Visceral obesity and incident cancer and cardiovascular disease: An integrative review of the epidemiological evidence

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Summary
Evidence shows a strong relationship between obesity, cancer and cardiovascular disease (CVD) risk. However, there is not enough evidence of the role of visceral obesity on both CVD and cancer. Visceral obesity may be more pro-oncogenic than total body fat. Therefore, it is important to know whether abdominal obesity can lead to both CVD and cancer. The present integrative review aimed at evaluating epidemiological evidence on the potential connection of visceral obesity in the occurrence of cancer and CVD. The following databases were searched: SCOPUS, PubMed, Science Direct, Lilacs, SciELO, Google Scholar, Web of Science, Scopus and ProQuest. The presence of visceral obesity can increase the risk of some specific cancer types, but there is controversial evidence about CVD risk based on sex-specific and ageing analyses. There is enough evidence that visceral obesity increases the risk of colorectal, pancreatic and gastro-oesophageal cancer. However, for some types of cancer such as breast, endometrial and renal, visceral obesity is a risk only in post-menopausal women. Regarding prostate cancer, the evidence is controversial. Despite the risk of visceral obesity being consistently associated with CVD in adults, this association disappears in sex-specific and older adults analyses. Moreover, in older adults, the results are controversial due to the use of different measures such as waist circumference and visceral adipose tissue. However, the evidence showing visceral obesity as a risk factor to CVD remains controversial. Sex differences, ageing and body mass index (BMI) category can potentially modify this association. Therefore, further epidemiological studies with analyses stratified by sex and samples including older adults aged 65 and older are needed.

KEYWORDS
aging, body composition, visceral adiposity, waist circumference

1 | INTRODUCTION

Cardiovascular disease (CVD) and cancer are the main leading causes of death globally and the world’s major disease burden. CVD continues to be the most prevalent non-communicable disease. There is growing consensus that obesity represents an important risk factor for both of these conditions. Obesity is increasing worldwide, and it is the most prevalent nutrition-related disorder in Western countries.
According to a recent report by the International Agency for Research on Cancer (IARC), which analysed more than 1000 epidemiological studies, there is sufficient evidence to classify obesity, measured by body mass index (BMI), as a causal cause for 13 types of cancers. Similarly, a cohort of 3.5 million adults in the United Kingdom has shown that higher BMI increases risk for coronary heart disease, cerebrovascular disease and heart failure.

However, BMI may not be the most adequate measure to assess obesity, characterized by excessive body weight and fat accumulation. Individuals with the same BMI may have different amounts of body fat and visceral fat. Some people can be classified as normal weight (BMI = 18.5–24.9 kg m\(^{-2}\)) as well as with abdominal obesity (waist circumference over than 102 cm in men and 88 cm in women). Therefore, the impact of adiposity distribution, mostly visceral obesity using sex-specific analyses, needs to be further explored. Despite the vast number of scientific papers on incident CVD and obesity, there are still some questions to be answered. Would an adipose distribution measure be more consistently associated to CVD risk than BMI? Do existing anthropometric measures explain the same CVD risk as the body composition variables measuring visceral adipose tissue? Is the impact of visceral obesity the same in men and women?

Unfortunately, there is not enough evidence for the role of abdominal obesity on cancer and CVD. Evidence of the effect of visceral obesity on the occurrence (incidence or prevalence) of both cancer and CVD in the same study is also scarce. Visceral obesity can be more pro-oncogenic than total body fat and is related to cardiometabolic conditions such as insulin resistance, diabetes, metabolic syndrome, hypertension and dyslipidaemia. Therefore, it is relevant to explore whether abdominal obesity can lead to both CVD and cancer, independently of total adiposity or BMI category. The objective of this study is to evaluate the epidemiological evidence on the association between visceral obesity and the incidence of cancer and CVD.

### 2 | METHODS

An integrative literature review was conducted. Observational studies, clinical trials and reviews exploring the role of visceral obesity on the occurrence of cancer and CVD were included. We considered as CVD the group of heart and blood vessels disorders including hypertension, coronary heart disease, cerebrovascular disease, peripheral vascular disease, heart failure, rheumatic heart disease and cardiomyopathies.

Currently, various studies are using BMI as a synonymous of adiposity measure. However, they measure different dimensions. We clarify in our review the differences between BMI and adiposity and visceral fat/obesity. BMI measures the excess of weight per height, but it is not the same of adiposity, which means the excess of body fat. Regarding visceral fat or visceral obesity, there are more appropriate anthropometric measures to evaluate it, such as waist circumference (WC), hip circumference (HP) and waist-hip ratio (WHR). There are also body composition methods to analyse visceral fat or total body fat, such as computed tomography and ultrasound.

An electronic search was performed using the following databases: SCOPUS, PubMed, Science Direct, Lilacs, SciELO, Google Scholar, Web of Science, Scopus and ProQuest. No language or year of publication restrictions were imposed. We analysed both titles and abstracts to decide whether a study could be included in our review. Articles were included if they fulfilled the following criteria: being peer-reviewed and/or research-based, investigating the association in adults and/or older adults and met the search criteria. Studies with incomplete data were excluded.

We described and analysed the evidence from epidemiological studies focusing on visceral obesity as a potential risk factor for both cancer and CVD. Preference was given to well-conducted observational epidemiological studies, mainly case–controls and cohort studies, that evaluated as outcome the incidence of cancer in general, specific types of cancers (breast, prostate, endometrial and others) and/or CVD. Few systematic reviews and umbrella reviews about both outcomes were also found.

### 3 | RESULTS

We summarized the evidence in two tables. Table 1 shows the association between visceral obesity with specific types of cancer, and Table 2 displays the association between visceral obesity with CVD. We highlighted in dark grey the non-significant associations between visceral obesity with cancer and/or CVD and in light grey protective significant associations.

In some of the included studies, visceral obesity was not the main independent variable (Tables 1 and 2), but it was instead included as a confounder variable or used as part of a group of variables to define/diagnosis the main independent variable such as metabolic syndrome (MetS). However, visceral obesity is more appropriate to investigate obesity-related health risks. Therefore, it was challenging to explore the role/connection of visceral obesity with both CVD and cancer. Only one epidemiological study, that is, the Framingham cohort, analysed the relationship between visceral obesity and both CVD and cancer. Other cohort studies analysed the risk of CVD in cancer patients, for example, breast cancer. This is called cardio-oncology field, a new cross-disciplinary field aiming to mitigate CVD morbidity and mortality in cancer patients.

MetS has been consistently associated with the risk of CVD, and recently, some studies investigated its association with several types of cancers, showing also a positive association. The prevalence of MetS is increasing worldwide and, consequently, the number of studies on its association with health outcomes. Some of the MetS components such as abdominal obesity, diabetes, hypertension and hyperlipidaemia had been associated with CVD and different types of cancer, most of them being sex specific.

