**PICO-1: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain, (I) is a single troponin versus (C) serial troponins needed for (O) ACS outcomes within 30 days?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Intervention Option(s)****:* Single troponin below detectable level then discharge home.
***Comparison(s) if relevant****:* >1 troponin levels separated by undefined time prior to discharge home
***Setting****:* Emergency Department
***Perspective****:* Emergency Medicine physicians and APP's (others?)

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐Probably yes<br>X Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain – and subsequent troponin testing choices?<br><br>Bryn – Musey 2018 paper has rates of 1+ return ED visits in patients with low-risk CP, both overall and stratified by low vs high anxiety | Likely source of significant practice variability and healthcare expense.<br><br>Ongoing research (example: LoDED RCT just published July 2020 )<br><br>**Most research for hsTrop**<br><br>**Bryn – about 50% of patients who undergo troponin testing receive single rather than serial trops**<br>Furmaga et al<br>Mumma *in press*<br><br>**Fernanda – does the single vs. serial troponin consider time since symptom onset.**<br><br>**Bryn – most guidelines require >3 hour since onset** |

**PICO-1: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| | | | **Deb – Roche assay study shows single trop not sufficient (Bryn: But this is in a mixed risk group, and we excluded these studies from our GRADE analysis)**<br><br>**Jeff – threshold problems, machine differences, gender differences (Peacock paper online AEM March 27)** |

**Detailed Judgments (Problem Priority)**

1) Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
2) Is the problem urgent?
3) Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-1: GRADE Evidence-to-Decisions Framework**

**SECTION A – Quality of the Evidence Base**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>✗ Low<br>☐ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified.<br><br>No indirect evidence on recurrent chest pain.<br><br>Indirect evidence of low-risk chest pain with 30-day MACE included 9 studies. Rate of 30-day MACE 72/15,715 (0.5%) | **Articles do not take into account time since symptom onset**<br><br>**Increased very low to low based on number of patients across 9 studies**<br><br>**Very early (?3-hours?) since symptom onset cannot use single trop to rule-out** |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>✗ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Theoretical benefits include decrease time in the ED and decrease hospital admission.<br><br>These beneficial outcomes were not addressed by the included studies. | **Clinical experience is time-savings judged as real.**<br><br>**Patients would value less blood draws (less pain)**<br><br>**John – patients appreciate less time in ED too. Would expect explanation from MD as to rationale for another troponin test** |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for each main outcome for which there is a desirable effect? | | | |

**PICO-1: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>✗ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Harms are missed AMI and/or 30-day MACE that serial troponin may more accurately identify.<br><br>The pooled incidence of AMI or MACE in low risk chest pain patients from indirect evidence is 3.4 per 1000 patients (95% CI, 2.0-4.8 per 1000). | **AMI/MACE rates heavily weighted towards hs-Trop**<br><br>**Conventional troponin data do not disagree with hs-Trop results** |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for each main outcome for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *balance* between desirable and undesirable effects favour the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>✗ Probably favors the intervention probably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>✗ Don't know | No evidence of benefit upon which to weigh.<br><br>Entirety of harms evidence based on indirect evidence. | **See above upgrade for criterion 3. Benefits probably outweigh potential harms.**<br><br>**Gottlieb – could we use boarding literature to hypothesize about harms. Problem is that boarding doesn't focus on harms to that patient, but to other patients.** |

**PICO-1: GRADE Evidence-to-Decisions Framework**

***Detailed Judgements (Balance of desirable vs undesirable effects)***

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

No direct evidence to quantify either benefits or harms. Indirect evidence suggests 30-day MACE low among low-risk chest pain patients with single troponin. Recurrent low-risk chest pain may be either lower or higher risk than undifferentiated low-risk pain patients.

**PICO-1: GRADE Evidence-to-Decisions Framework**

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ☒ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented. | **Jason has pending paper evaluating utility of 2nd troponin. Need to differentiate HEART score from HEART pathway in this question.**<br><br>**Hess may have some additional insights from Chest Pain Choice research** |

***Detailed question to consider:***

How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted?

**PICO-1: GRADE Evidence-to-Decisions Framework**

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br>☐ Varies<br>X Don't know | No cost-analysis of troponin testing strategies presented. | |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

**PICO-1: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource requirements (costs)?** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High<br>X No included studies | No cost-analysis of troponin testing strategies presented. | **Jeff posted Asher manuscript which showed cost considerations around serial troponin.**<br><br>**25622029 PMID – no difference in costs**<br><br>**Probst sent smaller Henry Ford manuscript 2 hospitals 150 patients.** |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-1: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness of troponin testing strategies presented. | https://pubmed.ncbi.nlm.nih.gov/28325612/<br>https://pubmed.ncbi.nlm.nih.gov/29121105/<br><br>None of these directly address our question, but suggest cost savings with accelerated ED evaluation |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-1: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation?<br><br>**Inequities with follow-up access but not in-ED work-up, probably heavily influenced by local practice patterns and resources. Local practice also includes susceptibility to malpractice if you are outlier.**<br><br>**The use of baseline troponin also important, but no research on usefulness or utility identified.** |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-1: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☒ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Important that patient understand what the troponin shows and additive value.<br><br>Need input from Cardiologist Mike Kontos on July 24.<br><br>New Cardiology guidelines due Nov 2020 which may differ from our recommendations. Specifically limit to hs-Trop and time since symptom onset lacking in our guidelines.<br><br>LOD vs. LOQ needs to be clarified and defined. Our recommendation needs to clarify the dependence on cutoffs and assay as well as whether troponin T or I. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No ☒ Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No ☒ Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No ☒ Don't know

**PICO-1: GRADE Evidence-to-Decisions Framework**

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes ☒ Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes ☒ Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-1: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☒ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | **Choice of troponin assay at our hospital's out of our control.**<br><br>**Single troponin using a standard assay generally going to be considered inadequate**<br><br>**The vast majority are hs-Trop from research (only 2 studies used conventional troponin-I)** |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies ☒ Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-1: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | X Very Low ☐ Low ☐ Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small ☐ Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp ☐ Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies X Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies ☐ Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no X Probably Yes ☐ Yes ☐ Varies ☐ Don't know |

**PICO-1: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low risk chest pain, we suggest a single ~~negative~~ high-sensitivity troponin (using a validated threshold) ~~below the measurable threshold~~ to reasonably exclude ACS within 30 days. (Conditional, For)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☒ For ☐ Either (neither) ☐ Against |

**PICO-1: GRADE Evidence-to-Decisions Framework**

| **Recommendation:** **In adult patients with recurrent low risk chest pain, we suggest a single ~~negative~~ high-sensitivity troponin (using a validated threshold) ~~below the measurable threshold~~ to reasonably exclude ACS within 30 days. (Conditional, For)** | | | | | |
|---|---|---|---|---|---|
| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
| | ○ | ○ | ○ | X | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* | | | |
| **Justification** | ??? | | | |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? | | | |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? | | | |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. | | | |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? | | | |

**PICO-2: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain and negative or non-diagnostic stress testing within the last 12-months, (I) does repeat provocative stress testing vs. (C) no stress test have an effect on (O) MACE within 30 days?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Intervention Option(s)****:* Repeat provocative stress test
***Comparison(s) if relevant****:* Single provocative stress test within 12-months.
***Setting****:* Emergency Department
***Perspective****:* Emergency Medicine physicians and APP's (others?)

