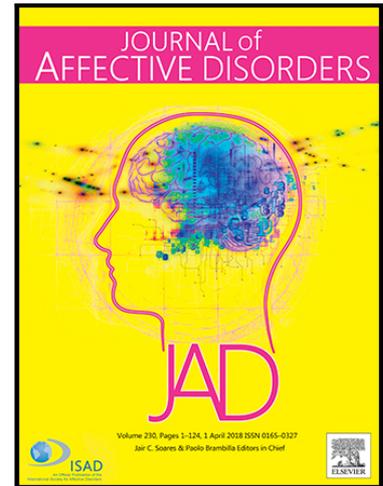


## Journal Pre-proof

Cancer diagnosis and suicide outcomes: umbrella review and methodological considerations

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## Highlights

- Cancer diagnosis is associated with increased suicide.
- The risk of suicide ranged from 1.5 to 1.7 for both sexes combined, but slightly higher in men.
- Other risk factors were identified, such as male sex, older age, a cancer diagnosis within the prior year, and some specific cancer sites.
- Results should be considered with caution and several methodological issues warrant attention.

Journal Pre-proof

**Cancer diagnosis and suicide outcomes: umbrella review and methodological considerations**

Running title: “*Cancer and suicide*”

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## Abstract

**Background:** Suicide outcomes in cancer patients represent a major public health concern. We performed an umbrella review (UR) including all systematic reviews (SRs) and meta-analyses (MAs) published on the association between cancer and suicide outcomes. **Methods:** Eligible studies were searched in the main scientific databases up to January 23<sup>rd</sup>, 2021. Eligible SRs/MAs focused on all suicidal phenotypes among cancer patients. Evidence of the association was extracted; the credibility and quality of the included studies were evaluated using ad-hoc tools, including “A MeaSurement Tool to Assess systematic Reviews-2” (AMSTAR-2-R). **Results:** Six MAs and 6 SRs were included. The standardized mortality ratio of suicide in cancer patients was 1.5 to 1.7-fold higher than in the general population. Risk factors for suicide outcomes among cancer patients were male sex and older age, a cancer diagnosis within the prior year, and some specific cancer sites. Among 107 associations, 90 (84.1%) were supported by high credibility of evidence (class II). However, all studies reported a large heterogeneity ( $I^2 > 50\%$ ) and the majority of them reported considerable heterogeneity ( $I^2 > 75\%$ ). All MAs used random-effects measures. All MAs but one assessed publication bias and only one disclosed it. The majority of MAs/SRs showed critically low quality based on AMSTAR-2-R. **Limitations:** We could not perform additional analyses due to the limited number of MAs. **Conclusions:** This UR underlines the inflated risk for suicide among cancer patients. Upcoming, well-designed studies are needed to account for a broader set of variables. Several methodological issues likewise warrant attention.

## Keywords

Suicide; suicidal behaviors; cancer; oncology; umbrella review; systematic review; meta-analysis.

### 1. Introduction

Cancer (Global Burden of Disease Cancer et al., 2019) and suicide (World Health Organization, 2019) stood out as two major public health concerns within the past decades. In particular, in the year 2017, incident tumor (i.e., all cancer types) cases were 24.5 million

worldwide and there were 9.6 attributable million cancer deaths (Global Burden of Disease Cancer et al., 2019). On the other hand, suicide accounted for 800,000 deaths per year, with one person dying every 40 seconds, and many more people who attempt suicide (World Health Organization, 2019). While the world population is steadily increasing over the years, the incident rate of cancers, worldwide, likewise increases at a worrisome faster pace (International Agency for Research on Cancer, 2019).

Mortality due to a given disease does not give a complete picture of its burden. Whilst dramatic, not even death directly attributable to cancer explains the complexity of the phenomenon in terms of subjective pain for the patient. The World Health Organization proposes several indexes to measure disease-related disability, including the disability-adjusted life years (DALY), a time-based measure that combines years of life lost due to premature mortality (YLLs), and years of life lost due to time lived in states of less than full health, or years of healthy life lost due to disability (YLDs) (Donev et al., 2010). However, no single metric could exhaust the variability of different types of pain, nor the complexity of the experience of suicidal behavior. The existing evidence points out an inflated risk for suicide among people diagnosed with cancer compared to the general population (Fang et al., 2012).

The association between psychological/psychiatric issues and cancer has been extensively investigated. One-third of cancer patients will experience distress (Gregurek et al., 2010); the most important distress factor being the fear of disease progression (Herschbach et al., 2004). People with a primary diagnosis of cancer may suffer from psychiatric disorders, especially depression, anxiety disorders, and adjustment disorders (Gregurek et al., 2010). They may also suffer from malnutrition (Movahed et al., 2021) and post-cancer fatigue (Goldstein et al., 2006).

Several systematic reviews (SRs) and meta-analyses (MAs) have been recently performed to appraise the association between cancer diagnosis and subsequent suicide. However, besides being preliminary, the existing qualitative or quantitative syntheses of the evidence need to be carefully

assessed for their credibility and quality to provide clinicians, public-health scientists, and policy-makers with solid guidance.

The aim of the present umbrella review (UR) is to appraise the most current evidence about the association between any type of cancer and suicide outcomes. In addition, the present UR accounts for different outcomes besides death due to suicide, thus including death wish (DW), suicidal ideation (SI), and suicide attempt (SA), phenotypes that are rarely explored as causes of disability despite their overall burden.

## **2. Methods**

### *2.1 Search Strategy and Selection Criteria*

The present UR summarizes the results from SRs and MAs assessing the association between cancer and suicidal outcomes (i.e., DW, SI, SA, and suicide). We followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines (Moher et al., 2009). We did not perform a new analysis of the included data, as elsewhere recommended by Fusar-Poli and Radua (Fusar-Poli and Radua, 2018), due to the limited number of available studies.

A bibliographic search was conducted throughout PubMed, PsycINFO, EMBASE, Scopus, and Cochrane Library from inception until January, 23<sup>rd</sup>, 2021, using combinations of the following MEDical Subject Headings terms: (“cancer” OR “carcinoma” OR “neoplasia” OR “tumor” OR “neoplasm” OR “maligna\*”) AND (“suicid\*” OR “self-harm” OR “self-poisoning”) AND (“review” OR “systematic review” OR “meta-analysis”). We also evaluated the retrieved cross-references. Two authors (RC and CF) independently searched titles and abstracts for eligibility. The full texts of potentially eligible articles were retrieved, and two raters (RC and CF) independently scrutinized each study for eligibility. Any discrepancy or issue during this process was solved through discussion.

We only included peer-reviewed studies meeting our inclusion criteria: a) SRs and/or MAs; b) documenting any association between cancer and suicidal outcomes; c) focusing on any type of

population and age; d) written in English, Italian or French. We also included studies that did not primarily focus on the association between cancer and suicidal risk (e.g., SRs on depression and hopelessness in patients with cancer). We excluded: a) non-systematic reviews; b) SRs or MAs that did not focus on the association between cancer and suicidal outcomes; c) original, primary studies.

## 2.2 Outcomes

### 2.2.1 Cancer

We included SRs or MAs that examined the impact of the diagnosis of any malignant neoplasm (International Classification of Diseases (ICD)-9: 140–209; ICD-10: C00–C97).

### 2.2.2 Suicidal outcomes

We referred to established nomenclature (Turecki and Brent, 2016). We separately considered all the suicidal events as reported by the original study authors: DW (death wish), SI (thinking about, considering, or planning suicide), SA (self-inflicted potentially injurious behavior with a non-fatal outcome and the intention to die), and suicide (self-inflicted death).

## 2.3 Data Extraction

CF performed the preliminary data extraction. Extracted data were independently further checked by WM and DC, and disagreements were solved upon reaching a consensus with a third investigator (RC). The following data were extracted using two standardized reporting forms, one for MAs and another for SRs. Concerning the MAs, we reported: source, eligibility criteria, cancer type, other risk factors, number of included studies, and number of included cases for the association between cancer and suicide, random-effects measure, main results, heterogeneity [ $I^2$  was reported considering Cochrane recommendations (Higgins et al., 2021)], Egger's test, the credibility of evidence classification using an ad-hoc tool and the assessment of the quality of reporting with a revised version of "A MeaSurement Tool to Assess systematic Reviews-2" - AMSTAR-2 (Shea et al., 2017), namely the AMSTAR-2-R. Concerning SRs, we reported: source, the main focus, range of years covered by the search, eligibility criteria, cancer type, suicidal

outcome, number of included studies, databases, other risk factors, main results, and AMSTAR-2-R.

