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ORIGINAL

Epidemiological and clinicopathological features of breast cancer in Mauritania

Características epidemiológicas y clinicopatológicas del cáncer de mama en Mauritania

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Abstract

Background: Breast cancer is the leading cause of death in African women. The aim of this cross –sectional study was to assess the incidence, clinic-pathological characteristics, risk factors and outcome of breast cancer in Mauritania.
Methods: Demographic and clinic pathological features of breast cancer were gathered from 11174 patient files of all cancer types referred to the Centre National d'Oncologie (CNO) between January 2009 and December 2020.
Results: Breast cancer was the most common type of cancer identified in women (30.7%). The disease incidence increased from 69 in 2009 to 209 in 2020 with a mean age of 49 year sat cancer detection. Grade 3 tumor was diagnosed in 31.8% patients. Stage 3 and metastasic stage were found respectively in 44.9 % and 22.6% of screened women. 40.4% of cancer patients with satisfactory immunohistochemical data were triple negative breast cancer (TNBC) but no significant variation was found in these features between TNBC and non TNBC groups. A 3-year survival rate of 63% was observed.
Conclusions: These results support the already published studies on the likely genetic basis of breast cancer in our population.

Key words: Breast cancer, triple negative breast cancer, women.

Resumen

Antecedentes: El cáncer de mama es la principal causa de muerte en las mujeres africanas. El objetivo de este estudio transversal fue evaluar la incidencia, las características clínico-patológicas, los factores de riesgo y el resultado del cáncer de mama en Mauritania.
Métodos: Las características demográficas y clínico-patológicas del cáncer de mama se recogieron de 11174 expedientes de pacientes de todos los tipos de cáncer remitidos al Centre National d'Oncologie (CNO) entre enero de 2009 y diciembre de 2020.
Resultados: El cáncer de mama fue el tipo de cáncer más común identificado en las mujeres (30,7%). La incidencia de la enfermedad aumentó de 69 en 2009 a 209 en 2020 con una edad media de 49 años de detección del cáncer. Se diagnosticó un tumor de grado 3 en el 31,8% de las pacientes. El estadio 3 y el estadio metastásico se encontraron, respectivamente, en el 44,9% y el 22,6% de las mujeres examinadas. El 40,4% de las pacientes con cáncer con datos inmunohistoquímicos satisfactorios eran cáncer de mama triple negativo (TNBC), pero no se encontraron variaciones significativas en estas características entre los grupos TNBC y no TNBC. Se observó una tasa de supervivencia a 3 años del 63%.
Conclusiones: Estos resultados apoyan los estudios ya publicados sobre la probable base genética del cáncer de mama en nuestra población.

Palabras clave: Cáncer de mama, cáncer de mama triple negativo, mujeres.

Abbreviations

Breast cancer (BC), Centre National d'Oncologie (CNO), Triple negative breast cancer (TNBC), Immunohistochemical (IHC), The American joint committee on cancer /Union for international cancer control (AJCC/UICC), Receptors of estrogen (ER), Progesterone (PR), Hormone epidermal growth factor receptor 2 (HER-2).

Background

Although breast cancer (BC) survival is continually improving in developed states[1], the disease remained a leading cause of death in women from low- and middle-income countries likely due to a late diagnosis, often at advanced stage, combined to the scarcity of adequate and personalized primary treatment[2-3]. The incidence and mortality rate from BC was also affected by other major risk factors such as age, family history and ethnic ascendance[4-6]. However, studies on the underlying etiologies and the prospect of recovery from the disease remained particularly limited in sub-Sahara African women[7-9]. We presented here a cross-sectional study gathered from the registries of the Centre National d'Oncologie (CNO), on the frequency, demographics, clinic-pathological features and prognosis of breast cancer in Mauritania. These variables were specifically evaluated in triple negative breast cancer (TNBC) patients and compared with data from non TNBC women.

