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Title page

**European Society of Cardiology quality indicators for the prevention and management of cancer therapy-related cardiovascular toxicity in cancer treatment**

Developed in collaboration with the Heart Failure Association of the European Society of Cardiology.

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Abstract and keywords

**Abstract**

**Aims:** To develop quality indicators (QIs) for the evaluation of the prevention and management of cancer therapy-related cardiovascular toxicity.

**Methods and results:** We followed the European Society of Cardiology (ESC) methodology for QI development which comprises (i) identifying the key domains of care for the prevention and management of cancer therapy-related cardiovascular toxicity in patients on cancer treatment, (ii) performing a systematic review of the literature to develop candidate QIs, and (iii) selecting of the final set of QIs using a modified Delphi process. Work was undertaken in parallel with the writing of the 2022 ESC Guidelines on Cardio-Oncology and in collaboration with the European Haematology Association, the European Society for Therapeutic Radiology and Oncology and the International Cardio-Oncology Society. In total, 5 main and 9 secondary QIs were selected across five domains of care: (i) Structural framework, (ii) Baseline cardiovascular risk assessment, (iii) Cancer therapy related cardiovascular toxicity, (iv) Predictors of outcomes, and (v) Monitoring of cardiovascular complications during cancer therapy.

**Conclusion:** We present the ESC Cardio-Oncology QIs with their development process and provide an overview of the scientific rationale for their selection. These indicators are aimed at quantifying and improving the adherence to guideline-recommended clinical practice and improving patient outcomes.

**Keywords:** Quality indicators, cardio-oncology, assessment, treatment, cancer therapy-related cardiovascular toxicity, outcomes

**European Society of Cardiology quality indicators for the prevention and management of cancer  
therapy-related cardiovascular toxicity in patients with cancer.**

Developed in collaboration with the Heart Failure Association of the European Society of Cardiology.

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## Introduction

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6 Cardio-oncology has emerged in recent years as a distinct entity that requires specialist expertise  
7  
8 different to that provided by cardiology and/or oncology services. The complexity of the acute  
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10 cardiovascular presentations from cytotoxic, targeted and immunotherapies necessitates co-  
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12 operation between various specialists to ensure holistic delivery of care that aims to identify and  
13  
14 mitigate the risks of cardiovascular complications during and after cancer therapy.<sup>1-3</sup> The greater  
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16 numbers of cancers that are treated with cardiotoxic therapies, alongside the better screening for  
17  
18 cancer therapy-related cardiovascular toxicity (CTR-CVT), create a need to develop tools to measure  
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20 the quality of cardio-oncology care and capture outcomes.  
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28 The European Society of Cardiology (ESC) strives to develop suites of quality indicators (QIs) for its  
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30 Clinical Practice Guidelines to facilitate the implementation of these evidenced-based guidelines and  
31  
32 enable the quantification of the quality-of-care delivery.<sup>4</sup> Thus, in parallel with the writing of the  
33  
34 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology  
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36 Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the  
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38 International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the  
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40 European Society of Cardiology (ESC),<sup>5</sup> and in collaboration with the European Haematology  
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42 Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the  
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44 International Cardio-Oncology Society (IC-OS), a group of domain experts in cardio-oncology was  
45  
46 formed to construct QIs that span the breadth of cardio-oncology care and capture the key aspects  
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48 of its care delivery and outcomes that are relevant to patients.  
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## Methods

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1 We used the ESC methodology for the development of QIs which comprises the following steps: (i)  
2 identifying key domains of care for the prevention and management of CTR-CVT in patients on  
3 cancer treatment, (ii) undertaking a systematic literature review to develop candidate QIs, and (iii)  
4 selecting of the final set of QIs using a modified Delphi process.<sup>4</sup> Structural QIs are the measures that  
5 evaluate care quality at institutional level, while process QIs are the measures that evaluate care  
6 quality at the patient level. Furthermore, QIs allow the capture of relevant outcomes that have an  
7 association with the quality-of-care delivery.  
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### 10 11 12 13 14 15 16 17 18 **Members of the development group**

19 The development group comprised Task Force members of the 2022 Guidelines on Cardio-Oncology,  
20 members of the ESC QI Committee, nominees from the Council of Cardio-Oncology (CO-Council) and  
21 the ESC Patient Forum, as well as international experts in Cardio-oncology field including  
22 representatives from IC-OS, EHA and ESTRO.  
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### 31 32 **Target population and domains of care**

33 The group initially defined the target population for whom the QIs will apply and the key domains of  
34 cardio-oncology care which encompass the developed indicators. The target population was defined  
35 as patients with an established cardiovascular disease prior to commencing cancer treatment and  
36 those who were at high risk of cardiovascular complications during or after receiving cancer  
37 treatment.  
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48 For each domain, the measurement period was specified to clarify the timepoint at which each QI is  
49 measured. These timepoints extended from the period before starting cancer treatment (for the  
50 assessment of the cardiovascular toxicity risks) to the long-term follow up after the completion of  
51 cancer therapy (for the identification of potential cardiovascular consequences of cancer treatment).  
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1 Further specifications were provided for individual QIs including a numerator, which is the criteria by  
2 which the QI is accomplished and a denominator, which is the eligibility criteria for the QIs. Given  
3  
4 that structural QIs are binary measurements of the availability of certain services, only numerators  
5  
6 are defined for the structural QIs. Both main and secondary QIs were developed based on the voting  
7  
8 scores on the validity and the feasibility of the candidate QIs.  
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## 11 12 13 14 15 **Systematic Review methods**