#### *2.4 Assessment of credibility and quality of the evidence*

In line with previously published URs (Bortolato et al., 2017; Dragioti et al., 2019; Veronese et al., 2018), we adapted and applied several criteria to assess the credibility of the evidence for the association provided in MAs. For details, please refer to Appendix 1 for details.

Concerning the AMSTAR-2-R (please see Appendix 2 for details), two authors (RC and WM) were in charge of the AMSTAR-2 adaptation for SRs and MAs piloting observational studies throughout meetings and discussions. In the AMSTAR-2-R the appointed investigators changed items 1, 3, 8, 9, 11, 12, and 13 referring to randomized controlled trials and non-randomized studies of interventions to better suit for observational studies.

Finally, the quality of reporting of each included SR and/or MA was independently assessed through AMSTAR-2-R by WM and DC, and disagreements were solved through discussion with RC.

### **3. Results**

Seventy-seven full-texts were assessed and ultimately 12 studies, 6 MAs, and 6 SRs were found to be eligible and were included in this UR. See Figure 1 for a detailed flowchart of the inclusion/exclusion process.

#### *3.1 Meta-analyses*

Descriptive characteristics of the 6 included MAs (Amiri and Behnezhad, 2020; Brunckhorst et al., 2020; Du et al., 2020; Guo et al., 2018; Harris and Barraclough, 1994; Ravaioli et al., 2020) are shown in Table 1. Four (66.7%) out of 6 MAs focused on any type of cancer (Amiri and Behnezhad, 2020; Du et al., 2020; Harris and Barraclough, 1994; Ravaioli et al., 2020), while 2 (33.3%) focused on prostate cancer (Brunckhorst et al., 2020; Guo et al., 2018). All focused on suicide death; one of them also accounted for SI (Brunckhorst et al., 2020).

Three MAs (50%) reported the standardized mortality ratio (SMR) (Amiri and Behnezhad, 2020; Harris and Barraclough, 1994; Ravaioli et al., 2020), 1 (16.7%) the risk ratio (RR) (Guo et al., 2018), 1 the pooled prevalence (Brunckhorst et al., 2020), and 1 the incidence (Du et al., 2020). Suicide death by sex was considered in 3 MAs (Amiri and Behnezhad, 2020; Du et al., 2020; Ravaioli et al., 2020), revealing an increased suicide risk in both sexes but especially in males (SMR=1.8, 95% CI: 1.6-2.0; SMR=1.7, 95% CI: 1.5-1.9) compared to females (SMR=1.4, 95% CI: 1.3-1.6; SMR=1.3, 95% CI: 1.2-1.5). Moreover, other risk factors were associated with the increase of suicide rates, specifically: continent (Amiri and Behnezhad, 2020; Du et al., 2020) and cancer site (Amiri and Behnezhad, 2020; Du et al., 2020; Harris and Barraclough, 1994). Contrasting results were reported concerning the geographical area of the study: Du et al. reported the highest suicide incidence in cancer patients in Asia, and the lowest in Oceania (Du et al., 2020), while Amiri and Behnezhad reported high relative suicide mortality risk in Europe and the Americas but not in Asia (Amiri and Behnezhad, 2020). With regards to cancer sites, Du et al. reported the highest rate of suicide among people diagnosed with esophagus cancer (Du et al., 2020). Amiri and Behnezhad found that suicide rates in patients with cancer in the bronchus, trachea, and lung (i.e., respiratory tract) triplicated the rates in other cancer sites such as the esophagus, stomach, pancreas, and liver (i.e., gastrointestinal tract), prostate, colon and rectum, female genital organs, breast, and finally melanoma and skin – malignant tumors ranked by frequency, top-down list (Amiri and Behnezhad, 2020). Likewise, Harris and Barraclough reported that the risk of suicide in patients with malignant neoplasms was higher for lung, upper airways, gastrointestinal tract, central nervous system, lymphoreticular system, pancreas, kidney, head, and neck cancer compared to breast cancer, female genital tract and localized cancers (i.e., in term of the extent of tumor) (Harris and Barraclough, 1994).

Two MAs (Brunckhorst et al., 2020; Guo et al., 2018) focused on prostate cancer only, reporting its association with suicide and confirming an increased suicide rate in cancer patients (RR=2.0; 95% CI: 1.5-2.6), especially if the diagnosis was made in the last six months (RR=2.2,

95% CI: 1.8-2.8) (Guo et al., 2018). The risk of suicide was also higher in 75-year-olds and over compared to younger men and among patients receiving hormonal therapy compared to those who were registered for curative treatment (Guo et al., 2018). Brunckhorst et al. reported a pooled prevalence of 9.85% (7.31–12.70) for SI and a suicide mortality rate of 47.1 (39.85–54.96) per 100,000 person-years (Brunckhorst et al., 2020).

Figures 2-4 show the studies included in more than one MA. Figure 2 shows that the 6 MAs included in the present UR are based on very different studies. As we stated before, this finding is partially explicable by the fact that 3 MAs reported the SMR (Amiri and Behnezhad, 2020; Harris and Barraclough, 1994; Ravaioli et al., 2020), 1 the RR (Guo et al., 2018), 1 the pooled prevalence (Brunckhorst et al., 2020), and 1 the incidence (Du et al., 2020). However, if we consider only studies reporting SMR (Figure 3), we find only 2 studies included in all the 3 MAs. In Figure 4, we can see that only 8 studies were included in both MAs (Brunckhorst et al., 2020; Du et al., 2020); however, this finding is more plausible because 1 MA was focused on any type of cancer (Du et al., 2020) and 1 considered prostate cancer only (Brunckhorst et al., 2020).

### 3.2 Systematic reviews

Descriptive characteristics of the included SRs (Cotter et al., 2017; Fassberg et al., 2016; Kawashima et al., 2019; Kolva et al., 2020; McDonough et al., 2019; Tang et al., 2015) can be found in Table 2. One of them focused on interventions to prevent suicidal outcomes in patients with cancer and it is described in a separate paragraph (Kawashima et al., 2019). Four (80%) out of the other 5 SRs focused on the association between suicide outcomes and cancer in all cancer sites (Fassberg et al., 2016; Kolva et al., 2020; McDonough et al., 2019; Tang et al., 2015), while 1 (20%) focused on prostate cancer (Cotter et al., 2017). Three (60%) SRs reported suicide as the main outcome (Cotter et al., 2017; Fassberg et al., 2016; McDonough et al., 2019); 1 (20%) focused on DW (Tang et al., 2015); and 1 (20%) focused on SI (Kolva et al., 2020).

Concerning the risk of suicide, two SRs reported an increased incidence of suicide in cancer patients (Cotter et al., 2017; Fassberg et al., 2016; McDonough et al., 2019). They also showed other risk factors associated with this increase, including male sex (Fassberg et al., 2016; McDonough et al., 2019), older age (Fassberg et al., 2016), and cancer sites (prostate and genital cancer, vertebral column or pelvis tumor, respectively) (Fassberg et al., 2016; McDonough et al., 2019).

Considering only prostate cancer, 1 SR (Cotter et al., 2017) reported that having received a diagnosis caused negative psychological states (i.e., shock, anxiety, fatalism, distress, sense of burden, depression, denial, loneliness, and psychological impact of sexual dysfunction) and higher suicide rates within the first five years.

Tang et al. considered DW as a component of demoralization (it is included in the Demoralization Scale) and found a high correlation between demoralization and depression in cancer patients (Tang et al., 2015). Regarding SI, Kolva et al. reported a prevalence in cancer patients ranging from 0.7% to 46.3% (Kolva et al., 2020). Additionally, they found the following risk factors for SI: age equal or over 60 years, cancer type (e.g. cancer affecting the primary central nervous system), treatment-related characteristics (i.e., history of chemotherapy and other treatment-related symptoms), physical symptoms, such as pain, fatigue, and sense of burden, as well as psychiatric/psychological factors (such as higher depression, anxiety, demoralization, and feelings of hopelessness or existential distress), and lower social support, including single status (i.e., divorced or separated, single, widowed) and caregiver characteristics. SI risk was independent on sex.