#### 3.1 | Evidence on the link between visceral obesity and the incidence of overall and specific types of cancer

A few prospective studies have investigated the association between multicancer sites and visceral adiposity. Two cohorts, one in Europe and another in the United States, analysed the association...
| Author/year       | Design          | Population                          | Outcome                                                                 | Visceral obesity measurement                                      | Visceral obesity results                          | Summary                                                                 |
|------------------|-----------------|-------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------|-------------------------------------------------------------------------|
| **Overall cancer** |                 |                                     |                                                                         |                                                                     |                                               |                                                                         |
| Britton (2013)   | Cohort          | Framingham Heart Study (n = 3086, 49% women, mean age 50.2 years Followed 5.0 years) | Incident of cancer Cancers were validated using medical records (pathology reports). Nonmelanoma skin cancers were not included. | Visceral adipose tissue (VAT) by computed tomography (CT)           | After adjustment for clinical risk factors and general adiposity/BMI: VAT was associated with cancer HR = 1.43 (1.12–1.84). Women HR = 1.27 (0.88–1.82) Men HR = 1.43 (1.06–1.94) | VAT Overall—risk Women—NS Men—risk                                    |
| Liu Y. (2016)    | Cohort          | 68 253 Chinese women                | Overall cancer Major site-specific cancers: postmenopausal breast cancer, endometrial, liver and ovarian | Waist-hip ratio (WHR)                                               | WHR was not associated with cancer risk after adjustment. | WHR Overall—NS                                                          |
| Lee (2018)       | Cohort          | 22.9 million Korean adults 769 871 cancer cases Followed 7 years | 23 of the most common cancers WC—quintiles of the cohort Site specific cancers | Positive association with 18 of 23 types of cancer varying by sex Adjust for BMI removed some association (premenopausal and postmenopausal uterus and ovary, postmenopausal breast and leukaemia) | WC Overall—risk Women—risk Men—risk 18 cancer—risk |                                                                        |
| Staunstrup (2019) | Prospective Epidemiological Risk Factor (PERF) cohort 4679 Danish postmenopausal women | Cancer diagnoses were extracted from the Danish Cancer Registry. Overall cancer Site specific cancers | Central obesity defined—trunk-to-peripheral fat ratio, calculated by fat mass in the trunk area/fat mass in arms and legs evaluate by dual-energy X-ray absorptiometry scanners High central obese—quartile 4 | Adjusted to BMI Overall cancer HR = 1.50 (1.20–1.88) Site-specific cancers: Respiratory (Q1 vs. Q4) HR = 2.01 (1.17–3.47) Gastrointestinal (Q1 vs. Q4: HR = 1.55 (0.99–2.41) Female genital organs (Q1 vs. Q4) HR = 1.95 (1.00–3.78) | Trunk-to-peripheral fat ratio Overall—risk Overall—NS (gastrointestinal) |                                                                        |
| Kyrgiou (2017)   | Umbrella review of systematic reviews and meta-analyses of observational studies | Colon cancer Pancreatic Breast premenopausal Breast postmenopausal Endometrial Ovarian Lung Melanoma Non-Hodgkin lymphoma Multiple myeloma Leukaemia Oesophageal adenocarcinoma Gastric Biliary tract | Waist circumference (WC) per 10 cm WHR per 0.1 units Continuous scale to measure adiposity | Colon WC HR = 1.25 (1.15–1.35) WC men 1.33 (1.18–1.50) WC women 1.16 (1.08–1.23) WHR HR = 1.29 (1.17–1.43) Men 1.43 (1.19–1.71) Women 1.20 (1.08–1.33) Pancreatic cancer WC 1.11 (1.05–1.18) WHR 1.20 (1.09–1.31) Endometrial WC 1.27 (1.17–1.39) WHR 1.21 (1.13–1.29) Ovarian | WC Overall—risk Women—risk Men—risk WHR Overall—risk Women—risk Men—risk Ovarian and all other sites—NS |                                                                        |
| Author/year | Design | Population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|------------|--------|------------|---------|-----------------------------|------------------------|---------|
| **Table 1 (Continued)** | | | | | | |
| **Colorectal cancer** | | | | | | |
| Chan (2007) | Case–control | Patients in Hong Kong, China, recruited after coronary angiography for suspected CAD. Age- and sex-matched control was recruited from the general population (n = 207). | Colorectal neoplasm | WC | Men ≥ 91.4 cm Women ≥ 81.3 cm | OR = 2.29 (1.29–3.72) | WC Overall—risk |
| Yamaji (2009) | Case–control study | 50–79 years old Screening in Tokyo, Japan 782 cases and 738 controls | Colorectal adenoma | Visceral fat area (VFA)—cm² by CT | OR = 1.58 (1.11–2.24) for men and women combined, independently of body mass index | VFA Overall—risk |
| Knag (2010) | Case–control study | 4276 subjects, Koreans that presented for health check-ups | Colorectal adenoma | VAT by CT | VAT Adjusted (OR) = 3.09 (2.19–4.36) WC | VAT Overall—risk WC Overall—NS |
| Tae-Hoon (2008) | Prospectively enrolled 200 asymptomatic adults, Seoul, Korea, 133 males, 67 females. Mean age, 50.9 8.5 years follow-up | Colorectal neoplasm | VAT by CT | 136.61 cm² versus VAT under 67.23 cm² WC > 90 cm | VAT After adjustment VAT WC | VAT Overall—risk WC Overall—NS |
| Keum (2015) | Meta-analysis of observational studies | 12 studies included 2776 cases | Colorectal adenomas | VAT—each 25 cm² increase Range of VAT area = 30–228 cm² | VAT OR = 1.13 (1.05–1.21) | VAT Overall—risk |
| Abar (2018) | Systematic review of prospective studies | 50 936 cases among 7 393 510 participants | Colorectal cancer (CRC) | WC per 10 cm | WC HR = 1.02 (1.02–1.03) WHR HR = 1.03 (1.01–1.05) | WC and WHR Overall—risk |
| **Prostate cancer** | | | | | | |
| Blanc-Lapierre (2015) | Population-based case–control study | 1937 men with incident prostate cancer, aged ≤75 years, diagnosed across hospitals, Montreal, Canada 1995 controls The Prostate Cancer & Environment Study (PROtEuS) | Prostate cancer Aggressiveness of PCa—defined by the Gleason score | WC cut-off of 102 cm for abdominal obesity | Cases had similar WC (98.6 vs. 98.5 cm) OR = 0.70 (0.60, 0.82) after considering potential confounders negative association did not vary according to PCa aggressiveness | WC Overall—protective |

