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Decision Aids for Preventive Treatment Alternatives for *BRCA1/2* Mutation Carriers: a Systematic Review

Entscheidungshilfen zu präventiven Handlungsalternativen für *BRCA1/2*-Mutationsträgerinnen: eine systematische Übersicht

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ABSTRACT

Introduction Women with a pathogenic *BRCA1/2* mutation have a markedly increased lifetime risk of developing breast and/or ovarian cancer. The current preventive treatment alternatives that are offered are an intensified breast cancer screening programme and risk-reducing operations. Before deciding on one option, medical and personal factors such as life situation and individual preferences must be weighed carefully. Decision aids are used internationally to support *BRCA1/2* mutation carriers during their decision-making process. In this study these are analysed structurally for the first time and their applicability to the German context is examined.

Material and Methods A systematic literature search in five electronic databases and a manual search were performed. The identified decision aids were evaluated with regard to formal criteria, medical content and quality. The qualitative assessment used the criteria of the International Patient Decision Aid Standards Collaboration (IPDASi v4.0), which examined various dimensions (e.g., information, probabilities, values).

Results Twenty decision aids, which were published between 2003 and 2019 in Australia (n = 4), the United Kingdom (n = 3), Canada (n = 2), the Netherlands (n = 2) and the USA (n = 9), were included. Nine focus on *BRCA1/2* mutation carriers and eleven include other risk groups. Eighteen include risk-reducing operations as decision options, 14 list screening methods for breast and/or ovarian cancer, and 13 describe the possibility of pharmacological prevention by means of selective oestrogen receptor modulators or aromatase inhibitors. Nine of the 20 decision aids meet fundamental quality criteria (IPDASi v4.0 qualification criteria).

Conclusion International decision aids can serve formally as a basis for a German decision aid for *BRCA1/2* mutation carriers. Some of them differ markedly in content from the recommendations of German guidelines. Only a few achieve a high quality.

ZUSAMMENFASSUNG

Einleitung Frauen mit einer pathogenen *BRCA1/2*-Mutation haben ein deutlich erhöhtes Lebenszeitrisiko, an Brust- und/oder Eierstockkrebs zu erkranken. Als derzeitige präventive Handlungsalternativen werden ein intensiviertes Brustkrebs-Früherkennungsprogramm und risikoreduzierende Operationen angeboten. Vor der Entscheidung für eine Option müssen medizinische und persönliche Faktoren wie die Lebenssituation und individuelle Präferenzen sorgfältig abgewogen werden. Um *BRCA1/2*-Mutationsträgerinnen während ihres Entscheidungsfindungsprozesses zu unterstützen, werden international Entscheidungshilfen eingesetzt. In dieser Studie werden diese erstmals strukturiert analysiert und auf ihre Übertragbarkeit auf den deutschen Kontext geprüft.

Material und Methoden Es wurden eine systematische Literaturrecherche in 5 elektronischen Datenbanken sowie eine Handsuche durchgeführt. Die identifizierten Entscheidungshilfen wurden bezüglich formaler Kriterien, medizinischer Inhalte und ihrer Qualität bewertet. Die qualitative Bewertung erfolgte mithilfe der Kriterien der International Patient Decision Aid Standards Collaboration (IPDASi v4.0), mit denen verschiedene Dimensionen überprüft wurden (z. B. Informationen, Wahrscheinlichkeiten, Wertevorstellungen).

Ergebnisse Es wurden 20 Entscheidungshilfen eingeschlossen, die zwischen 2003 und 2019 in Australien (n = 4), Großbritannien (n = 3), Kanada (n = 2), den Niederlanden (n = 2) und den USA (n = 9) veröffentlicht wurden. Neun richten sich an *BRCA1/2*-Mutationsträgerinnen, 11 schließen weitere Risikogruppen ein. 18 beinhalten als Entscheidungsoptionen risikoreduzierende Operationen, 14 benennen Früherkennungsverfahren für Brust- und/oder Eierstockkrebs, 13 beschreiben die Möglichkeit der medikamentösen Prävention mittels selektiver Östrogenrezeptor-Modulatoren oder Aromatase-Inhibitoren. Neun der 20 Entscheidungshilfen erfüllen grundlegende Qualitätskriterien (IPDASi v4.0-Qualifizierungskriterien).

Schlussfolgerung Formal können internationale Entscheidungshilfen als Grundlage für eine deutsche Entscheidungshilfe für *BRCA1/2*-Mutationsträgerinnen dienen. Inhaltlich weichen sie teils deutlich von den Empfehlungen deutscher Leitlinien ab. Nur wenige erreichen eine hohe Qualität.

Introduction

About one to three in a thousand women carry a pathogenic mutation in one of the two risk genes *BRCA1* and *BRCA2 (BReast CAncer genes 1* and *2)* [1 – 4]. They have a markedly increased risk of developing breast (BC) and/or ovarian cancer (OC) in the course of their life. According to population-based studies, the cumulative risk of *BRCA1* mutation carriers is 72 % for BC and 44 % for OC up to the age of 80 years [5]. Corresponding estimates for *BRCA2* are 69 % and 17 % [5]. In addition, patients with unilateral BC have a markedly increased risk of developing contralateral BC also, compared with the general population [5]. Women can be tested genetically if there is justified suspicion of *BRCA1/2* mutation [6, 7]. A positive gene result often confronts the women with difficult decisions. Mutation carriers without cancer must consider their personal values and life situation when deciding how to deal with the increased disease risk. Adequate understanding of risks is a fundamental precondition for decision-making. Women who already have unilateral BC must also consider various competing risks when deciding, such as the risk of ipsilateral recurrence or metastasis of the primary tumour. Current prevention and screening strategies that can be offered to mutation carriers include an intensified BC screening programme for women without BC (breast magnetic resonance imaging, breast ultrasound, mammography, medical breast palpation), an intensified BC screening and follow-up programme for women who already have BC and risk-reducing surgery of the breast and adnexa [7 – 10] (▶ **Table 1**).

Without comprehensive counselling and an adequate understanding of risk, decision conflicts may arise in *BRCA1/2* mutation carriers. Decision conflicts can lead to regretting important decisions or making recriminations [12 – 15]. Brehaut et al. showed the former in cohorts of women (hormone replacement therapy, adjuvant BC therapy) and men (prostate cancer therapy) [13], and the latter was found by Gattellari and Ward in a cohort of men (prostate specific antigen test) [14]. The right to be advised and informed was strengthened by the Patient Rights Act [16] and the importance of evidence-based patient information for decision-making was emphasised in the National Cancer Plan [17]. In Germany the information medium offered to patients to date has mainly been leaflets, which do not go beyond informing about the different treatment options. Decision aids (DAs) that in addition give the user the possibility of clarifying their own values and preferences as well as weighing treatment options are becoming increasingly important nationally and internationally. The International Patient Decision Aid Standards (IPDAS) Collaboration defines DAs as “tools designed to help people participate in decision making about health care options. They provide information on the options and help patients clarify and communicate the personal value they associate with different features of the options” [18]. DAs are used alone or in combination with other decision-making support tools, such as decision coaching, a non-directive discussion between a person seeking advice and trained health personnel [19].

DAs assist in weighing the benefits and risks of different treatment options and in clarifying one’s own values and preferences [18, 20]. They are helpful especially for complex decision when

1. There is more than one appropriate option,
2. No option has a clear advantage as regards the health outcome,
3. The options are preference-sensitive, that is, they are associated with advantages, disadvantages and uncertainties that can be assessed differently by the user,
4. The evidence is limited [18, 20].