### 16 17 18 19 20 21 **Search Strategy**

22 We conducted a systematic review of published literature using the Preferred Reporting for  
23  
24 Systematic Review and Meta-Analyses (PRISMA) statement.<sup>6</sup> A search strategy was developed using  
25  
26 keywords and medical subject headings that included Cardio-toxicity, Cardio-oncology, Oncology,  
27  
28 Haemato-oncology, Quality indicators and Outcome measures and medical subject headings such as  
29  
30 'Cancer', 'oncological treatment', 'risk factor' and 'quality indicator' (**Supplementary Material**  
31  
32 **online- Table 1**).  
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40 We developed separate search strategies for MEDLINE and Embase via OVID® using an iterative  
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42 process incorporating result of hand searching from reference lists and grey literature.  
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### 49 **Eligibility criteria**

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52 Studies included were those that evaluated the cardiovascular consequences of cancer therapy in  
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54 adult patients (>18 years old) who have been treated with at least one cardiotoxic treatment at any  
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56 point including chemotherapy, radiotherapy and immunotherapy. We included randomised  
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1 controlled trials and observational studies as well as consensus documents that are published in  
2 English between 01 January 2015 and 10 September 2021. We excluded systematic reviews, meta-  
3 analysis, conference abstracts and case reports. Studies with no defined intervention or outcome  
4 measures were also excluded.  
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## 10 **Study selection**

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16 Endnote X9 (Clarivate Analytics, London, UK) was used to manage references and remove duplicates.  
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18 Two authors (EB and GL) independently examined the abstracts of the retrieved studies which were  
19 assessed against the eligibility criteria. Disagreements were resolved through a third reviewer (SA)  
20 and full text article review.  
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## 29 **Data extraction**

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35 For each included study, the systematic review team extracted the definitions of the target  
36 population, intervention(s), comparison(s) and outcome measure(s). Data were collated using an  
37 Excel spreadsheet.  
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## 45 **Data synthesis**

### 46 **Modified Delphi process**

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52 The modified Delphi approach was used to evaluate the candidate QIs derived from the literature  
53 review.<sup>4</sup> The members of the group were made aware of the ESC criteria for QI development to  
54 standardize the voting process, and each candidate QI was ranked by each panellist on a 9-point  
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1 ordinal scale for both validity and feasibility using an online questionnaire (See supplement for  
2 criteria table). Two rounds of voting were conducted using the Delphi process with a series of virtual  
3 meetings between April 2021 until July 2022 to discuss the voting results and address concerns and  
4 queries.  
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### 10 11 12 13 14 15 16 17 18 19 **Analysis of voting results**

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22 The 9-point ordinal scale used for voting implied that ratings of 1–3 meant that the QI is not  
23 valid/feasible; ratings of 4–6 meant that the QI is of an uncertain validity/feasible; and ratings of 7–9  
24 meant that the QI is valid/feasible. For each candidate QI, the median and the mean deviation from  
25 the median were calculated to evaluate the central tendency and the dispersion of the votes.  
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27 Indicators, with median scores  $\geq 7$  for validity,  $\geq 4$  for feasibility, and with minimal dispersion, were  
28 included in the final set of QIs. The development group was asked to modify the phrasing of the  
29 candidate QIs to reach consensus on the inclusion of the indicator in the final set.  
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### 43 **Results**

#### 44 45 46 47 48 **Systematic review results**

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55 The domains of care identified were: (i) Structural framework, (ii) Baseline cardiovascular risk  
56 assessment, (iii) CTR-CVT, (iv) Predictors of outcomes and (v) Monitoring of cardiovascular complications  
57 during cancer therapy. The literature search retrieved 1081 articles, of which 64 met the inclusion  
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1 criteria (see **Figure 1**). These studies were used to extract 33 candidate QIs which were included in  
2 the first voting round. In total 5 (15%) of the candidate QIs were included as main QIs. Of the  
3 remaining indicators, 19 (58%) were excluded and 9 (27%) were considered in a second Delphi round  
4 and included as secondary QIs (see **Table 1**).  
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### 18 **Quality indicators**

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### 28 **Domain 1: Structural Framework**

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31 Two QIs have been selected in this domain. The first is a main QIs that captures the need for  
32 dedicated healthcare professionals for cardio-oncology patients (**Main 1**). The second defines the  
33 appropriate composition of a multidisciplinary team in this setting (**Secondary 1**), which should  
34 consist of at least an oncologist, cardiologist and a specialist nurse. The team should ideally have  
35 access to other services such as a radiologist, surgeon, haematologist, palliative care expert,  
36 physiotherapist, pharmacist, psychologist, general practitioner, and dietitian. Given the  
37 implementation of this QI may be challenging in some healthcare centres, it was included as a  
38 secondary one.  
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### 54 **Domain 2: Baseline cardiovascular risk assessment**

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57 The QIs under this domain relate to the importance of a comprehensive cardiovascular assessment  
58 prior to commencing cancer treatment. That is, the documentation of previous cardiovascular  
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1 history (for instance, history or clinical evidence of venous thrombo-embolism) (**Main 2.1**), as well as  
2 the identification of modifiable risk factors associated with cardiovascular complications such as  
3 diabetes and hypertension (**Main 2.2**). The other QI in this domain relates to the need to ensure that  
4 shared decision-making is discussed with the patient when determining the treatment strategy  
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9 (**Main 2.3**). In addition, the assessment of cardiovascular risk by performing a comprehensive clinical  
10 assessment may identify patients at higher risk and highlight strategies to mitigate this risk  
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14 (**Secondary 2.1**).  
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### 23 **Domain 3: Cancer therapy related cardiovascular toxicity (CTR-CVT)**