Methods

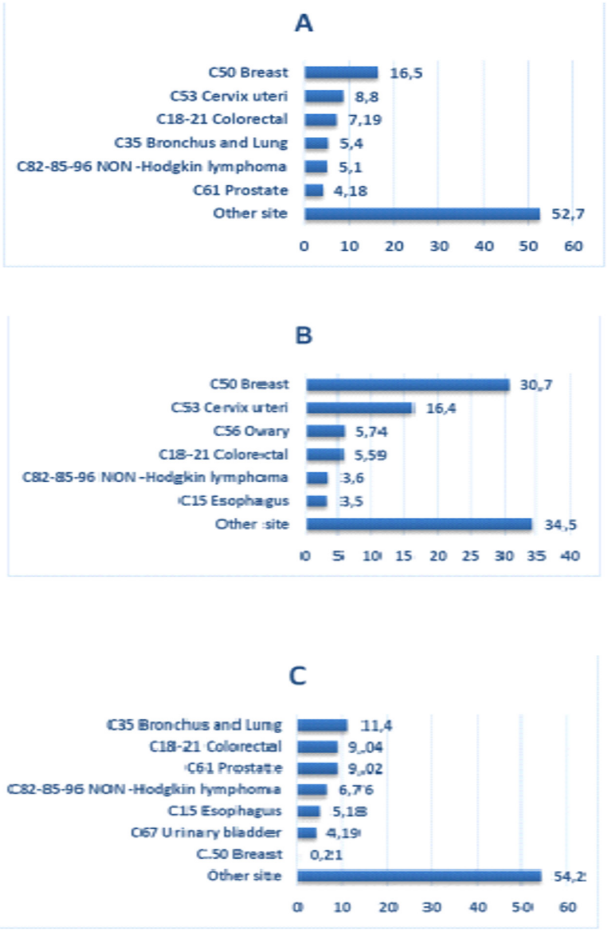
Medical files of 11174 patients of all cancer types followed at the CNO, the only referring center for oncology in the country, were examined from the period of January 2009, date of opening of the center, through to December 2020. Cancer type, Name and date of birth of each patient were recorded. In this study, detailed demographic and clinical characteristics, available at the center only from 01/2017 onwards, were analyzed for breast cancer patients and included age at diagnosis, body mass index (BMI) calculated as weight in kilograms/height in meters square (kg/m^2), family history of the disease, cancer staging, histological grading, received therapy and clinical outcome. Immunohistochemical staining (IHC) was carried out on patient tissue samples embedded in paraffin blocks. Patients with no slides or ambiguous pattern were excluded. Staging (from To to T4) was performed according to the American joint committee on cancer /Union for international cancer control (AJCC/UICC) systems. Evaluation (from 0 to 4) of cancer stage used TNM staging. Triple negative breast cancer (TNBC) subjects were patients with slides showing no antibody staining or a tumor cells fluorescence of less than 1% for, concurrently, receptors of estrogen (ER), progesterone (PR) and hormone epidermal growth factor receptor 2 (HER-2). Local or distant recurrence was defined by the time span from the end of primary treatment to date of return of the disease in the original site or other part of the body respectively. Survival duration was determined as the period between the dates of BC diagnosis to the patient death if recorded or the last missed appointment and loss of follow up. Data analysis was performed by SPSS version 23.0 software (Chicago, Ill). Comparison among clinical variables between TNBC and no TNBC was performed with Person Chi-square test using a statistical significance of $p<0.05$.

Results

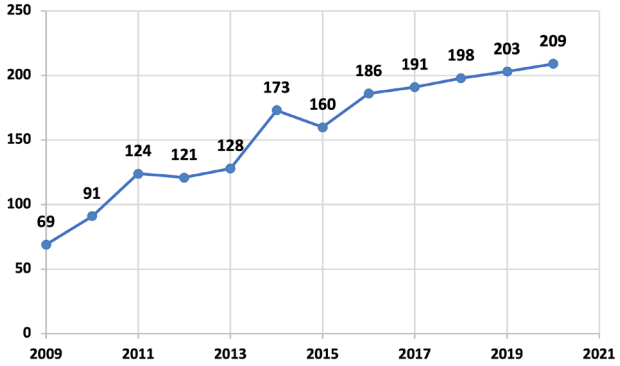
Demographic findings

Globally, out of the 11174 cancer files of all types (5989women and 5185men) referred to CNO during the period from January 2009 to December 2020, breast cancer was found in 1853(16.58%) patients (**Figure 1**). With a proportion of 30.75%, BC was the most common type of cancer identified in the female group. In the male group, the disease was much less frequent with only 11 cases (0.21%) of the total cancer male carriers. Overall, 99.79% of breast cancer cases were in females and less than 1% in males. The incidence rate showed a steady increase of the annual number of new women breast cancer cases with 69, 160 and 209 BC diagnosed in 2009, 2015 and 2020 respectively (**Graphic 1**). Adequate demographic and clinic-pathological characteristic, available from 01/2017 to 12/2020, concerned793 women (**Table I**). Median age of patients, at cancer detection, was 49 years with most breast cancers diagnosed between 35 to 55 years (52.4%) followed by the group of above 55 years (31%). The fraction in the 20s to 35s age represented 16.6%.Premenopausal status was observed in 63.7% of the records.