### 3.2.1 Effective interventions

Two SRs (Kawashima et al., 2019; Kolva et al., 2020), 1 of which focused specifically on suicidal prevention for cancer patients (Kawashima et al., 2019), cited one study (Hopko et al., 2011) reporting that behavioral activation and problem-solving therapies increased hopefulness and

reduced depression and SI (Kawashima et al., 2019; Kolva et al., 2020). In one study, spiritual care therapy was found to be effective for reducing SI in depressive cancer patients treated with antidepressants (Xiao-Qiu, 2015). Ketamine treatment (Fan et al., 2017) and a nursing care protocol including frequent assessment, psychoeducation, and empowerment for hospitalized patients (Xu et al., 2014) were associated with a reduction of SI. However, Kawashima et al. noted that none of the 22 studies they reviewed included an intervention specifically designed to prevent suicidal outcomes in cancer patients (Kawashima et al., 2019). Moreover, suicide rates varied among patients with different cancer sites, most trials were inadequate in terms of methodology and the incidence of SA or suicide was too low to produce adequate statistical power. According to the studies included in the SR, although depression was reported to be an important risk factor for suicide among cancer patients, treating depression seems to be insufficient, due to other risk factors, such as substance use, neurocognitive or sexual dysfunctions, sleep disturbance, stress-related or post-traumatic stress disorder, somatization, bipolar affective disorder and obsessive-compulsive disorder, pain, sense of burden and poor social support.

### *3.3. Rating credibility and quality of evidence in meta-analyses and systematic reviews*

Concerning the six assessed MAs, 90 (84.1%) out of 107 associations were supported by highly suggestive evidence (Class II: high credibility of the evidence) of the relationship between cancer and suicide risk (see Appendix 1 for eligibility criteria). Regarding gender differences, five associations were found to be non-significant and one showed female sex as a protective factor (Ravaioli et al., 2020). Otherwise, suggestive evidence (Class III: medium credibility of the evidence) was found in 17 (15.9%) associations, except for one study conducted in Canada in which the increased risk was not significant (Guo et al., 2018). No associations were supported by convincing evidence (Class I: the highest credibility of the evidence) due to the large between-study heterogeneity ( $I^2 > 50\%$ ). Concerning publication bias, except for one MA that did not calculate it (Harris and Barraclough, 1994), all others calculated it but only one disclosed it (Brunckhorst et al., 2020).

All 6 MAs showed a critically low-quality level based on AMSTAR-2-R. For details, see Table 3. On the other hand, 4 (66.7%) out of 6 SRs reached a critically low-quality level based on AMSTAR-2-R, while 2 (33.3%) had a low-quality level. None of the 12 included studies met the requirement for items 7 and 10.

#### 4. Discussion

The present up-to-date UR focusing on the association between cancer and suicidal risk included 12 studies, 6 MAs, and 6 SRs.

The MAs focusing on any type of cancer (Amiri and Behnezhad, 2020; Harris and Barraclough, 1994; Ravaioli et al., 2020) reported through SMR that suicide risk is 1.5 times higher in cancer patients than in the general population (Amiri and Behnezhad, 2020; Harris and Barraclough, 1994; Ravaioli et al., 2020) (2 of them with high credibility of the evidence, Class II) and that the overall pooled incidence of suicide in patients with cancer was 39.72 per 100,000 person-years (95% CI, 33.91–46.52) (Du et al., 2020). The following potential risk factors were also indicated: male sex (Kam et al., 2015; Saad et al., 2020), older age, cancer diagnosis within the first year, and some specific cancer sites (Kam et al., 2015; Saad et al., 2020), especially lung (Bjorkenstam et al., 2005), esophagus, stomach and pancreas (Bjorkenstam et al., 2005), and head and neck (Kam et al., 2015). A recent non-systematic (hence not included here) review (McFarland et al., 2019) classified some of the above risk factors as cancer-specific, including also the stage of cancer, treatment type, loss of physical ability, loss of meaning and social or personal status, symptoms of burden and being a survivor of childhood/adolescence cancer.

Concerning prostate cancer, 2 MAs (Brunckhorst et al., 2020; Guo et al., 2018) reported a high suicide risk especially among those patients diagnosed within the last six months or aged 50 and older.

It is important to observe that, in all included MAs, the psychiatric/psychological or social factors associated with suicide outcomes were not considered in the analyses, although a growing

body of evidence suggests their impact (Goldstein et al., 2006; Gregurek et al., 2010; Herschbach et al., 2004), and that people with severe mental illness often face delayed diagnosis and interventions for cancer (Solmi et al., 2020). In this vein, McFarland et al. have categorized the risk factors related to suicide in cancer patients in two groups: general risk factors, including a family history of suicide or child maltreatment, previous SA, and other psychological/psychiatric symptoms (e.g., demoralization, hopelessness, depression, anxiety, sense of burden, etc.), poor social support, physical symptoms (e.g. pain); and cancer-specific risk factors described above (McFarland et al., 2019). Juurlink et al. also showed a strong association between the cumulative number of illnesses, including physical illness (e.g., breast or prostate cancer, ischemic heart disease, chronic pain, etc.), mental disorders (e.g., depression, anxiety, sleep disorder, bipolar disorder, psychoses, and agitation) and the relative risk of suicide (Juurlink et al., 2004).

We can interpret these findings considering that some socio-demographic features (male, older age) are associated with higher suicide risk and that specific cancer sites might be linked to a poorer prognosis in the mind of the patients. However, at this stage of the research, we cannot push ourselves too far in interpretations. In fact, concerning the inclusion/exclusion of specific papers in the included 6 MAs (Figure 2-4), there are discrepancies. As we already stated, some of them can be explained by the fact that different MAs were performed (e.g., risk MAs versus incidence MA) and that some MAs considered any type of cancer and others prostate cancer only. However, if we consider only studies reporting the same risk measure (SMR) (Figure 3), we find only 2 studies included in all the 3 MAs and this means that there is a need to improve the comparability of MAs. Hence, we suggest starting to perform network graphs in future URs.

Considering the credibility of the evidence, although no Class I evidence exists, Class II (high credibility of the evidence) is present for 84.1% of the associations, representing an encouraging result. Considering the quality of reporting, critically low quality was reported for the majority of the included studies (100% for MAs and 66.7% for SRs). However, AMSTAR-2 (Shea et al., 2017), and our AMSTAR-2-R, have extremely strict criteria, and the chance of obtaining a “critically low

quality” evaluation is very high, so we underline the need for new expert panels on that in the future.

Concerning the five assessed SRs, 3 (Cotter et al., 2017; Fassberg et al., 2016; McDonough et al., 2019) focused on suicide (Cotter et al., 2017; Fassberg et al., 2016; McDonough et al., 2019), 1 on SI (Kolva et al., 2020), and 1 on DW (Tang et al., 2015). Psychological/social risk factors were found associated with suicide (McDonough et al., 2019): negative psychological health-related quality of life, self-image issues, anxiety symptoms in the diagnostic phase and depressive symptoms in the treatment phase (McDonough et al., 2019); negative psychological states (e.g. shock, anxiety, fatalism, distress, sense of burden, helplessness, depression, denial, loneliness, psychological impact of sexual dysfunction) (Cotter et al., 2017).

On the other hand, regarding SI only, we found one SR (Kolva et al., 2020) showing a prevalence of SI in cancer patients ranged from 0.7% to 46.3%, and its related risk factors (i.e., both sexes, age equal or over 60-year-old, cancer type, treatment-related characteristics, physical symptoms, and psychiatric/psychological and social factors). One SR (Tang et al., 2015) found a strong association between demoralization, comprising DW, and depression in cancer patients.

In our quantitative synthesis, we also included one SR focused on effective interventions to prevent SI and suicidal behaviors (Kawashima et al., 2019). However, no intervention was found to be specifically designed to prevent SI and suicidal behaviors and, although depression was reported as an important risk factor for suicide among cancer patients, it is fundamental to design specific interventions targeting suicidal risk.

Despite the handful of studies eligible for inclusion, we feel that the present UR is a prime since it is the first one to systematically assess the risk of suicide among cancer patients. Our aim was also to evaluate the credibility and quality of the included studies. Moreover, we performed some network graphs to show the number of commonly included studies in the different MAs and we suggest including these types of graphs in future URs.

However, some limitations occurred. First, the small number of included studies did not allow us to re-analyze the data, as suggested by Fusar-Poli and Radua (Fusar-Poli and Radua, 2018), hence we were not able to control for between-study heterogeneity. Secondly, some limitations were derived from the included studies (e.g., high between-study heterogeneity, lack of adjustment for possible confounders).