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28 Given CTR-CVT is associated with cardiovascular mortality during and after cancer treatment,<sup>7,8</sup>  
29 capturing the annual rate of hospitalisation due to CTR-CVT has been selected as a main QIs (**Main**  
30 **3**). After starting cancer treatment, it is important to perform a comprehensive cardiovascular  
31 assessment for patients developing signs and/or symptoms of CTR-CVT (**Secondary 3.2**). However,  
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33 CTR-CVT can sometimes be asymptomatic and at various time points. As such, two QIs have been  
34 selected to ensure appropriate follow up for high-risk individuals (**Secondary 3.3**) and within 3  
35 months from the completion of cancer treatment (**Secondary 3.3**).<sup>5,9</sup>  
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### 49 **Domain 4: Predictors of outcomes**

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51 Heart failure and in particular heart failure with reduced Ejection Fraction (HFrEF) is a well-  
52 documented complication of cancer treatment and patients should be closely monitored in the first  
53 year following completion of treatment.<sup>7,10</sup> Early diagnosis is an important measure along with  
54 appropriate management with guideline-directed medical therapy including beta-blockers, renin-  
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1 angiotensin-aldosterone inhibitors, and sodium glucose co-transporter2 inhibitors (**Secondary 4.1**).<sup>11</sup>

2 This QI has been aligned with the ESC guidelines for HF and the respective QI for HFrEF.<sup>12,13</sup> The  
3  
4 second QI in this domain is a more specific indicator that pertains to reducing the risk of  
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6 anthracycline and HER2 therapies by commencing prognostic treatment for moderate or severe  
7  
8 asymptomatic CTRCD (**Secondary 4.2**).  
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## 11 12 13 14 15 16 **Domain 5: Monitoring of cardiovascular complications during cancer therapy**

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18 Whilst different types of cancer treatment may have an impact on the cardiovascular system, certain  
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20 treatments are known to be more toxic than others.<sup>14</sup> As such, close monitoring for patients on HER2  
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22 therapies with a structured assessment to their side-effect profile may help identify and address  
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24 these adverse events early (**Secondary 5.1**). For those on tyrosine kinase inhibitors, the assessment  
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26 of blood pressure at every visit (**Secondary 5.2**) may have a role in recognising the potential  
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28 implications of this therapy.<sup>15</sup>  
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## 36 **Discussion**

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42 This document presents the ESC QIs for cardio-oncology and highlights the breadth of this field  
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44 which span across various clinical settings. These indicators have been developed in parallel with the  
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46 writing of the 2022 ESC guidelines on cardio-oncology and using the ESC methodology.<sup>4,5</sup> We have  
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48 identified 5 domains of care for cardio-oncology and selected 5 main and 9 secondary QIs across  
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50 these domains. They include structural indicators of care quality such as the availability of a multi-  
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52 disciplinary team, the benefits of which have been previously highlighted<sup>16</sup>, as well as process and  
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54 outcome QIs, with particular focus on shared decision-making as a key factor for successful  
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57 treatment.<sup>17</sup>  
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1 Cardio-oncology is expanding with increasing patient population and complexity, creating a need to  
2 standardize the methods by which care delivery is measured and outcomes captured given the  
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4 existing variation and the room for improvement.<sup>18</sup> Calls have been made to establish designated  
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6 cardio-oncology centres across Europe in line with the growing number of patients in need for  
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8 specialists' input and multidisciplinary management plans.<sup>19</sup> Patients on cancer treatment are at a  
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10 higher risk for developing cardiovascular complications, and a number of strategies may help  
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12 mitigate these risks. As such, we combined existing evidence with expert consensus to develop a  
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14 suite of QIs for patients considered for or receiving cancer treatment.  
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19 We are not aware of any previous initiative that aimed to develop internationally endorsed set of  
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21 QIs for cardio-oncology patients. The widespread implementation of these indicators enables the  
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23 conduction of meaningful comparative analyses across different centres and regions to highlight  
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25 disparities and standardise patient care. Besides, the integration of these QIs into a system of data  
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27 collection may facilitate the establishment of a unified registry for cardio-oncology that may help  
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29 generate evidence and monitor patterns of care delivery over time.  
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34 Although there are obvious strengths to the study, there are some limitations that need to be  
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36 acknowledged. The final QIs were determined by expert opinion via the Delphi process and  
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38 therefore reflects the views of the Working Group members. However, this was preceded by a  
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40 systematic literature review and the Delphi method used to independently record experts' votes to  
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42 select the QIs and also we applied the ESC criteria to standardise the voting process. The feasibility  
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44 of the QIs is an issue and relates to organisational barriers and limited resources in clinical practice  
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46 across Europe. We acknowledge that there is a variance of resources and the QIs may not be feasible  
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48 currently but can be used to standardise care and improve patient services in the future.  
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## 53 **Conclusion**

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55 We present the ESC Cardio-Oncology QIs along with the development process and provide an  
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57 overview of the scientific rationale for their selection. These indicators are aimed at quantifying and  
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1 improving adherence to guideline-recommended clinical practice and improving patient outcomes  
2 with particular focus on the cardio-toxic effects of cancer regimens and their effect on the  
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4 cardiovascular system.  
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7 **Conflict of Interest:**  
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10 G Lee: Grants: Horizon 2020.  
11

