SUPPLEMENTARY APPENDIX

Proportions and incidence of locally advanced cervical cancer: a global systematic literature review

Bradley J Monk,1 David S P Tan,2 José David Hernández Chagüi,3 Jitender Takyar,4 Michael J. Paskow,3 Ana Tablante Nunes,5 Eric Pujade-Lauraine6

Supplementary Methods

The search strategies shown below were created to support this locally advanced cervical cancer epidemiology systematic literature review as well as one focused on the natural history of locally advanced cervical cancer. Only the epidemiology publications are reported in this article. EMBASE, MEDLINE (PubMed), and Cochrane databases were searched using the search strategies below. Because some studies are not appropriately indexed in electronic databases, bibliographic searching and pearl growing techniques were used to identify any potentially relevant studies that were not captured by database searches.

Embase search strategy run on June 10, 2020

| Search number | Query                                                                 | Results     |
|---------------|-----------------------------------------------------------------------|-------------|
| #1           | 'uterine cervix cancer'/syn                                           | 114 434     |
| #2           | 'cervical tumor' OR 'cervical neoplasm' OR 'cervical tumour' OR 'cervical cancer' | 67 038     |
| #3           | cervi* NEAR/5 (cancer* OR oncolog* OR neoplas* OR carcinom* OR malignan* OR tumor* OR tumour* OR mass* OR growth* OR cyst* OR adenocarcinom* OR squamous) | 159 269 |
| #4           | #1 OR #2 OR #3                                                      | 159 271     |
| #5           | 'natural history'/exp OR 'natural history':ab,ti,kw OR 'natural course' | 423 926     |
| #6           | 'natural history study'                                              | 1649        |
| #7           | ('observational' OR 'prospective' OR 'retrospective' OR 'cross-sectional' OR 'cross sectional' OR 'longitudinal') NEAR/3 ('study' OR 'studies' OR analy*) | 2 513 311   |
| #8           | #5 AND #7                                                           | 18 090      |
| #9           | 'disease course':ab,ti,kw OR 'clinical course' OR ('natural history' NEAR/2 prognos*) | 113 467     |
| #10          | 'inception cohort' OR 'disease exacerbation'/syn OR 'disease progression' OR 'outcome assessment':ab,ti,kw | 246 377 |
| #11          | #5 OR #6 OR #8 OR #9 OR #10                                         | 770 081     |
| #12          | #4 AND #11                                                          | 3494        |
| #13          | 'locally advanced' OR 'local advanced' OR (local* NEAR/2 'advanced') OR 'stage one' OR 'stage two' OR 'stage three' OR 'stage four' OR 'stage ib2' OR 'stage ib' | 103 225    |
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### PubMed search strategy run on June 10, 2020

| Search number | Query                                                                 | Results     |
|---------------|-----------------------------------------------------------------------|-------------|
| #1            | Search: ‘uterine cervix cancer’[MeSH Terms]                          | 74 490      |
| #2            | Search: “cervical tumor” OR “cervical neoplasm” OR “cervical tumour” OR “cervical cancer” | 47 147      |
| #3            | Search: cervi* AND (cancer* OR oncolog* OR neoplas* OR carcinom* OR malignan* OR tumor* OR tumour* OR mass* OR growth* OR cyst* OR adenocarcinom* OR squamous) | 161 507     |
| #4            | Search: #1 OR #2 OR #3                                              | 161 507     |
| #5            | Search: (‘natural history’[MeSH Terms]) OR (‘natural history’[Title/Abstract]) OR ‘natural course’ | 84 236      |
| #6            | Search: “natural history study”                                     | 776         |
| #7            | Search: (‘observational’ OR “prospective” OR “retrospective” OR “cross-sectional” OR “cross sectional” OR “longitudinal”) AND (“study” OR “studies” OR analyses) | 2 332 275   |
| #8            | Search: #5 AND #7                                                   | 17 334      |
| #9            | Search: “disease course”:[Title/Abstract] OR “clinical course” OR (“natural history” AND prognos*) | 81 583      |
| #10           | Search: (“inception cohort”) OR (“disease exacerbation”[MeSH Terms]) OR “disease progression” OR (“outcome assessment”[MeSH Terms]) | 218 726     |
| #11           | Search: #5 OR #6 OR #8 OR #9 OR #10                                  | 360 274     |
| #12           | Search: #4 AND #11                                                   | 4419        |
| #13           | Search: “locally advanced” OR “local advanced” OR (local” AND “advanced”) OR “stage one” OR “stage two” OR “stage three” OR “stage four” OR “stage ib2” OR “stage ib” OR “stage iia” OR “stage iib” OR “stage iav” OR “stage 1b2” OR “stage 2b” OR “stage 3a” OR “stage 3b” OR “stage 4a” OR (“stage” AND (“ib2” OR “ib” OR “iia” OR “iib” OR “iva” OR “1b2” OR “2b” OR “3a” OR “3b” OR “4a”)) OR ‘non-metastatic’ OR ‘non metastatic’ OR ‘lacc’ | 100 166     |
The following conferences were also searched for relevant abstracts from meetings held between January 2017 and June 2020: American Society of Clinical Oncology, European Society for Medical Oncology, European Society of Gynaecological Oncology, Society of Gynecologic Oncology, American Association for Cancer Research, International Society for Pharmacoeconomics and Outcomes Research, International Gynecologic Cancer Society.