In conclusion, this study confirmed that cancer patients are at increased risk of suicide and that there are specific factors implicated in this association, such as male sex, older age, cancer diagnosis within the first year, and some specific cancer sites. However, no convincing evidence (Class I) exists, and both further original studies and methodologically robust MAs (including all the available studies) need to be performed to drive more definitive conclusions. The current published SRs and MAs on the topic offered only a scattered picture since they included partially different papers. For this reason, we proposed to introduce in future URs an innovative type of graphs, to help researchers and clinicians to evaluate the overlap among different SRs and MSs in terms of included papers. Further research should focus also on preventive interventions specifically targeting suicide outcomes among cancer patients.

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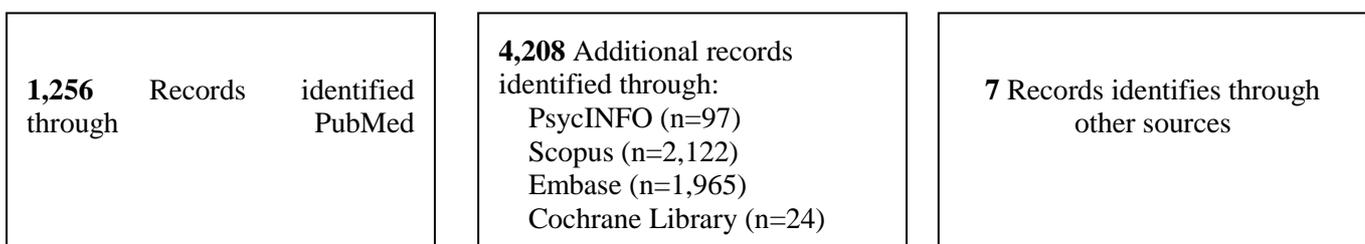
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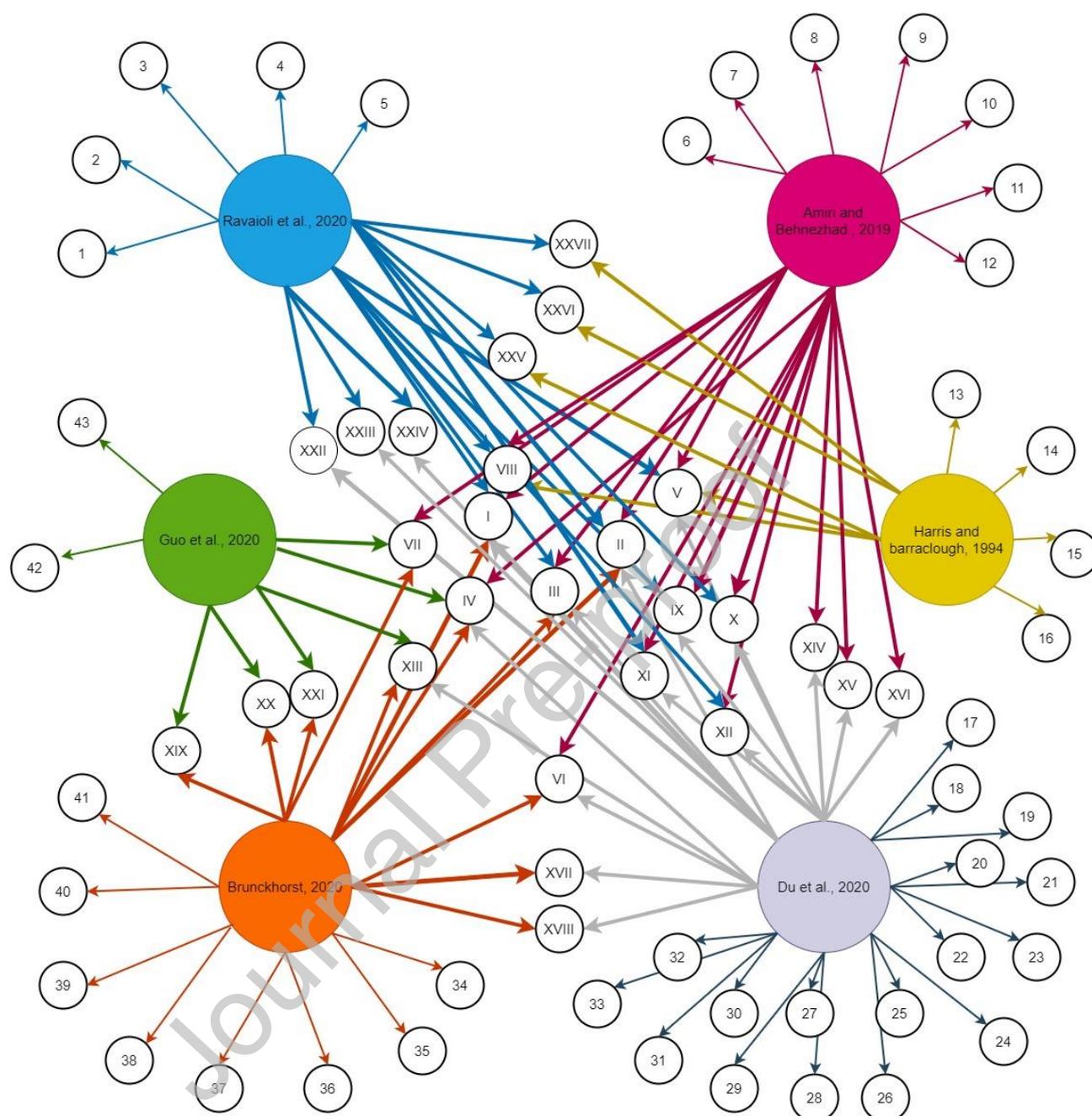
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**Figure 1.** Flowchart of the literature search and evaluation process.



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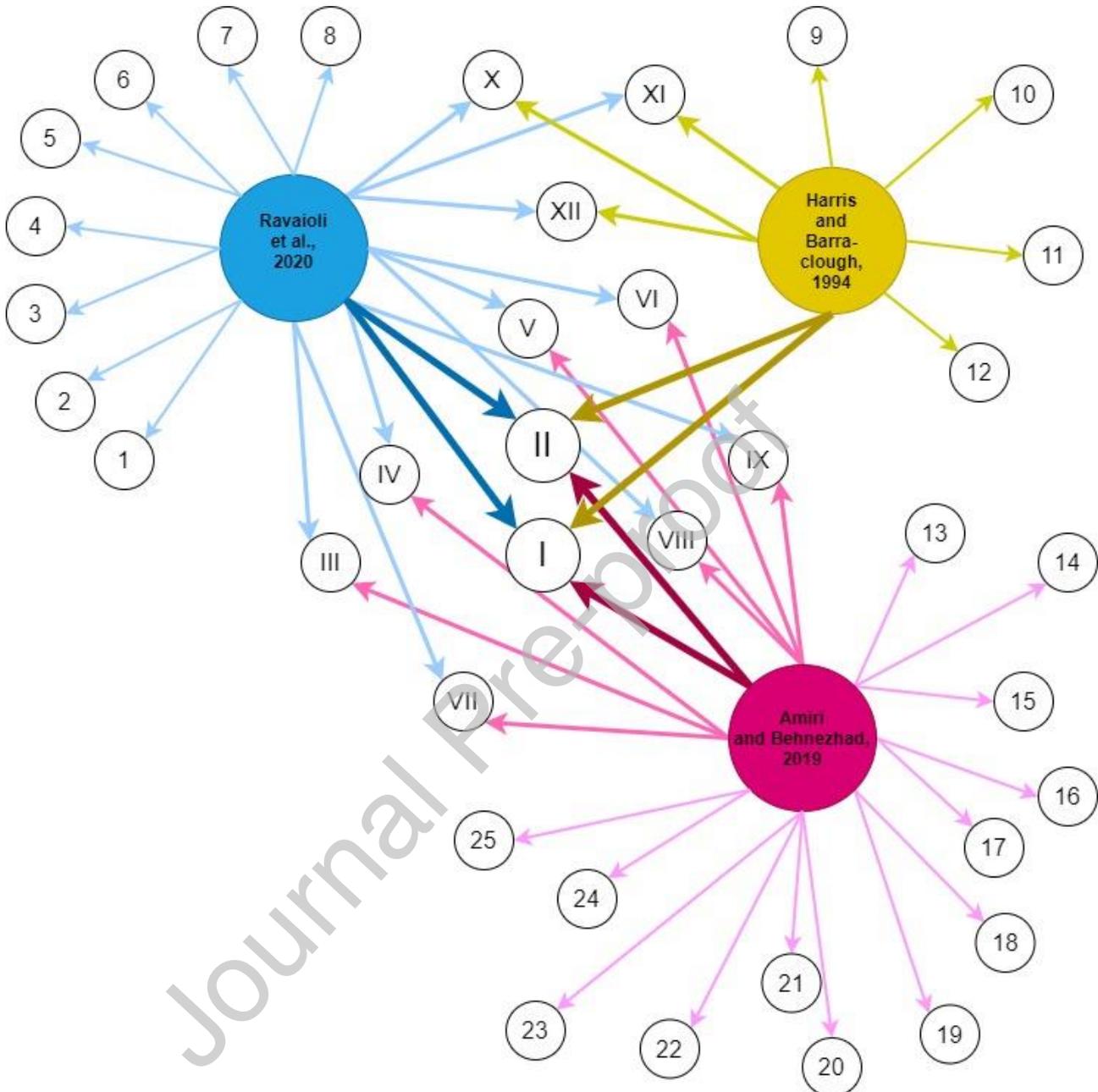
**Figure 2.** Graphic synthesis of studies included in the 6 included meta-analyses.