12 S Aktaa- Educational events (Wondr medical), European Society of Cardiology.  
13

14 E. Baker- Health Education England Post Doctoral Research Fellowship  
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16 C Gale: BHF, NIHR, Horizon 2020, Daichii Sankyo NHS Joint Working Party, Abbott Diabetes, BMS/Pfizer.  
17 Honoraria: Astra Zeneca, Boston Scientific, Menarini, Raisio Group, Wondr Medical, Zydus. Boards: Amgen,  
18 Bayer, BMS, Boehringer Ingelheim, Chiesi Ltd, Daichii Sankyo, Menarini Diagnostics UK, iRhythm. Leadership:  
19 NICE indicator advisory committee, Deputy Editor: EHJ Quality of Care and Clinical Outcomes, Oxford  
20 University Press, Chair ESC Quality Indicator Committee.  
21

22 G Gulati: Honoraria: AstraZeneca, BMS, Roche, Orion Pharma, Novartis. Leadership: Board member Norwegian  
23 Cardiology Society  
24

25 R. Asteggiano- Royalties from Springer.  
26

27 S Szmit: Amgen, Angelini, Astra Zeneca, BMS, Bayer, Gilead, Pfizer  
28

29 A Cohen Solal: Vifor, Novartis, MSD, Bayer, Sanofi, Boehringer Ingelheim, Amgen, Servier  
30

31 P Garrdio: Honoraria: Advisory Role: Abbvie, Amgen, Astra Zeneca, Bayer, BMS, Daichi, GSK, Janssen, Lilly,  
32 MSD, Novartis, Pfizer, Roche, Takeda, Sanofi. Speaker: Janssen, MSD, Novartis, Medscape, Takeda, TouchTime.  
33 Support attending meetings: Astra Zeneca, BMS. Leadership: ESMO Council member  
34  
35

36 A Sverdllov: Future Leader Fellowships (Awards IDs 101918 & 106025). Medical Research Future Fund  
37 (Australia). NSW Department of Health, RACE Oncology. Honorarora: Celgene Pty Ltd, BMS, Novarits, BMS,  
38 AstraZeneca, Boehringer Ingelheim. Leadership: ESC, Joint Cardiac Society of Australia and New Zealand and  
39 Clinical Oncology Society of Australia Cardio-Oncology Working Group, Global Cardio-Oncology Registry.  
40

41 CG Tocchetti: Italian Ministero della Salute RF 2016, VivaLyfe, Univers Formazione, Menarini, Amgen. Patients:  
42 P75NTR.  
43

44 P Zamorano: Honoraria: Novo Nordisk, Novaris, Philips, Bayer, Medtronic, Amgen.  
45

46 Z Lakobishvili: Grants: Novo-Nordisk. Consulting fees: Bayer, Pfizer, Boehringer Ingelheim. Honoraria: Pfizer,  
47 Astra Zeneca.  
48

49 R Pudil: Grants: COOPERATIO, AZV NV19-02-00297. Honoraria: Novartis, Boehringer Ingelheim.  
50

51 L Badimon: Grants: AstraZeneca, EU H2020, EU IMI, EU Sudoe. Honoraria: Amarin, Novartis, Pfizer. Patients:  
52 gly-APOJ, IVSTATINa, DJ1F. Data Safety Monitoring: Novartis, Novo Nordisk, Pfizer, Sanofi, International Aspirin  
53 Foundation, FICYE. Leadership: ESC.  
54

55 A Kirby: President of European Society of Radiation Therapy and Oncology  
56

57 D Farmakis: Consulting fees: Abbott, Bayer, Boehringer-Ingelheim, Leo  
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59 G Curigliano- Grants: Merck, Astra Zeneca. Consulting fees: Roche, BMS, Novartis, Lily, Pfizer, Seagen, Ellipsis,  
60 Gilead, Merck, Celcuity, Daichii Sankyo. Leadership: ESMO Council  
61

62 R Stephens. Honoraria: for being a cancer patient advocate working as a volunteer in cancer research  
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2 advisory board or consultancy fees and/or research grants from Pfizer, Novartis, Servier, Astra Zeneca, Bristol  
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4 Pharmaceuticals, Boehringer Ingelheim, Akcea Therapeutics, Myocardial Solutions, iOWNA Health and  
5 Heartfelt Technologies Ltd.

6 T Lopez-Fernandes: Philips, Janssem, Incyte  
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10 **Data Availability:** The data underlying this article are available and in the online supplementary material.  
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**Table 1: ESC Cardio-oncology quality indicators for the management of patients with cancer or cancer survivors**

**DOMAIN 1: Structural framework**

**Main 1:** Healthcare centres providing cancer treatment with available resources for patient education including dedicated health care professionals to optimise patient ability to manage self-care during and after treatment.

**Numerator:** centres providing cancer treatment with available resources for patient education including dedicated health care professionals to optimise patient ability to manage self-care during and after treatment.

**Secondary 1:** Healthcare centres providing cancer treatment with an available MDT for cardio-oncology. MDT should comprise as a minimum an oncologist\*\*, a cardiologist and a specialist nurse\*.

**Numerator:** centres providing cancer treatment with an available MDT for cardio-oncology.

**DOMAIN 2: Baseline cardiovascular risk assessment**

**Main 2.1:** Proportion of patients considered for cancer treatment<sup>§</sup> who are evaluated for prior history/clinical evidence of cardiovascular condition (including heart failure, coronary artery disease, arrhythmias, history of pulmonary embolism or deep vein thrombosis) prior to treatment

**Numerator:** patients considered for cancer treatment who are evaluated for a prior history of cardiovascular condition (including heart failure, coronary artery disease, arrhythmias, pulmonary embolism or deep vein thrombosis) prior to treatment

**Denominator:** patients considered for cancer treatment

**Measurement period:** prior to treatment

**Main 2.2:** Proportion of patients considered for cancer treatment who have their modifiable cardiovascular risk factors (Diabetes Mellitus, Hypertension etc) identified prior to treatment