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☒ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain with prior provocative test within 12-months and subsequent repeat provocative testing? | Likely source of significant practice variability and healthcare expense.<br><br>**Different stress test type or question about adequacy of prior stress test.** |

**Detailed Judgments (Problem Priority)**

4) Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
5) Is the problem urgent?
6) Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-2: GRADE Evidence-to-Decisions Framework**

## SECTION A – Quality of the Evidence Base

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☒ Low<br>☐ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified.<br><br>No indirect evidence on recurrent chest pain or recent stress testing.<br><br>Indirect evidence of ED patients with non-high-risk chest pain (not necessarily recurrent and without knowledge of prior stress testing) identified two RCTs and one retrospective study. 0/4906 died within 30 days, but 91/4906 (1.9%) had non-fatal significant cardiac event. | **Low risk defined differently**<br><br>**One RCT primary outcome was total charges, but secondary outcome was MACE**<br><br>**Increase to "Low" or "Moderate" because RCTs (one was quite small)**<br><br>**What type of stress test (nuclear, echo, MRI, treadmill)? Each have different "warranty" period**<br><br>**Probably worth discussing the adequacy of prior stress tests (heart rate, image quality, exercise duration).** |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☒ Trivial<br>☐ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Two RCT's that indirectly addressed the question did not demonstrate a reduction in significant cardiac events with stress testing during ED visit. Nor did the retrospective study demonstrate benefit of stress testing within 30 days. | Would recurrent low-risk chest pain patients have higher or lower baseline risk of 30-day MACE?<br><br>Probably lower MACE rates<br><br>Perhaps psychological benefits for patients?<br><br>Can only speak to 30 days for repeat stress testing. Longer event rates will need to be explicitly stated – do not know. |

| | | | |
|---|---|---|---|
| | | | Radiology appropriate use criteria suggest 2-years should not repeat nuclear stress test without new/different symptoms. |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Harms include potential allergic reaction, radiation exposure, procedural risks, and unnecessary downstream testing expenses/side effects. Additional harms might include inconvenience of time spent in the ED, psychological stress associated with false-positives.<br><br>Costs (see Frivoli paper) | **<u>John: Exercise stress tests difficult for some patients. Also query about safety of stress test with low EF.</u>**<br><br>**<u>Paul: Are patients unable to perform provocative stress testing still low risk? Probably depends on the issue (frailty vs. limb amputation)</u>**<br><br>**<u>Mike: The vast majority of tests are now pharmacologic (esp in COVID era which requires advanced testing for exercise testing)</u>**<br><br>**<u>Fernanda: Nuc med has 2x radiation exposure than CTA (historically). Nuc med primarily bladder, CT primary radiation exposure is breast and lung.</u>** |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect? | | | |

**PICO-2: GRADE Evidence-to-Decisions Framework**

| |
|---|
| |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *balance* between desirable and undesirable effects favour the intervention or the comparison?** | ☐ Favors the comparison<br>X Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>robably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | No evidence of benefit and theoretical risks of multiple harms. | Entirety of harms evidence based on indirect evidence. |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

**PICO-2: GRADE Evidence-to-Decisions Framework**

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

How to manage patient and some healthcare providers' bias towards technological tenesmus whereby a "test" provides higher quality/more accurate health information than does an individual clinician's gestalt or a guideline recommendation?

**PICO-2: GRADE Evidence-to-Decisions Framework**

**SECTION B – Patient Values/Preferences**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented.<br><br>Sex bias in cardiovascular testing: the contribution of patient preference. Mumma et al. PMID: 21146255<br>"both women and men preferred stress test to catheterization" | **Bryn study looked at stress testing, cath, and CABG (If your doctor recommended this how likely would you be to…with 30-day f/u did they actually get that treatment)**<br><br>**John – some patients not big proponent of stress testing.**<br><br>**Hess research suggests patients often choose d/c** |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | ~~No cost-analysis of repeat stress testing strategies presented.~~<br><br>**Frisoli TM, Nowak R, Evans KL, Harrison M, Alani M, Varghese S, Rahman M, Noll S, Flannery KR, Michaels A, Tabaku M, Jacobsen G, McCord J. Henry Ford HEART Score Randomized Trial: Rapid Discharge of Patients Evaluated for Possible Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2017 Oct;10.** | **Marc (Frisoli?) – total charges significantly less if directly discharged from ED**<br><br>**LOS and healthcare costs were lower in the early discharge group.** |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

**PICO-2: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource requirements (costs)?** | ☐ Very low<br>☐ **Low**<br>☐ Moderate<br>☐ High<br>X No included studies | ~~No cost-analysis of stress testing strategies presented~~.<br><br>**Frisoli TM, Nowak R, Evans KL, Harrison M, Alani M, Varghese S, Rahman M, Noll S, Flannery KR, Michaels A, Tabaku M, Jacobsen G, McCord J. Henry Ford HEART Score Randomized Trial: Rapid Discharge of Patients Evaluated for Possible Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2017 Oct;10.** | **Judgements: Change to "Low"?**<br><br>**LOS and healthcare costs were lower in the early discharge group.** |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-2: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ **Probably favors the comparison**<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>✗ No included studies | No cost-effectiveness of stress testing strategies presented.<br><br>**Frisoli TM, Nowak R, Evans KL, Harrison M, Alani M, Varghese S, Rahman M, Noll S, Flannery KR, Michaels A, Tabaku M, Jacobsen G, McCord J. Henry Ford HEART Score Randomized Trial: Rapid Discharge of Patients Evaluated for Possible Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2017 Oct;10.** | Change to → Probably favors the comparison. |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-2: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation?<br><br>Pre-authorization can require 3-4 days if discharged for stress test (may promote ordering in ED)<br><br>Compliance with follow-up is also a consideration. |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-2: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Need input from Cardiologist Mike Kontos on July 24. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-2: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>X Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-2: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐Don't know |
| **2. Overall Certainty of Evidence** | X Very Low ☐ Low ☐ Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | X Trivial ☐ Small ☐ Moderate ☐ Large ☐ Varies ☐ Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |

**PICO-2: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low risk chest pain, we do not recommend routine repeat stress testing with prior adequate stress test results available as it does not have an effect on MACE at 30 days. (Conditional, Against)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☐ For ☐ Either (neither) ☒ Against |

**PICO-2: GRADE Evidence-to-Decisions Framework**

| **Recommendation:** **In adult patients with recurrent low risk chest pain, we do not recommend routine stress testing as a means to decrease the incidence of MACE at 30 days. (Conditional, Against)** | | | | | |
|---|---|---|---|---|---|
| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
| | ○ | ○ | ○ | X | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* | | | |
| **Justification** | ??? | | | |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? | | | |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? | | | |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. | | | |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? | | | |