Figure 1: Proportions (%) of common cancers referred to the CNO during the period of 2009 to 2020: A (whole cohort); B (females); C (males).



Graphic 1: Breast cancer incidence between 2009 and 2020.



Family history (first- and second-degree relatives with breast cancer) was reported by 95 (14.5%) of patients and 388 women (59%) had parents with shared common ascendant. Of 785 patients, 31.3% were overweight and 49.3 % obese. The ethnic distribution of BC women showed that 397 (50.1%) patients were white Moors, 263 (33.16%) black Moors and 133 (16.7%) of black African descent.

Pathological feature

Out of the 793 included women, breast cancer was bilateral in 25 (3%) of cases. In 417 patients (52.6%), the right breast was affected. The average diameter (measured at the widest point) of the primary tumor was 4 cm with 68.1% of recorded patients having a tumor size smaller than 5 cm against 31.9% showing a diameter above 5 cm. Cells abnormality was diagnosed with poorly differentiated status (grade III) in 185 (31.8%) patients. Moderately differentiated (grade II) and differentiated (grade I) tumors were found respectively in 334 (57.2%) and 67 (11.4%) women. Breast cancer was at stage I in 7(0.13 %), stage II in 167 (31%), stage III in 242 (44.9%) and metastatic stage IV in124 (22.6%) patients. Cancer stretching into breast surrounding tissues showed presence of invasive ductal carcinomas (IDC) in 618 (79.6%) and invasive lobular carcinoma (ILC) in70 (9 %) slides. Less common types were also observed (11.4 %). In 425 breast cancer patients with satisfactory immunohistochemical data, 172 (40.4%) were classified triple negative breast cancer (TNBC) as no above cut off antibody staining was detected simultaneously for ER, PR and HER-2 receptors. Molecular classification of the remaining 253 (59.6%), non TNBC patients, gave in order 119(28 %) luminal A, 27 (6.2 %) luminal B and 107 (25.4%) HER2-positive (**Table I**). Comparison of the relevant demographic, clinical and immunohistochemical characteristics between TNBC and NTNBC patients showed, despite slight differences in percentages, no statistically significant difference ($p < 0.05$) in median age at diagnosis, family history, ethnicity, menopausal status, proportion of cases with clinical stage or histological grade, treatment and recurrence was observed (**Table II**).

Outcome

Out of 189 women diagnosed with breast cancer in 2017, 120 were still alive and only 26% of those diagnosed in 2018 have died giving a 3- and 2-year observed survival rate of 63% and 74% respectively. BC did not return in most of these patients, as 88% and 95% of women diagnosed respectively in 2017 and 2018 did not show any local or distant recurrence.

Table I: Demographic and clinico-pathological characteristic of the study population.

Parameters	*Cases (N)*	*Percentage (%)*
Age, years (N=793)		
<35	132	16,6
[35-55]	416	52,4
>55	245	31
Menopausal status (N=793)		
Premenopausal	505	63,7
Postmenpausal	288	36,3
Family history (N=658)		
Present	95	14,5
Absent	563	85,5
Consanguinity (N=658)		
Yes	388	59
Non	270	41
Body Mass Index kg/m² (N=785)		
Underweight <18	24	3
Normal weight [18-25[	128	16,3
Overweight [25-30[	246	31,4
Obesity [30-35]	354	45,1
Morbid obesity >35	33	4,2
Ethnicity (N=793)		
White Moors	397	50,1
Black Moors	263	33,2
Black Africans	133	16,7
Breast affected (N=793)		
Right	417	52,6
Left	351	44,3
Bilateral	25	3,1
Tumor size (N=404)		
<5 cm	275	68,1
>5cm	129	31,9
Histological grading (N=586)		
Grade I	67	11,4
Grade II	334	57
Grade III	185	31,6
Staging (N=540)		
STAGE I	7	1,2
STAGE II	167	31
STAGE III	242	44,9
STAGE IV	124	22,9
Histological type (N=777)		
Invasiv Ductal Carcinoma (IDC)	618	79,6
Invasive Lobular Carcinoma (ILC)	70	9
Other type	89	11,4
Immunohistochemistry (N=425)		
TNBC	172	40,4
luminal A	119	28
luminal B	27	6,4
HER2+	107	25,2
Treatment (N=777)		
Curative	604	77,7
Palliative	138	17,7
Not treated	35	4,6

Table II: Comparison of epidemiological and clinico-pathological features between TNBC and NON-TNBC patients.