**Numerator:** patients considered for cancer treatment who have their modifiable cardiovascular risk factors (Diabetes Mellitus, Hypertension, etc) identified

**Denominator:** patients considered for cancer treatment

**Measurement period:** prior to treatment

**Main 2.3:** Proportion of patients considered for cancer treatment who have been engaged in shared decision-making when deciding treatment strategy

**Numerator:** patients considered for cancer treatment who have been engaged in shared decision-making when deciding treatment strategy

**Denominator:** patients considered for cancer treatment

**Measurement period:** prior to treatment

**Secondary 2.1:** Proportion of patients considered for cardiotoxic cancer treatment<sup>#</sup> who have an assessment of their cardiovascular risk using diagnostic tools

1 **Numerator:** patients considered for cardiotoxic cancer treatment who have an assessment  
2 of their cardiovascular risk assessment using diagnostic tools

3 **Denominator:** patients considered for cancer treatment

4 **Measurement period:** prior to treatment

5 **DOMAIN 3: Cancer Therapy Related Cardiovascular Toxicity**

6  
7 **Main 3:** Annual rate of hospitalisation due to cancer therapy related cardiovascular  
8 toxicity

9  
10 **Numerator:** patients on or have recently been on cancer treatment who are hospitalised  
11 due to cancer therapy related cardiovascular toxicity

12 **Denominator:** patients on or have recently been on cancer treatment

13 **Measurement period:** during or after treatment

14 **Secondary 3.1:** Proportion of patients with symptoms and/or signs of cancer therapy  
15 related cardiovascular toxicity during/after cardiotoxic cancer treatment who have a  
16 cardiovascular assessment

17  
18 **Numerator:** patients with symptoms and/or signs of cancer therapy related cardiovascular  
19 toxicity during/after cardiotoxic cancer treatment who have a cardiovascular assessment

20 **Denominator:** patients with symptoms of cancer treatment-related toxicity during/after  
21 cardiotoxic cancer treatment

22 **Measurement period:** during and after treatment

23 **Secondary 3.2:** Proportion of patients at high risk<sup>&</sup> for cancer therapy related  
24 cardiovascular toxicity who are followed up after the completion of cardiotoxic cancer  
25 treatment to evaluate for adverse cardiac events

26 **Numerator:** patients at high risk<sup>&</sup> for cancer therapy related cardiovascular toxicity who  
27 are followed up after the completion of cardiotoxic cancer treatment to evaluate for  
28 adverse cardiac events

29 **Denominator:** patients after the completion of cardiotoxic cancer treatment

30 **Measurement period:** 1 and 5 years after treatment

31 **Secondary 3.3:** Proportion of patients who have a cardiovascular risk assessment 1 year  
32 after the completion of cardiotoxic cancer treatment<sup>#</sup>

33 **Numerator:** patients who have a cardiovascular risk assessment 1 year after the  
34 completion of cardiotoxic cancer treatment<sup>^</sup>

35 **Denominator:** patients within 1 year of the completion of cardiotoxic cancer treatment

36 **Measurement period:** 1 year after treatment

37 **DOMAIN 4: Predictors of outcomes**

38  
39 **Secondary 4.1:** Proportion of patients who develop symptomatic HFrEF during cancer  
40 treatment and are prescribed medications such as beta blockers, ACEI/ARB/ARNI, MRA  
41 and SGLT2 inhibitors

42 **Numerator:** patients who develop HF during cancer treatment and are prescribed beta  
43 blockers, ACEI/ARB/ARNI, MRA and SGLT2 inhibitors

44 **Denominator:** patients who develop HF during cancer treatment

45 **Measurement period:** during and after treatment

46 **Secondary 4.2:** Proportion of patients treated with anthracyclines or HER2 targeted  
47 therapies and develop asymptomatic moderate or severe CTRCD during cancer treatment  
48 who are prescribed beta blockers and/or ACEI/ARB

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1 **Numerator:** patients treated with anthracyclines or HER2 targeted therapies and develop  
2 asymptomatic moderate or severe CTRCD during cancer treatment who are prescribed  
3 beta blockers and/or ACEI/ARB

4 **Denominator:** patients treated with anthracyclines or HER2 targeted therapies and  
5 develop asymptomatic moderate or severe CTRCD during cancer treatment

6 **Measurement period:** during treatment

7 **DOMAIN 5 : Monitoring of cardiovascular complications during cancer therapy**  
8  
9

10  
11 **Secondary 5.1:** Proportion of patients on HER2-targeted therapies who have their  
12 cardiovascular assessment<sup>^</sup> every 3 months during the first year of treatment

13 **Numerator:** patients on HER2-targeted therapies who have their cardiovascular  
14 assessment every 3 months during the first year of treatment

15 **Denominator:** patients on HER2-targeted therapies

16 **Measurement period:** during & after treatment

17  
18 **Secondary 5.2:** Proportion of patients on TKI, including BTKi, who have their blood  
19 pressure assessed at every clinical visit.

20 **Numerator:** Proportion of patients on TKI (including BTKi) who have their blood pressure  
21 assessed at every clinical visit.