▶ **Table 1** Prevention strategies for *BRCA1/2* mutation carriers in Germany.

Intensified breast screening programme[1, 2]		
Women without cancer[3]		
▪ Medical breast examination	≥ 25 years	Half-yearly
▪ Breast ultrasound	≥ 25 to 70 years	Half-yearly
▪ Mammography	≥ 40 to 70 years	Every one to two years
▪ Breast MRI	≥ 25 to 70 years[4]	Annually
Women with unilateral BC[5]		
▪ Medical breast examination	≥ 25 years	Half-yearly
▪ Breast ultrasound	≥ 25 to 70 years	Half-yearly
▪ Mammography	≥ 40 to 70 years	Every one to two years
▪ Breast MRI	≥ 25 to 70 years[4]	Annually
Risk-reducing bilateral salpingo-oophorectomy[1, 6, 7]		
Without cancer, *BRCA1*[8]	≥ 35–40 years[9]	recommended
Without cancer, *BRCA2*[8]	≥ 40–45 years[9]	recommended
Women with unilateral BC[10]		
Risk-reducing bilateral or contralateral mastectomy[1, 7]		
Women without cancer[11]	Individual decision after detailed, non-directive counselling.	
Women with unilateral BC[12]		
Pharmacological prevention[1, 7]		
Currently no general recommendations for pharmacological prevention by the German Breast and Ovarian Cancer Consortium.		
Women without cancer		Pharmacological preventive measures should be considered only after detailed counselling and taking the individual risk profile and age into account.[1]
▪ Tamoxifen[13]	> 35 years	
▪ Raloxifen[14]	postmenopausal	
▪ Aromatase inhibitors[15]	postmenopausal	
Women with unilateral BC[16]		
▪ Tamoxifen[17]		
Life style[1, 18, 19]		
BMI 18,5–25 kg/m^2, prevention/good control of diabetes mellitus, reduction of alcohol consumption, no smoking, healthy diet (e.g., Mediterranean diet), physical activity		

BRCA1/2: BReast CAncer gene 1/2, MRI: magnetic resonance imaging, BC: breast cancer, OC: ovarian cancer, BMI: body mass index

[1] [9]

[2] [10]

[3] AGO: to identify early stages of BC (Oxford evidence level 2b).

[4] Or until good mammographic assessability is reached.

[5] AGO: to identify early stages of BC (Oxford evidence level 2a), to reduce mortality (Oxford evidence level 3a).

[6] [8]

[7] [7]

[8] AGO: reduces OC incidence, OC mortality and overall mortality (Oxford evidence level 2a). S3 OC guideline: reduces OC incidence and mortality (SIGN evidence level 2+). S3 BC guideline: reduces OC incidence and overall mortality (Oxford evidence level 2a).

[9] After family is complete and taking into account the earliest age of disease in a family member.

[10] AGO: reduces OC incidence and mortality and overall mortality (Oxford evidence level 2b). S3 BC guideline: reduces BC and overall mortality (Oxford evidence level 2a).

[11] AGO: reduces BC incidence (Oxford evidence level 2a) and BC mortality in *BRCA1*-positive women (Oxford evidence level 2b). S3 BC guideline: reduces BC incidence, reduction in BC mortality "not conclusively confirmed" (Oxford evidence level 2a).

[12] AGO: reduces contralateral BC incidence and mortality (Oxford evidence level 2b). S3 BC guideline: reduces contralateral BC incidence (Oxford evidence level 2a).

[13] AGO: reduces the risk for invasive BC, ductal carcinoma in situ and lobular neoplasia (Oxford evidence level 1a).

[14] AGO: reduces the risk for invasive BC (Oxford evidence level 1b).

[15] AGO: Anastrozole reduces the risk for OC, endometrial, colorectal, skin, thyroid, urinary tract and haematological cancers (Oxford evidence level 1b).

[16] S3 BC guideline: in oestrogen receptor-positive BC guided by pharmacological prevention recommendations for sporadic BC.

[17] AGO: reduces the incidence of contralateral BC (Oxford evidence level 2b).

[18] [11]

[19] AGO: general recommendations on BC prevention for women (*BRCA*-positive and negative). S3 OC guideline: increased BMI increases the OC risk.

The quality of a decision can be increased by DAs [20, 21]. A decision is high-quality or, as O'Connor terms it, "effective" when it is informed and in agreement with one's own values and is acted on accordingly [22].

In recent years, several DAs have been developed internationally for *BRCA1/2* mutation carriers. These have not yet been collated systematically or classified with regard to their content or quality. In Germany to date, no DAs for *BRCA1/2* mutation carriers are provided routinely in clinical practice. Two German DAs were developed in conjunction with the present study and are currently undergoing clinical investigation [23, 24]. The aim of this study is

1. To provide a completely up-to-date systematic overview of available DAs for *BRCA1/2* mutation carriers,
2. To record the formal criteria of the DAs,
3. To analyse the medical content of the DAs and
4. To assess their quality.

Material and Methods

Search strategy

A systematic literature search was performed in MEDLINE, Embase, PsycINFO, ERIC and the Cochrane Database of Systematic Reviews. The search strategy was adapted individually to each database and comprised two categories of terms: decision-making/decision aid and *BRCA1/2* (Appendix 1). The search followed the PRISMA guidelines [25]. The bias potential of the studies was not investigated as this was already done in a previous article [21] and the focus of this article was not on the screened studies but on the DAs described therein. In addition, a manual search was performed using Google and on the websites of various institutions (e.g., Ottawa Hospital Research Institute). The IPDAS Collaboration definition of DA was used in the search [18].

Inclusion criteria

- Documents that are designated by the authors as DA, without limitation of the format, including
  - DAs that are described in primary studies, without limitation of the study design plus
  - DAs that can be accessed on the internet.
- Target group of the DA: women aged 18 to 75 years with positive *BRCA1/2* genetic test result.
- Content of the DA: preventive treatment alternatives for confirmed pathogenic *BRCA1/2* mutation.
- Languages of the DA: German, English, French, Spanish, Italian, Dutch.

Exclusion criteria

- DAs on the question of whether genetic testing for a *BRCA1/2* mutation should be performed,
- DAs on communicating a positive *BRCA1/2* genetic test result to relatives,
- DAs on questions about family planning if there is a positive *BRCA1/2* genetic test result,
- Other forms of decision support, e.g., decision coaching.

Screening

Screening of titles, abstracts and full texts was performed by two reviewers independently. A third reviewer was added in the event of disagreements in the screening process. The DAs described in the primary studies were requested or, if available, accessed online.

Analysis of formal criteria

The included DAs were analysed according to formal criteria: target group addressed, publication year or last update, site of production, language and format.

Analysis of content criteria

The content was analysed as to whether the offered treatment alternatives refer to the prevention of BC, OC or both diseases, which options are named specifically, which tools are offered to support decision making, what information is present and whether it is possible to individualise information.

