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Editorial

Model of care for women at increased risk of breast and ovarian cancer

Women with a family history of breast and/or ovarian cancer have a substantially higher risk of developing these cancers and at a much younger age when compared to the general population [1]. For women with a proven *BRCA1* or *BRCA2* mutation, this life time risk can reach up to 65% for breast cancer and up to 45% for ovarian cancer by the age of 70, according to two large meta-analyses [2,3].

In The Netherlands, the care for these high risk women is mainly concentrated in university hospitals because of the availability of highly specialized expertise. Our university hospital is situated in the North of The Netherlands, covering an area of 3.4 million inhabitants. In our hospital, the care for these women is provided by a multidisciplinary team consisting of clinical geneticists, surgical oncologists, gynecological oncologists, oncology nurses, a psychologist, a radiologist, plastic surgeons, and a pathologist. The team is supported by two epidemiologists.

Interventions comprise a four-stage approach consisting of risk assessment and genetic counselling, gene-mutation analysis, oncologic counselling and medical screening or intervention strategies (preventive surgery) [4]. When an increased cancer risk is assumed because of a personal or family history, women are referred to our family cancer clinic [5,6]. The clinical geneticists assess the breast and/or ovarian cancer risk based on a confirmation of the family history, and whether there is an indication for DNA-testing. The women are extensively counselled on the pros and cons of DNA-testing, its timing and the possible personal and familial consequences. If women need support with their decision making, they are referred to the psychologist of the team.

The surgical oncologists counsel patients in their choice of risk reducing strategies. Regarding breast cancer, they can opt for screening or for a preventive mastectomy with or without reconstructive surgery [7,8]. The latter service is provided by the plastic surgeons. All women opting for preventive mastectomy are referred to the psychologist to discuss this option and the consequences.

Regarding ovarian cancer, women with a positive family history or a *BRCA1/2* mutation are counselled by a gynecological oncologist on risk reducing strategies for ovarian cancer. Women are counselled on lifestyle, family planning and on the optimal timing of risk-reducing salpingo-oophorectomy (RRSO) and the short- and long-term sequelae [9–11]. Since ovarian cancer screening is not effective, from 2009 this option is not offered anymore. After RRSO, women visit the family cancer clinic for advice regarding prevention or treatment of hot flushes, psychosexual functioning and osteoporosis [12–14].

By offering the care for these women in such an integrated way, the university hospital can take the lead as initiating participant

in a managed clinical network of the catchment area [15,16]. In a managed clinical network, one of the major challenges is to develop better access to relevant generic information for women and clinicians (sharing knowledge) – from general practitioner's data, to hospital units including surgeons and gynecologists, to cancer centre registries and back.

From 1994, all newly referred women are entered into the BrOCa registration. Included are women with a *BRCA1* or *BRCA2* mutation, not tested women with a first degree relative with a *BRCA1* or *BRCA2* mutation and women with a life time risk of more than 30% to develop breast cancer or a risk of more than 10% to develop ovarian cancer.

For all registered patients, there is a linkage connection with the municipal registry to check whether a person is alive and still living in the catchment area in the North of the Netherlands, a linkage with diagnoses and care data of the general practitioner and with pharmacy prescriptions is planned. In 1994, when our family cancer clinic started, patient data were entered in lists guaranteeing a prospective registration of a consecutive cohort of all women attending. Nowadays, all information concerning a contact is put into the database during the consultation. For these registrations we have developed a prospective system with an entry interface in which most of the collected information is predefined. The physician can just click and upon finishing the consultation, the database is filled with the entered information and a letter to the referring physician is produced automatically as well. Information not entered during the consult (among others results of mammography or serum level of CA125) is retrieved from the hospital information system by using the unique identifiers on a regular basis.

For each research project relevant data are retrieved from the registration and linked by the use of a unique identifier. These new datasets are anonymized. In all research projects, the involved care providers participate as well as one of the epidemiologists. All new patients are asked for informed consent. Every research project based on the BrOCa registration and tissue/serum bank has to be approved by the Medical Ethical Committee.