**PICO-3: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain is (I) admission to the hospital versus (C) dismissal home vs. Observation Unit preferred (O) for ACS outcomes within 30 days?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Intervention Option(s)****:* *Admission to hospital or observation unit*
***Comparison(s) if relevant****:*. *Discharge home*
***Setting****:* *Emergency Department*
***Perspective****:* *Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain with admission to the hospital? | Likely source of significant practice variability, healthcare expense, and potentially imbalances in health equity. |

**Detailed Judgments (Problem Priority)**

7) Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
8) Is the problem urgent?
9) Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-3: GRADE Evidence-to-Decisions Framework**

## SECTION A – Quality of the Evidence Base

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High<br><br>✗ No included studies | No direct or indirect evidence identified. | **Jason – conducted independent medical librarian search and also unable to find any supporting literature.**<br><br>**How do disentangle from admission for stress test vs. admission without stress test?**<br><br>**Probst paper randomized**<br><br>**Chest pain choice paper also assessed admission multi-center BMJ (no difference in outcome at 30 days?) – what was comparison (decision aid vs. no decision aid OR admit vs. discharge)**<br><br>**Should we define components of "Observation Unit" (location vs. protocol). Observation pathway vs. Observation unit. Anna Marie data on ED Obs Unit vs. Inpatient Obs Unit** |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>✗ Don't know? | No desirable effects hypothesized. | Ability to rapidly identify and manage true-positive ACS for admitted |

**PICO-3: GRADE Evidence-to-Decisions Framework**

| |
|---|
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☐ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>✗ Don't know? | No desirable effects hypothesized. | **<u>Missed MI for patient discharged (malpractice risk).</u>**<br><br>**<u>Increased cost of hospital admission (for patient unlikely to benefit).</u>**<br><br>**<u>Iatrogenic problems with hospital admission.</u>** |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *<u>balance</u>* between <u>desirable</u> and <u>undesirable</u> effects favour the <u>intervention or the</u> comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the | No evidence of benefit and theoretical risks of multiple harms. | Entirety of harms evidence based on indirect evidence.<br><br>**<u>All based on expert consensus without published evidence.</u>** |

| | | | |
|---|---|---|---|
| | intervention or the comparison<br>☐ Probably favors the intervention<br>robably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>X Don't know | | **Admitting to hospital when Obs Unit available may be misuse of resources.**<br><br>**Individual cases (based on story) may require inpatient evaluation and our recommendation should not rob ED providers of ability to admit those patients.** |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

How to manage patient and some healthcare providers' bias towards technological tenesmus whereby a "test" provides higher quality/more accurate health information than does an individual clinician's gestalt or a guideline recommendation?

**PICO-3: GRADE Evidence-to-Decisions Framework**

**PICO-3: GRADE Evidence-to-Decisions Framework**

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented. | |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

**PICO-3: GRADE Evidence-to-Decisions Framework**

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of admission vs. observation vs. discharge home presented. | **Simon Mahler paper on accelerated diagnostic pathways looked at cost?**<br><br>**Cost savings of chest pain units (Brian Gibler?)**<br><br>**Rob Reilly paper on HEART pathway cost-effectiveness**<br><br>**Asher paper that Kline sent out**<br><br>**JAMA 2016 cost of admitted vs. unplanned revisits (not chest pain)** |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

**PICO-3: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource requirements (costs)?** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High<br>X No included studies | No cost-analysis of admission vs. observation vs. discharge home presented. | |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-3: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness of admission vs. observation vs. discharge home presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-3: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>☒ Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation? |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes ☒ Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No ☒ Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No ☒ Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-3: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Need input from Cardiologist Mike Kontos on July 24. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | **Add component of why this question is so hard to research.** |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies ☒ Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-3: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | ☐ Very Low ☐ Low ☐ Moderate ☐ High X No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small ☐ Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate ☐ Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp ☐ Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies X Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |

**PICO-3: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low risk chest pain, there is not enough evidence to recommend admission to the hospital or observation unit versus discharge home in relationship with ACS outcomes within 30 days. (No evidence, Either)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☐ For ☒ Either (neither) ☐ Against |

**PICO-3: GRADE Evidence-to-Decisions Framework**

**Recommendation: In adult patients with recurrent low risk chest pain, there is not enough evidence to recommend admission to the hospital versus home versus observation unit in relationship with ACS outcomes within 30 days. (No evidence, Either)**

| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|---|---|---|---|---|---|
| | ○ | ○ | X | ○ | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* | | | |
| **Justification** | ??? | | | |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? | | | |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? | | | |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. | | | |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? | | | |

**PICO-4: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain and within the last 5-years a negative cardiac cath defined as less than 50% stenosis (E) what is their risk of subsequent ACS or time to ACS?

***Problem****: (What is the background for this problem, and objective for resolution): ???*
***Exposure****: Less than 50% stenosis on cardiac catheterization within the last 5-years*
***Comparison(s) if relevant****: No prior cardiac cath.*
***Setting****: Emergency Department*
***Perspective****: Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain with accessible planar cardiac catheterization within the preceding 5 years? | Likely source of significant practice variability, healthcare expense, and potentially imbalances in health equity.<br><br>**Can patient be considered "low-risk" after they've had a cardiac cath (regardless of findings)? What is warranty on that negative cardiac cath. Most of literature from 1980's-90's (limited diagnostic options) – less relevant now with CTCA? Warranty varies (higher event rate later, lower earlier)**<br><br>**How do we account for changing definition of MACE over time? Overall event rates remained below despite varying definitions of MACE.** |

**Detailed Judgments (Problem Priority)**

**PICO-4: GRADE Evidence-to-Decisions Framework**

| |
|---|
| 10)Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?<br>11)Is the problem urgent?<br>12)Is it a recognized priority (e.g. based on a political or policy decision)? |

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SECTION A – Quality of the Evidence Base

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☐ Low<br>☒ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified. Indirect evidence (not necessarily low risk or recurrent chest pain) in one meta-analysis of 54 studies including 35039 patients comparing outcomes in those with <50% coronary obstruction vs. 0% obstruction with significant statistical heterogeneity ($I^2$ = 91%). The 5-year risk of non-fatal MI or all-cause death was 3.6% and 4.1%, respectively. | **30 day outcomes don't make sense for recurrent chest pain? Should all PICO questions have same timeframe for outcomes? Should GRACE-1 exclude evidence that has different timeframes (30 days vs. 5 years)?**<br><br>**John – what is criteria for cath vs. stress test decision for low-risk patients? Also, question about what is being sought with cath (looking for anatomic obstruction) vs. stress test (looking for limited flow to heart muscle)**<br><br>**Is "recurrent" truly lower risk? Consensus = probably but need GRACE-1 to discuss differential diagnosis & avoidance of anchoring bias** |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Avoiding low-yield hospital admissions in lieu of expedited outpatient re-evaluation could save substantial patient-time and money. | How important to John are these desirable anticipated effects? If doctor feels admission for more testing is indicated that is more important than time/$ - patients want certainty. |
| ***Detailed Question to consider:*** | | | |