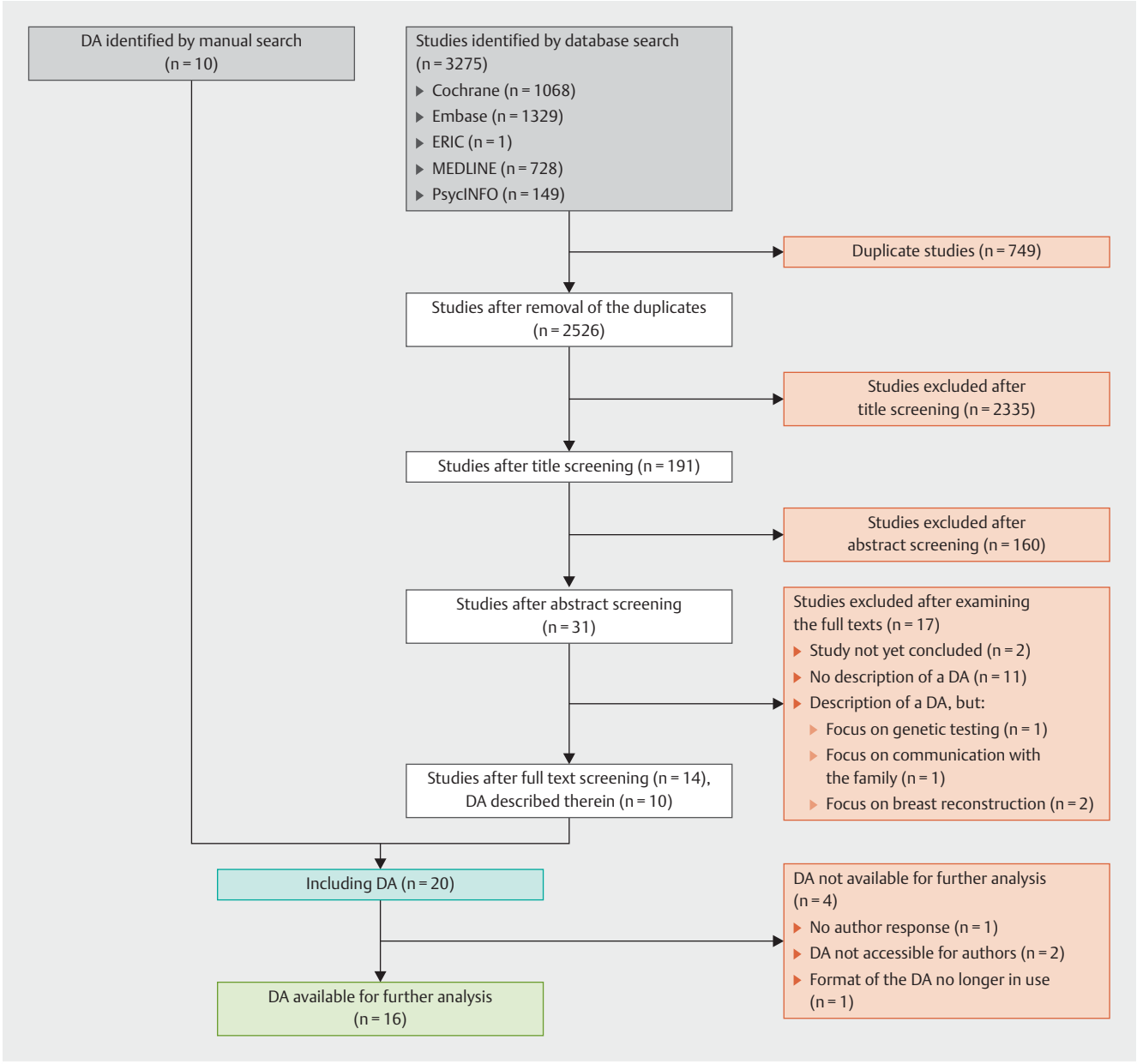
Analysis of qualitative criteria

The quality of the DA was examined with the aid of the International Patient Decision Aid Standards tool (IPDASi v4.0). This comprises 44 criteria in ten dimensions (information, probabilities, values, support of decision-making, decision-making, development process, evidence, disclosure, readability, evaluation, diagnostic test). The IPDASi dimension "Diagnostic test" was not included as it does not apply for the present study aim and as a DA. The IPDASi criteria are divided into three groups: qualification criteria, certification criteria and quality criteria (▶ **Table 6**). The qualification criteria were given a binary assessment (yes/no) and define a DA as such. The certification criteria, which are assessed on a scale of 1 to 4, are intended to avoid decision bias. If a DA is to be certified as such, each certification criterion must reach a score of at least 3. The quality criteria are desirable as they increase the quality of the DA but are not essential (assessment scale from 1 to 4). The quality of the DA was assessed independently by two reviewers. A third reviewer was included if the assessments differed.

Results

Search results

Twenty DAs in total were included (▶ **Fig. 1**). Ten DAs are described in primary studies and were found in the database search [27 – 36]. Six of these were available as full version [28, 29, 32 – 35]. Four DAs were not available as full version as two authors could no longer access the DA [27, 31], the format of the DA was no longer in use [36] or our enquiry was not answered [30]. Ten other DAs were identified by manual search and were available for further analysis [37 – 46].



▶ **Fig. 1** Flowchart of the search results based on the PRISMA guidelines [25]. Search results of the systematic literature search in MEDLINE, Embase, PsycINFO, ERIC and the Cochrane Database of Systematic Reviews; the search strategy included the two categories decision-making/ decision aid and *BRCA1/2*. A manual search was performed in addition. DA: decision aid(s). Date of the last database search: 29.10.2019. Date of the last manual search: 31.12.2019.

Formal criteria

All 20 included DAs could be used for formal assessment. They were published between 2003 and 2019 (▶ **Table 2**). Nine DAs were produced explicitly for *BRCA1/2* mutation carriers [27–31, 33–36], and eleven were additionally addressed to women who have an increased OC and/or BC risk for other reasons [32, 37–46]. These include increased familial incidence of OC and/or BC [32, 37–44], Lynch syndrome [38, 40, 41, 43, 44], TP53, STK11, PTEN or E-cadherin mutation [45, 46] and radiotherapy of the thorax [42]. Of the nine DAs produced explicitly for *BRCA1/2* mutation carriers, one is addressed exclusively to women with a history of BC [27] and four are addressed exclusively to women who so far have neither BC nor OC [28–30, 33]. Nine DAs were developed in the USA [27, 29, 31, 33, 36, 37, 40, 42, 43], four in Australia [32, 38, 39, 44], three in the United Kingdom [41, 45, 46], two in Canada [28, 30] and two in the Netherlands [34, 35]. All except the last two are written in English. Thirteen DAs are web-based or accessible online [27, 29, 32, 33, 37, 39–46] and seven were produced in paper, video or CD-ROM format [28, 30, 31, 34–36, 38]. Information about how the women could access the DAs could not be analysed as there was no clear information in this regard in several DAs or in the corresponding studies.

▶ **Table 2** Basic decision aid data.