The publication timeframe for conference searching was limited to the previous 3 years.
based on the assumption that research presented at conferences is usually published within 3–4 years as a full-text article or indexed in different biomedical literature databases as a conference paper, conference review, etc.

Inclusion and exclusion criteria used to identify relevant studies are shown in the table below.

| Parameter       | Inclusion/exclusion criteria                                                                 |
|-----------------|---------------------------------------------------------------------------------------------|
| Study design    | • Retrospective observational study                                                         |
|                 | • Prospective observational study                                                           |
|                 | • Case-control studies                                                                      |
|                 | • Surveys and cross-sectional studies                                                        |
|                 | • Registry/database studies                                                                 |
|                 | • Excluded: controlled trials (randomized controlled trial, non-randomized controlled study, or single-arm study) |
| Population      | • Adult population (aged ≥18 years)                                                          |
|                 | • Any race                                                                                  |
|                 | • Locally advanced cervical cancer: stages IB2-IVA per any version of the FIGO staging criteria |
|                 | • Excluded: studies that only include patients with early-stage or metastatic cervical cancer |
| Line of therapy | • Not restricted                                                                             |
|                 | • Studies of patients with locally advanced cervical cancer (both untreated and treated)     |
| Countries       | • Not restricted                                                                             |
| Language        | • Englisha                                                                                  |
| Time-frame      | • 2010–2020                                                                                 |
| Data reported   | • Proportion of patients with cervical cancer by disease stage                               |
Incidence of cervical cancer by disease stage

English language was a criterion from the beginning of the systematic literature review process and was used as an exclusion criterion in database search queries.

FIGO, International Federation of Gynecology and Obstetrics.

Data extraction

The following information was extracted from the final set of published reports, where available: study details (sample size, inclusion/exclusion criteria, disease stage, stage classification criteria, treatment details, study limitations, time-frame of data collection, data source, location), patient demographics (age, race/ethnicity), clinical characteristics (histology, prior therapy), the proportion of patients with locally advanced stages of cervical cancer, prevalence (rate, odds ratio, risk ratio), and incidence (rate, risk ratio).

Calculation of the Proportion of Locally Advanced Cervical Cancer

The Surveillance, Epidemiology, and End Results summary stage categorizes the extent of cancer spread in a basic set of criteria. In the past, this classification system has also been referred to as General Stage, California Stage, historic stage, and Surveillance, Epidemiology, and End Results Stage. Summary stage uses all information available via medical records (ie, both clinical and pathologic documentation). Below are the criteria as per the most recent version (v2.0) published in 2020; however, studies included in the systematic literature review may have used older versions of the criteria. A summary of changes between the last available version (v1.7) and version 2.0 is available at https://seer.cancer.gov/tools/ssm/change-log.pdf. The 2020 criteria were used to determine which SEER Summary stages were equivalent to FIGO stage IB2-IVA.

| Code | Stage | Definition |
|------|-------|------------|
| 0    | In situ | Noninvasive, intraepithelial lesions. Includes cancer in situ with endocervical gland involvement, cervical intraepithelial neoplasia Grade III, preinvasive. |
| 1    | Localized | Clinically visible lesion (macroscopic), including superficial invasion. |
Confined to cervix uteri or uterus NOS, except corpus uteri NOS, including if not clinically visible or unknown if clinically visible. Measured stromal invasion less than 5 mm from the base of the epithelium AND horizontal spread of 7.0 mm or less. Includes FIGO stage IA1, IA2, IA NOS, IB1, IB2, IB NOS, I NOS.

2 Regional (direct extension) Extension to the bladder wall; bladder NOS excluding mucosa; bullous edema of bladder mucosa; confined to corpus uteri, size, depth and horizontal spread unknown; corpus uteri NOS; Cil de sac (rectouterine pouch); fallopian tube(s); “frozen pelvis” (clinically described); hydrenephrosis or nonfunctioning kidney; invasion beyond uterus NOS; ligament(s) (broad, cardinal, uterosacral); ovary/ovaries; parametrial (paracervical soft tissue) invasion; pelvic wall(s); rectal wall; rectum NOS excluding mucosa; upper two-thirds of vagina including fornices; ureter (intra- and extramural); urethra; vagina (lower third [not extending into pelvic wall], NOS); vaginal wall NOS; vulva. Includes FIGO stage IIA, IIB, II NOS, IIIA, IIIB, III NOS.

3 Regional (lymph node involvement only) Localized tumor WITH regional lymph node involvement. Involvement of the following types of lymph nodes: para-aortic, iliac NOS, paracervical, parametrial, sacral NOS, regional NOS. Includes FIGO stages IIIC1, IIIC2, IIIC NOS.

4 Regional (both direct extension and regional lymph nodes involved) Any combination of codes 2 and 3 above.

7 Distant (sites or lymph nodes) Cervical cancer that has metastasized. Includes bladder mucosa, rectal mucosa, sigmoid colon, small intestine, inguinal (femoral) lymph node, mediastinal lymph node, scalene lymph node, supraclavicular lymph node; or cancers labeled as carcinomatosis or distant metastasis with or without distant lymph nodes. Includes FIGO stage IVA, IVB, IV NOS.

9 Unknown Unknown if extension or metastasis. FIGO, International Federation of Gynecology and Obstetrics; NOS, not otherwise specified.
**Supplementary Fig 1.** Countries represented by the studies included in the systematic literature review.