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| Author/year       | Design Population                                                                 | Outcome                                                                 | Visceral obesity measurement | Visceral obesity results                                                                 | Summary                      |
|------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------|------------------------------|--------------------------------------------------------------------------------------------|-------------------------------|
| Pischon (2008)   | 29,502 men without cancer at baseline from eight countries of the EPIC             | Follow-up of 8.5 years                                                  | WHR per 0.1 unit             | RR advanced prostate cancer = 1.06 (1.01–1.1)                                               | Overall—risk                  |
|                  |                                                                                   | Prostate cancer diagnosis at biopsy.                                    |                              | WHR RR = 1.21 (1.04–1.39)                                                                   |                               |
|                  | De Nunzio (2016)                                                                  | Patients with moderate/high cardiovascular risk evaluated for prostate cancer diagnosis. | WC                           | WC was not associated with prostate cancer (p = 0.669).                                       | WC Overall—NS                 |
|                  |                                                                                   | Prostate cancer diagnosis at biopsy.                                    |                              | WC was associated with Gleason score (p = 0.028).                                             |                               |
| De Nunzio (2016) |                                                                                   | Secondary end point                                                    |                              | WC was associated with Gleason score (p = 0.028).                                             |                               |
| Breast cancer    |                                                                                   | High-grade disease—Gleason score of ≥ 7                                 |                              | Highest WC between Gleason score ≥ 7                                                           |                               |
| Agnoli (2010)    |                                                                                   | Breast cancer postmenopausal                                            | WC > 86 cm                   | WC                                                                                           |                               |
|                  |                                                                                   |                                                                         |                              | Adjusted RR = 1.23 (0.83–1.81)                                                               | Women—NS (post)               |
|                  | Case-control study postmenopausal women, ORDET cohort.                             |                                                                         |                              |                                                                                              |                               |
|                  |                                                                                   | Follow-up 13.5 years                                                    |                              |                                                                                              |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              |                               |
| Agnoli (2015)    |                                                                                   | Breast cancer (BC)                                                      | WC > 80 cm                   | WC                                                                                           |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              | Women—NS (pre and post)       |
|                  |                                                                                   | Postmenopausal and premenopausal                                       |                              |                                                                                              |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              |                               |
| Bandera (2015)   |                                                                                   | Breast cancer                                                           | WHR                          |                                                                                              |                               |
|                  |                                                                                   | Premenopausal and postmenopausal Categorized according to hormone receptor status ER+, ER− and TN (ER−, PR− and HER2−) |                              |                                                                                              |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              |                               |
| Park (2017)      |                                                                                   | Breast cancer                                                           | WC (88 cm)                   |                                                                                              |                               |
|                  |                                                                                   |                                                                         | WHR (0.85)                   |                                                                                              |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              |                               |
|                  |                                                                                   |                                                                         |                              |                                                                                              |                               |

(Continues)
| Author/year | Design Population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|-----------------------------|-------------------------|---------|
| Chen (2016) | Meta-analysis of prospective studies | Breast cancer | WC per 10 cm, WHR per 0.1 unit | Premenopausal BC–adjusted RRs | Women WC–risk (post), WC–NS (pre), WHR–NS (pre and post) |
| Amankwah (2013) | Population-based case–control study | Endometrial cancer | WC, HP, WHR | WC > 84.8–96.0, OR = 2.34 (1.59–3.43), WC > 96.0, OR = 4.21 (2.90–6.10), HP > 104.7–112.7, OR = 1.48 (1.03–2.11), HP > 112.7, OR = 2.87 (2.05–4.00), WHR > 0.81–0.86, OR = 1.86 (1.28–2.69), WHR > 0.86, OR = 2.57 (1.80–3.67) | Women WC–risk, HP–risk, WHR–risk |
| Reeves (2011) | Cohort | Endometrial cancer | WHR | WHR HR = 1.33 (1.04–1.70) | Women WHR–risk |
| Sponholtz (2016) | Cohort | Endometrial cancer | WC ≥ 88 cm, HC highest quartile, WHR ≥ 0.85 | After adjustment | Women WC–NS, HC–NS, WHR–NS |
| Author/year       | Design Population                                                                 | Outcome                                      | Visceral obesity measurement | Visceral obesity results | Summary                     |
|------------------|------------------------------------------------------------------------------------|----------------------------------------------|------------------------------|--------------------------|-----------------------------|
| Raglan (2019)    | Umbrella review analysed systematic reviews or meta-analyses of observational studies | Endometrial cancer                           | WHR 0.1 unit                 | RR = 1.21 (1.13–1.29)    | Women                       |
| Luo (2008)       | Cohort                                                                             | Pancreatic cancer                            | WC per 10 cm                 | WC 1.08 (0.98–1.18)      | Women                       |
|                  | 138 503 women followed for 7.7 years Women’s Health Initiative in the United States |                               | WHR per 0.1 unit             | WHR 1.32 (1.12–1.56)     | WC–NS                       |
|                  | 846 340 individuals 2135 individuals were diagnosed with pancreatic cancer          |                               |                              |                          | WHR–risk                    |
| Genkinger (2011) | Analysis of 14 cohort studies on 846 340 individuals                               | Pancreatic cancer                            | WHR                          | RR = 1.35 (1.03–1.78)    | Overall WHR–risk            |
|                  |                                                                                   |                               | Highest versus lowest quartile|                          |                             |
| Aune (2012)      | Systematic review and meta-analysis of prospective studies                         | Pancreatic cancer                            | WC 10-cm increase            | WC RR = 1.11 (1.05–1.18) | Overall WC–Risk             |
|                  |                                                                                   |                               | WHR 0.1-unit increment       | WHR RR = 1.19 (1.09–1.31) | WHR–risk                    |
| Du (2017)        | Systematic review and meta-analysis of prospective studies                         | Gastro-oesophageal cancer: total gastro-oesophageal cancer, gastric cancer and oesophageal cancer | WC                           | Gastro-oesophageal cancer | Overall WC–risk             |
|                  | Total of 2130 gastro-oesophageal cancer cases diagnosed among 913 182 participants |                               | WHR                          | WC RR 1.68 (1.38–2.04)   | WHR–risk                    |
|                  |                                                                                   |                               |                              | WHR RR 1.49 (1.19–1.88)  |                             |
|                  |                                                                                   |                               |                              | Gastric cancer            |                             |
|                  |                                                                                   |                               |                              | WC RR 1.48 (1.24–1.78)   |                             |
|                  |                                                                                   |                               |                              | WHR RR 1.33 (1.04–1.70)  |                             |
|                  |                                                                                   |                               |                              | Oesophageal cancer        |                             |
|                  |                                                                                   |                               |                              | WC RR 2.06 (1.30–3.24)   |                             |
|                  |                                                                                   |                               |                              | WHR RR 1.99 (1.05–3.75)  |                             |
| Steffen (2015)   | European Prospective Investigation into Cancer and Nutrition (EPIC) study           | Oesophageal adenocarcinoma (EAC)             | WC–highest versus lowest quintile | EAC                        | Overall WC–risk             |
|                  | 11 years of follow-up                                                             | Gastric cardia adenocarcinoma (GCC)         | HC–highest versus lowest quintile | Adjusted for BMI           | WHR–risk                    |
|                  | 391 456 individuals                                                                | Gastric noncardia adenocarcinoma (GNCC)     | WHR–highest versus lowest quintile | WC                        |                             |
|                  |                                                                                   |                               |                              | HR = 3.76 (1.72–8.22)    |                             |