22 **Denominator:** patients on TKI (including BTKi)

23 **Measurement period:** during and after treatment  
24  
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28 ABBREVIATIONS: ACEI = angiotensin converting enzymes inhibitors, ARBs = angiotensin receptors blockers,  
29 ARNI = angiotensin receptor neprilysin inhibitor, BTKi = bruton tyrosine kinase inhibitors, CTR-CVT = Cancer  
30 therapy related cardiovascular toxicity DM = diabetes mellitus, DVT = deep venous thrombosis, HCPs =  
31 healthcare professionals, HF = heart failure, HFrEF = heart failure with reduced ejection fraction, HTN =  
32 hypertension, LVSD = left ventricular systolic dysfunction, MDT = multidisciplinary team, MRA =  
33 mineralocorticoid receptor antagonists, PE = pulmonary embolism, SGLT2 = sodium–glucose cotransporter 2  
34 (SGLT2), TKI = tyrosine kinase inhibitors.  
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39 *\*Ideally MDT should also involve a radiologist, surgeon, palliative care expert, physiotherapist,  
40 pharmacist, psychologist, general practitioner, and dietitian.*

41 *&High-risk patients are those with >10% risk of future cardiovascular toxicity according to HFA-ICOS  
42 risk assessment (Lyon AR et al. 2020)*

43 *#Cardiotoxic cancer treatment is defined as any cancer treatment with potential cardiovascular side  
44 effects*

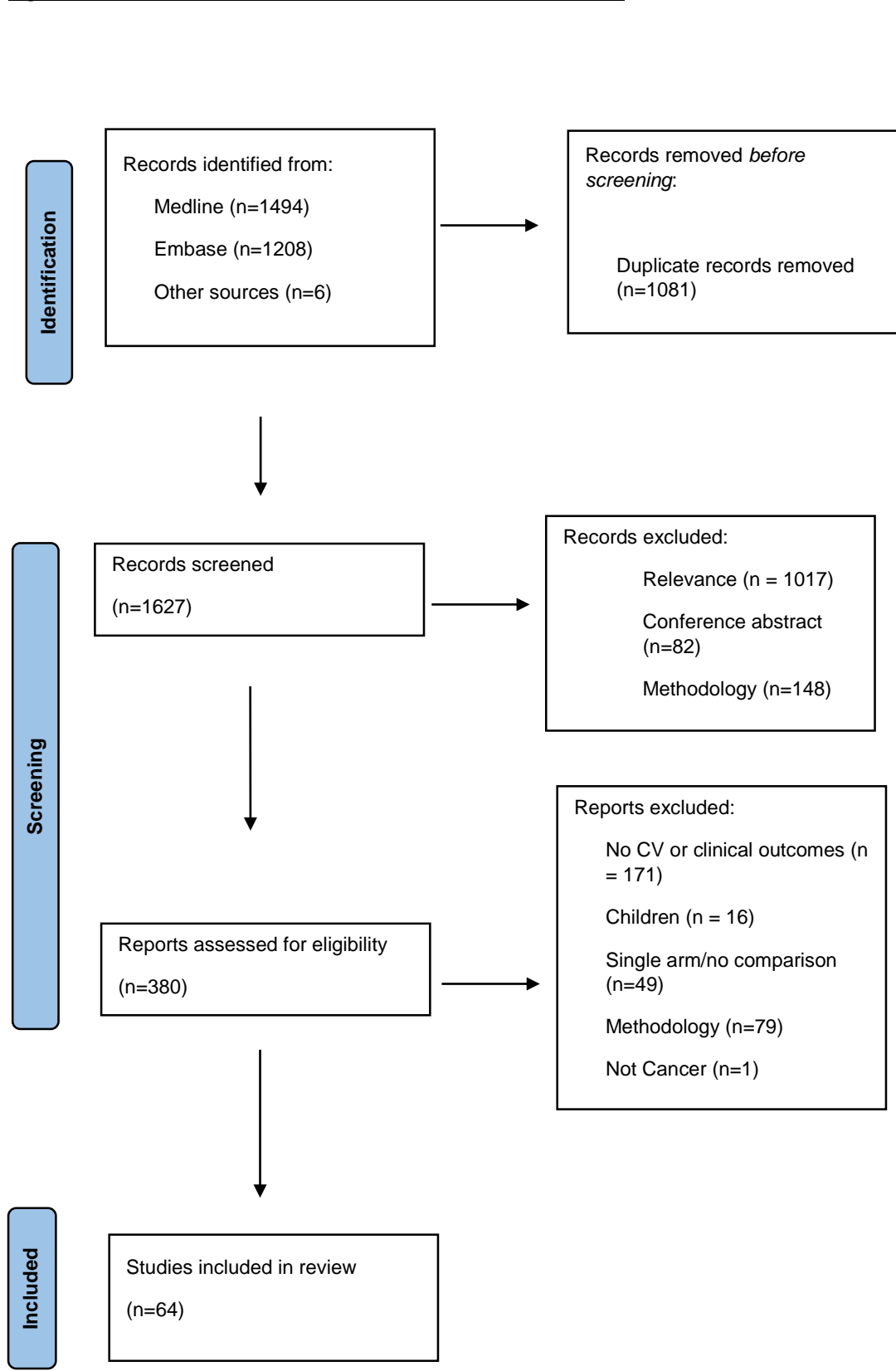
45 *^Assessment includes an echocardiography (at baseline and within 12 months after completing  
46 treatment and include a documentation of LVEF and GLS assessment), cardiac troponins and NPs in  
47 high and very high-risk patients (at baseline, before every anthracycline cycle and 3 and 12 months  
48 after therapy completion).*

49 *\*\*Oncologist includes three specialists: medical oncologist, haematologist and radiation oncologist*  
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*\$ Cancer treatment includes chemotherapy, targeted agents, hormone therapies, immune therapies,  
and radiation therapy*

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**Figure 1: PRISMA Flow Chart for selection of included studies**



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**Supplementary Table 1: Summary of Systematic Search Strategy:**