Included countries are the United States, Canada, China, India, Japan, Jordan, collective Gulf countries [Saudi Arabia, United Arab Emirates, Qatar, Oman, Kuwait, Bahrain], Kazakhstan, Korea, Taiwan, Belarus, Bulgaria, Estonia, France, Germany, Ireland, Lithuania, the United Kingdom, Morocco, Kenya, South Africa, Brazil, and Trinidad & Tobago.
**Supplementary Fig 2.** Estimated proportion of locally advanced cervical cancer by type of data source

| Study                  | ES (95% CI)       | Region               | Time period | N |
|------------------------|-------------------|----------------------|-------------|---|
| Registry               |                   |                      |             |   |
| Kosgei 2016            | 0.31 (0.25-0.37)  | Africa               | 2010-2014   | 265 |
| Bouchoik 2013          | 0.42 (0.39-0.46)  | Africa               | 2005-2007   | 816 |
| Somdyala 2020          | 0.29 (0.23-0.39)  | Africa               | 2005-2012   | 1315|
| Wang 2015              | 0.51 (0.49-0.53)  | Asia                 | 1993-2008   | 3641|
| Cheung 2011            | 0.44 (0.43-0.46)  | Asia                 | 1997-2006   | 4407|
| Akhtarali 2019         | 0.59 (0.57-0.61)  | Gulf countries       | 1996-2012   | 2332|
| Yagi 2019              | 0.39 (0.37-0.42)  | Asia                 | 1976-2012   | 25820|
| Sharkas 2017           | 0.10 (0.07-0.12)  | Asia                 | 2000-2013   | 591 |
| Kaidarova 2018         | 0.69 (0.65-0.70)  | Asia                 | 2012        | 1641|
| Lee 2014               | 0.50 (0.46-0.55)  | Asia                 | 1999-2010   | 49203|
| Chiang 2016            | 0.31 (0.30-0.33)  | Asia                 | 2004-2008   | 8238|
| Warner 2016            | 0.29 (0.27-0.31)  | Caribbean            | 1995-2009   | 1812|
| Samson 2016            | 0.54 (0.53-0.55)  | Europe               | 1995-2013   | 21736|
| Djamaa 2016            | 0.38 (0.35-0.40)  | Europe               | 2005-2014   | 1795 |
| Lorin 2015             | 0.41 (0.35-0.47)  | Europe               | 1998-2010   | 311 |
| Rottmann 2020          | 0.26 (0.24-0.28)  | Europe               | 2007-2016   | 2291|
| Ulinikes 2013          | 0.64 (0.63-0.65)  | Europe               | 1990-2004   | 6680|
| Mshmud 2011            | 0.38 (0.34-0.41)  | North America        | 1985-2001   | 714 |
| Machida 2018           | 0.27 (0.27-0.27)  | North America        | 1973-2013   | 87151|
| Skaznik-Wikle 2012     | 0.36 (0.36-0.37)  | North America        | 2002-2006   | 19003|
| Ciha 2014              | 0.27 (0.26-0.27)  | North America        | 1973-2010   | 27002|
| Herley 2010            | 0.36 (0.36-0.37)  | North America        | 2004-2006   | 36076|
| Subtotal (I²=99.87, p=0.00) | 0.38 (0.34-0.43) |                     |             |   |

Multiple centers

- Elmaajouli 2016: 0.89 (0.85-0.90) Africa 2006 646
- Rodrigues 2018: 0.73 (0.69-0.76) South America 2016-2017 631
- Subtotal

Single center

- Agarwal 2012: 0.68 (0.65-0.71) Asia 2000-2009 927
- Srivastu 2014: 0.97 (0.94-0.99) Asia NR (1-year period) 189
- Subramaniem 2010: 0.14 (0.11-0.16) North America 2002-2007 430
- Carmo 2011: 0.69 (0.67-0.70) South America 2012-2015 3341
- Possati-Resende 2018: 0.06 (0.02-0.13) South America 2003-2015 NR
- Subtotal (I²=98.94%, p=0.00) 0.51 (0.22-0.79)

Heterogeneity between groups: p=0.000

Overall (I²=99.89%, p=0.00) 0.43 (0.38-0.49)

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Proportion of cervical cancer patients with locally advanced disease

Estimated proportion for each study (ES) and the 95% confidence intervals are plotted according to data source (registry, multicenter institution, or single institution). Overlapping timeframes and duplicate data from the same study have been removed. Red triangles represent the range of the subtotal estimated proportion, and the red dashed line represented the overall estimated proportion of locally advanced cervical cancer from this dataset. Heterogeneity of studies is reflected in the I² value; a score of >60% = high heterogeneity. Single center studies provided the most unreliable data with the largest variance (estimated range, 6–97%). N indicates the total number of women with cervical cancer. NR, not reported.
Supplementary Table 1. Strengthening the Reporting of Observational studies in Epidemiology checklist items