**PICO-4: GRADE Evidence-to-Decisions Framework**

| |
|---|
| How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☒ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐Don't know? | Adverse consequences of additional testing include allergic reactions to ancillary testing (stress tests) or iatrogenic harms of hospital admission. | **<u>Additional complications (physical pain, pseudoaneurysm, coronary artery dissection), psychological.</u>** |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *<u>balance</u>* between <u>desirable</u> and <u>undesirable</u> effects favour the <u>intervention or</u> the comparison?** | ☐ Favors the comparison<br>☒ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention | Indirect evidence likely favors not repeating cardiac cath or admitting for additional cardiac evaluation, though multiple potential benefits and harms are not studied. | The risk of outcomes (3.6% and 4.1%) may exceed some patients' or providers' threshold to favor additional testing. Formal test-treatment threshold analyses would be beneficial, including whether admission of low-risk recurrent chest pain patients with <50% stenosis within last 5-years improves outcomes.<br><br>The decision not as simple as cath or not cath – decision for the provider is more |

| | | | |
|---|---|---|---|
| | robably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | | complex (call cardiology, obs admission for serial troponin) |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

How to manage patient and some healthcare providers' bias towards technological tenesmus whereby a "test" provides higher quality/more accurate health information than does an individual clinician's gestalt or a guideline recommendation?

Need decision-instrument showing harms of cath.

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented. | **Bryn – women get less testing (2 papers). Does that reflect MD presentation to female patient OR women's testing preferences.** |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-4: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource requirements (costs)?** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High<br>X No included studies | No cost-analysis of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | **Bias in upfront decision-making (admit vs. obs)? Differences in costs to patients (with obs vs. admission) worth contemplating.**<br><br>**Marc Probst has one cost-analysis manuscript to add to Intro** |

***Detailed question to consider:***

See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-4: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation?<br><br>**Really depends on practice-setting and local resources.**<br><br>**Also, associated costs of missing work and lost wages/vacation time with higher impact on low/middle income patients.**<br><br>**Is there evidence of health inequity in chest pain evaluations?**<br><br>**Co-pay costs and ability to pay (outpatient vs. inpatient work-up)?**<br><br>**Differences in healthcare systems like Kaiser (ability to discharge with reliable follow-up)?** |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

**PICO-4: GRADE Evidence-to-Decisions Framework**

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-4: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Need input from Cardiologist Mike Kontos on July 24.<br><br>Mike – helpful to standardize work-up, does not contradict Cardiology guidelines.<br><br>John – encouraged us to interpret guidelines individually for each patient (not one-size-fits-all). |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-4: GRADE Evidence-to-Decisions Framework**

| |
|---|
| |

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | **Lang/Wyer 2011 paper on Guideline attributes to facilitate KT – summary table at beginning with strength of recommendations; probably unable to create clinical care paths with these disparate PICO questions.**<br><br>**AGREE-II recommends audit-and-feedback component of guideline recs** |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies ☒ Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-4: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | ☐ Very Low ☐ Low X Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small X Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |

**PICO-4: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In low-risk (HEART </= 3) adult patients with recurrent chest pain and with prior minimally occlusive CAD (<50%) on angiography <5 years generally demonstrate low MACE rates, we suggest that such patients may not need to be admitted for inpatient evaluation and should be referred to expedited outpatient testing as warranted. (Conditional, Either)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☐ For ☒ Either (neither) ☐ Against |

## PICO-4: GRADE Evidence-to-Decisions Framework

**Recommendation:** **In adult patients with recurrent low-risk chest pain and with prior minimally occlusive CAD (<50%) on angiography <5 years generally demonstrate low MACE rates, we suggest that such patients may not need to be admitted for inpatient evaluation and should be referred to expedited outpatient testing as warranted. (Conditional, Either)**

| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|---|---|---|---|---|---|
| | ○ | X | ○ | ○ | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |

| | |
|---|---|
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* |
| **Justification** | ??? |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? |

**PICO-5: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain a negative cardiac cath defined as complete clean coronaries (0% stenosis) (E) what is their risk of subsequent ACS/time to ACS?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Exposure****: 0% stenosis on cardiac catheterization within the last 5-years*
***Comparison(s) if relevant****:. No prior cardiac cath.*
***Setting****: Emergency Department*
***Perspective****: Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>X Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain with accessible planar cardiac catheterization within the preceding 5 years? | Likely source of significant practice variability, healthcare expense, and potentially imbalances in health equity.<br><br>**Same as PICO 4** |

**Detailed Judgments (Problem Priority)**

13)Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
14)Is the problem urgent?
15)Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-5: GRADE Evidence-to-Decisions Framework**

**SECTION A – Quality of the Evidence Base**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☐ Low<br>☒ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified. Indirect evidence (not necessarily low risk or recurrent chest pain) in one meta-analysis of 54 studies including 35039 patients comparing outcomes in those with any coronary obstruction vs. 0% obstruction. The 5-year risk of non-fatal MI or all-cause death was 2.88% and 2.97%, respectively. | **Probably alter wording of recommendation as with PICO-4**<br><br>**Heterogeneous data because most studies include all catheterization results up to 50% stenosis as "clean coronary"** |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Avoiding low-yield hospital admissions in lieu of expedited outpatient re-evaluation could save substantial patient-time and money. | |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for each main outcome for which there is a desirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-5: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>X Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐Don't know? | Adverse consequences of additional testing include allergic reactions to ancillary testing (stress tests) or iatrogenic harms of hospital admission. | **Suneel – is risk of incremental caths additive? Mike – in-between risks probably the same with each cath**<br><br>**Marc – decision to cath outside realm of EM influence. EM only decides admit vs. discharge, but EM can decide on stress testing** |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for each main outcome for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *balance* between desirable and undesirable effects favour the intervention or the comparison?** | ☐ Favors the comparison<br>X Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention robably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | Indirect evidence likely favors not repeating cardiac cath or admitting for additional cardiac evaluation, though multiple potential benefits and harms are not studied. | The risk of outcomes (2.88% and 2.97%) may exceed some patients' or providers' threshold to favor additional testing. Formal test-treatment threshold analyses would be beneficial, including whether admission of low-risk recurrent chest pain patients with 0% stenosis within last 5-years improves outcomes.<br><br>**Event rate improved looking at 1-year would be even lower than the 5-year rate.**<br><br>**Risk potentially not evenly distributed over time period.** |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

**PICO-5: GRADE Evidence-to-Decisions Framework**

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

How to manage patient and some healthcare providers' bias towards technological tenesmus whereby a "test" provides higher quality/more accurate health information than does an individual clinician's gestalt or a guideline recommendation?

