ASCO GUIDELINES

Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: ASCO Clinical Practice Guideline

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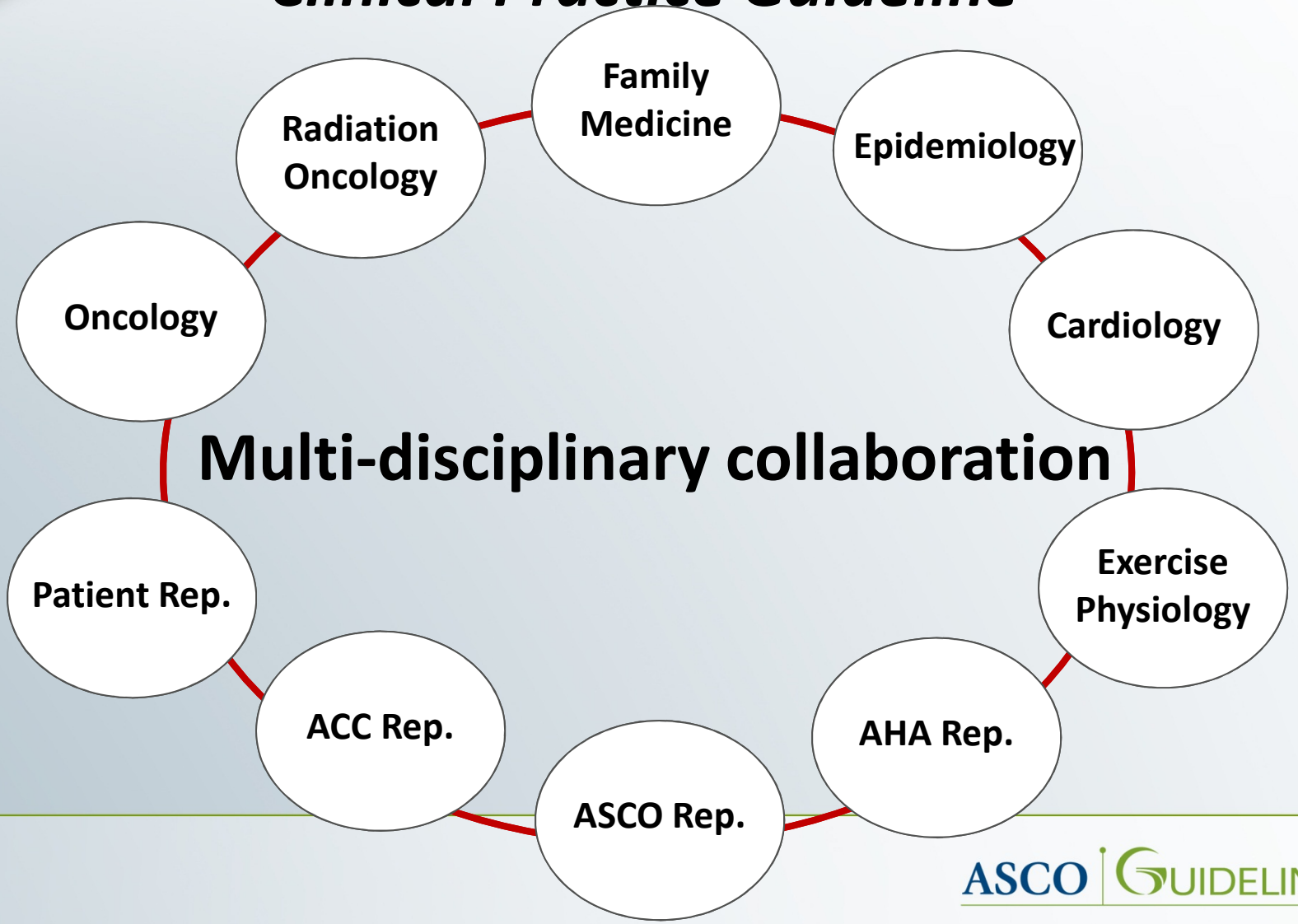
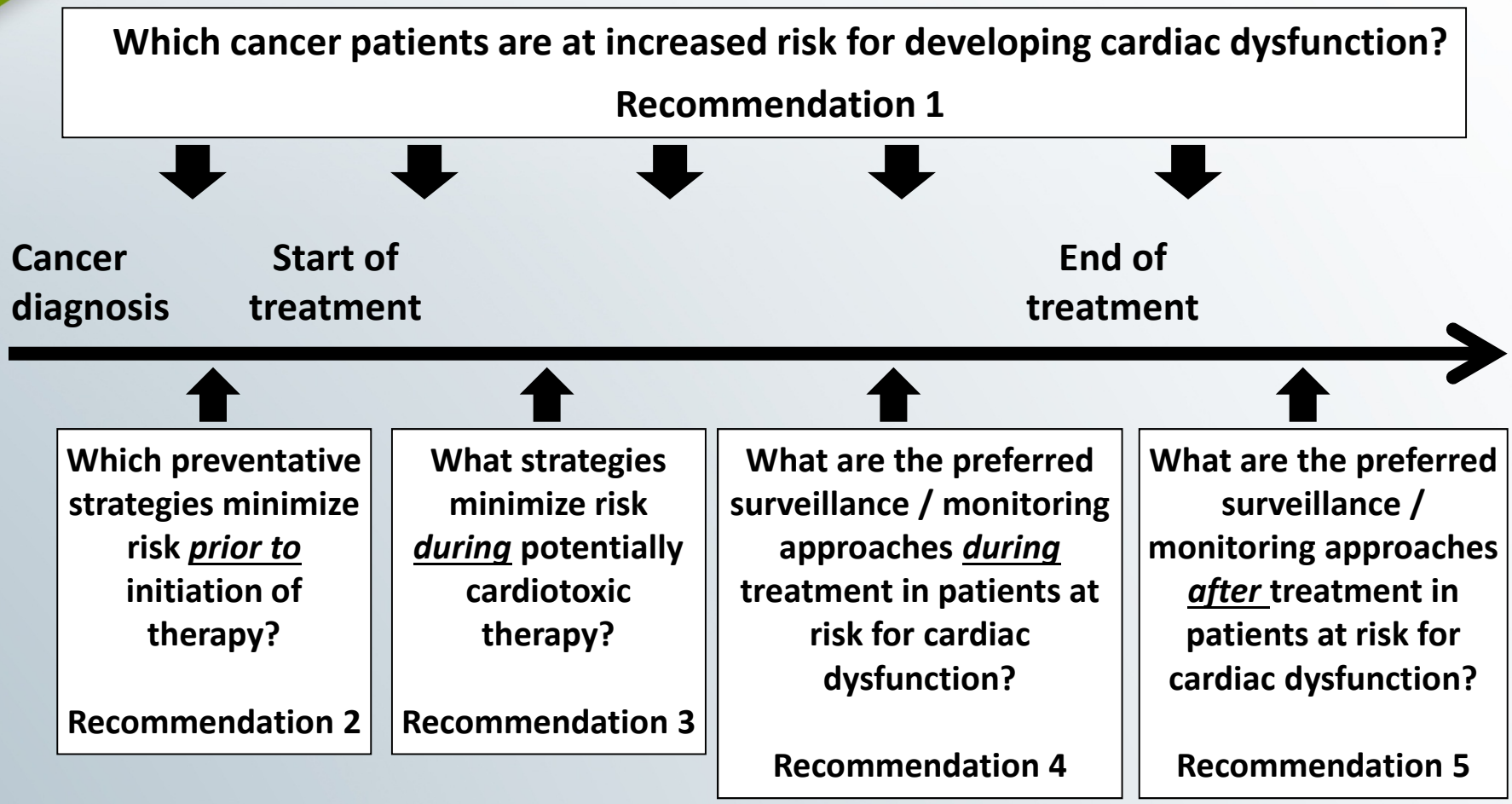
- **Objectives:**
  - Improve the quality of care of adult (>21 y.o.) cancer survivors by identifying and providing guidance on prevention and monitoring of **cardiac dysfunction** resulting from cancer therapy
  - Evidence-based
    - Strength of the Evidence
    - Strength of the Recommendation
  - Identify gaps in knowledge and develop research priorities to help address these gaps.