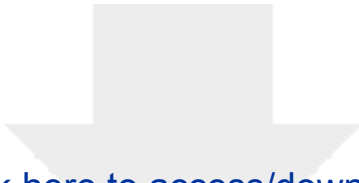
Overview:			
Interface	Ovid		
Databases	Ovid MEDLINE (1946-09/2021)		
	OVID Embase (1996 – 09/2021)		
Date of Search	10/09/2021		
Study Types	Randomised controlled trials		
	Observational Studies		
Limits	English language		
	Publication date (01/2015 – 09/2021)		
	Human participants		
Multi-database search strategy			
Line	Syntaxes	Medline Count	Embase Count
1	Cancer.mp or exp Neoplasms/	4062443	5979401
2	Oncolog*.mp.	192715	433643
3	(Cardi* adj2 Oncolog*).mp.	2054	
4	Exp Hematologic Neoplasms/	22630	2683889
5	Exp Neoplasm Metastasis/	212519	726618
6	Tumor.mp.	1751026	3248675
7	1 OR 2 OR 3 OR 4 OR 5 OR 6	64536526	7958749
8	Chemotherapy.mp. or Drug Therapy/	1680342	3345858
9	Exp Radiotherapy/	195119	650486
10	Exp Immunotherapy/	295456	251265
11	Hormone Therapy.mp.	451409	321092

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12	Exp Anthracyclines/	73107	24044
13	Anti-HER2.mp.	2783	5245
14	Interferon therapy.mp.	179072	324111
15	Exp Molecular Targeted Therapy/	32361	45045
16	8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15	2595775	4314485
17	Exp Risk Factors/ or Exp Myocardial Infarction/ or Exp Coronary Artery Disease/ or Cardiac Risk Factor.mp. or Exp Cardiovascular Disease	3148169	4747672
18	Exp Hypertension/	298582	
19	Hypercholesterolaemia.mp. or exp Hypercholesterolemia	29939	80112
20	Exp Diabetes Mellitus/	454034	1098310
21	Exp obesity/	231117	581631
22	Exp smoking/	153832	427178
23	Exp Sedentary Behaviour/	11444	16400
24	(Genetic adj4 cardi*).mp.	4339	6731
25	17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24	372322	5977616
26	7 AND 16 AND 25	106343	443506
27	(Quality adj3 indicator*).mp.	28024	23010
28	Exp Quality indicators, Health Care/	23282	3557512
29	Exp Cardiotoxicity	2952	47561
30	Patient reported outcomes.mp. or exp patient reported outcome measures/	21756	46722
31	Risk adj2 (assessment or stratification).mp.	358906	711406
32	Exp Risk Assessment/	291461	631873
33	Risk stratification.mp.	35915	62686

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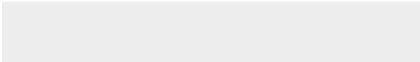
34	(Palliative adj2 Care).mp.	71410	56306
35	Exp Patient Satisfaction/ or patient experience.mp.	94943	160638
36	Care pathway.mp.	3167	5919
37	Antithrombotic therapy.mp. or exp anticoagulants/	233281	741542
38	Exp mortality/	405758	1253302
39	Exp morbidity/	600267	401283
40	27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39	1662667	5789671
41	26 AND 40	28501	224365
42	Limit step 41 to English and published since 2015	1494	1208

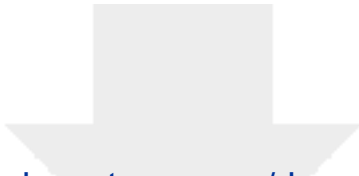


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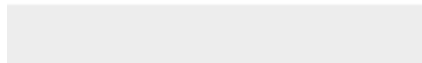
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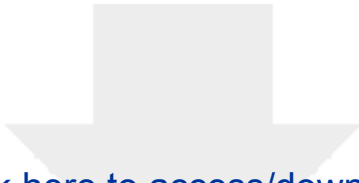




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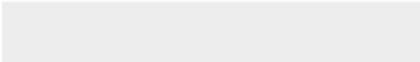


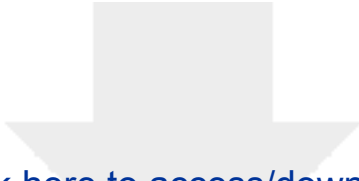


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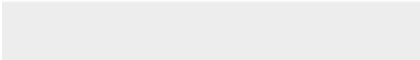


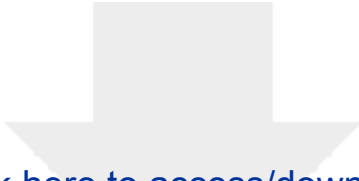


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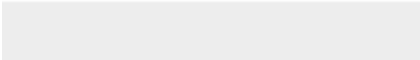


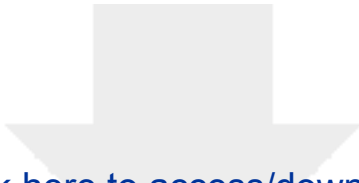


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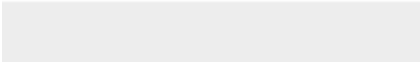




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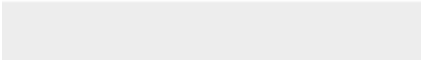
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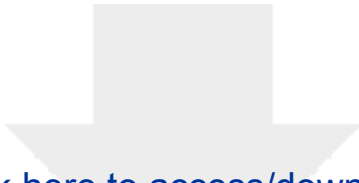




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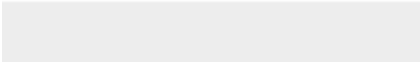
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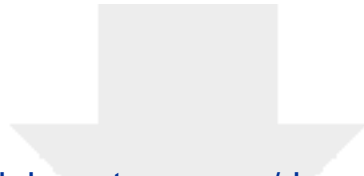