This diagram was performed using the software Draw.io made available in the public domain. The studies included in more than one meta-analysis are indicated with Roman numbers, while studies included in one meta-analysis only are indicated with Arabic numbers. Different colors indicated the six meta-analyses included in our umbrella review, respectively blue, purpura, green, yellow, orange, and lilac (Ravaioli et al., 2020; Amiri and Behnezhad, 2019; Guo et al., 2018; Harris and Barraclough, 1994; Brunckhorst et al., 2020; Du et al., 2020). Arrows are also different in terms of thickness: lower thickness was used for studies included in one meta-analysis only while higher thickness for studies included in at least two meta-analyses.

<b>First authors of the meta-analyses</b>	<b>Included studies</b>
Amiri, Brunckhorst, Du and Ravaioli	I. Hem et al., 2004 II. Misono et al., 2008 III. Vyssoki et al., 2015
Amiri, Brunckhorst, Du and Guo	IV. Fall et al., 2009
Amiri, Du, Harris and Ravaioli	V. Levi et al., 1991
Amiri, Brunckhorst and Du	VI. Smailyte et al., 2013
Amiri, Brunckhorst and Guo	VII. Llorente et al., 2005
Amiri, Harris and Ravaioli	VIII. Louhivuori et al., 1979
Amiri, Du and Ravaioli	IX. Dormer et al., 2008 X. Innos et al., 2003 XI. Robinson et al., 2009 XII. Yousaf et al., 2005
Brunckhorst, Du and Guo	XIII. Bill-Axelsson et al., 2010
Amiri and Du	XIV. Crocetti et al., 1998 XV. Tanaka et al., 1999 XVI. Yamauchi et al., 2014
Brunckhorst and Du	XVII. Klaassen et al., 2015 XVIII. Smith et al., 2018
Brunckhorst and Guo	XIX. Carlsson et al., 2013 XX. Dalela et al., 2016 XXI. Fang et al., 2010
Du and Ravaioli	XXII. Ahn et al., 2010 XXIII. Lin et al., 2017 XXIV. Oberaigner et al., 2014
Harris and Ravaioli	XXV. Allebeck et al., 1989 XXVI. Fox et al., 1982 XXVII. Storm et al., 1992
Ravaioli	1. Camidge et al., 2007 2. Kaceniene et al., 2017 3. Miccinesi et al., 2004 4. Nasser et al., 2012 5. Ravaioli et al., 2020
Amiri	6. Ahn et al., 2015 7. Lin et al., 2009 8. Lu et al., 2013 9. Miller et al., 2008 10. Muff Christensen et al., 2006 11. Nakash et al., (1) 2013

	12. Nakash et al., (2) 2013
Harris	13. Barton et al., 1965 14. Davidson et al., 1988 15. Henk et al., 1977 16. Shaw et al., 1965
Du	17. Alanee and Russo, 2012 18. Anderson and Park, 2018 19. Bowden et al., 2017 20. Dai et al., 2008 21. Dulskas et al., 2019 22. Henson et al., 2019 23. Guo et al., 2019 24. Mahdi et al., 2011 25. Osazuwa-Peters et al., 2018 26. Peng et al., 2005 27. Pham et al., 2019 28. Rahouma et al., 2018 29. Schairer et al., 2006 30. Shen et al., 2020 31. Siracuse et al., 2017 32. Turaga et al., 2011 33. Zaorsky et al., 2019
Brunckhorst	34. Chen et al., 2019 35. Lehto et al., 2015 36. Lehluante and Fransson, 2014 37. Louda et al., 2012 38. Perry et al., 2018 39. Recklitis et al., 2014 40. Rice et al., 2018 41. Zhou et al., 2015
Guo	42. Juurlink et al., 2004 43. Smith et al., 2015

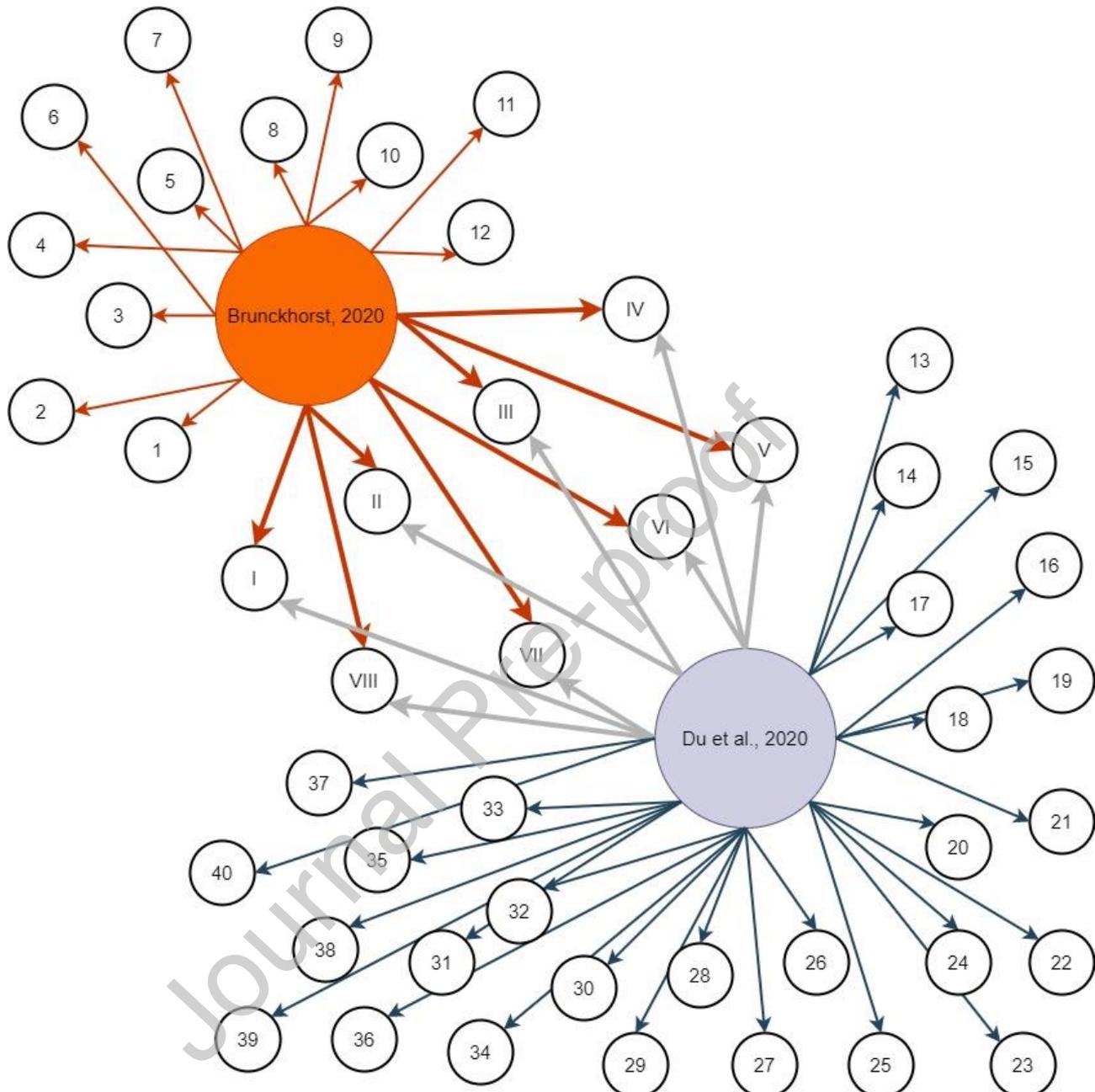
**Figure 3.** Graphic synthesis of studies included in the 3 included meta-analyses reporting standardized mortality ratio (SMR).