American Society of Clinical Oncology:
Clinical Practice Guideline



ASCO GUIDELINES

Clinical Questions



Type of Recommendation

Recommendation	Definition
Evidence-based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
(In)Formal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., “strong,” “moderate,” or “weak”).
No Recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Adapted from: AHRQ Methods Guide for Comparative Effectiveness Reviews 2011; ICSI; GRADE; and USPSTF

Clinical Questions

Which cancer patients are at increased risk for developing cardiac dysfunction?

Recommendation 1

Study design and analysis:

- **Large population-based cohort studies**
- **Long-term and complete follow-up**
- **Validated CV outcomes**
- **Treatment dose-specific information**
- **Comparison to no exposure**
- **Multivariable regression analysis (adjusting for confounders)**

Cancer patients at increased risk

- High dose anthracycline (e.g. ≥250 mg/m^2 doxorubicin, ≥600 mg/m^2 epirubicin)
- High dose (≥30 Gy) radiotherapy where the heart is in the treatment field
- Lower dose anthracycline (e.g. <250 mg/m^2 doxorubicin) in combination with lower dose radiotherapy (<30 Gy) where the heart is in the treatment field
- Treatment with lower dose anthracycline (e.g. <250 mg/m^2 doxorubicin) *or* trastuzumab alone, and presence of any of the following risk factors:
  - Multiple (≥2) CV risk factors: smoking, hypertension, diabetes, dyslipidemia, obesity
  - Older (≥60 years) age at cancer treatment
  - Compromised cardiac function (e.g. borderline low LVEF [50-55%], history of myocardial infarction, ≥moderate valvular heart disease)
- Treatment with lower dose anthracycline (e.g. <250 mg/m^2 doxorubicin) followed by trastuzumab (sequential therapy)
- ***(Evidence-based; Benefits outweigh harms; Evidence quality: Intermediate; Strength of the Recommendation: Moderate)***

No Determination of Risk

- Lower dose anthracycline (e.g. <250 mg/m^2 doxorubicin, <600 mg/m^2 epirubicin) *or* trastuzumab alone, and no additional risk factors
- Lower dose radiotherapy (<30 Gy) where the heart is in the treatment field, and no additional cardiotoxic therapeutic exposures or risk factors
- Kinase inhibitors
- ***(Evidence-based; Evidence quality: Low)***

Clinical Questions

Recommendation 2

Which preventative strategies minimize risk *prior to* initiation of therapy?

Cancer diagnosis → Start of treatment → End of treatment

Recommendation 2.1

Avoid or minimize the use of potentially cardiotoxic therapies if established alternatives exist that would not compromise cancer-specific outcomes.

(Consensus-based; Benefits outweigh harms; Strength of Recommendation: Strong).

Recommendation 2.2

Comprehensive assessment in cancer patients that includes an H&P, screening for cardiovascular disease risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking), and an echocardiogram prior to initiation of potentially cardiotoxic therapies.

(***Evidence and consensus-based; Benefits outweigh harms; Evidence quality: High; Strength of Recommendation: Strong***)

Clinical Questions

Recommendation 3

Which preventive strategies are effective in minimizing risk *during* the administration of potentially cardiotoxic cancer therapy?

- Considerations:
  - Prior exposure considerations for clinical trials evaluating more established cardioprotection (e.g. dexrazoxane, liposomal, continuous)
  - Newer strategies (ACE-inhibitors, B-Blockers, ARB-blockers, statins)
    - Single arm vs. randomized
    - +/- Clinical (e.g. heart failure prevention) endpoints
  - Paucity of info on long-term CVD prevention with changes in RT practice

Which preventive strategies are effective in minimizing risk *during* the administration of potentially cardiotoxic cancer therapy?