Title	Developer	Publication year or last update	Origin	Format	Target group	Treatment alternatives offered
DA with preventive measures regarding BC and OC						
Keuzen bij een erfelijk verhoogd risico op borst- en/of eierstokkanker	van Roosmalen	2004	Netherlands	Brochure, video	*BRCA1/2* mutation carriers, with or without BC/OC (no RR-BM + RR-BO, no distant metastases)[4]	BC-S (self-examination, medical examination, mammography, MRI), RR-M, OC-S, RR-O, pharmacological prevention (tamoxifen), use of oral contraceptives
Individualized Survival Curves Improve Satisfaction With Cancer Risk Management Decisions in Women With *BRCA1/2* Mutations	Armstrong	2005	USA	Brochure	*BRCA1/2* mutation carriers, with or without BC (no RR-BM + RR-BO, no BC with metastases, no OC)[4]	BC-S, RR-M, RR-O, pharmacological prevention (tamoxifen, raloxifene), HRT
Development an Evaluation of a Decision Aid for *BRCA* Carriers with Breast Cancer	Culver	2011	USA	Web-based	*BRCA1/2* mutation carriers aged > 21 years, with BC[4]	BC-S (mammography, MRI), RR-M, RR-O, EK-F, pharmacological prevention (tamoxifen)
Decision Tool for Women with *BRCA* Mutations	Kurian	2011	USA	Web-based	*BRCA1/2* mutation carriers aged 25–69 years, without cancer (no BC-S such as MRI or mammography, no RR-M, no RR-O, no RR-S, no preventive medication)	BC-S (mammography, mammography + MRI), RR-M, RR-O
BRCA decision aid (for unaffected *BRCA+* women)	Jabaley	2019	USA	Web-based	Healthy *BRCA1/2* mutation carriers	Intensified surveillance (BC-S including self-examination, medical examination, mammography, MRI; RR-SO; OC-S including CA-125 testing and vaginal ultrasonography), RR-M, RR-BSO, pharmacological prevention (tamoxifen or raloxifene), use of oral contraceptives
DA with preventive measures regarding BC[1]						
Personal Aid to Health: Making Decisions that Work	Kaufman	2003	USA	CD-ROM	*BRCA1/2* mutation carriers aged 25–75 years, with or without BC/OC (no RR-BM, no metastases)[4]	BC-S (self-examination, medical examination, mammography), RR-M, OC-S, RR-O, pharmacological prevention (tamoxifen, raloxifene), use of oral contraceptives
What are my Options for Breast Cancer Prevention? Facts and Decision Aid for Women with a *BRCA1* or *BRCA2* Mutation	Metcalfe	2007	Canada	Brochure	*BRCA1/2* mutation carriers without BC/OC who are undecided with regard to a preventive measure[4]	BC-S (self-examination, medical examination, mammography, MRI), RR-M, RR-SO, pharmacological prevention (tamoxifen)
Information for women considering preventive mastectomy	Centre for Genetics Education, NSW Health	2012	Australia	Web-based, brochure	Women with increased BC risk (*BRCA1/2* mutation carriers, increased familial incidence of BC)	BC-S (examinations, mammography, MRI), RR-M, pharmacological prevention (anastrozole), lifestyle (avoidance of hormones, fat-reduced diet, reduce alcohol consumption)
Taking tamoxifen to reduce the chance of developing breast cancer. Decision aid for premenopausal women at high risk	NICE	2017	United Kingdom	Web-based, PDF	Premenopausal women with increased BC risk (mutations in *BRCA1/2*, TP53, STK11, PTEN, E-cadherin), without BC	No medication, tamoxifen daily for a period of 5 years
Taking a medicine to reduce the chance of developing breast cancer. Decision aid for postmenopausal women at high risk	NICE	2017	United Kingdom	Web-based, PDF	Postmenopausal women with increased BC risk (mutations in *BRCA1/2*, TP53, STK11, PTEN, E-cadherin), without BC	No medication, tamoxifen daily for a period of 5 years, anastrozole daily for a period of 5 years, raloxifene daily for a period of 5 years

Continued next page

▶ **Table 2** Basic decision aid data. *(Continued)*

Title	Developer	Publication year or last update	Origin	Format	Target group	Treatment alternatives offered
iPrevent®	Collins	2017	Australia	Web-based	Women including women with increased BC risk (age 18–70 years, no BC, no RR-BM, no radiotherapy of the breast, no mutations in cancer genes apart from *BRCA1/2* in themselves or blood relatives, no half sibling with OC/BC/prostate cancer/pancreatic cancer)	Personalised options for BC risk reduction
Effect of decision aid for breast cancer prevention on decisional conflict in women with a *BRCA1* or *BRCA2* mutation: a multisite, randomized, controlled trial	Metcalfe	2017	Canada	Brochure	*BRCA1/2* mutation carriers aged 25–60 years, without BC/OC (no RR-M, no RR-O, no tamoxifen)[4]	RR-M, RR-BSO, pharmacological prevention (tamoxifen)
Breast Cancer: What Should I Do if I'm at High Risk?	Healthwise	2019	USA	Web-based	Women with increased BC risk (*BRCA1/2* mutation carriers, increased familial incidence of BC)	BC-S (medical examinations, Mammography, MRT), RR-M, RR-O, pharmacological prevention (tamoxifen, raloxifene, aromatase inhibitors like anastrozole)
Preventive (prophylactic) mastectomy: Surgery to reduce breast cancer risk	Mayo Clinic	2019	USA	Web-based	Women with increased BC risk (*BRCA1/2* mutation carriers, increased familial incidence of BC, radiotherapy of the thorax)	BC-S (self-examination, medical examination, mammography, MRI), RR-M, P-O, pharmacological prevention (tamoxifen, raloxifene, exemestane, anastrozole), lifestyle (weight normalisation, physical activity, reduction of alcohol consumption, no HRT during menopause, Mediterranean diet)
DA with preventive measures regarding OC[2]						
Risk Management options for women at increased risk of developing ovarian cancer. Information Booklet and Decision Aid	Tiller	2008	Australia	Brochure	Women with increased OC risk aged ≥ 30 years, with or without BC (without OC; without RR-BO; no women in whom a risk mutation for OC was excluded)[4]	Watchful waiting, OC-S, RR-SO, tubal ligation, hysterectomy, use of oral contraceptives, HRT
OvDex. Oophorectomy Decision Explorer[3]	Cardiff University	2014	United Kingdom	Web-based, PDF	Women with increased OC risk (*BRCA1/2* mutation carriers, increased familial incidence of OC and/or BC, Lynch syndrome)	RR-SO, lifestyle (healthy diet, healthy weight, physical activity), HRT
Surgery to Reduce the Risk of Ovarian Cancer. Information for Women at Increased Risk	Centre for Genetics Education, NSW Health	2017	Australia	Web-based, brochure	Women with increased OC risk (BRCA1/2 mutation carriers, increased familial incidence of OC, Lynch syndrome)	RR-BSO (laparoscopy or laparotomy), hysterectomy, tubal ligation, use of oral contraceptives, HRT
A patient decision aid for risk-reducing surgery in premenopausal *BRCA1/2* mutation carriers: Development process and pilot testing	Harmsen	2018	Netherlands	Brochure	Premenopausal *BRCA1/2* mutation carriers[4]	No operation, RR-SO, RR-S with delayed RR-O, HRT, no HRT

Continued next page

▶ **Table 2** Basic decision aid data. *(Continued)*

Title	Developer	Publication year or last update	Origin	Format	Target group	Treatment alternatives offered
Ovarian Cancer: Should I Have My Ovaries Removed to Prevent Ovarian Cancer?	Healthwise	2019	USA	Web-based	Women with increased OC risk (*BRCA1/2* mutation carriers, increased familial incidence of OC, Lynch syndrome)	OC-S (CA-125 testing, vaginal ultrasonography), RR-O, use of oral contraceptives
Prophylactic oophorectomy: Preventing cancer by surgically removing your ovaries	Mayo Clinic	2019	USA	Web-based	Women with increased BC/OC risk (*BRCA1/2* mutation carriers, increased familial incidence of OC and/or BC, Lynch syndrome)	P-O, OC-S (CA-125 testing, vaginal ultrasonography), P-BM, HET, use of oral contraceptives

BRCA1/2: BReast CAncer gene 1/2, BC: breast cancer, DA: decision aid(s), OC: ovarian cancer, BC-S: breast cancer screening, OC-S: ovarian cancer screening, RR-M: risk-reducing mastectomy, RR-BM: risk-reducing bilateral mastectomy, RR-O: risk-reducing oophorectomy, RR-BO: risk-reducing bilateral oophorectomy, RR-S: risk-reducing salpingectomy, RR-SO: risk-reducing salpingo-oophorectomy, RR-BSO: risk-reducing, bilateral salpingo-oophorectomy, HRT: hormone replacement therapy

[1] Focus on BC prevention based on title of the DA or authors' information on the DA. Options for OC prevention are sometimes mentioned also.