This diagram was performed using the software Draw.io made available in the public domain. The studies included in more than one meta-analysis are indicated with Roman numerals, while studies included in one meta-analysis only are indicated with Arabic numbers. Different colors indicated the three meta-analyses included in our umbrella review considering standardized mortality ratio (SMR), respectively blue, yellow, and purpura (Ravaoli et al., 2020; Harris and Barraclough, 1994; Amiri and Behnezhad, 2019). Arrows are also different in terms of thickness: lower thickness was used for studies included in one meta-analysis only, medium thickness for studies included in two meta-analyses, and high thickness for studies included in three meta-analyses.

<b>First authors of the meta-analyses</b>	<b>Included studies</b>
Amiri, Harris and Ravaioli	I. Levi et al., 1991 II. Louhivuori et al., 1979
Amiri and Ravaioli	III. Dormer et al., 2008 IV. Hem et al., 2004 V. Innos et al., 2003 VI. Misono et al., 2008 VII. Robinson et al., 2009 VIII. Vyssoki et al., 2015 IX. Yousaf et al., 2005
Harris and Ravaioli	X. Allebeck et al., 1989 XI. Fox et al., 1982 XII. Storm et al., 1992
Ravaioli	1. Ahn et al., 2010 2. Camidge et al., 2007 3. Kaceniene et al., 2017 4. Lin et al., 2017 5. Miccinesi et al., 2004 6. Nasser et al., 2012 7. Oberaigner et al., 2014 8. Ravaioli et al., 2020
Harris	9. Barton et al., 1965 10. Davidson et al., 1988 11. Henk et al., 1977 12. Shaw et al., 1965
Amiri	13. Ahn et al., 2015 14. Crocetti et al., 1998 15. Lin et al., 2009 16. Lu et al., 2013 17. Miller et al. 2008 18. Muff Christensen et al., 2006 19. Nakash et al., (1) 2013 20. Nakash et al., (2) 2013 21. Smailyte et al., 2013 22. Tanaka et al., 1999 23. Yamauchi et al., 2014 24. Fall et al., 2009 25. Llorente et al., 2005

**Figure 4.** Graphic synthesis of studies included in the 2 included meta-analyses reporting prevalence and incidence of suicidal risk.



This diagram was performed using the software Draw.io made available in the public domain. The studies included in more than one meta-analysis are indicated with Roman numbers, while studies included in one meta-analysis only are indicated with Arabic numbers. Different colors indicated the two meta-analyses included in our umbrella review considering prevalence and incidence of suicidal risk, respectively orange and lilac (Brunckhorst et al., 2020; Du et al., 2020). Arrows are also different in terms of thickness: lower thickness was used for studies included in one meta-analysis only while higher thickness for studies included in both meta-analyses.

<b>First authors of the meta-analyses</b>	<b>Included studies</b>
Brunckhorst and Du	I. Bill-Axelsson et al., 2010 II. Fall et al., 2009 III. Hem et al., 2004 IV. Klaassen et al., 2015 V. Misono et al., 2008 VI. Smailyte et al., 2013 VII. Smith et al., 2018 VIII. Vyssoki et al., 2015
Brunckhorst	1. Carlsson et al., 2013 2. Chen et al., 2019 3. Dalela et al., 2016 4. Fang et al., 2010 5. Lehto et al., 2015 6. Lehluante and Fransson, 2014 7. Llorente et al., 2005 8. Louda et al., 2012 9. Perry et al., 2018 10. Recklitis et al., 2014 11. Rice et al., 2018 12. Zhou et al., 2015
Du	13. Ahn et al., 2010 14. Alanee and Russo, 2012 15. Anderson and Park, 2018 16. Bowden et al., 2017 17. Crocetti et al., 1998 18. Dai et al., 2008 19. Dormer et al., 2008 20. Dulskas et al., 2019 21. Henson et al., 2019 22. Innos et al., 2003 23. Guo et al., 2019 24. Levi et al., 1991 25. Lin et al., 2017 26. Mahdi et al., 2011 27. Oberaigner et al., 2014 28. Osazuwa-Peters et al., 2018 29. Peng et al., 2005 30. Pham et al., 2019 31. Rahouma et al., 2018 32. Robinson et al., 2009 33. Schairer et al., 2006 34. Shen et al., 2020 35. Siracuse et al., 2017 36. Tanaka et al., 1999 37. Turaga et al., 2011 38. Yamauchi et al., 2014

39. Yousaf et al., 2005  
40. Zaorsky et al., 2019

**Table 1.** Descriptive characteristics of the meta-analyses focused on the association between cancer and suicide outcomes included in the umbrella review.

Source	Eligibility criteria	Cancer type	Other risk factors	No. incl. studies/ No. Cases	Risk measure	Rem, ES (95% CI)					Main results	Heterogeneity Q-test (df) I <sup>2</sup> (95% CI)	Egger's test, p Begg's test, p	CE/AMSTAR-2-R
						for both sexes	for men	for women	for cancer sites	for other risk factors				
Brunchorst et al., 2020 (UK)	<ul style="list-style-type: none"> <li>Observational studies with data for depressive and anxiety disorders or symptoms, and suicidal ideation prevalence or suicide mortality rates, after cancer diagnosis; longitudinal, cross-sectional, prospective; retrospective studies;</li> <li>English language.</li> </ul>	Prostate	Age	8 on suicidal ideation 12 on suicide/—	Prevalence	<b>Suicidal ideation:</b> pooled prevalence 9.85 (7.31–12.70) <b>Suicide:</b> pooled incidence 47.1 (39.85–54.96) per 100,000 person-years	—	—	Non localized disease: 1.71 (1.38–2.13)	<b>Suicide:</b> No association in patients aged 65 or older at the time of the first diagnosis (p= .11)	↑ risk for suicidal ideation and suicide	<b>Suicidal ideation:</b> — Substantial 88.17 (—)  <b>Suicide:</b> — Considerable 96.76 (—)	—, .01 —, .09	II/Cr. low
	PubMed Scopus PsycINFO Cochrane Library/ Up to 26 <sup>th</sup> May 2020													
Du et al., 2020 (China)	<ul style="list-style-type: none"> <li>The cause of death was “suicide or self-inflicted</li> </ul>	Any type	<ul style="list-style-type: none"> <li>Sex</li> <li>Cancer sites</li> <li>Continent</li> <li>Time</li> </ul>	36/—	Incidence	Pooled incidence of suicide	57.78 (47.31–70.56)	14.47 (11.27–18.57)	<b>Both sexes:</b> 87.71 (27.42–280.54) <b>Esophagus:</b> 61.02 (53.66–69.40) <b>Oceania:</b> 61.02 (53.66–69.40)	<ul style="list-style-type: none"> <li>Continent: Asia: 61.02 (53.66–69.40)</li> <li>Oceania: 61.02 (53.66–69.40)</li> </ul>	↑ risk for suicide	8786.79 (—) Considerable 99.6 (—)	1.32, .20 0.45, .65	II/Cr. low