- **Recommendation 3.1**
- Clinicians should screen for and actively manage modifiable cardiovascular risk factors (smoking, hypertension, diabetes, dyslipidemia, obesity) in all patients receiving potentially cardiotoxic treatments.
- ***(Informal consensus and evidence-based; Benefits outweigh harms; Evidence quality: Insufficient; Strength of Recommendation: Moderate)***

- **Recommendation 3.2**
- Clinicians may incorporate a number of strategies, including use of the cardioprotectant dexrazoxane, or continuous infusion, or liposomal formulation of doxorubicin for prevention of cardiotoxicity in patients planning to receive high-dose (e.g. ≥250 mg/m2 doxorubicin) anthracyclines.
- ***(Evidence-based; Benefits outweigh harms; Evidence quality: Intermediate; Strength of Recommendation: Moderate)***

Clinical Questions

Recommendation 4

What are the preferred surveillance / monitoring approaches *during* treatment in patients at risk for cardiac dysfunction?

Consideration

- Detects injury before irreversible impairment
- Non-invasive
- Inexpensive
- Widely available
- Reproducible (esp. for asymptomatic dz)
- Actionable in guiding therapy
- Highly predictive of clinically significant disease

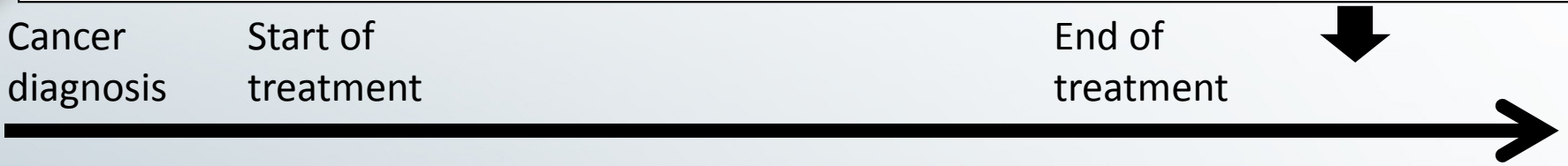
What are the preferred surveillance / monitoring approaches *during* treatment in patients at risk for cardiac dysfunction?

- Routine surveillance imaging may be offered during treatment in *asymptomatic* patients considered to be at increased risk (Recommendation 1.1) of developing cardiac dysfunction. In these individuals, echocardiography is the surveillance imaging modality of choice that should be offered. Frequency of surveillance should be determined by healthcare providers based upon clinical judgment and patient circumstances.
- ***(Evidence-based; Benefits outweigh harms; Evidence quality: Intermediate; Strength of Recommendation: Moderate)***

- No recommendations can be made regarding continuation/discontinuation of cancer therapy in individuals with evidence of cardiac dysfunction. This decision, made by the oncologist, should be informed by close collaboration with a cardiologist, fully evaluating the clinical circumstances, and considering the risks/benefits of continuation of therapy responsible for the cardiac dysfunction.
- ***(Informal consensus; Benefits outweigh harms; Evidence quality: Insufficient)***

Recommendation 5

What are the preferred surveillance / monitoring approaches *after* treatment in patients at risk for cardiac dysfunction?



- An echocardiogram may be performed between 6 to 12 months after completion of cancer-directed therapy in asymptomatic patients considered to be at increased risk (Recommendation 1.1) of cardiac dysfunction.
- ***(Evidence-based; Benefits outweigh harms; Evidence quality: Intermediate; Strength of Recommendation: Moderate)***

- Cardiac MRI or MUGA may be offered for surveillance in asymptomatic individuals if an echocardiogram is not available or technically feasible (e.g. poor image quality), with preference given to cardiac MRI.
- **(Evidence-based; Benefits outweigh harms; Evidence quality: Intermediate; Strength of Recommendation: Strong**)

- **Knowledge Gaps**
  - Risk of new-onset Stage B disease in patients with normal baseline/6-12 month echocardiograms (above and beyond gen. pop)
  - Optimal pharmacologic/other interventions & their duration
  - Cost-effectiveness of different screening frequencies/strategies
  - PPV, NPV of echocardiography by risk category

- No recommendations can be made regarding the frequency and duration of surveillance in patients at increased risk (Recommendation 1.1) who are asymptomatic and have no evidence of cardiac dysfunction during their 6-12 month post-treatment echocardiogram.
- ***(Informal consensus; Relative balance of benefits and harms; Evidence quality: Insufficient)***

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