[2] Focus on OC prevention based on title of the DA or authors' information on the DA. Options for BC prevention are sometimes mentioned also.

[3] Currently not accessible online.

[4] Information on target group from corresponding study.

Content

Based on their content, the DAs were divided into three groups: 5 of the 20 DAs (25%) describe preventive measures for both BC and OC [27, 29, 31, 33, 35], 9 (45%) focus on BC preventive measures [32, 37, 39, 42, 45, 46] and 6 (30%) on OC preventive measures [34, 38, 40, 41, 43, 44]. Further analysis of the contents of the DAs was possible only for the 16 DAs that were present in full version. The results are presented in ▶ **Tables 3** to **5** and compared to the German guidelines. None of the existing DAs corresponds completely in content to the German recommendations.

Four DAs offer those seeking advice the possibility of individualised information. This ranges from differentiating the mutation status *(BRCA 1* or *2)* [34] to the possibility of individualising the information by means of detailed filter variables such as mutation status, age, menopause status and family history [32]. Thirteen of the 16 DAs contain instruments for decision-making, including the possibility of weighting advantages and disadvantages for oneself, step-by-step decision instructions and note fields for writing down thoughts, fears etc.

Quality

Sixteen of the 20 DAs were evaluated using the IPDASi v4.0 instrument (▶ **Table 6**). Ten DAs (63%) met all qualification criteria and could be declared as DAs according to the IPDASi v4.0 definition [28, 32, 34, 35, 37–41, 44]. The other DAs were unable to meet one to two of the qualification criteria and therefore by definition do not count as DAs. For example, six of the DAs report insufficiently on how a decision impacts on further life, and two DAs do not adequately present the disadvantages of a decision option.

The certification criteria are met fully by one DA (6%) [28]. The other DAs meet between two and five of the six criteria. The certification criteria most often reported as inadequate are updating of the DA, the degree of uncertainty of the information and the financing of the DA.

As regards the quality criteria, one DA meets 19 of the 23 criteria (82%) [28], whereas one DA meets none of the criteria [42].

Discussion

This study is the most up-to-date systematic review of DAs for *BRCA1/2* mutation carriers. Despite an international consensus on quality criteria and evidence-based guidelines, the picture is heterogeneous regarding the content, form and quality of the analysed DAs. A recommendation or translation of international DAs for *BRCA1/2* mutation carriers without prior examination cannot be made based on these results.

The assessed formal criteria included the target group and format. A precise definition of the target group is necessary as prevention and treatment recommendations differ depending on the genetic mutation and disease stage. For example, the recommendations on BC prevention in the German S3 and S2 guidelines vary depending on whether a *BRCA1/2* mutation carrier does not have BC or has unilateral disease [7, 9]. Three of the DAs with statements on BC prevention do not differ in the definition of the target group with regard to BC disease history [37, 39, 42]. Five DAs address "Women with an increased OC risk" and also include women with Lynch syndrome as a target group as well as *BRCA1/2* mutation carriers [38, 40, 41, 43, 44]. According to German guidelines, both groups should be advised with regard to risk-reducing (salpingo-)oophorectomy because of the increased OC risk, which is also done in the aforementioned DA, but further specific preventive measures are recommended to women with Lynch syndrome, including investigations such as colonoscopy, oesophago-gastro-duodenoscopy, transvaginal ultrasound and

endometrial biopsy [8, 47]. Thirteen of 15 DAs have an online downloadable format. They can thereby be more readily individualised and updated. The 16 analysed DAs show large differences in content, both in the extent of the information provided in the text and in the treatment alternatives offered. Risk-reducing operations are mentioned in 14 of the 16 DAs. Here, the recommendations, apart from vagueness regarding the difference between salpingo-oophorectomy and oophorectomy or contralateral and bilateral mastectomy, largely agree with the German guidelines [7 – 9]. There is similar agreement between the DAs and the recommendations in the German guidelines [9] on BC screening. The breast ultrasonography recommended in the guidelines is mentioned in only 3 of the 10 DAs in question. As regards pharmacological prevention as an option, there are no clear recommendations in the German guidelines (▶ **Tables 3** to **5**), and the lack of clarity with this option is also reflected in the DAs; in one of the DAs in question, pharmacological prevention is not even listed [33], while all currently discussed options (raloxifene, tamoxifen, aromatase inhibitors) are mentioned in three DAs [37, 42, 45]. A point of criticism is that screening for OC by CA-125 testing and/or transvaginal ultrasound is cited in seven DAs as a possible prevention option, including three DAs from 2019 [29, 40, 43]. The German S3 OC guideline [8] and international guidelines [48, 49] advise clearly against such screening.

Another critical point is that crucial contents are mentioned only briefly or not at all in a few DAs. For instance, in the Mayo Clinic DA on OC prevention, it is not mentioned that an immediate loss of fertility is associated with oophorectomy. As Kim et al. show, this knowledge cannot be assumed; in their study, published in 2014, on women's knowledge about the subjects of oophorectomy and fertility, 38 % of the *BRCA1/2* mutation carriers stated that they did not know that a woman cannot have any more biological offspring when her ovaries have been removed [50].

The 16 DAs analysed differ very greatly in quality. Only ten met all IPDASi v4.0 qualification criteria, which, according to Joseph-Williams et al., define a tool as a DA thus: "Tools would not be considered a patient decision aid unless all of these criteria are met" [26]. The opposite conclusion means that six of the tools assessed here are not DAs according to the IPDAS Collaboration. It is problematic that nearly all these tools call themselves DAs (▶ **Table 2**). The IPDASi v4.0 certification criteria are met fully only in the DA of Metcalfe et al. [28], which was developed following the quality criteria of the IPDAS Collaboration. In the case of all other tools, decision bias due to the DA cannot be excluded. It is particularly difficult when the certification criterion of balanced representation is not met. For instance, in the Mayo Clinic tool for BC prevention, the possibility of risk-reducing mastectomy including the advantages, disadvantages and risks is explained in detail but, by contrast, BC screening is mentioned in only one sentence. A weakness of this study is that a DA in Chinese had to be excluded because of the lack of capacity to translate this. In addition, a recent DA could be included but qualitative analysis was not possible as a full version was not obtained from the authors.

The strengths of this study are the clear search protocol, the inclusion of five different databases, no limitations of the design of the primary studies or format of the DAs, as well as assessment of the DAs by three independent reviewers. The quality of the DAs was examined using the IPDAS collaboration tool, which allows a detailed analysis of DAs and meets the current international standard in DA quality assessment.