**PICO-5: GRADE Evidence-to-Decisions Framework**

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented. | **See prior paper with PICO-4**<br><br>**Paul (EM perspective): Would conversation differ with 0% stenosis vs. <50% stenosis?** |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

| | | | |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High | No cost-analysis of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | |

| | | | |
|---|---|---|---|
| **requirements (costs)?** | X No included studies | | |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-5: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness of alternative diagnostic pathways for patients with <50% stenosis within last 5-years presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-5: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation? |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-5: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Need input from Cardiologist Mike Kontos on July 24. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-5: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>X Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | **Recommendations need to be interpreted through lens of local practice patterns and resources** |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-5: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | ☐ Very Low ☐ Low X Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small X Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |

**PICO-5: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with low risk chest pain (</= 3 HEART) and no occlusive CAD (0%) on angiography <5 years, we recommend that such patients not be admitted for inpatient evaluation and should be referred to expedited outpatient testing as warranted. (Conditional, Either)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong X Conditional |
| **Direction of Recommendation** | X For X Either (neither) ☐ Against |

**PICO-5: GRADE Evidence-to-Decisions Framework**

| **Recommendation:** **In adult patients with recurrent low risk chest pain and no occlusive CAD (0%) on angiography within 5 years, we recommend that such patients not be admitted for inpatient evaluation and should be referred to expedited outpatient testing as warranted. (Conditional, Either)** | | | | | |
|---|---|---|---|---|---|
| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
| | ○ | X | ○ | ○ | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* | | | |
| **Justification** | ??? | | | |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? | | | |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? | | | |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. | | | |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? | | | |

**PICO-6: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain and a "negative" coronary computed tomography angiogram (E) what is their risk of subsequent ACS/time to ACS?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Exposure****: CT coronary angiogram without evidence of coronary artery disease*
***Comparison(s) if relevant****:. No prior coronary imaging.*
***Setting****: Emergency Department*
***Perspective****: Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain with subsequent evaluation including coronary CTA? | Likely source of significant regional practice variability, healthcare expense, radiation exposure, and potentially imbalances in health equity.<br><br>Likely variability with access to CCTA and insurance reimbursement. |

**Detailed Judgments (Problem Priority)**

16)Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
17)Is the problem urgent?
18)Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-6: GRADE Evidence-to-Decisions Framework**

**SECTION A – Quality of the Evidence Base**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☐ Low<br>☒ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified. Indirect evidence identified of 18 studies in patients without necessarily recurrent chest pain but as a predictor of long-term coronary events in patients following coronary CTA. These studies included RCTs comparing CTCA with stress echo or stress myocardial perfusion, as well as ED observation studies and registries.<br><br>CONFIRM Registry with "negative" CTA 0.08% MI, 0.4% all-cause mortality, and 0.6% death/MI/revascularization at median 2-year follow-up. Those with 1%-49% stenosis had 1.3% MI, 0.5% all-cause mortality, and 2.4% composite outcome rates.<br><br>PROMISE evaluated 3800 patients with negative coronary CTA. Within 90 days 8% had subsequent non-invasive testing and 4% had coronary angiography. | Most studies define "normal" as 0% stenosis vs. mild stenosis as 1-49% stenosis.<br><br>Common contraindications included renal failure, IV dye allergy, prior CCTA, or dysrhythmias.<br><br>These studies were not recurrent chest pain. Low risk patients with an initial "negative" coronary CTA would be expected to have even lower rates of AMI or MACE.<br><br>Cite Anna Marie study on calcium score |

**PICO-6: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Accurate rule-out of 30-day MACE while avoiding low-yield hospital admissions or Observation Unit evaluations could improve operational flow and reduce healthcare costs. Additional benefits for recurrent low risk chest pain is avoidance of extensive coronary ischemia evaluation following "normal" coronary CTA within 1-year. | Limitations of ED CTA studies is focus or strategy rather than test accuracy.<br><br>Deb's team working on separate SR. |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? | | | |

**PICO-6: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☒ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐Don't know? | Adverse consequences of additional testing include risk of beta-blocker (CTA protocol), renal injury, incidentaloma (and downstream work-up costs, including some level of coronary stenosis), allergic reactions to contrast dye, higher levels of medical radiation exposure, more costly initial ED evaluation medical bill, and longer ED length of stay compared with a no-test strategy. | CTA often associated with increased coronary cath rates.<br><br>John had IV contrast reaction with 4 extra hospital days then AKI requiring post-discharge follow-up |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *<u>balance</u>* between <u>desirable</u> and <u>undesirable</u> effects favour the <u>intervention or the</u> comparison?** | ☐ Favors the comparison<br>☒ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention probably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | Indirect evidence likely favors not pursing repeat ischemic evauation other than troponin and EKG (as per HEART score) for patients with recurrent low-risk chest pain after a negative coronary CTA within last 2-years.<br><br>Additional research explicitly evaluating the risk of ischemic events in patients who have recurrent chest pain with HEART </= 3 after negative coronary CTA is essential. | Accurately identifying the warranty of a negative CTA is also important.<br><br>**<u>Many studies used TIMI rather than HEART. Need statement that others use different risk scores (esp. historically) Barb Backus comparative research?</u>**<br><br>**<u>Correlation between HEART and EDACS? Discuss in Intro</u>** |

**PICO-6: GRADE Evidence-to-Decisions Framework**

***Detailed Judgements (Balance of desirable vs undesirable effects)***

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

How to manage patient and some healthcare providers' bias towards technological tenesmus whereby a "test" provides higher quality/more accurate health information than does an individual clinician's gestalt or a guideline recommendation?

**PICO-6: GRADE Evidence-to-Decisions Framework**

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain presented. | |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-6: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of alternative diagnostic pathways for patients with 0% stenosis on coronary CTA is presented. | **Studies comparing CTA to stress testing for costs and outcomes.**<br><br>**Initial costs or downstream costs?**<br><br>**Relook at judgment** |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High | No cost-analysis of alternative diagnostic pathways for patients with 0% stenosis on coronary CTA is presented. | |

| | | | |
|---|---|---|---|
| **requirements (costs)?** | X No included studies | | |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-6: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness of alternative diagnostic pathways for patients with 0% stenosis on coronary CTA is presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-6: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation? |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-6: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24 = made comments about AKI with dye exposure. Relies upon advice of physician for optimal diagnostic and management strategy.<br><br>Need input from Cardiologist Mike Kontos on July 24 = same as PICO-4 and PICO-5<br><br>Jeff – need to mention cancer risk in terms of acceptability (female <45 breast cancer risk, 1:300 =3 years of background radiation in 15 seconds). How often is this risk actually discussed (with CTA or coronary cath)? |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

**PICO-6: GRADE Evidence-to-Decisions Framework**

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes ☒ Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-6: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | Does every hospital have requisite CT image acquisition protocol, equipment, and Radiologist interpretation expertise for coronary CTA? |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies ☒ Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-6: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | ☐ Very Low ☐ Low X Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small X Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no X Probably Yes ☐ Yes ☐ Varies ☐ Don't know |

**PICO-6: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low risk chest pain and negative prior CTA, we suggest no further diagnostic testing other than an ECG and a single negative troponin below the measurable threshold to rule-out ACS for the next 2-years. (Conditional, For)**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | X For ☐ Either (neither) ☐ Against |

**Do we need statement that recommendation has nothing to do with calcium scoring?**

**PICO-6: GRADE Evidence-to-Decisions Framework**

**Recommendation: In adult patients with recurrent low risk chest pain and negative prior CTA, we suggest no further diagnostic testing other than an ECG and a single negative troponin below the measurable threshold to rule-out ACS for the next 2-years. (Conditional, For)**

| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|---|---|---|---|---|---|
| | ○ | ○ | ○ | X | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |

| | |
|---|---|
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* |
| **Justification** | ??? |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? |

**PICO-7: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain, (I) what is the yield of depression and anxiety screening tools vs. (C) routine care in (O) healthcare use/return ED visits?