(Continues)
| Author/year | Design Population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|------------|------------------|---------|-----------------------------|------------------------|---------|
| O’Doherty (2012)<sup>41</sup> | Prospective NIH–AARP cohort 218 854 participants | Oesophageal adenocarcinoma (EAC) Gastric cardia adenocarcinoma (GCC) | WC WHR | HR = 0.35 (0.18–0.68) WHR = 4.05 (1.85–8.87) GCC WC (HR = 1.91 (1.09–3.37)) HC (HR = 0.38 (0.42–1.13)) WHR HR = 1.95 (1.12–3.38) GNCC WC HR = 1.25 (0.75–2.08) HC HR = 0.69 (0.41–1.15) WHR HR = 2.05 (1.19–3.52) | Overall WC—risk WHR—risk (EAC) WHR—NS (GC) |

**Renal cancer**

| Author/year | Design Population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|------------|------------------|---------|-----------------------------|------------------------|---------|
| Luo (2007)<sup>15</sup> | Cohort Women's Health Initiative 7.7 years of follow-up 140 057 postmenopausal women aged 50–79 years | Renal cell carcinoma | WHR—highest vs. lowest quartile | RR = 1.8 (1.2–2.5) | Women WHR—risk |
| Pischon (2006)<sup>43</sup> | European Prospective Investigation into Cancer and Nutrition (EPIC)—eight countries 348 550 men and women 6.0 years of follow-up | Renal cell carcinoma | WC HC quintile WHR quintile | Multivariable adjustment Women WC RR = 1.80 (1.18–2.75) HC RR = 1.65 (0.64–4.23) WHR RR = 1.01 (0.54–1.89) Men WC RR = 1.19 (0.98–1.97) HC RR = 0.44 (0.20–0.98) WHR RR = 1.86 (0.97–3.56) | Women WC—risk HC—NS WHR—NS Men WC—NS HC—protective WHR—protective |
| Nam (2019)<sup>54</sup> | 23 313 046 Korean adults 5.4 years of follow-up, 18 036 cases | Kidney cancer | WC per 5 cm WC male ≥ 1000, female ≥ 95.0 | HR increased with increasing waist circumference (WC) (p for trend < 0.001) WC per 5 cm Adjusted HR = 1.09 (1.08–1.11) | Overall WC—risk |
| Author/year                          | Design Population                          | Population | Outcome                                      | Visceral obesity measurement | Visceral obesity results | Summary                      |
|-------------------------------------|-------------------------------------------|------------|----------------------------------------------|------------------------------|--------------------------|-------------------------------|
| **Several types of cancer**         |                                           |            |                                              |                              |                          |                               |
| Montella (2015)                     | Case-control study                        | Italy—hospital-based | Bladder cancer Urothelial carcinoma of the bladder (UCB) | WC ≥ 94 cm for men           | Adjusted HR = 1.18 (1.09–1.28) | Overall WC—risk              |
|                                     | 690 incident UCB                          |            |                                              | WC ≥ 80 cm for women         |                          |                               |
|                                     | 665 controls                              |            |                                              |                              |                          |                               |
|                                     |                                           |            |                                              |                              |                          |                               |
| Britton (2008)                      | European Prospective Investigation into Cancer and Nutrition (EPIC), 371 983 cancer-free individuals. 8.5 years of follow-up, 1219 histologically confirmed incident cases |            | Hodgkin’s lymphoma (NHL) and multiple myeloma (MM) | WC ≥ 102 cm men, ≥ 88 cm women | Visceral obesity was not associated with NHL and MM in men and women. | Men WC—NS, Women ≥ NS          |
|                                     |                                           |            |                                              | WHR ≥ 0.95 men, ≥ 0.80 women | Sex-specific analyses      |                               |
| Schlesinger (2013)                  | European Prospective Investigation into Cancer and Nutrition study 359 525 men and women in the follow-up of 8.6 years |            | Hepatocellular carcinoma (HCC), intrahepatic (IBDC) extrahepatic bile duct system cancer (EBDSC) including gallbladder cancer (GBC) | WC and WHR—extreme tertiles | All anthropometric measures were positively associated with risk of HCC and GBC. | Overall WC—risk, WHR—risk (IBDC and EBDSC) |
|                                     |                                           |            |                                              |                             | WC and WHR—extreme tertiles |                               |
|                                     |                                           |            |                                              |                             | HCC RR = 3.51 (2.09–5.87)   |                               |
|                                     |                                           |            |                                              |                             | GBC RR = 1.56 (1.12–2.16)   |                               |
|                                     |                                           |            |                                              |                             | No association was observed between abdominal obesity and risk of IBDC and EBDSC. |                               |
|                                    |                                           |            |                                              |                             |                           |                               |
| Gaudet (2015)                       | 20 cohort studies Pooled data from 1 941 300 participants, including 3760 cases |            | Head and neck cancer | WC per 5 cm: WHR per 0.1 unit | After adjustment for BMI WC, HR = 1.04 (1.03–1.05) | Overall WC—risk |
|                                    |                                           |            |                                              |                             | WHR RR = 1.07 (1.05–1.09)   |                               |
|                                    |                                           |            |                                              |                             | Larger HC was not associated. |                               |
|                                    |                                           |            |                                              |                             |                           |                               |
| Kitahara (2016)                     | Pooled analysis of 22 prospective studies |            | Thyroid cancer | WC (per 5 cm) | HR = 1.03 (1.01–1.05) | Overall WC—risk |
|                                    |                                           |            |                                              |                             |                           |                               |
|                                    |                                           |            |                                              |                             |                           |                               |
| Aune (2015)                         | Systematic review and meta-analysis of prospective studies |            | Ovarian cancer | WC per 10 cm HC, WHR | RR = 1.06 (1.00–1.12) | Overall WC—NS, HC—NS |

(Continues)
### TABLE 1 (Continued)

| Author/year | Design Population                          | Outcome                  | Visceral obesity measurement | Visceral obesity results                        | Summary             |
|-------------|-------------------------------------------|--------------------------|-----------------------------|------------------------------------------------|---------------------|
| Hidayat (2016) | Meta-analyses of observational studies | Lung cancer              | WC—10-cm increase          | WC RR = 1.10 (1.04–1.17)                         | Overall WC—Risk     |
|             |                                           |                          | WHR—0.1-unit increase       | WHR RR = 1.05 (1.00–1.11)                         |                     |
|             |                                           |                          |                             | Highest versus lowest categories:                |                     |
|             |                                           |                          |                             | WC RR = 1.32 (1.13–1.54)                         |                     |
|             |                                           |                          |                             | WHR RR = 1.10 (1.00–1.23)                         |                     |
|             |                                           |                          |                             | WC Never smokers RR = 1.11 (1.00–1.23)            |                     |
|             |                                           |                          |                             | Former smokers RR = 1.12 (1.03–1.22)              |                     |
|             |                                           |                          |                             | Current smokers RR = 1.16 (1.08–1.25)             |                     |
| Abar (2019) | Meta-analysis of prospective studies      | Lymphohaematopoietic cancers | WC                          | Higher WC—no associated with multiple myeloma    | WC—NS              |
|             |                                           |                          | WHR                         | WHR associated with diffuse large β-cell lymphoma |                     |