This study has the following implications for practice: *BRCA1/2* mutation carriers should be managed with evidence-based and high-quality DAs in counselling centres since

1. Unlike pure patient information leaflets, DAs also include clarification of the patient's own values and preferences,
2. Those seeking advice are protected from incorrect information due to poor-quality decision tools.

The development of DAs should be guided by the quality criteria of the IPDAS collaboration and precise target group definition and various formats (printed version, App) should be provided.

Conclusion

To date there is still no DA for *BRCA1/2* mutation carriers for German-speaking countries that is used routinely in clinical practice. Various support tools for *BRCA1/2* mutation carriers are currently in development or clinical testing, however, including two DAs [23, 51 – 53]. In developing a German DA, already existing international DAs can serve formally as a basis and the content regarding treatment recommendations must be adapted to the German guidelines. To ensure high DA quality, it is crucial to follow the quality criteria of IPDAS Collaboration when developing it.

▶ **Table 3** Content of the decision aids: treatment alternatives for breast cancer prevention.

	Recommendations in Germany[3]										
	S3 BC guideline, women without BC	S3 BC guideline, women with BC	AGO Guidelines Breast, women without BC	AGO Guidelines Breast, women with BC	S3 OC guideline						
Decision aids						**With preventive measures regarding BC and OC**					**With preventive measures**
Developer						**van Roosmalen**	**Armstrong**	**Culver**	**Kurian**	**Jabaley**	**Kaufman**	**Metcalfe**
Publication year or last update						**2004**	**2005**	**2011**	**2011**	**2019**	**2003**	**2007**
Origin						**NL**	**USA**	**USA**	**USA**	**USA**	**USA**	**Canada**
Target group												
Risk												
▪ Explicitly women with *BRCA1/2* mutation	X	X	X	X	X	X	X	X	X	X	X	X
▪ Increased BC/OC risk												
▪ Increased BC risk												
▪ Increased OC risk												
Disease history												
▪ With/without BC/OC[1]						X	X				X	
▪ Without BC	X		X						X	X		X
▪ With BC		X		X				X				
▪ Without OC									X	X		X
Individualisation of the information									X		X	
Treatment alternatives BC prevention												
Intensified screening												
▪ Self-examination	0	0	0	0	0	X	(X)[18]			X	X	X
▪ Medical examination	0	0	+	+	0	X	(X)[18]			X	X	X
▪ Breast ultrasonography	0	0	+	+	0	X	(X)[18]					
▪ Mammography	0	0	+	+	0	X	(X)[18]	X	X	X	X	X
▪ Breast MRI	0	0	+	+	0	X	(X)[18]	X	X	X		X
Risk-reducing operations												
▪ Mastectomy	(+)[4, 5]	(+)[8]	(+)[4]	(+)[4]	0	X	X	X	X	X	X	X
▪ Salpingo-oophorectomy	±[6]	+[9]	0	0	0			X				X
▪ Salpingectomy	0	0	0	0	0							
▪ Oophorectomy	0	0	0	0	0							
Pharmacological prevention												
▪ Raloxifene	0	0	(+)[4, 11]	0	0		X			X	X	
▪ Tamoxifen	±[7]	(+)[10]	(+)[4, 13]	(+)[11]	0	X	X	X		X	X	X
▪ Aromatase inhibitors	0	(+)[10, 11]	(+)[4, 11]	(+)[11]	0							
Miscellaneous												
▪ Weight normalisation	0	+[12]	+[12]	+[12]	0							
▪ Healthy diet	0	+[12]	(+)[12]	(+)[12]	0							
▪ Physical activity	0	+[12]	+[12]	+[12]	0							
▪ No smoking	0	+[12]	+[12]	+[12]	0							
▪ Low alcohol consumption	0	+[12]	(+)[12]	(+)[12]	0							
▪ No oral contraceptives	0	±[12]	0	0	0							
▪ No HRT (peri-/postmenopausal)	0	+[12]	(+)[12]	(+)[12]	0							

BRCA1/2: BReast CAncer gene 1/2, BC: breast cancer, DA: decision aid, OC: ovarian cancer, MRI: magnetic resonance tomography, HRT: hormone replacement therapy, +: unlimited recommendation. (+): recommendation with limitation. ±: no clear recommendation possible, e.g., because of limited data. 0: no information.

regarding BC[19]								With preventive measures regarding OC[24]					
	Centre for Genetics Education, NSW Health	NICE (pre-menopausal)	NICE (post-menopausal)	Metcalfe	Collins	Healthwise	Mayo Clinic	Tiller	Cardiff University	Centre for Genetics Education, NSW Health	Harmsen	Health-wise	Mayo Clinic
	2012	2017	2017	2017	2017	2019	2019	2008	2014	2017	2018	2019	2019
	Australia	GB	GB	Canada	Australia	USA	USA	Australia	GB	Australia	NL	USA	USA
				X							X		
													X
	X	X	X		X	X	X						
								X	X	X		X	
		X	X	X	X			X					
								X					
				X				X					
					X[22]				X[25]		X[26]		
	(X)[20]						X						
	(X)[20]				X	X	X						
	X				X								
	X				X	X	X						
	X				X	X	X						
	X			X	X	X	X						X
					X	X					X		
						X	X						X
			X			X[23]	X						
		X	X	X	X	X[11]	X						
	X[21]		X			X[11]	X						
					X		X						
	X						X						
					X		X						
					X								
	X				X		X						
	X												
	X				X		X						

NSW: New South Wales, NICE: National Institute for Health and Care Excellence, grey field: full version of the DA not available

–: no recommendation. [1–26] See ▶ **Table 5**.

▶ **Table 4** Content of the decision aids: treatment alternatives for ovarian cancer prevention.

	Recommendations in Germany[3]										
	S3 BC guideline, women without OC	S3 BC guideline, women without BC	S3 BC guideline, women without OC	S3 BC guideline, women without BC	S3 OC guideline						
Decision aids						With preventive measures regarding BC and OC					With preventive measures
Developer						van Roosmalen	Armstrong	Culver	Kurian	Jabaley	Kaufman	Metcalfe
Publication year or last update						2004	2005	2011	2011	2019	2003	2007
Origin						NL	USA	USA	USA	USA	USA	Canada
Target group												
Risk												
▪ Explicitly women with *BRCA1/2* mutation	X	X	X	X	X	X	X	X	X	X	X	X
▪ Increased BC/OC risk												
▪ Increased BC risk												
▪ Increased OC risk												
Disease history												
▪ With/without BC/OC[1]						X	X				X	
▪ Without BC	X		X						X	X		X
▪ With BC		X		X				X				
▪ Without OC									X	X		X
Individualisation of the information									X		X	
Treatment alternatives OC prevention												
Screening												
▪ Medical examination	0	0	0	0	–	X						
▪ CA-125 test	0	0	0	0	–	X		X		X	X	
▪ Vaginal ultrasonography	0	0	0	0	–	X		X		X	X	
Risk-reducing operations												
▪ Salpingo-oophorectomy	+[6]	+[6]	+	(+)	+			X	X	X		X
▪ Salpingectomy	0	0	0	0	(+)[14]							
▪ Oophorectomy	0	0	0	0	0	X	X		X		X	
▪ First salpingectomy, then oophorectomy	0	0	0	0	0							
▪ Tubal ligation	0	0	0	0	±[15]							
▪ Hysterectomy	0	0	0	0	0							
Miscellaneous												
▪ Watchful waiting	0	0	0	0	0							
▪ Weight normalisation	0	0	0	0	+[16]							
▪ Healthy diet	0	0	0	0	0							
▪ Physical activity	0	0	0	0	0							
▪ No smoking	0	0	0	0	0							
▪ Low alcohol consumption	0	0	0	0	0							
▪ Oral contraceptives	0	0	0	0	+	X				X	X	
▪ No HRT	0	0	0	0	(+)[17]		X					