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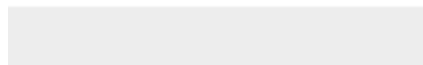
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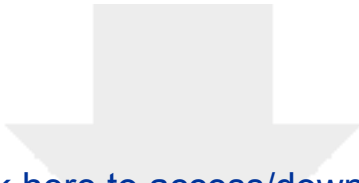




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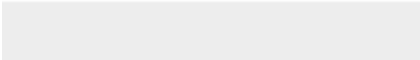


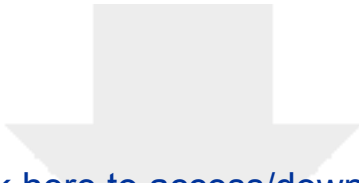


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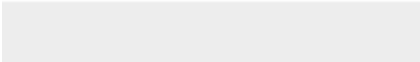
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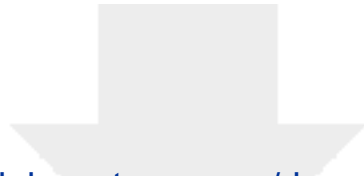




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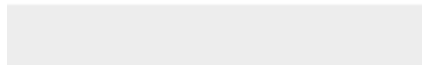
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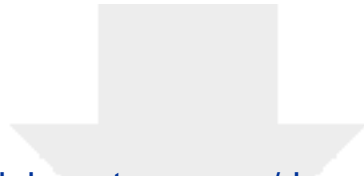




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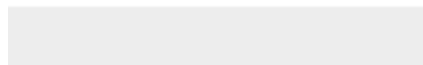




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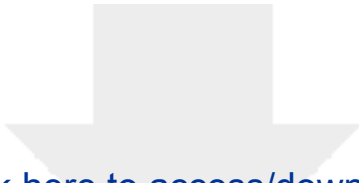




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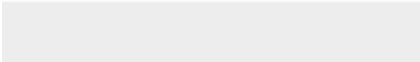




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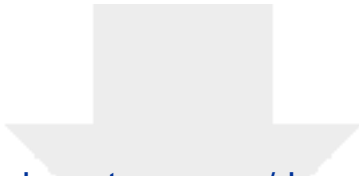




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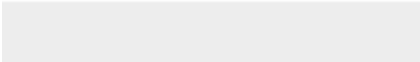


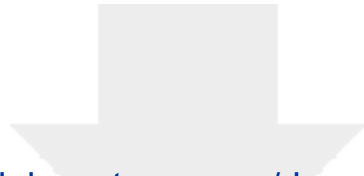


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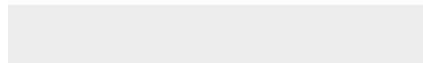


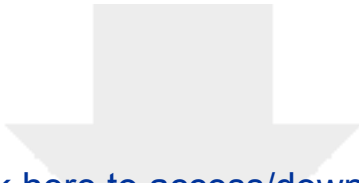


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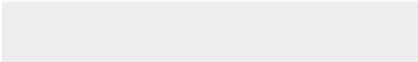


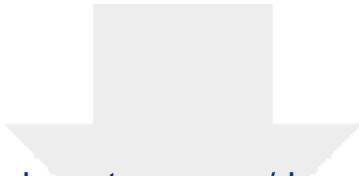


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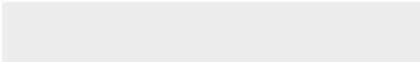
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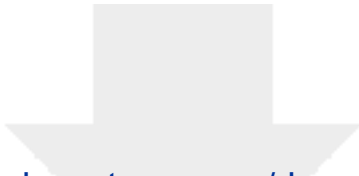




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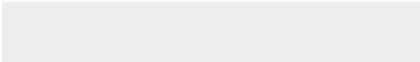


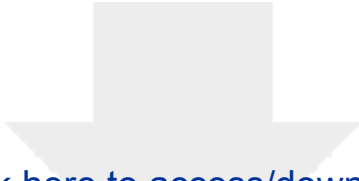


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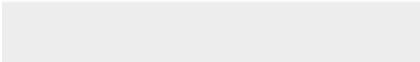
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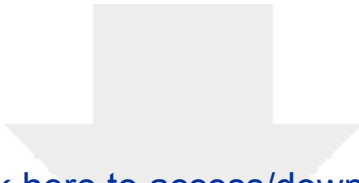




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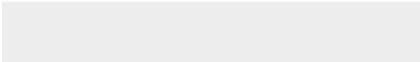
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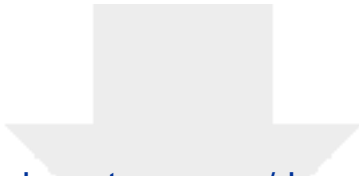




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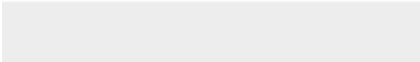


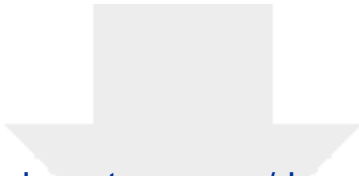


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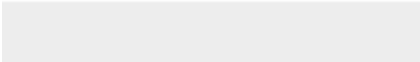


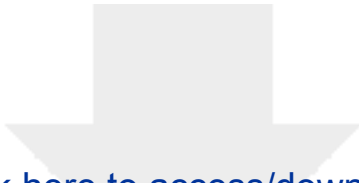


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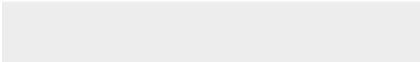




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