WHR—NS
**TABLE 2**  Epidemiological evidence on the association between visceral obesity and incident cardiovascular disease in adults and/or older adults

| Author/year          | Design population                                                                 | Outcome                                      | Visceral obesity measurement | Visceral obesity results     | Summary               |
|----------------------|-----------------------------------------------------------------------------------|----------------------------------------------|------------------------------|------------------------------|------------------------|
| **Anthropometric measures—All sample**                                                                                     |                                               |                              |                              |                        |
| Chan (2007)\(^{28}\) | Case control study Hong Kong, China Presence of CAD (\(n = 206\)) Control group general population (\(n = 207\)) | Coronary artery disease                      | WC ≥ 91.4 cm for men or ≥81.3 cm for women | WC OR = 2.29 (1.29–3.72)    | WC Overall—risk       |
| The Emerging Risk Factors Collaboration (2011)\(^{53}\)                  | Cohort—collaborative analysis of 58 prospective studies 221 934 people in 17 countries 14 297 incident cardiovascular disease outcome | First-onset cardiovascular disease          | WC                            | After adjustment: WC HR = 1.10 (1.05–1.14) WHR HR = 1.12 (1.08–1.15) | Overall WC—risk WHR—risk |
| van Wijk (2016)\(^{51}\)                                         | Cohort—European Prospective Investigation of Cancer—Norfolk 7279 participants EPIC-Norfolk—10-country collaborative EPIC study | Coronary heart disease                      | WC                            | Stratified by C-reactive protein levels (≥2 mg L\(^{-1}\)) WC HR = 1.38 (1.08–1.75) | WC Overall—risk       |
| Feliciano (2017)\(^{52}\)                                         | Cohort—population of Kaiser Permanente Northern California (KPNC) 3109 early-stage breast cancer (stage I–III) 18 to 80 years without pre-existing CVD Follow-up 8.28 years | Cardiovascular disease (CVD) among breast cancer patients | WC—comparing 100 vs. 80 cm | HR: 1.93 (1.31–2.84) WC increased risk of CVD, independent of pre-existing risk factors. | WC Women—risk         |
| Aune (2016)\(^{56}\)                                                  | Systematic review and meta-analysis of prospective studies 23 prospective studies >15 905 incident cases 647,388 participants | Heart failure                               | WC—10-cm increase WHR—0.1-unit increase | WC RR = 1.29 (CI 1.21–1.37) WHR RR = 1.29 (CI 1.13–1.47) | Overall WC—risk WHR—risk |
| **Anthropometric measures—Sex-specific and BMI class analyses**                                                            |                                               |                              |                              |                        |
| Li (2006)\(^{52}\)                                                 | Prospective population-based study, Malmo, Sweden 7 years follow-up 10 369 men and 16 638 women 45–73 years old | Incidences of first-cardiac event (CE) and ischemic stroke | WHR Cut-off points for tertiles of WHR | WHR after adjustments Men Normal weight RR = 1.24 (1.13–1.37) Overweight RR = 1.06 (0.94–1.20) Obesity RR = 1.04 (0.87–1.24) Women Normal weight RR = 1.24 (1.11–1.39) Overweight RR = 1.31 (1.18–1.46) Obesity RR = 1.27 (1.07–1.51) | WHR Men—risk in normal weight Men—NS in overweight Women—risk in normal end overweight |
| Carlsson (2013)\(^{54}\)                                         | Population-based study—the Malmö | Cardiovascular disease                       | WC                            | CVD risk factor-adjusted: Men WC—NS |                        |

(Continues)
| Author/year | Design population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|------------------------------|--------------------------|---------|
| Diet and Cancer study-cardiovascular cohort | 1751 men and 1990 women, aged 60 years without CVD at baseline 11 years of follow-up | Visceral obesity measurement | Waist-hip-height ratio (WHHR) WC-to-height ratio (WCHR) SAD-to-height ratio (SADHR) Sagittal abdominal diameter (SAD) | Men WC, WHR and WCHR were not associated SAD 1.16 (1.02–1.30) WHHR 1.19 (1.05–1.36) SADHR 1.19 (1.07–1.32) | WHR NS WCHR NS SAD risk WHHR risk Women CVD HR = 1.19 (1.04–1.35) Adjustments for established risk factors. Women overweight/obese None of the measures were significantly associated. Men overweight/obese All measures were significant predictors WHR 1.24 (1.04–1.47) WC 1.19 (1.00–1.42) SAD 1.21 (1.00–1.46) WHHR 1.23 (1.05–1.44). |
| Carlsson (2014) | Cohort N 3741 (53% women) 60-year old without CVD followed for 11-years | CVD All cases of fatal and nonfatal | WHR WC Sagittal abdominal diameter (SAD) Waist-hip-height ratio (WHHR) | Women normal weight (BMI < 25) WHR 1.91 (1.35–2.70) WC 1.81 (1.02–3.20) SAD 1.25 (0.74–2.11) WHHR 1.97 (1.40–2.78) Men normal weight (BMI < 25) WHR, WHHR and WC were not associated SAD only associated CVD HR = 1.19 (1.04–1.35) Adjustments for established risk factors. Women overweight/obese None of the measures were significantly associated. Men overweight/obese All measures were significant predictors WHR 1.24 (1.04–1.47) WC 1.19 (1.00–1.42) SAD 1.21 (1.00–1.46) WHHR 1.23 (1.05–1.44). | Women normal weight WHR—risk WC—risk SAD—risk WHHR—risk Women overweight WHR—NS WC—NS SAD—NS WHHR—NS Men normal weight WHR—NS WC—NS SAD—NS WHHR—NS Men overweight WHR—risk WC—risk SAD—risk WHHR—risk |

Table 2 (Continued)

| Author/year | Design population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|------------------------------|--------------------------|---------|
| Fox (2007) | Framingham Heart Study—population-based 3001 participants free of clinical cardiovascular disease Mean age 50 years | Systolic and diastolic blood pressure (SBP) and (DBP) | Visceral adipose tissue (VAT) Measured by computed tomography | VAT was associated with SBP and DBP (p ≤ 0.0001) in men and women | VAT Overall—risk |
| Mahabadi (2009) | Framingham Heart Study Offspring cohort 1267 participants Mean age 60 years | Prevalence of cardiovascular disease (CVD). | VAT by computed tomography | VAT OR = 1.23 (0.92–1.63) adjustment for traditional risk factor | VAT Overall—NS |
| Britton (2013) | Cohort Framingham Heart Study n = 3086, 49% women, mean age 50.2 years | Incident cardiovascular disease | VAT by computed tomography | VAT HR 1.44 (1.08–1.92) By sex VAT | VAT Overall—risk Women—NS Men—risk |