Parameters	*NON-TNBC (N=253)*	*TNBC (N=172)*	*X^2 Value*	*P Value*
Age			4,845	0,088
< 35	39 (15,67%)	34 (19,56%)		
[35-55]	147 (58,2%)	75 (43,475%)		
>55	67 (26,11%)	63 (36,9%)		
Family history			1,616	0,204
Present	15 (6%)	32 (18,93%)		
Absent	238 (94%)	139 (80,07%)		
Ethnicity			5,343	0
Moors white Moors	103 (40,7%)	49 (28,5%)		
Black Moors	16 (9,3%)	107 (62,7%)		
Black Africans	56 (22,13%)		16 (9,3%)	
Menopause			,704	0,401
Premenopause	149 (59%)	113 (66%)		
Postmenopause	104 (40%)	59 (34%)		
Histological type			,099	0,753
Invasive carcinoma	209 (83,58%)	143 (83,5%)		
Others	44 (16,4%)	29 (16,5%)		
Histological grading			4,813	0,185
Grade I	30 (11,11%)	6 (3,2%)		
Grade II	158 (62,8%)	111 (64,8%)		
Grade III	65 (26,11%	55 (32%)		
Staging			3,652	0,455
STAGE I	2 (0,14%)	0(0%)		
STAGE II	70 (27,6%)	56 (32,9%)		
STAGE III	101 (40,2%)	66 (38,4%)		
STAGE IV	48 (19%)	24 (14,2%)		
Treatment			2,549	0,28
Curative	208 (82,2%)	146 (84,6%)		
Palliative	45 (17,8%)	26 (15,4%)		
Local recurrence or distant metastasis	(n=58) 22,9%	(n=68) 39,5%	4,041	0
Local recurrence	2	3		
Distant metastasis	56	65		

Discussion

In this study, we have first addressed the main demographic and clinical characteristics of breast cancer in a cohort of patient women referred to the CNO (Centre National d'Oncologie) and assessed the outcome of cancer in the context of these factors. Out of 11175 patient files of all cancer types, BC was the most common in the cohort population (16.56%), particularly in women (30.9%). This standing was also reported by a ten years study (from 2000 to 2009) which included 3305 histological samples analyzed by the department of anatomic pathology (Hopital National de Nouakchott) and showed a prevalence of 14.6% in the whole cohort and 25.2% among the female population[10-11]. As our study was conducted in the following decade of the previous work and covered the single state referring facility for cancer, the data generated were therefore likely representative of the disease evolution in the country. Their concordance reflected an increase in the incidence of breast cancer in our population. Similar percentages of breast cancer in women were reported in neighboring populations such as in Morocco (36%)[8,12] and Senegal (26.1%)[13]. Most women diagnosed with breast cancer (69%) in our study were ages 55 or less. Registries and community-based studies showed that 70% of women with breast cancer in Sub-Saharan Africa were in the same age group[14]. The mean age of 49 years we observed was thus close to the 48 years reported globally in Africa[15] and 46 years in British black women[16]. This relatively early onset of breast cancer was lower than late age of 67 years at presentation in white British women [16]. Pre-menopausal status was also predominant in our cohort (63 %) as in two-thirds of black African women with BC[17-18] while most of European women (80 %) were postmenopausal at presentation with the disease[19]. We also observed that most patients (66%) had moderate to poorly differentiated tumors with widely spread stage 3 (44%) or metastasized (22%) cancer when diagnosed with BC. A similar outline was reported in a 12 sub-Saharan countries study (Zimbabwe, Benin, Seychelles, Ethiopia, Mauritius, South Africa, Kenya, Mozambique, Mali, Namibia, Uganda and Cote d'Ivoire) showing that 64.9% of women patients were diagnosed in late stages, when treatment became weakly effective, of which 18.4% being metastatic at diagnosis[20]. This late advanced stage at presentation, very likely accentuated by poor socioeconomic conditions and lack of access to adequate healthcare. Therefore could be determinant in the low 2- and 3-year observed survival rate of 74% and 64% observed in our cohort and the overall relative