	<p>injury”;</p> <ul style="list-style-type: none"> <li>Only data that could be calculated using the reported suicides and the number of person-years in which the suicides occurred</li> </ul> <p>PubMed Web of Science CNKI/ Up to 20<sup>th</sup> May 2020</p>		<p>since diagnosis</p> <ul style="list-style-type: none"> <li>Stage</li> <li>Age</li> <li>Marital status</li> </ul>			<p>death: 39.72 (33.91 – 46.52) per 100,000 person-years</p>			<ul style="list-style-type: none"> <li><b>Pancreas:</b> 75.39 (41.80-135.97)</li> <li><b>Bone and Sarcoma:</b> 60.99 (17.37-214.19)</li> <li><b>Head and Neck:</b> 53.76 (19.92-145.10)</li> <li><b>Gastric:</b> 51.83 (36.18-74.26)</li> <li><b>Lung:</b> 44.89 (26.37-76.43)</li> <li><b>Liver:</b> 38.13 (15.64-92.96)</li> <li><b>Prostate:</b> 35.82 (26.29-48.80)</li> <li><b>Testis:</b> 32.01 (18.58-55.15)</li> <li><b>Kidney:</b> 30.61 (22.14-42.34)</li> </ul> <p><b>Men:</b></p> <ul style="list-style-type: none"> <li><b>Pancreas</b> ranked first: 195.70 (129.55-295.61), followed by oesophagus, gastric, head and neck, sarcoma</li> </ul> <p><b>Women:</b></p> <ul style="list-style-type: none"> <li><b>Esophagus</b> ranked first: 18.34 (5.92-56.84), followed by head and neck, vaginal, gastric,</li> </ul>	<p>24.07 (20.78–27.88)</p> <ul style="list-style-type: none"> <li><b>Time diagnosis (&lt;6 mo.):</b> 89.33 (50.64–157.58)</li> <li><b>Stage:</b> from 42.39 (28.63-62.77) for distant metastasis to 22.78 (17.02-30.49) for localized cancer</li> <li><b>Age:</b> from 19.37 (14.38-26.08) for age <math>\leq 39</math> to 43.68 (35.32-54.02) for age <math>\geq 80</math></li> <li><b>Marital status:</b> from 44.39 (14.72-133.84) for divorced to 25.18 (20.87-30.37) for married patients</li> </ul>					
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									colorectal					
Ravaioi et al., 2020 (Italy)	<ul style="list-style-type: none"> <li>English language;</li> <li>Death due to suicide;</li> <li>Population-based or cancer-registry-based study;</li> <li>Original data;</li> <li>All tumor sites combined;</li> <li>Data for the one or the other gender or both genders combined;</li> <li>Information on the no. of deaths and the SMR or the HR.</li> </ul>	Any type	Sex	20/19,883	SMR	1.7 (1.5-1.9) from 14 studies included	1.8 (1.6-2.0) from all 20 studies included	1.4 (1.3-1.6) from all 20 studies included	—	—	↑ risk for suicide	<b>Both sexes:</b> Considerable 833 (13) 98.4 (98-99)	—	II/Crit. Low
	PubMed/Up to 6 <sup>th</sup> Nov. 2017											<b>Men:</b> Considerable 615 (19) 96.9 (96-98)	-2.5, .26	
												<b>Women</b> Considerable 246 (19) 92.3 (89-94)	-.9, .5	
Amiri and Behnezhad, 2019 (Iran)	<ul style="list-style-type: none"> <li>Prospective cohort, retrospective cohort, case-control studies;</li> <li>Cancer and its type as the exposure variable;</li> <li>Suicide mortality as an outcome</li> </ul>	Any type & localized	<ul style="list-style-type: none"> <li>Sex</li> <li>Cancer sites</li> <li>Continent</li> </ul>	22/—	SMR	1.55 (1.37-1.74)	1.67 (1.48-1.89)	1.34 (1.20-1.50)	<ul style="list-style-type: none"> <li><b>Bronchus, trachea, lung:</b> 3.07 (2.20-4.28)</li> <li><b>Esophagus, stomach, pancreas, liver:</b> 2.06 (1.32-3.23)</li> <li><b>Prostate:</b> 1.71 (1.38-</li> </ul>	<ul style="list-style-type: none"> <li><b>Continent:</b>  <b>Europe:</b> 2.63 (1.51-4.57)  <b>America:</b> 1.52 (1.36-1.70)  <b>Asia:</b> 1.18 (.94-1.49)</li> </ul>	↑ risk for suicide	<b>Cancer sites:</b> <ul style="list-style-type: none"> <li><b>Bronchus, trachea, lung:</b> — Considerable 95.9 (—)</li> <li><b>Esophagus, stomach, pancreas, liver:</b> — Considerable 91.2 (—)</li> <li><b>Prostate:</b></li> </ul>	—, .83	II/Crit. Low

	<ul style="list-style-type: none"> <li>SMR, RR, OR, HR or adequate result for calculating SMR;</li> <li>Only the most comprehensive studies.</li> </ul>							2.12) <ul style="list-style-type: none"> <li><b>Colon, rectum:</b> 1.57 (1.26-1.97)</li> <li><b>Female genital organs:</b> 1.26 (.79-1.99)</li> <li><b>Breast:</b> 1.24 (1.03-1.48)</li> <li><b>Melanoma and skin:</b> .93 (.75-1.16)</li> </ul>		— Substantia 1 88.9 (—) <ul style="list-style-type: none"> <li><b>Colon, rectum:</b> — Substantia 1 87.5 (—)</li> <li><b>Female genital organs:</b> — Considera ble 94.3 (—)</li> <li><b>Breast:</b> — Substantia 1 87.8 (—)</li> <li><b>Melano ma and Skin:</b> — Substantia 1 71.4 (—)</li> </ul> <hr/> Considera ble <b>Tot.</b> 96.9 (—)			
Guo et al., 2018 (China)	<ul style="list-style-type: none"> <li>Men diagnosed with prostate cancer (any type) only;</li> <li>Original studies that investigated the association between any suicidal outcome and its relevant risk factors and any type of prostate cancer;</li> <li>Studies that reported sufficient data of risk estimates;</li> <li>Studies that used either case-control,</li> </ul>	Prostate (Any type)	<ul style="list-style-type: none"> <li>Time since diagnosis</li> <li>Age;</li> <li>Treat. mod.</li> <li>Disease risk category</li> <li>SSE</li> <li>Marital status</li> <li>Race</li> </ul>	8/—	RR	—	2.01 (1.52-2.64)	—	<ul style="list-style-type: none"> <li><b>Time diagnosis (&lt;6 mo.):</b> 2.24 (1.77-2.85)</li> <li><b>Age ≥75:</b> 1.51 (1.04-2.18)</li> <li><b>Treat. mod.: Hormonal:</b> 1.80 (1.54-2.12)</li> </ul>	↑ risk for suicide	<b>Other risk factors:</b> <ul style="list-style-type: none"> <li><b>Men:</b> — Considera ble 91.8 for men</li> <li><b>Time since diagnosis is:</b> — Moderate 61.1</li> <li><b>Age ≥ 75:</b> — Considera ble 91.5</li> <li><b>Treat. mod.:</b> — Absent 0</li> </ul>	—, .29 —	III/Crit. . Low

	cross-sectional, retrospective cohort, or prospective cohort design.													
	PubMed EMBASE Cochrane Library PsycINFO / Up to April 2018													
Harris and Barraclough, 1994 (UK)	<ul style="list-style-type: none"> <li>▪ Describe the mortality of a cohort with the defined medical disorder with a mean or median follow-up of 2 years or more;</li> <li>▪ Published in an English language peer-reviewed journal;</li> <li>▪ Lost less than 10% of cases at follow-up;</li> <li>▪ Gave observed/expected numbers of suicide.</li> </ul>	Any type & head, neck	Cancer site	9 <sup>+</sup> / 1,634	SMR	—	—	—	—	—	↑ risk for suicide	—	—	III/Critical . Low
	PubMed/ From 1966 to 1992													

<sup>+</sup> Studies on all cancer sites (k=5) and head and neck cancer (k=4).

—=not available; Rem=Random-effect model (only significant effects); ES=effect size; SMR=standardized mortality ratio; RR=risk ratio; OR=odds ratio; CI=confidence interval; CNKI=China National Knowledge Infrastructure; Treat. mod.=Treatment modality; CE=Class of Evidence; Crit.=critically; ↑=increased; AMSTAR-2-R=A revised MeaSurement Tool to Assess systematic Reviews 2 Revised.

**Table 2.** Descriptive characteristics of the systematic reviews focused on the association between cancer and suicide outcomes included in the umbrella review.