Body composition variables

| Author/year | Design population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|------------------------------|--------------------------|---------|
| Fox (2007) | Framingham Heart Study—population-based 3001 participants free of clinical cardiovascular disease Mean age 50 years | Systolic and diastolic blood pressure (SBP) and (DBP) | Visceral adipose tissue (VAT) Measured by computed tomography | VAT was associated with SBP and DBP (p ≤ 0.0001) in men and women | VAT Overall—risk |
| Mahabadi (2009) | Framingham Heart Study Offspring cohort 1267 participants Mean age 60 years | Prevalence of cardiovascular disease (CVD). | VAT by computed tomography | VAT OR = 1.23 (0.92–1.63) adjustment for traditional risk factor | VAT Overall—NS |
| Britton (2013) | Cohort Framingham Heart Study n = 3086, 49% women, mean age 50.2 years | Incident cardiovascular disease | VAT by computed tomography | VAT HR 1.44 (1.08–1.92) By sex VAT | VAT Overall—risk Women—NS Men—risk |
between overall cancer with body composition variables, visceral adipose tissue (VAT) and trunk-to-peripheral fat (TPF) ratio using computed tomography (CT) and body dual-energy X-ray (DXA) (Table 1). In both cohorts, VAT and TPF, after adjustment for clinical risk factors and BMI, were associated to overall cancer risk in all participants. However, this association remained significant only among men after stratification by sex. The European cohort also found that respiratory and gynaecological cancer were associated with abdominal obesity, whereas gastrointestinal cancer was not. In contrast, a cohort with Chinese women that analysed overall cancer, ovarian, endometrial and postmenopausal breast cancer did not find an association with visceral obesity measured by WHR. An umbrella review that analysed 36 cancer sites using WC and WHR as visceral obesity measures found the following associations: WC and WHR with colon cancer in all participants, men and women; WC and WHR with pancreatic and endometrial cancer; and WC with ovarian cancer. The other 32 cancer sites were not associated with visceral obesity measured by WC and WHR, which may be a consequence of multiple test corrections, because studies investigating the association between visceral adiposity and each cancer site separately showed more positive associations.

Several studies analysed the association between colorectal cancer and visceral obesity using body composition, anthropometric measures such as WC and WHR or both and methods (Table 1). An increase in visceral adiposity was associated with colorectal adenoma risk in the general healthy population. These studies, including a meta-analysis of 12 observational studies, found an association between colorectal adenoma and colorectal cancer with visceral obesity measured by VAT or visceral fat area. In this meta-analysis, every 25-cm² increase of VAT resulted in 13% more risk of colorectal adenoma. Visceral obesity measured by WC was associated in some studies but not in others with colorectal cancer. A recent systematic review of prospective studies found a positive association between colorectal cancer and WC and between colorectal adenoma and WHR. There is clear evidence linking visceral obesity measured by body composition or anthropometric measures to

### Table 2 (Continued)

| Author/year | Design population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|-------------------------------|--------------------------|---------|
| Kouli (2017) | Prospective study in Europe—ATTICA study | Fatal/nonfatal CVD incidence | Visceral adiposity index (VAI) by CT | After adjusting for multiple confounders, VAI OR = 1.05 (1.01–1.10) Men HR = 1.06 (1.00–1.11) Women HR = 1.06 (0.96–1.10) | Overall—risk or Men—NS |
| Nicklas (2004) | Health, Ageing and Body Composition Study | Incident myocardial infarction (MI) | WC waist-to-thigh ratio (WTR) VAT (per 66.23-cm² increase) VAT/SAT (per 0.30 increase) VAT/fat mass (per 2.17 increase) Computed tomography | Women WC and WTR were not associated VAT HR = 1.67 (1.28–2.17) VAT/SAT area HR = 1.42 (1.08–1.87) VAT/fat mass HR = 1.67 (1.20–2.31) Men No association were observed WC, WTR, VAT and VAT/SAT | Women WC—NS WTR—NS VAT—risk VAT/SAT—risk VAT/fat mass—risk Men WC—NS WTR—NS VAT—NS VAT/SAT—NS VAT/fat mass—NS |
| Jasper (2017) | ‘SMART’ cohort—secondary manifestations of arterial disease | Vascular events | WC VAT%—visceral fat to total abdominal fat measured by ultrasound | WC Men HR = 1.13 (CI 0.97–1.32) Women HR = 1.00 (CI 0.76–1.32) VAT% HR = 1.15 (0.99–1.34) | Women VAT%—NS Men—NS VAT—NS |

### Table 2

| Author/year | Design population | Outcome | Visceral obesity measurement | Visceral obesity results | Summary |
|-------------|-------------------|---------|-------------------------------|--------------------------|---------|
| Followed up 5.0 years | 3,042 adults 10 years follow-up | | | | |
| Kouli (2017) | Prospective study in Europe—ATTICA study | Fatal/nonfatal CVD incidence | Visceral adiposity index (VAI) by CT | OR = 1.05 (1.01–1.10) Men HR = 1.06 (1.00–1.11) Women HR = 1.06 (0.96–1.10) | Overall—risk or Men—NS |
| Nicklas (2004) | Health, Ageing and Body Composition Study | Incident myocardial infarction (MI) | WC waist-to-thigh ratio (WTR) VAT (per 66.23-cm² increase) VAT/SAT (per 0.30 increase) VAT/fat mass (per 2.17 increase) Computed tomography | Women WC and WTR were not associated VAT HR = 1.67 (1.28–2.17) VAT/SAT area HR = 1.42 (1.08–1.87) VAT/fat mass HR = 1.67 (1.20–2.31) Men No association were observed WC, WTR, VAT and VAT/SAT | Women WC—NS WTR—NS VAT—risk VAT/SAT—risk VAT/fat mass—risk Men WC—NS WTR—NS VAT—NS VAT/SAT—NS VAT/fat mass—NS |
| Jasper (2017) | ‘SMART’ cohort—secondary manifestations of arterial disease | Vascular events | WC VAT%—visceral fat to total abdominal fat measured by ultrasound | WC Men HR = 1.13 (CI 0.97–1.32) Women HR = 1.00 (CI 0.76–1.32) VAT% HR = 1.15 (0.99–1.34) | Women VAT%—NS Men—NS VAT—NS |
colorectal cancer. Based on the existing evidence, the World Cancer Research Fund (WCRF) and the American Institute of Cancer have classified body fatness as a risk factor for colorectal cancer.\(^{21}\)

The evidence for the association between prostate cancer and visceral obesity show conflicting results. WC and WHR were associated with prostate cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, including data from eight countries.\(^{17}\) However, a study using data from Italian men with moderate to high cardiovascular risk did not find an association between WC and prostate cancer.\(^{18}\) In a Canadian case–control study, WC was a protective factor to prostate cancer after adjustment for potential confounders ($OR = 0.70 \,[0.60–0.82]$).\(^{19}\) Prostate cancer and its association with visceral obesity have been evaluated only by anthropometric measures such as WC and WHR and the data are still very controversial. In line with this, the WCRF classified as 'probable' the current evidence for the association between body fatness, including WC and WHR measures, and prostate cancer.\(^{21}\) There is still no evidence of an association between visceral obesity and prostate cancer.

