cancer in pregnancy.

Although cancer during pregnancy does not meet the official WHO criteria of a rare disease, this unique situation raises similar issues [20,31,32]. These include the small number of patients spread over a country, logistic problems in reaching expert centres, lack of validated diagnostic tools and treatments, limited clinical expertise and lack of evidence-based guidelines. Dedicated guidelines for the specialised treatment of different medical conditions are increasingly developed to optimise patient care but have not yet been published for all the different types of cancer encountered during pregnancy; however, no hospital could fulfil all these requirements. Membership in a national CIP-MDT and (inter)national registration can resolve this problem.

Fig. 4 shows the steps necessary to establish a CIP-MDT. The enthusiasm of stakeholders to participate in an on-demand virtual CIP-MDT will ultimately determine its success and sustainability. The variety of questions received by the CIP-MDT underlines the importance of including experts from various disciplines. Agreements must be made concerning means of communication of the CIP-MDT, how to be contacted by requesting physicians, the timing of response, formation of the board and planning of regular meetings. Visibility is key to success and acknowledgement of national medical societies and a yearly conference can be the next step in achieving this [33,34].

As stated previously, the CIP-MDT offers recommendations on how and if standard treatment is possible during pregnancy. A presentation of pros and cons as discussed by the CIP-MDT can be outlined in the recommendations to support a shared decision between healthcare professionals and patients. It should always be taken into account that the requesting physician has the most insight into their patient's preferences, characteristics and social situation and remains responsible for the initiated treatment plan.

Our study shows that logistic difficulties and geographical barriers to expertise needed can be overcome by a virtual CIP-MDT. Based on the results of this CIP-MDT, an overarching international CIP-MDT has been launched this year (www.ab-cip.org) and facilitates the establishment of several national CIP-MDTs. Although platforms to collect data and answer research questions regarding cancer and pregnancy, like the International Network on Cancer, Infertility and Pregnancy (INCIP), already exist, the CIP-MDT has the potential to improve clinical care for these patients as it draws on the expertise and information gained from registering pregnant patients with cancer in higher numbers than any single institution can accrue [35].

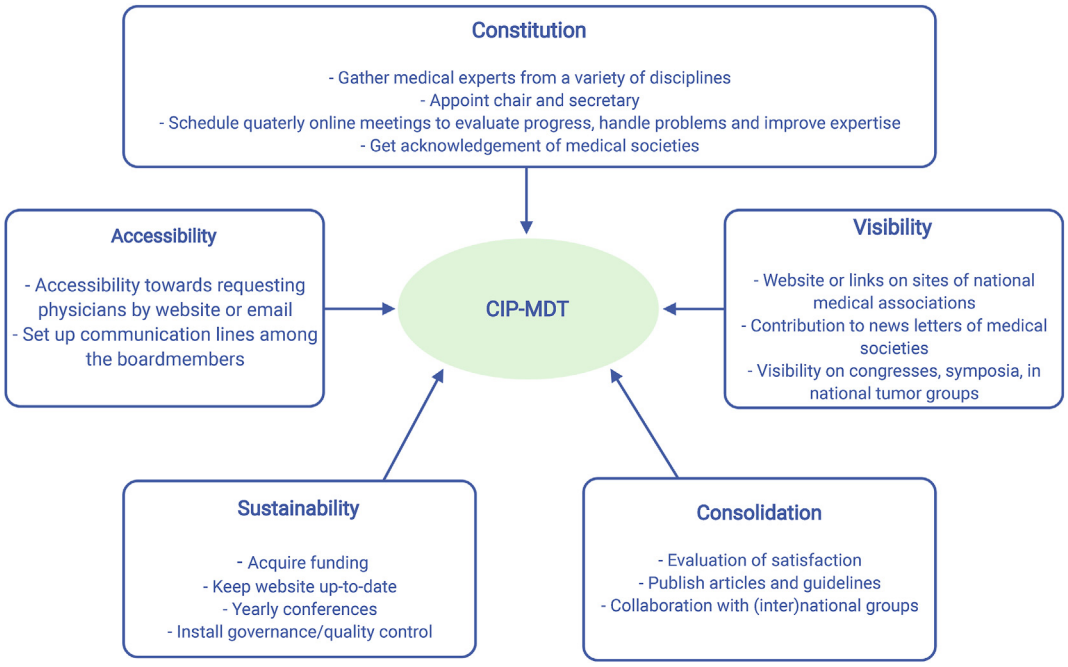

Fig. 4. **Flowchart of the steps taken at the foundation of a CIP-MDT**. Figure created with BioRender.com.