Our prospective system guarantees that no patient contacts are missed and that information exchange with the referring doctor is much faster and more accurate than before. Due to the interface with a predefined format, the data reliability is enhanced. The time between the hospital consultation and the written report to the referring doctor has come down to 5 days at a maximum.

The evaluation of the effectiveness and cost-effectiveness of the provided care has been performed on the following topics: the penetrance of *BRCA1* and *BRCA2* mutations and variants [17–23], the effectiveness of surveillance [24–29], psychological and familial

aspects [7,13,30,31] and on the safety and effects of RRSO [11,14]. Because there is increasing evidence that ovarian cancer screening is not effective in detecting early ovarian cancer, since 2009 ovarian cancer screening has been abandoned and women are counselled on lifestyle, family planning and on the optimal timing of risk-reducing salpingo-oophorectomy (RRSO) and the short- and long-term sequelae [9–11].

The strength of this prospective cohort registration is that it improves the quality of care for this patient group. As a consequence of this systematic evaluation of care we nowadays include not only the doctors' perspective on the trade off between surveillance and preventive surgery (preventive surgery to prevent dying from cancer) but also patients perspective (preventive surgery to diminish cancer worries and prevent getting cancer). This database allows us to pool data with other (inter)national centres. The main weakness is that the amount of items on which data is collected is as yet limited. This can also be considered as an advantage because it makes this registry complete and up to date but, when research is planned, for most research questions additional information from the patient files is needed.

Women with an inherited increased risk of breast and ovarian cancer should be seen in a multidisciplinary setting to deliver up to date and optimal care and evaluate the short term and long term consequences of the given care.

Contributors

JdV, HH, JPJ, PMW, JCO, MJM contributed to the multidisciplinary care for these women. All authors contributed to the data registration and to this manuscript. All authors have read and approved this manuscript and agree with publication of their names.

Competing interests

The authors have no financial of any other kind of personal conflicts with this manuscript.

Provenance and peer review

Commissioned, not externally peer reviewed.

References

- [1] Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. *Cancer* 1994;73:643–51.
- [2] Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unscreened for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003;72:1117–30.
- [3] Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. *J Clin Oncol* 2007;25:1329–33.
- [4] Roukos DH, Briasoulis E. Individualized preventive and therapeutic management of hereditary breast ovarian cancer syndrome. *Nat Clin Pract Oncol* 2007;4:578–90.
- [5] King MC, Marks JH, Mandell JB. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science* 2003;302:643–6.
- [6] Anderson K, Jacobson JS, Heitjan DF, et al. Cost-effectiveness of preventive strategies for women with a BRCA1 or a BRCA2 mutation. *Ann Intern Med* 2006;144:397–406.
- [7] Van Roosmalen MS, Stalmeier PF, Verhoef LC, et al. Randomized trial of a shared decision-making intervention consisting of trade-offs and individualized treatment information for BRCA1/2 mutation carriers. *J Clin Oncol* 2004;22:3293–301.
- [8] Spear SL, Carter ME, Schwarz K. Prophylactic mastectomy: indications, options, and reconstructive alternatives. *Plast Reconstr Surg* 2005;115:891–909.
- [9] Domchek SM, Friebel TM, Neuhausen SL, et al. Mortality after bilateral salpingo-oophorectomy in BRCA1 and BRCA2 mutation carriers: a prospective cohort study. *Lancet Oncol* 2006;7:223–9.
- [10] Mourits MJ, de Bock GH. Managing hereditary ovarian cancer. *Maturitas* 2009;64:172–6.
- [11] Kenkhuis MJ, de Bock GH, Elferink PO, et al. Short-term surgical outcome and safety of risk reducing salpingo-oophorectomy in BRCA1/2 mutation carriers. *Maturitas* 2010;66:310–4.