***Problem****: (What is the background for this problem, and objective for resolution):* ???
***Intervention****: ED-based depression/anxiety screening*
***Comparison(s) if relevant****:. Routine care (presumably without depression/anxiety screening).*
***Setting****: Emergency Department*
***Perspective****: Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☒ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain attributable to anxiety or depression? | Potential source of cognitive disposition to respond medical-decision making error by some healthcare providers.<br><br>Paul can add some context |

**Detailed Judgments (Problem Priority)**

19)Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
20)Is the problem urgent?
21)Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-7: GRADE Evidence-to-Decisions Framework**

**SECTION A – Quality of the Evidence Base**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☒ Very low<br>☐ Low<br>☐ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified. Indirect evidence included patients with or without coronary artery disease (not purely low-risk) with recurrent chest pain.<br><br>**Depression:** Kim et al included 365 low- to moderate-risk ED patients admitted to a chest pain unit noting increased risk of recurrent chest pain when screening positive for clinically significant depression using validated PHQ-8 score >10 (OR 2.11, 95% CI 1.18-3.79).<br><br>**Anxiety:** Three prospective observational studies provided indirect evidence. Kim et al no increase of recurrent chest pain with anxiety (aOR 1.59, 95% CI 0.80 – 3.79). Musey et al. showed increased recurrence (OR 2.36, 95% CI 1.09-5.15). Kim and Musey showed increased risk of ED returns with anxiety, but Schwarz showed no difference. | Only one depression screening tool reported.<br><br>A variety of anxiety screening tools used including: Clinical Anxiety Scale (25-items), Hospital Anxiety Depression Scale – Anxiety Subscale (7-items), and the Generalized Anxiety Disorder-7 (GAD-7). Do these instruments identify different subsets of anxiety? Are each equally feasible to implement in ED settings?<br><br>Downgrade certainty because of small effect size, small sample size, and limited number of studies (with heterogeneity)<br><br>Instruments can be self-administered (to increase feasibility). |

**PICO-7: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Identification of previously unrecognized depression or anxiety in ED patients with low- or moderate-risk chest pain (meeting the patient where they are and facilitating appropriate handoff).<br><br>Benefits may extend to non-chest pain patients too (example frequent utilizers) | Should discuss the evidence hierarchy of decision-aids – uncertain whether identification of subsets with anxiety or depression will find patients amenable to interventions to reduce recurrent chest pain, ED visits, or improved mental health.<br><br>Need to provide reliability citations for instruments (preferably in ED)<br><br>Potential temporal trigger – not screen for anxiety/depression at first visit but on repeat visits (looking for alternative etiologies) |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? | | | |

**PICO-7: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☐ Small<br>X Moderate<br>☐ Large<br>☐ Varies<br>☐Don't know? | Added burden of screening for ED. Risk of increasing patient depression or anxiety with screening test result. Open Pandora's box without adequate resources to ethically address in mental healthcare system. Increased patient healthcare expenses (or insurance) or harm to employment status. | Adds to ED burden of screening for mental illness (suicide screening).<br><br>Increased risk of litigation documenting depression.<br><br>Add discussion about how doctors feel about this issue. |
| ***Detailed question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect? | | | |

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *<u>balance</u>* between <u>desirable</u> and <u>undesirable</u> effects favour the <u>intervention or</u> the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>X Probably favors the intervention probably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | Indirect evidence likely favors depression and anxiety screening in recurrent low risk chest pain patients. | In following hierarchy of decision-aid evidence both the potential benefits and potential harms of this recommendation require further evaluation.<br><br>**<u>John: How do doctors get at the cause-effect relationship between chest pain causing anxiety vs. anxiety causing chest pain? (see Paul's studies – a subset of patients have persistent elevation of anxiety/depression symptoms beyond their ED visit).</u>** |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

**PICO-7: GRADE Evidence-to-Decisions Framework**

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).
- People's attitudes towards desirable effects (how risk seeking they are)

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain or detection of previously unrecognized anxiety or depression is presented. | **See Paul research on ED provider survey results.** |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-7: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of recurrent low-risk chest pain diagnostic pathways that include anxiety/depression screening is presented. | **Unaware of any cost-analyses of anxiety/depression screening for any ED condition (or chest pain). Function of cost-shifting – theoretical downstream saving with less ED returns?** |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High | No cost-analysis of recurrent low-risk chest pain diagnostic pathways that include anxiety/depression screening is presented. | |

| | | | |
|---|---|---|---|
| **requirements (costs)?** | X No included studies | | |

***Detailed question to consider:***
See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed

Have all important items of resource use that may differ between the options being considered been identified?

How certain is the cost of the items of resource use that differ between the options being considered?

Is there important variability in the cost of the items of resource use that differ between the options being considered?

**PICO-7: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness estimates of recurrent low-risk chest pain diagnostic pathways that include anxiety/depression screening are presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-7: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to healthcare after ED evaluation?<br><br>**Fernanda – women historically mislabeled as anxiety rather than ACS. Historical diagnosis of "hysteria".**<br><br>**Paul – also people of color also mislabeled with risk of premature closure attributing to psychiatric etiology.**<br><br>**How many f/u after abnormal screening result?** |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

**PICO-7: GRADE Evidence-to-Decisions Framework**

| |
|---|
| ☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know |

**PICO-7: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>☐ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br><br>Need input from Cardiologist Mike Kontos on July 24.<br><br>Screening trigger do PCP – does not need to even involve the EP. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**PICO-7: GRADE Evidence-to-Decisions Framework**

**PICO-7: GRADE Evidence-to-Decisions Framework**

## SECTION E – Feasibility

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>X Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | Do emergency medicine physicians and APP's have sufficient training in the administration, interpretation, and/or explanation of anxiety/depression screeners?<br><br>Does every ED have pragmatic access to mental health resources in response to these results, regardless of patient's insurance status?<br><br>Does documentation of previously unrecognized depression increase ED providers' malpractice risk?<br><br>Screening trigger to PCP or mental health – does not need to even involve the EP.<br><br>If not using MD/RN may require some adaptations to less resourced hospitals, but first need to evaluate effect at higher resourced settings |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-7: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | X Very Low ☐ Low ☐ Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small X Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no X Probably Yes ☐ Yes ☐ Varies ☐ Don't know |

**PICO-7: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low risk chest pain, we suggest depression and anxiety screening as these might have an effect on healthcare use/return ED visits. (Conditional/Either).**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☐ For X Either (neither) ☐ Against |

**PICO-7: GRADE Evidence-to-Decisions Framework**

| **Recommendation:** **In adult patients with recurrent low risk chest pain, we suggest depression and anxiety screening as these might have an effect on healthcare use/return ED visits. (Conditional/Either).** | | | | | |
|---|---|---|---|---|---|
| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
| | ○ | ○ | X | ○ | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |

| | |
|---|---|
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* |
| **Justification** | ??? |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest? |

## PICO-7: GRADE Evidence-to-Decisions Framework

| | |
|---|---|
| | What are the next steps needed for research (short/middle/long-term)? |

**PICO-8: GRADE Evidence-to-Decisions Framework**

***Guideline Question:*** (P) In adult patients with recurrent low risk chest pain, (I) what is the role of referral for anxiety/depression vs. (C) routine care in (O) healthcare use/return ED visits?