survival (RS) of 61.4% (59.1–63.5) at year 3 and 52.3% (49.9–54.6) at year 5[20] in BC patients across sub-Saharan Africa. In contrast, 79% and 89% of women with breast cancer respectively in Europe and the US had not died from their cancer 5 years later after diagnosis[21]. Despite evidences reported from many large cohort studies linking overweight to breast cancer risk[22-23], nearly 40% of women worldwide were overweight in 2020[24]. We have shown a high cumulative prevalence of overweight and obesity among our patients. Obesity was for centuries desirable and a sign of wealth in various African countries[25]. A traditional practice of force-feeding teenage girls (known as leblouh in our country) has indeed been prevalent in Mauritania and several other African populations[26-27]. Although lifestyle choices and low provision of healthcare services in African populations may be determinant in the disease expected development, various studies have shown that other risk factors may take part in BC prognosis such as patient race or ethnic origin, parents 'consanguinity and age at onset[28-30]. The comparable early age at breast cancer onset observed in our cohort, globally in Sub-Saharan[14] and British black women[16] against a relatively late age of 67 years in white British women at presentation[19] was in this context relevant. African-American women have also higher rates of grade 3 than their Caucasian counterparts[31-32]. Race related differences among BC patients have been attributed to various hereditary grounds including breast cancer susceptibility genes and endogenous hormones[33]. For instance, in the US, the frequency of samples tested negative for receptors of progesterone, estrogen and HER2 protein (TNBC) was higher in African-American women (28%) compared to Caucasian women (12%)[34]. The Mauritanian population is composed of three main groups all Muslims but of different race origin[35]: the white Maures (WM) speaking Hassaniya, a berber-arab dialect. This group ethnically and culturally self-identifies with the neighboring North Africa populations. The black Maures (BM) also speaking Hassaniya but share the same race origin with the third group, the black African Mauritanians (BAM), as both descended from native sub-Saharan Africans.

The global TNBC prevalence (40.4%) observed in this study was intermediate between the percentages of 28.5% in the white Moors and 71.51% in the black Moors-black Africans group respectively. The frequency observed in the white Moors (28.5%) although slightly higher, was comparable to the percentages in North African populations[36-37]. The frequencies in black Moors-black Africans group, is also similar to those reported in sub-Saharan African women-based studies[38-39] which is consistent with the common African ascendance above mentioned. This ethnically associated repartition of percentages in TNBC also concords with the distribution of other biomarkers we reported previously in our population[40-41]. However, although differences of percentages between TNBC and NTNBC patients were observed, all parameters we analyzed did not reach the level of statistical significance set.

Limitations

One of the limitation of this study was that all the parameters were not available in all patients for various reasons of which we could mention disappearance of patients and lack of consent to participate. As a result of this failing we could not set a statistical significance of all patient characteristics.

Conclusion

We have provided data from a representative cohort on the frequencies of BC in Mauritania, evaluated the main demographic and clinical characteristics, which may affect the disease prognosis. The results, consistent with already published studies support a genetic basis of breast cancer in our population. Further studies increasing the cohort size and extending the time span of following the patients may optimize data for significant correlation assessment.

What is already know on this topic

- High prevalence of breast cancer in sub-Saharan African women
- Poor outcome due to late diagnosis
- Gene susceptibility is reported to a great extent

What this study adds

- Present recent epidemiological and clinic-pathological data on breast cancer in Mauritania
- Provide first data (diagnosis, incidence and survival rate) on triple negative breast cancer patients in Mauritania.
- Compare the data found with data available in neighboring populations

Ethics approval and consent

Approval to this study was given by the ethics committee of the Université de Nouakchott Al-Asriya, Mauritania. The informed consent of patients referred to the CNO was obtained. All methods were carried out in accordance with relevant guidelines and regulations.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interest.

Funding

No specific funding was obtained for this study carried out between the UNA and the CNO.

Authors' contributions

Selma MOHAMED BRAHIM: collected and organized all cancer files; She contributed to epidemiological and Immunohistochemistry data analysis;
Cheikh Tijani HAMED: contributed in pathological data analysis;
Ekht Elbenina ZEIN: initiated the paper conception and contributed to the manuscript progress; MS contributed to epidemiological data analysis;
Fatimetou VETEN: contributed to epidemiological data analysis;
Mohamed Vall ZEIN: contributed to patholgical data analysis;
Meriem KHYATTI: contributed in paper conception and paper writing;
Ahmed HOUMEIDA: were the major contributor in coordinating all data analysis and writing the manuscript;
Ahmedou TOLBA: examined Immunohisto chemical slides (IHC) and contributed in paper conception and writing.
All authors read and approved the final manuscript.

Annex

STROBE Statement—checklist of items that should be included in reports of observational studies.

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	3
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	2
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	4
		(c) Consider use of a flow diagram	4
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	4
		(b) Indicate number of participants with missing data for each variable of interest	4
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	4
		Cross-sectional study—Report numbers of outcome events or summary measures	4
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(b) Report category boundaries when continuous variables were categorized	4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	4
Discussion			
Key results	18	Summarise key results with reference to study objectives	4
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	5
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6
Generalisability	21	Discuss the generalisability (external validity) of the study results	6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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