- [12] Buijs C, Mom CH, Willemse PH, et al. Venlafaxine versus clonidine for the treatment of hot flashes in breast cancer patients: a double-blind, randomized cross-over study. *Breast Cancer Res Treat* 2009;115:573–80.
- [13] Madalinska JB, Hollenstein J, Bleiker E, et al. Quality-of-life effects of prophylactic salpingo-oophorectomy versus gynecologic screening among women at increased risk of hereditary ovarian cancer. *J Clin Oncol* 2005;23:6890–8.
- [14] Madalinska JB, van Beurden M, Bleiker EM, et al. The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women after prophylactic salpingo-oophorectomy. *J Clin Oncol* 2006;24:3576–82.
- [15] Introduction of managed clinical networks within the NHS in Scotland. NHS MEL (Management Executive Letter) 10. Edinburgh, UK: St Andrews House; 1999.
- [16] Gregor A. Managed clinical network in practice—is it working? *Clin Oncol (R Coll Radiol)* 2003;15:169–71.
- [17] van der Kolk DM, de Bock GH, Leegte BK, et al. Penetrance of breast cancer, ovarian cancer and contralateral breast cancer in BRCA1 and BRCA2 families: high cancer incidence at older age. *Breast Cancer Res Treat* 2010;124:643–51.
- [18] Rijnsburger AJ, Obdeijn IM, Kaas R, et al. BRCA1-associated breast cancers present differently from BRCA2-associated and familial cases: long-term follow-up of the Dutch MRISC screening study. *J Clin Oncol* 2010;28:5265–73.
- [19] Gómez García EB, Oosterwijk JC, Timmermans M, et al. A method to assess the clinical significance of unclassified variants in the BRCA1 and BRCA2 genes based on cancer family history. *Breast Cancer Res* 2009;11:R8.
- [20] Mohammadi L, Vreeswijk MP, Oldenburg R, et al. A simple method for co-segregation analysis to evaluate the pathogenicity of unclassified variants; BRCA1 and BRCA2 as an example. *BMC Cancer* 2009;9:211.
- [21] Leegte B, Van der Hout AH, Deffenbaugh, et al. Phenotypic expression of double heterozygosity for BRCA1 and BRCA2 germline mutations. *J Med Genet* 2005;42:e20.
- [22] Bodmer D, Ligtenberg MJ, van der Hout AH, et al. Optimal selection for BRCA1 and BRCA2 mutation testing using a combination of 'easy to apply' probability models. *Br J Cancer* 2006;95:757–62.
- [23] Verhoog LC, van den Ouweland AM, Berns E, et al. Large regional differences in the frequency of distinct BRCA1/BRCA2 mutations in 517 Dutch breast and/or ovarian cancer families. *Eur J Cancer* 2001;37:2082–90.
- [24] van der Velde NM, Mourits MJ, Arts HJ, et al. Time to stop ovarian cancer screening in BRCA1/2 mutation carriers? *Int J Cancer* 2009;124:919–23.
- [25] Hermesen BB, Olivier RI, Verheijen RH, et al. No efficacy of annual gynaecological screening in BRCA1/2 mutation carriers; an observational follow-up study. *Br J Cancer* 2007;96:1335–42.
- [26] Vasen HF, Tesfay E, Boonstra H, et al. Early detection of breast and ovarian cancer in families with BRCA mutations. *Eur J Cancer* 2005;41:549–54.
- [27] Kriege M, Brekelmans CT, Obdeijn IM, et al. Factors affecting sensitivity and specificity of screening mammography and MRI in women with an inherited risk for breast cancer. *Breast Cancer Res Treat* 2006;100:109–19.
- [28] Kriege M, Brekelmans CT, Peterse H, et al. Tumor characteristics and detection method in the MRISC screening program for the early detection of hereditary breast cancer. *Breast Cancer Res Treat* 2007;102:357–63.
- [29] Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med* 2004;351:427–37.
- [30] Ockhuysen-Vermey CF, Henneman L, Van Asperen CJ. Design of the BRISC study: a multicentre controlled clinical trial to optimize the communication of breast cancer risks in genetic counselling. *BMC Cancer* 2008;8:283.
- [31] Vos J, Stiggelbout AM, Oosterwijk J, et al. A counsellor-oriented perspective on risk communication in genetic counseling: explaining the inaccuracy of the counselees' risk perception shortly after BRCA1/2 test result disclosure. *Genet Med* 2011;13:800–11.

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