BRCA1/2: BReast CAncer gene 1/2, BC: breast cancer, DA: decision aid, OC: ovarian cancer, MRI: magnetic resonance tomography, HRT: hormone replacement therapy, +: unlimited recommendation. (+): recommendation with limitation. ±: no clear recommendation possible, e.g., because of limited data. 0: no information.

regarding BC[19]								With preventive measures regarding OC[24]					
	Centre for Genetics Education, NSW Health	NICE (pre-menopausal)	NICE (post-menopausal)	Metcalfe	Collins	Healthwise	Mayo Clinic	Tiller	Cardiff University	Centre for Genetics Education, NSW Health	Harmsen	Health-wise	Mayo Clinic
	2012	2017	2017	2017	2017	2019	2019	2008	2014	2017	2018	2019	2019
	Australia	GB	GB	Canada	Australia	USA	USA	Australia	GB	Australia	NL	USA	USA
				X							X		
													X
	X	X	X		X	X	X						
								X	X	X		X	
		X	X	X	X			X					
								X					
				X				X					
					X[22]				X[25]		X[26]		
								X				X	X
								X				X	X
				X	X	X		X	X	X	X		X
						X	X					X	X
											X		
								X		X			
								X		X			X
								X					
									X				
									X				
									X				
								X		X		X	X
						X		X	X	X	X		X

NSW: New South Wales, NICE: National Institute for Health and Care Excellence, grey field: full version of the DA not available

–: no recommendation. [1–26] See ▶ **Table 5**.

▶ **Table 5** Content of the decision aids: information, instruments for supporting decision-making.

	Recommendations in Germany[3]										
	S3 BC guideline, women without BC	S3 BC guideline, women with BC	S3 BC guideline, women without BC	S3 BC guideline, women with BC	S3 OC guideline						
Decision aids						With preventive measures regarding BC and OC				With preventive measures	
Developer						van Roosmalen	Armstrong	Culver	Kurian	Jabaley	Kaufman	Metcalfe
Publication year or last update						2004	2005	2011	2011	2019	2003	2007
Origin						NL	USA	USA	USA	USA	USA	Canada
Target group												
Risk												
▪ Explicitly women with *BRCA1/2* mutation	X	X	X	X	X	X	X	X	X	X	X	X
▪ Increased BC/OC risk												
▪ Increased BC risk												
▪ Increased OC risk												
Disease history												
▪ With/without BC/OC[1]						X	X				X	
▪ Without BC	X		X						X	X		X
▪ With BC		X		X				X				
▪ Without OC									X	X		X
Individualisation of the information									X		X	
Information												
BC/OC disease risks (text)						X			X	X		X
BC/OC disease risks (graphics)									X	X		X
Advantages/disadvantages of the preventive options						X				X		
Experience reports						X						X
Instruments for supporting decision-making												
Step-by-step decision instructions										X		X
Personal weighting of advantages/ disadvantages										X		X
Note field (for own values, fears etc.)						X				X		
List of questions to doctors/ counselling staff												
Test of knowledge												
Miscellaneous												
Addresses and/or internet links										X		X
References[2]						X			X	X		X

BRCA1/2: BReast CAncer gene 1/2, BC: breast cancer, DA: decision aid, OC: ovarian cancer, MRI: magnetic resonance tomography, HRT: hormone replacement therapy, NSW: New South Wales, NICE: National Institute for Health and Care Excellence, grey field: full version of the DA not available

+: unlimited recommendation. (+): recommendation with limitation. ±: no clear recommendation possible, e.g., because of limited data. 0: no information. −: no recommendation.

[1] No precise details of disease history in the DA or no limitation of the target group. [2] In DA or corresponding primary study. [3] [7 – 9, 11] [4] Individual decision after detailed non-directive counselling. [5] S3 BC guideline, p. 62: Bilateral prophylactic mastectomy leads to a reduction in breast cancer incidence. "A reduction in breast cancer-specific mortality or overall mortality by bilateral prophylactic mastectomy has not been adequately confirmed." [6] S3 BC guideline, p. 62: "Prophylactic bilateral salpingo-oophorectomy reduces the ovarian cancer risk by 97 %. Whether the breast cancer risk is also reduced by this prophylactic operation has currently not been conclusively established." [7] S3 BC guideline, p. 63: "A possible risk reduction by prophylactic administration of tamoxifen has not been clearly shown." [8] S3 BC guideline, p. 64: Contralateral, secondary prophylactic mastectomy leads to a reduction in the contralateral cancer risk. "The prognosis of the first cancer should be considered when determining if contralateral secondary prophylactic mastectomy is indicated." [9] S3 BC guideline, p. 64: Prophylactic adnexectomy leads to a reduction in breast cancer-specific mortality and to an increase in overall survival. [10] Recommendation in hormone receptor-positive sporadic breast cancer.

regarding BC[19]								With preventive measures regarding OC[24]					
	Centre for Genetics Education, NSW Health	NICE (pre-menopausal)	NICE (post-menopausal)	Metcalfe	Collins	Healthwise	Mayo Clinic	Tiller	Cardiff University	Centre for Genetics Education, NSW Health	Harmsen	Health-wise	Mayo Clinic
	2012	2017	2017	2017	2017	2019	2019	2008	2014	2017	2018	2019	2019
	Australia	GB	GB	Canada	Australia	USA	USA	Australia	GB	Australia	NL	USA	USA
				X							X		
													X
	X	X	X		X	X	X						
								X	X	X		X	
		X	X	X	X			X					
								X					
				X				X					
					X[22]				X[25]		X[26]		
	X	X	X		X	X		X	X	X	X	X	X
		X	X		X	X			X	X	X	X	
	X	X	X		X	X		X	X	X	X	X	
	X					X		X				X	
								X	X		X	X	
		X	X			X		X	X		X	X	
	X	X	X			X		X	X			X	
	X									X			X
												X	
	X							X	X	X			
	X	X	X		X	X	X	X	X	X	X	X	X

[11] Postmenopausal women. [12] Recommendation for all women (with/without *BRCA1/2* mutation). [13] Women > 35 years. [14] S3 OC guideline, p. 45: "Bilateral salpingectomy alone also has a risk-minimising but lower protective effect." [15] S3 OC guideline, p. 45–46: "The operation leads to a reduction in the ovarian cancer risk by 34%. […] It has currently not been conclusively established whether the risk reduction can also be shown in *BRCA1/2* mutation carriers." [16] S3 OC guideline, p. 46: "A comprehensive meta-analysis, which included 28 studies, showed that obesity in adulthood was associated with an increased risk for ovarian cancer." (Statement not specific for *BRCA1/2* mutation carriers) [17] S3 OC guideline, p. 44: "It must be considered […] that ovariectomy of premenopausal women leads to an increase in the risk of myocardial infarction and osteoporosis-related fractures, among other things, so that short-term hormone therapy […]with a preventive aim also should be considered." [18] No clear statement on BC screening. [19] Focus on BC prevention based on title of the DA or information from the authors on the DA. OC prevention options are sometimes cited also. [20] No clear differentiation between self- and medical examination. [21] Anastrozole for postmenopausal women in the ITO II study. [22] Example of details for 44-year-old premenopausal *BRCA1* mutation carrier. [23] Recommendation especially for women under 50 years. [24] Focus on OC prevention based on title of the DA or information from the authors on the DA. BC prevention options are sometimes cited also. [25] Example of details for under 35-year-old *BRCA1* mutation carrier without a history of BC. [26] Different DA for *BRCA1* and *BRCA2*.