| Section                     | Item No | Recommendation                                                                 |
|-----------------------------|---------|---------------------------------------------------------------------------------|
| Title and abstract          | 1       | (a) Indicate the study’s design with a commonly used term in the title or the abstract |
|                             |         | (b) Provide in the abstract an informative and balanced summary of what was done and what was found |
| Introduction                |         |                                                                                 |
| Background/rationale        | 2       | Explain the scientific background and rationale for the investigation being reported |
| Objectives                  | 3       | State specific objectives, including any prespecified hypotheses                  |
| Methods                     |         |                                                                                 |
| Study design                | 4       | Present key elements of study design early in the paper                          |
| Setting                     | 5       | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants                | 6       | (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up |
|                             |         | Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls |
| Section                                      | Instruction                                                                 |
|----------------------------------------------|-----------------------------------------------------------------------------|
| Cross-sectional study                       | Give the eligibility criteria, and the sources and methods of selection of participants |
| (b) Cohort study                             | For matched studies, give matching criteria and number of exposed and unexposed |
| Case-control study                           | For matched studies, give matching criteria and the number of controls per case |
| Variables                                    | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement                   | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias                                         | Describe any efforts to address potential sources of bias |
| Study size                                   | Explain how the study size was arrived at |
| Quantitative variables                       | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods                          | (a) Describe all statistical methods, including those used to control for confounding |
|                                              | (b) Describe any methods used to examine subgroups and interactions |
|                                              | (c) Explain how missing data were addressed |
(d) **Cohort study**—If applicable, explain how loss to follow-up was addressed

*Case-control study*—If applicable, explain how matching of cases and controls was addressed

*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

**Results**

| Participants | 13* |
|--------------|-----|
| (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| (b) Give reasons for non-participation at each stage |
| (c) Consider use of a flow diagram |

| Descriptive data | 14* |
|------------------|-----|
| (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| (b) Indicate number of participants with missing data for each variable of interest |
| (c) **Cohort study**—Summarise follow-up time (eg, average and total amount) |

| Outcome data | 15* |
|--------------|-----|
| **Cohort study**—Report numbers of outcome events or summary measures over time |
| **Case-control study**—Report numbers in each exposure category, or summary measures of |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. |
| Other analyses | 17 | (b) Report category boundaries when continuous variables were categorized. |
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. |
| Other analyses | 17 | Report other analyses done—eg, analyses of subgroups and interactions, and sensitivity analyses. |
| Discussion | 18 | Summarise key results with reference to study objectives. |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results. |
Information should be given separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Items as reported on the Strengthening the Reporting of Observational studies in Epidemiology website (https://www.equator-network.org/reporting-guidelines/strobe/).

| Other information          |
|----------------------------|
| Funding                    |

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.
Supplementary Table 2. Strengthening the Reporting of Observational studies in Epidemiology – Abstract version – checklist items

| Item          | Recommendation                                                                 |
|---------------|-------------------------------------------------------------------------------|
| Title         | Indicate the study’s design with a commonly used term in the title (e.g cohort, case-control, cross sectional) |
| Authors       | Contact details for the corresponding author                                   |
| Study design  | Description of the study design (e.g cohort, case-control, cross sectional)    |
| Objective     | Specific objectives or hypothesis                                              |
| Methods       |                                                                                   |
| Setting       | Description of setting, follow-up dates or dates at which the outcome events occurred or at which the outcomes were present, as well as any points or ranges on other time scales for the outcomes (e.g., prevalence at age 18, 1998-2007). |
| Participants  |                                                                                   |
| Cohort study  | Give the most important eligibility criteria, and the most important sources and methods of selection of participants. Describe briefly the methods of follow-up |
| Case-control study | Give the major eligibility criteria, and the major sources and methods of case ascertainment and control selection |
| Cross-sectional study | Give the eligibility criteria, and the major sources and methods of selection of participants |
| Cohort study  | For matched studies, give matching and number of exposed and                      |
| Variables                  | Clearly define primary outcome for this report. |
|---------------------------|-------------------------------------------------|
| Statistical methods       | Describe statistical methods, including those used to control for confounding |

### Results

| Participants              | Report Number of participants at the beginning and end of the study |
|---------------------------|---------------------------------------------------------------------|
| Main results              | Report estimates of associations. If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
|                           | Report appropriate measures of variability and uncertainty (e.g., odds ratios with confidence intervals) |

### Conclusions

General interpretation of study results

Checklist items were obtained from the EQUATOR network website: https://www.equator-network.org/reporting-guidelines/strobe-abstracts/.
### Supplementary Table 3. Strengthening the Reporting of Observational studies in Epidemiology checklist for included studies[2-30]

| Study name | Title & abstract | Introduction | Methods | Results | Discussion | Other information |
|------------|-----------------|--------------|---------|---------|------------|-------------------|
| Henley 2010 | Y Y Y Y | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Gorg 2011 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Skaznik-Wikel 2012 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Ojha 2014 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Machida 2018 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Zahnd 2018 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Hou 2019 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Bruegl 2020 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Tian 2020 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Mahmud 2011 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Jarmo 2011 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Possati-Risende 2018 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Warner 2018 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Lorin 2015 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Samson 2016 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Djamaa 2018 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Ullinskas 2013 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |
| Bouchbika 2013 | Y Y Y Y | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N | Y Y Y N |