Globally, breast cancer is the most incident type of cancer in women. The overall prevalence of obesity, measured by BMI, is also the highest in women. The association between breast cancer and visceral adiposity has been investigated in several studies using anthropometric measures such as WC and WHR, that is, the ORDET cohort, EPIC, AMBER Consortium, Sister Study and a meta-analysis.\(^{11,19,32–34}\) In premenopausal women, breast cancer was not associated with WC,\(^{11,19,32,34}\) only with WHR in Estrogen receptor-positive tumours.\(^{33}\) Similarly, a meta-analysis and the Sister Study,\(^{11,34}\) which stratified analyses by body status, WC and WHR were not associated with premenopausal breast cancer. On the other hand, in postmenopausal women, although WC was not associated in two studies,\(^{19,32}\) a meta-analyses found a positive association,\(^{11}\) despite the small magnitude of the effect (RR = 1.06 [1.04–1.09]). In the Sister Study, the most recent study and with the largest sample investigating this topic, WC and WHR were associated with breast cancer in postmenopausal women classified as normal or overweight/with obesity.\(^{34}\) Like other well-known risk factors for breast cancer, there are also differences between postmenopausal and premenopausal risk for visceral obesity. These results suggest that high WC and WHR are not important risk factors for breast cancer among premenopausal but increase considerably the risk in postmenopausal despite overall adiposity.

The associations between endometrial cancer and visceral adiposity, assessed by WC, WHR and HC, were positive in all studies including an umbrella review.\(^{12,35,36}\) The exception was the Black Women’s Health Study,\(^{37}\) a cohort of almost 48 000 black women, which did not find an association between endometrial cancer and WHR, WC or HC. Similarly to the findings with breast cancer, visceral obesity was associated with increased risk of endometrial cancer in postmenopausal women independently of their BMI.\(^{23,34,35,38}\)

Pancreatic cancer was also positively associated with visceral obesity, measured by WC and WHR, in a systematic review.\(^{13,39}\) Similar association was observed for WHR but not for WC in the Women’s Health Initiative study.\(^{40}\) There is strong evidence suggesting that visceral obesity increases the risk of pancreatic cancer. However, it is important to conduct sex-specific analyses to support such evidence.

Regarding gastro-oesophageal cancer, a systematic review showed that higher WC and WHR were associated with all subtypes of gastric and oesophageal cancers\(^{14,41}\) even after adjustment for BMI.\(^{42}\) HP does not show the same association probably because it does not measure visceral fat but obesity pear-shaped body, that is, more fat tissue around the hips than in the abdomen itself.

The association between renal and visceral adiposity shows conflicting results. Renal cancer was found to be associated in postmenopausal women with WHR\(^{15}\) and with WC in the EPIC study.\(^{43}\) Among men, visceral obesity measured by WC, WHR and HC were not associated to renal cancer. However, a recent article showed a positive association between WC and kidney cancer in 23.3 million East Asians.\(^{44}\)

There is also some evidence on the association between other types of cancer such as ovarian,\(^{45}\) hepatocellular, gallbladder, intrahepatic/extrahepatic bile duct system,\(^{46}\) bladder and urothelial,\(^{20}\) Hodgkin’s lymphoma, multiple myeloma,\(^{47}\) lung,\(^{48}\) head and neck cancer\(^{49}\) and visceral adiposity. All these studies used conventional anthropometric measures, that is, WC, WHR and HC, and also included new ones such as waist-to-height ratio (WHtR).\(^{46}\) However, none had included body composition variables. WC was positively associated with ovarian,\(^{45}\) hepatocellular carcinoma,\(^{46}\) gallbladder cancer,\(^{46,48}\) urothelial carcinoma of the bladder,\(^{20}\) lung,\(^{48}\) head and neck\(^{49}\) and thyroid cancer,\(^{50}\) whereas WHR was associated with hepatocellular carcinoma,\(^{46}\) gallbladder cancer,\(^{46,48}\) head and neck\(^{49}\) and lung cancer,\(^{58}\) even after adjustment for smoking status. Visceral obesity evaluated by WC was no associated with intrahepatic extrhepatic bile duct system,\(^{46}\) Hodgkin’s lymphoma and multiple myeloma.\(^{47}\) WHtR was strongly associated with hepatocellular carcinoma.\(^{46}\) The identification of visceral obesity risk in several types of cancer is important in order to determine the specific targets of preventive public health programs.

### 3.2 Evidence of visceral obesity on incident CVD

Obesity is a well-known risk factor of CVD in adults, and in this section, we investigate the evidence on visceral obesity and CVD. Most studies included in this review article had used anthropometric measures, mainly WC and WHR, to evaluate the association between CVD risk and visceral obesity\(^{22,28,51–56}\) (Table 2). There were studies that used body composition measured by computed tomography, DXA or ultrasonography.\(^{57–59}\) VAT is the most used body composition variable to describe visceral fat. Fewer studies had used both methods to analyse visceral obesity.\(^{28,58}\)

A positive association between WC and WHR with CVD risk (heart failure, coronary artery disease or CVD risk factor) was found in few cohort studies and in a systematic review.\(^{22,28,51,53,56}\) However, in three cohort studies that performed sex-specific analyses, the association between WC and myocardial infarction\(^{60}\) or CVD risk\(^{54,58}\) disappeared in women and not significant in men. A similar pattern was
observed for WHR and CVD risk, which was not associated in both sexes. The findings, however, from cohort studies that analysed visceral obesity with more sophisticated methods of body composition, such as computed tomography, the variables VAT or visceral adiposity index (VAI) were associated with CVD in all participants. However, when the analysis was stratified by sex, VAT remained associated with blood pressure risk in both men and women, but it was not associated with CVD risk in women in two cohorts.

In addition to the importance of sex-specific analyses in understanding the association between CVD risk and visceral obesity using anthropometrics or body composition methods, the influence of ageing should also be considered. The Health, Aging and Body Composition Study with individuals aged 70 and older did not find an association for WC and myocardial infarction risk in both men and women. However, they found an association with VAT in all participants. In contrast, in the Framingham Heart Study Offspring cohort, mean age was 60 years old; VAT was not associated with CVD risk. The impact of visceral obesity in CVD remains controversial in older adults.

Other significant question is about the influence of nutritional status in visceral obesity associated with incident CVD. It is also important to stratified data by nutritional body status and sex. A Swedish cohort stratified their analyses of WHR by sex and BMI and found that the highest tercile of WHR was associated with CVD in women independent of BMI class and in men only among those classified as normal weight. In contrast, another cohort found that WC and WHR were associated with CVD only among women with normal BMI and in overweight and men with obesity.