▶ **Table 6** Quality of the decision aids according to IPDASi v4.0 criteria [26].

	DA with preventive measures regarding BC and OC			DA with preventive measures regarding BC							DA with preventive measures regarding OC					
Publication	**van Roosmalen (2004)**	**Kurian (2011)**	**Jabaley (2019)**	**Metcalfe (2007)**	**NSW Health (2012)**	**NICE, premenopausal (2017)**	**NICE, postmenopausal (2017)**	**Collins (2017)**	**Healthwise (2019)**	**Mayo Clinic (2019)**	**Tiller (2008)**	**Cardiff University (2014)**	**NSW Health (2017)**	**Harmsen (2018)**	**Healthwise (2019)**	**Mayo Clinic (2019)**
Criteria																
Information																
Qualification criteria (5)																
▪ Description of the health status/problem	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
▪ Index decision is addressed	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
▪ Available options	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
▪ Advantages	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
▪ Disadvantages	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Certification criteria (1)																
▪ Balanced presentation	4	2	4	4	3	4	4	4	4	2	4	4	3	4	4	2
Quality criteria (2)																
▪ Description of the natural course	1	4	4	4	1	4	4	4	4	1	4	4	3	4	4	2
▪ Possibility of comparing features	1	3	3	4	2	4	4	3	3	1	3	4	1	3	3	2
Probabilities																
Quality criteria (6)																
▪ Event probability	3	4	2	4	3	4	4	4	1	2	3	4	1	4	1	3
▪ Reference class	4	4	3	3	3	2	2	4	3	2	4	4	2	4	3	3
▪ Event rate	1	4	1	4	3	4	4	4	1	1	1	4	1	4	1	3
▪ Possibility of comparing probabilities	1	4	1	4	1	4	4	4	1	1	1	3	1	4	1	3
▪ Comparison with the same denominator	4	4	1	4	1	4	4	4	1	1	1	3	1	4	1	4
▪ Varied representation of probabilities	1	4	1	4	1	4	4	4	1	1	1	4	1	4	1	1

Continued next page

▶ **Table 6** Quality of the decision aids according to IPDASi v4.0 criteria [26]. *(Continued)*

	DA with preventive measures regarding BC and OC			DA with preventive measures regarding BC							DA with preventive measures regarding OC					
Publication	**van Roosmalen (2004)**	**Kurian (2011)**	**Jabaley (2019)**	**Metcalfe (2007)**	**NSW Health (2012)**	**NICE, premenopausal (2017)**	**NICE, postmenopausal (2017)**	**Collins (2017)**	**Healthwise (2019)**	**Mayo Clinic (2019)**	**Tiller (2008)**	**Cardiff University (2014)**	**NSW Health (2017)**	**Harmsen (2018)**	**Healthwise (2019)**	**Mayo Clinic (2019)**
Criteria																
Values																
Qualification criteria (1)																
▪ Experiencing the consequences	+	–	–	+	+	–	–	+	+	–	+	+	+	+	+	+
Quality criteria (1)																
▪ Personal importance	1	1	3	4	3	4	4	1	4	1	4	4	2	4	4	2
Support of decision-making																
Quality criteria (2)																
▪ Step-by-step instructions	1	4	1	4	1	2	1	1	4	1	4	4	1	4	4	1
▪ Worksheets or lists of questions	1	1	3	4	4	3	3	1	4	1	4	4	2	4	4	4
Development process																
Quality criteria (6)																
▪ Patients' needs	1	1	2	4	2	?	?	1	?	?	4	4	?	4	?	?
▪ Health staff's needs	4	1	2	?	?	?	?	4	?	?	?	4	?	4	?	?
▪ Independent review (patients)	1	1	1	1	?	1	1	1	?	?	1	1	?	3	?	?
▪ Independent review (staff)	1	1	1	4	?	1	1	1	?	?	4	3	?	4	?	?
▪ Tested with patients	4	4	4	4	?	1	1	4	?	?	4	3	?	1	?	?
▪ Tested with health staff	4	4	4	1	?	1	1	4	?	?	1	1	?	1	?	?
Evidence																
Certification criteria (4)																
▪ References	1	4	4	4	4	4	4	4	4	4	4	4	4	2	4	4
▪ Production date	1	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
▪ Method of updating	1	2	2	3	2	1	1	1	1	1	2	3	1	2	2	1
▪ Degree of uncertainty	1	1	1	4	1	1	1	1	1	1	1	1	1	4	1	1
Quality criteria (2)																
▪ Synthesis of the research evidence	1	3	2	4	1	2	2	1	1	1	4	1	1	3	1	1
▪ Quality of the research evidence	1	1	2	4	1	2	2	1	1	1	1	1	1	3	1	1

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▶ **Table 6** Quality of the decision aids according to IPDASi v4.0 criteria [26]. *(Continued)*

	DA with preventive measures regarding BC and OC			DA with preventive measures regarding BC							DA with preventive measures regarding OC					
Publication	**van Roosmalen (2004)**	**Kurian (2011)**	**Jabaley (2019)**	**Metcalfe (2007)**	**NSW Health (2012)**	**NICE, premenopausal (2017)**	**NICE, postmenopausal (2017)**	**Collins (2017)**	**Healthwise (2019)**	**Mayo Clinic (2019)**	**Tiller (2008)**	**Cardiff University (2014)**	**NSW Health (2017)**	**Harmsen (2018)**	**Healthwise (2019)**	**Mayo Clinic (2019)**
Criteria																
Disclosure																
Certification criteria (1)																
▪ Information on financing	4	4	4	4	4	1	1	4	1	1	4	4	1	4	1	1
Quality criteria (1)																
▪ Author information	1	2	2	4	4	1	1	1	4	1	4	2	2	4	4	1
Readability																
Quality criteria (1)																
▪ Readability level	1	1	1	1	1	1	1	1	1	1	4	1	1	1	1	1
Evaluation																
Quality criteria (2)																
▪ Knowledge	4	1	1	4	1	1	1	3	1	1	3	1	1	1	1	1
▪ Improved decision quality	1	1	1	4	1	1	1	1	1	1	3	1	1	1	1	1
Qualification criteria (6)	**6**	**4**	**5**	**6**	**6**	**5**	**5**	**6**	**6**	**5**	**6**	**6**	**6**	**6**	**6**	**5**
Certification criteria (6)	**2**	**3**	**4**	**6**	**4**	**3**	**3**	**4**	**3**	**2**	**4**	**5**	**3**	**4**	**3**	**2**
Quality criteria (23)	**7**	**10**	**7**	**19**	**6**	**9**	**9**	**12**	**7**	**0**	**12**	**15**	**1**	**18**	**7**	**6**

IPDASi: International Patient Decision Aid Standards instrument, BC: breast cancer, DA: decision aid, OC: ovarian cancer

Supplementary Material

Appendix 1: Search strategy for each database

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Conflict of Interest

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