**Legend:**
- **Y:** Yes
- **N:** No

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Checklist items are explained in Online Supplementary Table 1.
Supplementary Table 4. Strengthening the Reporting of Observational studies in Epidemiology – Abstract version - checklist for included studies [31-41]

| Study Name       | Title                           | Authors | Study Design | Objective | Setting | Participants | Variables | Statistics | Results - Participants | Main results | Conclusions |
|------------------|---------------------------------|---------|--------------|-----------|---------|--------------|-----------|------------|------------------------|--------------|-------------|
| Subramaniam 2010 | N                               | Y       | Y            | Y         | Y       | Y            | Y         | Y          | Y                      | N            | Y           |
| McLean 2012      | N                               | Y       | Y            | Y         | Y       | Y            | Y         | Y          | Y                      | N            | Y           |
| (Int J Gyn Can)  |                                  |         |              |           |         |              |           |            |                        |              |             |
| McLean 2012      | N                               | Y       | Y            | Y         | Y       | Y            | Y         | Y          | Y                      | Y            | Y           |
| (Gyn Oncol)      |                                  |         |              |           |         |              |           |            |                        |              |             |
| Popadiuk 2010    | N                               | N       | Y            | Y         | Y       | Y            | N         | N          | Y                      | N            | Y           |
| Rodrigues 2018   | N                               | Y       | Y            | Y         | Y       | Y            | N         | Y          | Y                      | Y            | Y           |
| Nathani 2012     | N                               | Y       | N            | Y         | Y       | Y            | Y         | N          | Y                      | N            | Y           |
| Garry 2018       | N                               | Y       | Y            | Y         | Y       | Y            | N         | N          | Y                      | N            | Y           |
| Rottmann 2020    | Y                               | Y       | Y            | Y         | Y       | Y            | Y         | Y          | Y                      | Y            | Y           |
| Litvinova 2017   | M                               | Y       | Y            | Y         | Y       | Y            | Y         | N          | Y                      | N            | N           |
| Kosgel 2018      | N                               | Y       | N            | Y         | Y       | Y            | Y         | N          | Y                      | N            | Y           |
| Kaidarova 2018   | N                               | Y       | N            | Y         | Y       | Y            | Y         | N          | Y                      | Y            | Y           |

Checklist items are explained in Online Supplementary Table 2.
### Supplementary Table 5. Study characteristics

| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|-------------------------|----------|--------------------------------|------------|-------------|--------------------------|-------------------------------------|------------|-----------------------------------|
| Henley 2010[11]         | USA      | Retrospective, National registry| 2004–2006  | National Program of Cancer Registries and SEER database | ICD-O-3: C53 Collaborative Stage classification | Localized, regional, distant • Invasive cervical, breast, or colon/rectum cancers • ≥20 years of age for cervical cancer | 36,076     |
| Subramaniam 2010[41]    | Birmingham, Alabama, USA | Retrospective cohort, Single center institution | 2002–2007  | University-based gynecologic oncology program | NR | I, II, III, IV • Invasive cervical cancer | 430         |
| Garg 2011[10]           | USA      | Retrospective, National registry | 1988–2005  | SEER database 17 registries used | NR FIGO staging | IIA (IIA1, IIA2) • Stage IIA cervical cancer • Primary treatment with RH or RT | 560         |
| McLean 2012[36]         | USA      | Retrospective, Healthcare database | 1992–2007  | SEER-Medicare database | NR | I, II, III, IV • Any stage cervical cancer • Aged 65–100 years | 6718        |
| McLean 2012[35]         | USA      | Case-control, Healthcare database | 1992–2007  | SEER-Medicare database | NR | I, II, III, IV • Diagnosed with cervical cancer after age 70 (n=734) • Matched non-cancer controls (n=2936) | 734         |
| Skaznik-Wikel 2012[22]  | USA      | Retrospective, National registry | 2000–2006  | SEER database 17 registries used | NR FIGO staging | I, II, III, IV • Cervical cancer diagnosis | 18,003      |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|--------------------------|----------|---------------------------------|------------|-------------|--------------------------|-----------------------------------|------------|------------------------------------|
| Ojha 2014[17] Manuscript | USA      | Longitudinal/cohort, National registry | 1973–2010 | SEER database | NR                       | 1 – localized 2/3 – locally advanced 4 – metastatic | NR         | 27 002                             |
|                          |          |                                 |            | Only 9 registries used: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah | SEER summary staging |                       |                       |                                      |
|                          |          |                                 |            | SEER-PAYA cancer survivors’ cohort |                       |                       |                       |                                      |
|                         |          |                                 |            | SEER database | I, II, III, IV | **PAYA**: females diagnosed with any cancer before age 30 years, had survived ≥5 years post-diagnosis, and were later diagnosed with invasive cervical cancer (n=46) Females in the general population aged ≤56 years at primary cervical cancer diagnosis (n=26,956) |                       |                                      |
| Machida 2018[14] Manuscript | USA      | Retrospective cohort, National registry | 1973–2013 | SEER database | ICD-O-3 and WHO classifications (histology) TNM: AJCC 7th ed. staging | I, II, III, IV |                       | 87 151                             |
|                         |          |                                 |            | SEER database |                       |                       |                       |                                      |
| Zahnd 2018[29] Manuscript | USA      | Retrospective cohort, National registry | 2009–2013 | North American Association of Central Cancer Registries | NR | Localized and distant | All stageable cancer types combined HPV-associated cancers Tobacco-associated cancers | NR |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|-------------------------|----------|--------------------------------|------------|-------------|--------------------------|-----------------------------------|------------|----------------------------------|
| Hou 2019[12] Manuscript | USA      | Retrospective cohort, National registry | 1988–2011 | SEER database | ICD-O-3: C53.0-53.9 FIGO staging | I, II, III, IV | White and Asian-American patients with cervical cancer | 58 780 |