***Problem****: (What is the background for this problem, and objective for resolution):* *Large number of ED visits for recurrent chest pain. Also impacts patient quality of life.*
***Intervention****: ED referral for abnormal depression/anxiety screening*
***Comparison(s) if relevant****:. Routine care (presumably without screening or referral).*
***Setting****: Emergency Department*
***Perspective****: Emergency Medicine physicians and APP's (others?)*

**Evidence to Decision Criteria:**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **1. Is the problem a priority?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | Is there any epidemiological evidence on the numbers of patients arriving to ED annually with recurrent low-risk chest pain attributable to anxiety or depression and referred or not referred? | |

**Detailed Judgments (Problem Priority)**

22)Are the consequences of the problem serious (i.e. severe or important in terms of the potential benefits or savings)?
23)Is the problem urgent?
24)Is it a recognized priority (e.g. based on a political or policy decision)?

**PICO-8: GRADE Evidence-to-Decisions Framework**

**SECTION A – Quality of the Evidence Base**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **2. What is the *overall certainty* of the evidence?**<br><br>**(No detailed judgements)** | ☐ Very low<br>☐ Low<br>✗ Moderate<br>☐ High<br><br>☐ No included studies | No direct evidence identified. Indirect evidence was derived from two systematic reviews, neither based on ED depression/anxiety screening. | One SR multi-component psychological intervention<br><br>One SR assessing anti-depressant intervention |

**PICO-8: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **3. How substantial are the *desirable* anticipated effects?** | ☐ Trivial<br>☐ Small<br>☒ Moderate<br>☐ Large<br>☐ Varies<br>☐ Don't know? | Kisely et al included 17 RCTs totaling 1006 participants exploring a range of interventions (cognitive behavioral therapy, relaxation, hyperventilation control, hypnotherapy, other counseling) and reported reduction in chest pain reports in the subsequent 3-months (RR 0.70, 95% CI 0.53-0.92), more chest pain free days (mean difference 3.0, 95% CI 0.23-5.77), and reduced chest pain frequency but no effect on chest pain severity.<br><br>Wang et al. included 7 RCTs totaling 319 patients evaluating antidepressants as symptom management for functional chest pain. Antidepressants associated with pain reduction (SMD – 1.26, 95% CI -2.34 to – 0.19), improved psychological symptoms (SMD -0.87, 95% CI -1.67 to -0.08) without improved health-related quality of life (WMD 2.00, 95% CI 2.54- to -6.65). | How is "functional chest pain" defined and operationalized? Both SRs required normal coronary angiography.<br><br>Are the psycho-behavioral interventions interchangeable or do some recurrent chest pain subtypes respond differently to various modalities? Cochrane generally lumped them together as interchangeable. Probably should not be lumped together (rather analyzed as qualitative review).<br><br>Similarly, are antidepressants interchangeable? Subgroup analyses also provided.<br><br>Most readers are not going to care about these specifics since they won't be delivering it.<br><br>Does non-pharmacological psychological therapy for recurrent chest pain require specialized training (fidelity of intervention)?<br><br>If able to refer to center that does these specific therapies, may be helpful<br><br>More important question is if referred, how do patients do?<br>John questioned communication with PCP or Cardiology by EP after episode of ED care (does it occur, how do we decide who |

| | | | |
|---|---|---|---|
| | | | to communicate with, what to communicate)<br><br>These last PICO questions have population health implications because we're striving to reduce previously untreated suffering |
| ***Detailed Question to consider:***<br><br>How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is a desirable effect? | | | |

**PICO-8: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **4. How substantial are the *undesirable* effects?** | ☐ Trivial<br>☒ Small<br>☐ Moderate<br>☐ Large<br>☐ Varies<br>☐Don't know? | No adverse effects of behavioral interventions assessed.<br><br>Antidepressants associated with increased side effects (OR 0.35, 95% CI 0.15 to 0.78). | Do all antidepressants carry same side effect risk and profile?<br><br>Other undesirable effects on ED operations could include prolonged length of stay awaiting resources for referral. What do emergency departments do in scenario where nobody will accept uninsured patients referred? Or if the nearest referral center is hundreds of miles away and patient lacks transportation?<br><br>Deb: Already mandated to screen for suicide risk/depression, so this burden may not be additive and high-risk group may already be taken out of denominator.<br><br>PHQ-8 doesn't ask about suicidal risk and score >20 requires close follow-up. The majority of high-risk patients (but not 100%) will be identified by Triage suicide screening. |

***Detailed question to consider:***

How substantial is the anticipated effect (difference) for <u>each main outcome</u> for which there is an undesirable effect?

**PICO-8: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **5. Does the *balance* between desirable and undesirable effects favour the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>X Probably favors the intervention probably favors the comparison<br>☐ Favours the intervention<br>☐ Varies<br>☐ Don't know | Indirect evidence likely favors referral for anxiety/depression management in recurrent low risk chest pain patients. | Additional research to provide direct evidence on NNT, NNH, cost-effectiveness, and healthcare disparities desperately needed. |

***Detailed Judgements (Balance of desirable vs undesirable effects)***

BALANCE OF EFFECTS: **Does the balance between desirable and undesirable effects favor the intervention or the comparison?**

Detailed judgements for this criterion include judgements regarding each of the four preceding criteria:

- Is there important uncertainty about or variability in how much people value the main outcomes?
- What is the overall certainty of the evidence of effects?
- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?

In addition, panels might want to consider (and, if relevant document) the extent to which the following considerations might influence the balance between the desirable and undesirable effects:

- How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)?
- People's attitudes towards undesirable effects (how risk averse they are).

**PICO-8: GRADE Evidence-to-Decisions Framework**

- People's attitudes towards desirable effects (how risk seeking they are)

## SECTION B – Patient Values/Preferences

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **6. Is there important uncertainty about how much people value the main outcomes?** | ✗ Important uncertainty or variability<br>☐ Possibly important uncertainty or variability<br>☐ Probably no important uncertainty of variability<br>☐ No important uncertainty of variability | No evidence on patient values for recurrent low risk chest pain or detection of previously unrecognized anxiety or depression is presented. | **Many psychotherapy studies show beneficial short-term effect (1- to 3-months) but not long-term benefit (12-months)**<br><br>**Antidepressants also 5-weeks median duration (range 3-16 weeks)** |
| ***Detailed question to consider:***<br><br>How were patient values/preferences for main outcomes ascertained? Has a formal GRADE evaluation of PVP been conducted? | | | |

## SECTION C – Resource Implications

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-8: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **7. How large are the resource requirements/ costs ?** | ☐ Large costs<br>☐ Moderate costs<br>☐ Negligible costs and savings<br>☐ Moderate savings<br>☐ Large savings<br><br>☐ Varies<br>X Don't know | No cost-analysis of recurrent low-risk chest pain management pathways that include anxiety/depression referral is presented. | |

***Detailed questions to consider:***

How large is the difference in each item of resource for which fewer resources are required?