This study gives retrospective insight in the working methods of a national CIP-MDT. Almost 10 years of experience and increasing numbers of requests show that this initiative is highly appreciated and addresses a clinical need. Limitations of this study are the observational and retrospective character, taking into consideration that prospective or randomised studies are barely possible in this field. Outcomes and patient satisfaction were not documented. Therefore, the impact our CIP-MDT had on the treatment plan and outcome of patients could not be described. Future documentation of the advice next to inclusion of these patients in (inter)national registries, will give insight whether CIP-MDTs improves clinical outcome of patients [35].

Funding

None.

Author's contributions

Joosje H. Heimovaara: Conceptualisation, Methodology, Formal analysis, Visualisation, and Writing – Original draft.
Ingrid A. Boere: Project administration, Writing- Reviewing and Editing.
Jorine de Haan: Writing- Reviewing and Editing.
Kristel van Calsteren: Conceptualisation, Writing- Reviewing and Editing.
Frédéric Amant: Conceptualisation, Writing- Reviewing and Editing.
Lia van Zuylen: Project administration, Writing- Reviewing and Editing.
Christine A.R. Lok: Supervision, Conceptualisation, Methodology, and Writing- Reviewing and Editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of interest

None declared

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejca.2022.04.040.

References

[1] Han SN, Kesic VI, Van Calsteren K, et al. Cancer in pregnancy: a survey of current clinical practice. Eur J Obstet Gynecol Reprod Biol 2013;167(1):18–23. https://doi.org/10.1016/j.ejogrb.2012.10.026.
[2] de Haan J, Verheecke M, Van Calsteren K, et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. Lancet Oncol 2018;19(3):337–46. https://doi.org/10.1016/s1470-2045(18)30059-7.
[3] Thenappan A, Halaweish I, Mody RJ, et al. Review at a multidisciplinary tumor board impacts critical management decisions of pediatric patients with cancer. Pediatr Blood Cancer 2017;64(2):254–8. https://doi.org/10.1002/pbc.26201.