- Individual cancers with screening recommendation from the United States Preventive Services Task Force and has current recommendations (colorectal, female breast, cervical, and lung)
- Cancers for which screening was recommended for most of the study period (prostate)
- Cancers with insufficient evidence for recommended screening but for which screening may be performed regularly in clinical practice (skin and oral)
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|--------------------------|----------|---------------------------------|------------|-------------|--------------------------|------------------------------------|------------|-----------------------------------|
| Bruegl 2020[5] Manuscript | Idaho, Oregon, Washington, USA | Retrospective cohort, Regional registry | 1996–2016 | Cancer Data Registry of Idaho, Oregon State Cancer Registry, Washington State Cancer Registry | ICD-O-3: C53.0-53.9 NR | Localized, regional, distant | • Non-Hispanic White and American Indian/Alaskan Native women diagnosed with a gynecological cancer | 7222 |
| Tian 2020[24] Manuscript | USA | Retrospective cohort, National registry | 2010–2015 | SEER database 18 registries used | NR FIGO staging | IB2–IVA | • Cervical cancer stages IB2 to IVA • Pathological biopsy confirmed SCC and AC • No distant metastases • Aged 20–69 years | 4131 |
| Mahmud 2011[15] Manuscript | Saskatchewan, Canada | Retrospective cohort, Regional registry | 1987–2001 | Provincial cancer registry-Saskatchewan | NR FIGO staging | I, II, III, IV | • Cervical cancer diagnosis | 714 |
| Popadiuk 2010[38] Congress abstract | Newfoundland, Canada | Retrospective cohort, Regional registry | 1992–2008 | Newfoundland Cancer Registry | NR | IA, IB, IIB, IVA | • Invasive cervical cancer • Aged 19–29 years | 37 |
| Carmo 2011[6] Manuscript | Rio de Janeiro, Brazil | Retrospective cohort, Single center institution | 1999–2004 | Brazilian National Cancer Institute | NR FIGO staging | I, II, III, IV | • Cervical cancer diagnosis | 3341 |
| Rodrigues 2018[39] Congress abstract | Brazil | Prospective, Multiple institutions | 2016–2017 | 16 sites, representing 5 Brazilian regions | NR | I, II, III, IV | • Invasive cervical cancer • Aged ≥18 years | 631 |
| Possati-Resende 2018[18] Manuscript | Barretos, Brazil | Retrospective cohort, Single center institution | 2003–2015 | Prevention Institute at Barretos Cancer Hospital | NR | I, II, III, IV | • Cervical cancer diagnosis | NR |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|-------------------------|----------|---------------------------------|------------|-------------|--------------------------|-----------------------------------|------------|----------------------------------|
| Warner 2018[27] Manuscript | Trinidad and Tobago | Retrospective cohort, National registry | 1995–2009 | Dr. Elizabeth Quamina Cancer Registry (aka National Cancer Registry of Trinidad and Tobago) | ICD-10: C53 NR | Localized, regional, distant | • Any cancer diagnosis | 1812 |
| Nathani 2012[37] Congress abstract | Bradford, UK | Retrospective cohort, Single center institution | 2007–2011 | Bradford Royal Infirmary database | NR | IA1, IA2, IB1, III | • Cervical cancer diagnosis • Aged 19–30 years | 19 |
| Garry 2018[31] Congress abstract | Dublin, Ireland | Retrospective cohort, Single center institution | 2006–2015 | Electronic case report forms from a tertiary oncology center | NR FIGO staging | IA, IB, II, III, IV | • Cervical cancer diagnosis • Aged ≥60 years | 119 |
| Lorin 2015[13] Manuscript | Côte-d’Or, France | Retrospective cohort, Regional registry | 1998–2010 | Côte d’Or gynecological registry | NR FIGO staging | I, II, III, IV | • Invasive cervical cancer | 311 |
| Rottmann 2020[40] Congress abstract + poster | Upper Bavaria, Germany | Retrospective cohort, Regional registry | 2007–2016 | Munich Cancer Registry | NR | IA1–IV, M1 | • Cervical cancer diagnosis | 2291 |
| Litvinova 2017[34] Congress abstract | Minsk City, Belarus | Retrospective cohort, National registry | 2012–2016 | National Cancer Registry | NR | IIB, III, IVA | • Unresectable cervical cancer diagnosis • Only young women discussed for proportions of disease by stage | 324 |
| Samson 2016[19] Manuscript | Bulgaria | Retrospective cohort, National registry | 1993–2013 | Bulgarian National Cancer Registry | ICD-O: C53.0, C53.1, C53.8, and C53.9 | I, II, III, IV | • Cervical cancer diagnosis | 21 737 |