Source	Main focus	Range pub. years	Eligibility criteria	Cancer type	Suicidal outcome <sup>†</sup>	No. incl. studies		Databases	Other risk factors	Main results	AMSTAR-2-R
						Total	Per association <sup>†</sup>				
Kolva et al, 2019 (USA)	SI and Cancer	From Jan. 2008 to Sept. 2018	<ul style="list-style-type: none"> <li>Adults previously diagnosed with cancer;</li> <li>SI stated as an outcome.</li> </ul> <p>Excluded if:</p> <ul style="list-style-type: none"> <li>a) included participants 17 years of age or younger;</li> <li>b) findings were based on qualitative data methods;</li> <li>c) did not include experimental analyses (i.e., case studies, SR/MA, letter to the Editor, or commentary)</li> </ul>	Any type & Breast, Prostate, Stomach, Head, and Neck, Brain	SI	44	44	PubMed, PsycINFO, EMBASE, CINAHL, CDSR and CC	<ul style="list-style-type: none"> <li>Age;</li> <li>sex;</li> <li>disease/treat. - rel. charact.;</li> <li>Social support including living alone, marital status, and caregiver charact.;</li> <li>Psych. factors.</li> </ul>	<ul style="list-style-type: none"> <li>Prevalence of SI in cancer patients ranged from .7% to 46.3%;</li> <li>Single items drawn from validated measures were the most frequent method of assessing SI (n=20, 45%);</li> <li>Commonly risk factors for SI included: age ≥ 60, both sexes; &lt; social support; disease/treat.-rel. charact. (childhood cancers survivors/ history of chemotherapy, physical symptom and burden, pain and fatigue), psych. factors (dep., anxiety, demor., hopelessness, existential or general psych. distress, history or current psychiatric diagnosis, poorer psych. or existential well-being).</li> </ul> <p><i>Effective interventions:</i></p> <ul style="list-style-type: none"> <li>for depr., SI, hopelessness: BA therapy and P-S therapy and SC Interv.;</li> <li>only for SI: MHCN Interv., including frequent assessment, education and empowerment for hospitalized patients, and the use of a single dose of ketamine.</li> </ul>	Low
Kawashima et al., 2019 (Japan)	Interv. to prevent SOs for cancer patients	Up to July 2018	<ul style="list-style-type: none"> <li>Patients with cancer;</li> <li>The study was a randomized controlled trial (RCT) or another intervention study that prospectively examined the effect of intervention;</li> <li>Suicide death, SA, self-harm, SI were reported in the manuscript</li> </ul>	Any type	Suicide/SA/SI	22	19	PubMed, PsycINFO, CINAHL, Cochrane Library	<ul style="list-style-type: none"> <li>Depr.;</li> <li>Sub. Use;</li> <li>Neuro. dysf.;</li> <li>Sexual dysf.;</li> <li>Sleep disease;</li> <li>Stress-related/PTS;</li> <li>Somatization;</li> <li>Bipolar Disorders;</li> <li>OCD;</li> <li>Pain;</li> <li>Sense of burden;</li> <li>Poor Social support</li> </ul>	<ul style="list-style-type: none"> <li>No interv. designed to prevent SOs for cancer patients;</li> <li>SOs reported as secondary outcomes;</li> <li>7 on 8 trials designed to treat dep.;</li> <li>Treating dep. might be not an effective way to reduce suicide due to the presence of other risk factors.</li> <li>Suicide rates vary among patients with different types of cancers;</li> <li>Breast cancer was the most frequent cancer type;</li> <li>Most trials demonstrated inadequate study quality.</li> </ul> <p><i>Effective interventions for reducing SI:</i></p> <ul style="list-style-type: none"> <li>BA therapy;</li> <li>P-S therapy;</li> <li>Ketamine use.</li> </ul>	Low



Fässberg et al., 2016 (Sweden)	MDs and SOs	Up to Nov. 2014	<ul style="list-style-type: none"> <li>Peer-reviewed publication in English;</li> <li>Focused on persons &gt; 64 years of age;</li> <li>Examined a) deaths wishes, SI, nonfatal suicidal behaviors/ self-harm, or suicide, and b) an indicator of physical health.</li> </ul>	Any type	Suicide/SA/SI	65	9	ERIC Google Scholar PsycINFO PubMed Scopus	<ul style="list-style-type: none"> <li>Age;</li> <li>sex;</li> <li>cancer site.</li> </ul>	<ul style="list-style-type: none"> <li>↑ suicide in cancer patients, specifically in older males with lung, prostate, and genital cancer.</li> <li>Cancer ↔ SOs;</li> <li>Physical illness ↔ SOs.</li> </ul>	Crit. Low
Tang et al., 2015 <sup>++</sup> (China)	Demor., Dep. and Cancer	Up to August 2012	<ul style="list-style-type: none"> <li>Correlational studies that explored the psych. factors that influence demor. in patients with cancer.</li> <li>English or Chinese language.</li> </ul>	Any type	DW	5	3	CINAHL Cochrane Library PubMed PsycINFO CEPS	<ul style="list-style-type: none"> <li>Hopelessness;</li> <li>DW;</li> <li>Anxiety;</li> <li>Poor comfort.</li> </ul>	Demor. (including DW) ↔ Depression	Crit. Low

<sup>+</sup>Cancer and Suicidal outcomes (i.e. Death Wish, Suicidal Ideation, Suicide Attempt, and Suicide). <sup>++</sup> Only the systematic review was considered because the main focus was not the association between cancer and suicide.

*Abbreviations:* SR=systematic review; MA=meta-analysis; SOs=suicidal outcomes; DW=death wish; SI=suicidal ideation; SA=suicide attempt; CDSR and CC=Cochrane Database of Systematic Reviews and Cochrane Central; CEPS=Centre for European Policy Studies; ERIC=Education Resources Information Center; MDs=Medical Disorders; uHNs=unmet health needs; incl.=included; Treat. mod.=treatment modality; SSE=socio-economic status; demor.=demoralization; dep.=depression; treat.-rel. charact.=treatment related characteristics; interv.=interventions; BA=Behavioral Activation, P-S=Problem-Solving; SC=Spiritual Care; MHCN=Mental Health Clinical Nursing; HRQoL=Health Related Quality of Life; psych.=psychological; funct.=functioning; PC=Prostate Cancer; AAA=Abdominal Aortic Aneurism; Sub. Use=Substance Use; Neuro.=Neurocognitive; disf.=dysfunctions; PTS=post-traumatic stress; OCD=Obsessive-Compulsive Disorders; AMSTAR-2-R=A Revised Measurement Tool to Assess systematic Reviews 2 Revised; Crit.=critically; ↑=increased; ↓=decreased; <=minor; >=major; —=negative; ↔=association.

**Table 3.** Assessment of the quality of the included meta-analyses and systematic reviews using A Measurement Tool to Assess systematic Reviews 2 Revised (AMSTAR-2-R).

Source	1	2	3	4	5	6	7	8	9	10	11	12
Brunckhorst et al., 2020	Yes	Yes	No	Part. yes	Yes	Yes	No	Part. yes	Yes	No	No	Yes
Du et al., 2020	No	No	No	No	Yes	Yes	No	Part. yes	Yes	No	No	No
Ravaioli et al., 2020	Yes + optional	No	No	No	Yes	No	No	Yes	No	No	No	Yes
Amiri and Behnezhad, 2019	Yes + optional	No	No	Part. yes	No	Yes	No	Yes	Yes	No	No	Yes
Guo et al., 2018	Yes + optional	No	No	Part. yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Harris and Barraclough, 1994	Yes	No	No	No	No	No	No	Yes	No	No	No	No
Kolva et al., 2019	Yes	Part. yes	No	Part. yes	Yes	Yes	No	Yes	Yes	No	No MA	No MA
Kawashima et al., 2019 <sup>+</sup>	Yes	Part. yes	Yes	Part. yes	Yes	Yes	No	Yes	Yes	No	No MA	No MA
McDonough et al., 2018	Yes	No	No	Part. yes	Yes	Yes	No	Yes	Yes	No	No MA	No MA
Cotter et al., 2017	Yes + optional	No	No	Part. yes	Yes	Yes	No	Part. yes	Yes	No	No MA	No MA
Fässberg et al., 2016	Yes	No	No	Part. yes	No	No	No	Yes	No	No	No MA	No MA
Tang et al., 2015 <sup>++</sup>	Yes	No	No	Part. yes	No	No	No	Part. yes	Yes	No	No MA	No MA

<sup>+</sup> This Systematic Review is focused on treatments to prevent suicidal ideation and behaviors among cancer patients.

<sup>++</sup> All included data are related to the Systematic Review only.

MA=meta-analysis; Cr.=Critically; Part.=partial.