[4] La Nasa M, Gaughan J, Cardonick E. Incidence of neonatal neutropenia and leukopenia after in utero exposure to chemotherapy for maternal cancer. American Journal of Clinical Oncology 2019;42(4):351–4. https://doi.org/10.1097/COC.0000000000000527.
[5] Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. The Lancet Oncology 2004;5(5):283–91. https://doi.org/10.1016/s1470-2045(04)01466-4.
[6] Peccatori FA, Azim Jr HA, Orecchia R, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(Suppl 6):vi160–70. https://doi.org/10.1093/annonc/mdt199.
[7] Bézu C, Coutant C, Salengro A, et al. Anaphylactic response to blue dye during sentinel lymph node biopsy. Surgical Oncology 2011;20(1):e55–9. https://doi.org/10.1016/j.suronc.2010.10.002.
[8] Amant F, Berveiller P, Boere IA, et al. Gynecologic cancers in pregnancy: guidelines based on a third international consensus meeting. Annals of Oncology 2019;30(10):1601–12.
[9] Van den Broek NR, Lopes AD, Ansink A, et al. "Microinvasive" adenocarcinoma of the cervix implanting in an episiotomy scar. Gynecol Oncol 1995;59(2):297–9. https://doi.org/10.1006/gyno.1995.0025.
[10] Baloglu A, Uysal D, Aslan N, et al. Advanced stage of cervical carcinoma undiagnosed during antenatal period in term pregnancy and concomitant metastasis on episiotomy scar during delivery: a case report and review of the literature. Int J Gynecol Cancer 2007;17(5):1155–9. https://doi.org/10.1111/j.1525-1438.2007.00926.x.
[11] Arakawa A, Ichikawa H, Kubo T, et al. Vaginal transmission of cancer from mothers with cervical cancer to infants. N Engl J Med 2021;384(1):42–50. https://doi.org/10.1056/NEJMoa2030391.
[12] Bhatla N, Aoki D, Sharma DN, et al. Cancer of the cervix uteri. Int J Gynecol Obstetrics 2018;143:22–36. https://doi.org/10.1002/ijgo.12611.
[13] Santolaria A, Perales A, Montesinos P, et al. Acute promyelocytic leukemia during pregnancy: a systematic review of the literature. Cancers (Basel) 2020;12(4). https://doi.org/10.3390/cancers12040968.
[14] Maggen C, Dierickx D, Lugtenburg P, et al. Obstetric and maternal outcomes in patients diagnosed with Hodgkin lymphoma during pregnancy: a multicentre, retrospective, cohort study. Lancet Haematol 2019;6(11):e551–61. https://doi.org/10.1016/S2352-3026(19)30195-4.
[15] Lishner M, Avivi I, Apperley JF, et al. Hematologic malignancies in pregnancy: management guidelines from an international consensus meeting. J Clin Oncol 2016;34(5):501–8. https://doi.org/10.1200/JCO.2015.62.4445.
[16] Palani R, Milojkovic D, Apperley JF. Managing pregnancy in chronic myeloid leukaemia. Ann Hematol 2015;94(Suppl 2):S167–76. https://doi.org/10.1007/s00277-015-2317-z.
[17] Borgers JSW, Heimovaara JH, Cardonick E, et al. Immunotherapy for cancer treatment during pregnancy. Lancet Oncol 2021;22(12):e550–61. https://doi.org/10.1016/s1470-2045(21)00525-8.
[18] Pavlidis N, Pentheroudakis G. Metastatic involvement of placenta and foetus in pregnant women with cancer. Recent Results Cancer Res 2008;178:183–94. https://doi.org/10.1007/978-3-540-71274-9_16.
[19] Vandecaveye V, Amant F, Lecouvet F, et al. Imaging modalities in pregnant cancer patients. Int J Gynecol Cancer 2021;31(3):423–31. https://doi.org/10.1136/ijgc-2020-001779.
[20] Gatta G, van der Zwan JM, Casali PG, et al. Rare cancers are not so rare: the rare cancer burden in Europe. Eur J Cancer 2011;47(17):2493–511. https://doi.org/10.1016/j.ejca.2011.08.008.
[21] Verheecke M, Halaska MJ, Lok CA, et al. Primary brain tumours, meningiomas and brain metastases in pregnancy: report on 27 cases and review of literature. Eur J Cancer 2014;50(8):1462–71. https://doi.org/10.1016/j.ejca.2014.02.018.
[22] McGrane J, Bedford T, Kelly S. Successful pregnancy and delivery after concomitant temozolomide and radiotherapy treatment of glioblastoma multiforme. Clin Oncol (R Coll Radiol) 2012;24(4):311. https://doi.org/10.1016/j.clon.2012.01.005.
[23] Evans AC, Nelson MB, Dhall G. Pregnancy in a patient with a malignant brain tumor taking temozolomide: case report and review of the literature. J Pediatr Oncol Nurs 2015;32(5):326–8. https://doi.org/10.1177/1043454214563414.
[24] Vandenbroucke T, Han SN, Van Calsteren K, et al. Psychological distress and cognitive coping in pregnant women diagnosed with cancer and their partners. Psychooncology 2017;26(8):1215–21. https://doi.org/10.1002/pon.4301.
[25] Smith LH, Danielsen B, Allen ME, et al. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. Am J Obstet Gynecol 2003;189(4):1128–35. https://doi.org/10.1067/s0002-9378(03)00537-4.
[26] Lee YY, Roberts CL, Dobbins T, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study. BJOG 2012;119(13):1572–82. https://doi.org/10.1111/j.1471-0528.2012.03475.x.
[27] Parazzini F, Franchi M, Tavani A, et al. Frequency of pregnancy related cancer: a population based linkage study in lombardy, Italy. Int J Gynecol Cancer 2017;27(3):613–9. https://doi.org/10.1097/igc.0000000000000904.
[28] Netherlands. CBoSot. Bevolking en bevolkingsontwikkeling per maand. 1995-2018. https://opendata.cbs.nl/statline/#/CBS/nl/dataset/37943ned/table. [Accessed 27 January 2021].
[29] de Haan J, Verheecke M, Van Calsteren K, et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. Lancet Oncol 2018;19(3):337–46.
[30] Commission E. Conference report. 3rd conference on European reference networks. 2017 March 9-10. https://ec.europa.eu/health/sites/health/files/ern/docs/ev_20170309_frep_en.pdf2017. [Accessed 27 January 2021].
[31] Organization WH. Priority diseases and reasons for inclusion - rare diseases. https://www.who.int/medicines/areas/priority_medicines/Ch6_19Rare.pdf. [Accessed 27 January 2021].
[32] Lok C, Amant F. Editorial: the challenge of treating and investigating rare gynaecologic cancers. Curr Opin Oncol 2021;33(5):432–4. https://doi.org/10.1097/cco.0000000000000761.
[33] Blay JY, Coindre JM, Ducimetière F, et al. The value of research collaborations and consortia in rare cancers. Lancet Oncol 2016;17(2):e62–9. https://doi.org/10.1016/s1470-2045(15)00388-5.
[34] Ray-Coquard I, Pujade Lauraine E, Le Cesne A, et al. Improving treatment results with reference centres for rare cancers: where do we stand? Eur J Cancer 2017;77:90–8. https://doi.org/10.1016/j.ejca.2017.02.006.
[35] Maggen C, Wolters V, Cardonick E, et al. Pregnancy and cancer: the INCIP project. Curr Oncol Rep 2020;22(2):17. https://doi.org/10.1007/s11912-020-0862-7.