| Ojamaa 2018[16] Manuscript | Estonia | Retrospective cohort, National registry | 1968–2014 | Estonian Cancer Registry | ICD-O-3: C53.0; C53.1, C53.8, and C53.9 | I, II, III, IV | • Invasive cervical cancer | 3403 |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|--------------------------|----------|---------------------------------|------------|-------------|--------------------------|-----------------------------------|------------|-----------------------------------|
| Ulinskas 2013[25]        | Lithuania | Retrospective cohort, National registry | 1990–2004 | Lithuanian cancer registry | TNM (AJCC 7th ed) for staging | I, II, III, IV | Cervical cancer diagnosis | 6680 |
| Kosgei 2018[33]          | Uasin Gishu, Kenya | Retrospective cohort, Regional registry | 2010–2014 | Eldoret Cancer Registry | NR | I, II, III, IV | Cervical cancer diagnosis | 265 |
| Bouchbika 2013[4]        | Casablanca, Morocco | Retrospective cohort, Regional registry | 2005–2007 | Greater Casablanca Registry | ICD-O-3, converted to ICD-10: C53 | Localized, regional, distant | Any cancer diagnosis | 816 |
| Elmajjaoui 2016[9]       | Morocco | Retrospective cohort, Multiple institutions | 2006 | National Institute of Oncology, Mohammed V Hospital, Rabat Cheikh Khalifa Ibn Zaid Hospital, Université Mohammed VI des Sciences de la Santé, Casablanca | NR | I, II, III, IV | Invasive cervical cancer | 646 |
| Somdyala 2020[23]       | Eastern Cape Province, South Africa | Retrospective cohort, Regional registry | 1998–2012 | Eastern Cape Cancer Registry | ICD-O: C53.0–C53.9 | I, II, III, IV | Cervical cancer diagnosis | 1315 |
| Sharkas 2017[20]        | Jordan | Retrospective cohort, National registry | 2000–2013 | Jordan Cancer Registry | ICD-10: C53 | Localized, regional, distant | Cervical cancer diagnosis | 591 |
| Kaidarova 2018[32]      | Kazakhstan | Retrospective cohort, National registry | 2012 | Kazakhstan Cancer Registry | NR | IA, IB, IIA, IIB, III | Cervical cancer diagnosis | 1641 |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|--------------------------|----------|---------------------------------|------------|-------------|-------------------------|------------------------------------|------------|------------------------------------|
| Alkhalawi 2019[3]        | Gulf countries | Retrospective cohort, Multinational registry | 1998–2012 | Gulf Centre for Cancer Control and Prevention Database | ICD-O-3: C53.0, C53.2, C53.8, C53.9 SEER summary staging | Localized, regional, distant | • Invasive cervical cancer | 2332 |
| Agarwal 2012[2]          | Delhi, India | Retrospective cohort, Single center institution | 2000–2009 | Guru Teg Bahadur Hospital | NR FIGO staging | I, II, III, IV | • Any primary gynecologic cancer diagnosis | 927 |
| Shruthi 2014[21]         | Kolar, India | Retrospective cohort, Single center institution | NR 1-year period | Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research | NR TNM staging | I, II, III, IV | • Cervical cancer diagnosis | 199 |
| Wang 2015[26]            | Beijing, China | Retrospective cohort, Regional registry | 1993–2008 | Statistics Database of Beijing Cancer Registry | ICD-O FIGO staging | I, II, III, IV | • Cervical cancer diagnosis | 3641 |
| Cheung 2011[7]           | Hong Kong, China | Retrospective cohort, Regional registry | 1997–2006 | Hong Kong Cancer Registry | NR FIGO and TNM staging | I, II, III, IV | • Cervical cancer diagnosis | 4407 |
| Yagi 2019[28]            | Osaka Prefecture, Japan | Retrospective cohort, Regional registry | 1976–2012 | Osaka Cancer Registry | C53, C54, C55 (C55 later sorted to C53 or C54 using a multiple imputation estimation) TNM staging | Localized (T1N0M0), regional lymph nodes (N1), adjacent organs (T2, 3, 4), distant (M1) | • Cervical cancer diagnosis | 25 826 |
| Seol 2014[30]            | Korea | Retrospective cohort, National registry | 1999–2010 (total population) 1999-2004 (with stage information) | Korea Central Cancer Registry | NR FIGO staging | IA1-IvB | • Cervical cancer diagnosis | 49 503 (total population) 19 282 (with stage information) |
| Study / publication type | Location | Study design & data source type | Time-frame | Data source | Classification criteria* | Stages of cervical cancer included | Population | Total patients with cervical cancer |
|-------------------------|----------|---------------------------------|------------|-------------|-------------------------|-----------------------------------|------------|----------------------------------|
| Chiang 2016[8] Manuscript | Taiwan   | Retrospective cohort, National registry | 2002–2012 | Taiwan Cancer Registry | ICD-O-3: C53 TNM staging | I, II, III, IV Any invasive cancer Age ≥15 years | 8238       |                                  |