In most studies, visceral obesity was defined based on anthropometric measurements, but with variations in their anthropometric assessment methods, mainly anatomical points used and different cut-off points. These differences across studies can affect the accuracy and comparisons between them as well as the understanding of which specific body size measures, that is, WC or WHR better identifies those at high risk for different types of cancer. There is also evidence of several sex-specific associations between visceral obesity and several types of cancer that used sex-specific cut-offs sometimes and did not other times. Regarding the anatomical points, we observed a great variation in measurements for WC: narrowest point between the iliac crest and the lower rib, midpoint between the lowest rib and the top of the iliac crest and narrowest torso circumference. It is important to use standard measures and cut-offs for the same anatomical point to improve results.

The anthropometric measurements were the most widely used methods to define abdominal obesity, that is, WC and WHR. On one hand, this is a positive aspect because they are the most accessible and cheaper methods to be used in clinical settings and in the general population compared with body composition methods. However, the specific body composition components are more relevant to understand how the visceral obesity can affect both CVD and cancer risks. Body composition methods are more accurate than a single anthropometric measurement to assess the components of visceral obesity: SAT and VAT. WC reflects both.

4 | CONCLUSIONS AND FUTURE RESEARCH

This integrative review aimed to investigate further the role of visceral obesity on incident cancer and CVD. The impact of visceral obesity on CVD is overall clear in adults but remains controversial by sex, age and BMI categories, regardless the method used to measure visceral obesity. The predictive capacity of different visceral obesity variables needs further investigation. Moreover, visceral obesity can increase the risk of some specific cancer types, but there were controversial findings about CVD risk according to sex specific and in older adults varying with different measures used such as WC and VAT. There is enough evidence showing that visceral obesity increases the risk of colorectal, pancreatic and gastro-oesophageal cancer. However, for some types of cancer such as breast endometrial, visceral obesity is a risk only in postmenopausal women. Regarding prostate and renal cancer, the evidence is still unclear, and there is a need for more studies. For certain cancers, such as postmenopausal breast and endometrial cancers, it was observed that visceral obesity increased their risk regardless overall individual’s BMI.

Despite the evidence on visceral obesity showing an association with CVD risk, this association disappears in sex-specific analyses and in older adults. The link between visceral obesity and CVD risk remains unclear because sex differences, changes with ageing and BMI category can modify it. Therefore, further epidemiological studies with analyses stratified by sex and samples including older adults aged 65 and older are needed.

CONFLICT OF INTEREST

No conflict of interest was declared.

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REFERENCES

1. World Health Organization. Global Strategy on Diet, Physical Activity and Health. WHO Press: Geneva (Switzerland); 2008.
2. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC Working Group. N Engl J Med. 2016; 375(8):794-798.
3. Caleyachetty R, Thomas GN, Toulis KA, et al. Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. J Am Coll Cardiol. 2017;70(12):1429-1437.
4. World Health Organization. Global Action Plan for the Prevention and Control of Noncommunicable Diseases (2013-2020). Geneva (Switzerland): WHO Press; 2013.
5. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO consultation. Geneva (Switzerland): WHO Press; 2000.
6. Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. J Am Coll Cardiol. 2013;62(10):921-925.
dose-response meta-analysis of prospective studies. *Int J Cancer*. 2015;136(8):1888-1898.

46. Schlesinger S, Aleksandrova K, Pisichon T, et al. Abdominal obesity, weight gain during adulthood and risk of liver and biliary tract cancer in a European cohort. *Int J Cancer*. 2013;132(3):645-657.

47. Britton JA, Khan AE, Rohrmann S, et al. Anthropometric characteristics and non-Hodgkin’s lymphoma and multiple myeloma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Haematologica*. 2008;93(11):1666-1677.

48. Hidayat K, Du X, Chen G, Shi M, Shi B. Abdominal obesity and lung cancer risk: systematic review and meta-analysis of prospective studies. *Nutrients*. 2016;8(12):810.

49. Gaudet MM, Kitahara CM, Newton CC, et al. Anthropometry and head and neck cancer: a pooled analysis of cohort data. *Int J Epidemiol*. 2015;44(2):673-681.

50. Kitahara CM, McCullough ML, Franceschi S, et al. Anthropometric factors and thyroid cancer risk by histological subtype: pooled analysis of 22 prospective studies. *Thyroid*. 2016;26(2):306-318.

51. van Wijk DF, Boekholdt SM, Arsenault BJ, et al. C-reactive protein identifies low-risk metabolically healthy obese persons: the European prospective investigation of Cancer-Norfolk prospective population study. *J Am Heart Assoc*. 2016;5:1-8.

52. Li C, Engström G, Hedblad B, Calling S, Berglund G, Janzon L. Sex differences in the relationships between BMI, WHR and incidence of cardiovascular disease: a population-based cohort study. *Int J Obes (Lond)*. 2006;30(12):1775-1781.

53. The Emerging Risk Factors Collaboration. Separate and combined associations of body mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet*. 2011;377:1085-1095.

54. Carlsson AC, Risérus U, Engström G, et al. Novel and established anthropometric measures and the prediction of incident cardiovascular disease: a cohort study. *Int J Obes (Lond)*. 2013;37(12):1579-1585.

55. Carlsson AC, Risérus U, Årnlöv J, et al. Prediction of cardiovascular disease by abdominal obesity measures is dependent on body weight and sex—results from two community based cohort studies. *Nutr Metab Cardiovasc Dis*. 2014;24(8):891-899.

56. Aune D, Sen A, Norat T, et al. Body mass index, abdominal fatness, and heart failure incidence and mortality. *Circulation*. 2016;133(7):639-649.

57. Mahabadi AA, Massaro JM, Rosito GA, et al. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. *Europace*. 2009;11(7):850-856.

58. Jaspers NEM, Dorresteijn JAN, Van Der Graaf Y, et al. Relation between adiposity and vascular events, malignancy and mortality in patients with stable cerebrovascular disease. *Int J Obes (Lond)*. 2017;41(12):1775-1781.

59. Kouli G-M, Panagiotakos DB, Kyrou I, et al. Visceral adiposity index and 10-year cardiovascular disease incidence: the ATTICA study. *Nutr Metab Cardiovasc Dis*. 2017;27(10):881-889.

60. Nicklas BJ, Penninx BWJH, Cesari M, et al. Association of visceral adipose tissue with incident myocardial infarction in older men and women: the health, aging and body composition study. *Am J Epidemiol*. 2004;160(8):741-749.

61. Lee KR, Seo MH, Do Han K, Jung J, Hwang IC, Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. Waist circumference and risk of 23 site-specific cancers: a population-based cohort study of Korean adults. *Br J Cancer*. 2018;119(8):1018-1027.

62. Abar L, Sobieckij AO, Cariolou M, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. *Ann Oncol*. 2019;30(4):528-541.

How to cite this article: Silveira EA, Kliemann N, Noll M, Sarrafzadegan N, de Oliveira C. Visceral obesity and incident cancer and cardiovascular disease: An integrative review of the epidemiological evidence. *Obesity Reviews*. 2020;1–17. https://doi.org/10.1111/obr.13088