*Two types of classifications were found in the included studies. Disease coding classification criteria was used to identify patients with cervical cancer in large registries and databases and included different versions of the ICD or ICD-O criteria. The specific codes used to identify cervical cancer patients are also summarized where available. The second classification types found in the included studies were used to determine the stage of disease, and included FIGO, TNM, SEER summary, and Collaborative Stage criteria.

AC, adenocarcinoma; AJCC, American Joint Committee on Cancer; FIGO, International Federation of Gynecology and Obstetrics; HPV, human papillomavirus; ICD-10, International Classification of Diseases, 10th edition; ICD-O, International Classification of Diseases, Oncology; NR, not reported; PAYA, pediatric and young adult cancers; RH, radical hysterectomy; RT, radiotherapy; SCC, squamous cell carcinoma; SEER, Surveillance, Epidemiology, and End Results; TNM, tumor, node, metastasis; USA, United States of America; WHO, World Health Organization.
Supplementary Table 6. Studies reporting incidence by stage of cervical cancer.

| Reference  | Region          | Location / data collection period | N     | Incidence of cervical cancer by stage | Incidence of locally advanced cervical cancer |
|------------|-----------------|-----------------------------------|-------|--------------------------------------|-----------------------------------------------|
| Bruegl 2020[5]a | North America | USA Idaho, Oregon, Washington 1996–2016 | 7222  | Age-standardized rate per 100 000 population | Age-standardized rate per 100 000 population |
|            |                 |                                   |       | American Indian/Alaskan Natives       | American Indian/Alaskan Natives               |
|            |                 |                                   |       | Localized, 4.3                        | Regional, 3.6                                 |
|            |                 |                                   |       | Regional, 3.6                         |                                              |
|            |                 |                                   |       | Distant, 1.8                          | Regional, 3.6                                 |
|            |                 |                                   |       | Unknown, 0.9                          | Regional, 3.6                                 |
|            |                 |                                   |       |                                      |                                              |
| Henley 2010[11] | North America | USA 2004–2006                    | 36,076| Age-standardized rate per 100 000 population | Age-standardized rate per 100 000 population |
|            |                 |                                   |       | Localized, 5.3                        | Regional, 4.0                                 |
|            |                 |                                   |       | Regional, 4.0                         |                                              |
|            |                 |                                   |       | Distant, 1.2                          |                                              |
|            |                 |                                   |       | Unknown, 0.9                          |                                              |
| Zahnd 2018[29]b | North America | USA 2009–2013                    | Not reported | Age-standardized rate per 100 000 population | Not calculable |
|            |                 |                                   |       | Rural                                 |                                              |
|            |                 |                                   |       | Localized, 3.7                        |                                              |
|            |                 |                                   |       | Distant, 1.1                          |                                              |
| McClean 2012[36] | North America | USA 1992–2007                    | 6718  | Women aged 65–100 years, Age-adjusted incidence rate | Women aged 65–100 years, Age-adjusted incidence rate |
|            |                 |                                   |       | Stage I, decreased by 2.4% per year   | Stage III, increased by 2.0% per year         |
Stage III, increased by 2.0% per year

| Litvinova 2017[34] | Europe | Belarus | Incidence per 100 000 female population |
|--------------------|--------|---------|----------------------------------------|
|                    |        | Minsk City 2012–2016 | IIB, decreased from 3.8 to 1.9 |
|                    |        |                     | III, decreased from 3.2 to 2.3 |
|                    |        |                     | IVA, increased from 0.4 to 0.7 |

The Bruegl 2020 study only included patients who were American Indian/Alaskan Natives or non-Hispanic White.

In the Zahnd 2018 study, only the incidence of localized and distant cervical cancer was compared in urban and rural areas; neither of these stages was considered locally advanced disease according to our method of estimation (ie, only “regional” disease is considered).

USA, United States of America.
| Section and Topic | Item # | PRISMA Checklist Item | Location where item is reported |
|-------------------|--------|-----------------------|---------------------------------|
| **TITLE**         |        |                       |                                 |
| Title             | 1      | Identify the report as a systematic review. | Page 1                          |
| **ABSTRACT**      |        |                       |                                 |
| Abstract          | 2      | See the PRISMA 2020 for Abstracts checklist. | Page 3                          |
| **INTRODUCTION**  |        |                       |                                 |
| Rationale         | 3      | Describe the rationale for the review in the context of existing knowledge. | Page 5                          |
| Objectives        | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 5                          |
| **METHODS**       |        |                       |                                 |
| Eligibility criteria | 5    | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Pages 5-6, Supplementary Appendix pages 1-3 |
| Information sources | 6    | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 5, Supplementary Appendix pages 1-3 |
| Search strategy   | 7      | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supplementary Appendix pages 1-3 |
| Selection process | 8      | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 6                          |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 6                          |
| Data items        | 10a    | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Supplementary Appendix page 5 |
|                  | 10b    | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Supplementary Appendix page 5 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | N/A |
| Effect measures   | 12     | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | N/A |
| Synthesis methods | 13a    | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Supplementary Appendix page 5 |
| Section and Topic | Item # | PRISMA Checklist item | Location where item is reported |
|-------------------|--------|-----------------------|---------------------------------|
| 13b               | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Page 6-7, Supplementary Appendix page 5-6 |
| 13c               | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Page 6-7, Supplementary Appendix page 5-6 |
| 13d               | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 6-7, Supplementary Appendix page 5-6 |
| 13e               | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Supplementary Appendix page 8 |
| 13f               | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | N/A |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | N/A |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | N/A |
| RESULTS           | Study selection | 16a Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 7 and Figure 1 |
|                   |                    | 16b Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | N/A |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Pages 7-8, Supplementary figure 1, Supplementary figures 3, 4, 5 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | N/A |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Pages 8-11, Figure 2, Tables 1-3, Supplementary Figure 2 |
| Section and Topic | Item # | PRISMA Checklist item | Location where item is reported |
|------------------|--------|-----------------------|---------------------------------|
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Pages 8-11, Figure 2, Tables 1-3 |
|                  | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Pages 8-11, Figure 2, Tables 1-3, Supplementary Figure 2 |
|                  | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Page 9, Supplementary Figure 2 |
|                  | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | N/A |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | N/A |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | N/A |
| DISCUSSION | 23a | Provide a general interpretation of the results in the context of other evidence. | Pages 11-12 |
|            | 23b | Discuss any limitations of the evidence included in the review. | Page 12-13 |
|            | 23c | Discuss any limitations of the review processes used. | Page 12-13 |
|            | 23d | Discuss implications of the results for practice, policy, and future research. | Page 13 |
| OTHER INFORMATION | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 6 |
| Registration and protocol | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 6, Supplementary Appendix page 1 |
|            | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | N/A |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 15 |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 15 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | N/A |

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: [http://www.prisma-statement.org/](http://www.prisma-statement.org/)

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| Page | Reference |
|------|-----------|
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