How large is the difference in each item of resource use for which more resources are required?

Cost of the intervention alone, not necessarily the downstream outcomes.

May depend on who's perspective as payor: individual, insurance company, gov't coverage plans, etc.? May need to know burden of illness numbers in the population of interest?

Can list the per-person costs, and then the aggregate costs of the payor (if not individual?); specify the viewpoint being judged for ratings (individual vs. system vs. societal, etc.)

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **8. What is the certainty of the evidence of resource** | ☐ Very low<br>☐ Low<br>☐ Moderate<br>☐ High | No cost-analysis of recurrent low-risk chest pain management pathways that include anxiety/depression referral is presented. | |

**PICO-8: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **requirements (costs)?** | X No included studies | | |
| ***Detailed question to consider:***<br>See specific costing resources if possible...CADTH, EED, other databases if available? Cut/paste links to relevant resources as needed<br><br>Have all important items of resource use that may differ between the options being considered been identified?<br><br>How certain is the cost of the items of resource use that differ between the options being considered?<br><br>Is there important variability in the cost of the items of resource use that differ between the options being considered? | | | |

**PICO-8: GRADE Evidence-to-Decisions Framework**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **9. Does the cost-effectiveness of the intervention favor the intervention or the comparison?** | ☐ Favors the comparison<br>☐ Probably favors the comparison<br>☐ Does not favor either the intervention or the comparison<br>☐ Probably favors the intervention<br>☐Favors the intervention<br>☐ Varies<br>X No included studies | No cost-effectiveness estimates of recurrent low-risk chest pain management pathways that include anxiety/depression referral are presented. | |

***Detailed questions to consider:***

Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses? No cost-effectiveness studies.

Is the cost-effectiveness ratio sensitive to multi-variable sensitivity analysis? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based reliable? No cost-effectiveness studies.

Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?
No cost-effectiveness studies.

**PICO-8: GRADE Evidence-to-Decisions Framework**

## SECTION D – Equity & Stakeholder Considerations

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|
| **10. What would be the impact on health inequity?**<br><br>Summary of GRADE equity articles? | ☐ Increased<br>☐ Probably increased<br>X Uncertain<br>☐ Reduced<br>☐ Varies | No evidence on health equity in ED or post-ED evaluation of low risk recurrent chest pain presented. | Will low income, under-insured individuals with recurrent low-risk chest pain have access to these recommended referrals after ED evaluation?<br><br>Access to resources (same as PICO-7)<br><br>Anna Marie: Different psycho-behavioral therapy of different acceptance or perceived value (example CBT). |

***Detailed question to consider:***

Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there important considerations that should be made when implementing the intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

| | | | |
|---|---|---|---|
| **11. Is the option acceptable to key stakeholders?** | ☐ No<br>☐ Probably no<br>X Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented. | Need input from patient representative John on July 24.<br>John's perspective is ED referral for psychiatric problems appropriate and probably beyond the therapeutic scope of emergency care ("not a fan of taking those tests in the emergency department")<br><br>Need input from Cardiologist Mike Kontos on July 24. |

***Detailed question to consider:***

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future?

Are there key stakeholders that would not accept the distribution of the benefits, harms and costs?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)?

☐ Yes ☐ Probably yes ☐ Probably no ☐ No X Don't know

Would the intervention (option) adversely affect people's autonomy?

☐ Yes ☐ Probably yes X Probably no ☐ No ☐ Don't know

Are there key stakeholders that would disapprove of the intervention (option) morally, for reasons other than its effects on people's autonomy (i.e. in relationship to ethical principles such as non-maleficence, beneficence or justice)?

☐ Yes X Probably yes ☐ Probably no ☐ No ☐ Don't know

**SECTION E – Feasibility**

| Criterion | Judgments | Research Evidence | Other Considerations |
|---|---|---|---|

**PICO-8: GRADE Evidence-to-Decisions Framework**

| | | | |
|---|---|---|---|
| **12. Is the option feasible to implement?** | ☐ No<br>☐ Probably no<br>☒ Uncertain<br>☐ Probably yes<br>☐ Yes<br>☐ Varies | No evidence presented on knowledge translation, healthcare provider acceptability, or process change by which to evaluate "feasibility". | Do emergency medicine physicians and APP's have sufficient training in the administration, interpretation, and/or explanation of anxiety/depression screeners?<br><br>Does every ED have pragmatic access to mental health resources in response to these results, regardless of patient's insurance status?<br><br>Does documentation of previously unrecognized depression increase ED providers' malpractice risk?<br><br>This topic is a health system feasibility issue (not provider or department). |

***Detailed question to consider:***

Is the intervention (option) sustainable?

☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies ☒ Don't know

Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?

☐ No ☐ Probably No X Probably Yes ☐ Yes ☐ Varies ☐ Don't know

**PICO-8: GRADE Evidence-to-Decisions Framework**

## SUMMARY OF JUDGEMENTS

**Statement of Question:** _____

_____

**(Comp: comparison, Int: intervention)**

| | |
|---|---|
| **1. Problem Priority** | ☐ No ☐ Probably No ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **2. Overall Certainty of Evidence** | ☐ Very Low ☐ Low X Moderate ☐ High ☐ No included studies |
| **3. Desirable Effects** | ☐ Trivial ☐ Small X Moderate ☐ Large ☐ Varies X Don't know |
| **4. Undesirable Effects** | ☐ Large ☐ Moderate X Small ☐ Trivial ☐ Varies ☐ Don't know |
| **5. Balance of Effects** | ☐ Favors Comp X Probably favors Comp ☐ Favors neither Comp/ Int ☐ Probably favors Int ☐ Favours Int ☐ Varies ☐ Don't know |
| **6. Patient Values & Preferences (Uncertainty/varability – U/V)** | ☐ Important U/V ☐ Possibly important U/V ☐ Probably no important U/V ☐ No U/V X Don't know |
| **7. Resources Required** | ☐ Large costs ☐ Moderate costs ☐ Negligible costs/savings ☐ Moderate savings ☐ Large savings ☐ Varies X Don't know |
| **8. Certainty of Evidence of Required Resources** | ☐ Very low ☐ Low ☐ Moderate ☐ High X No included studies |
| **9. Cost Effectiveness** | ☐ Favors Comp ☐ Probably favors Comp ☐ Neither Comp/Int ☐ Probably favors Int ☐ Favors Int ☐ Varies X No included studies |
| **10. Equity** | ☐ Reduced ☐ Probably reduced ☐ No impact ☐ Probably increased ☐ Increased ☐ Varies X Don't know |
| **11. Acceptability** | ☐ No ☐ Probably no ☐ Probably Yes ☐ Yes ☐ Varies X Don't know |
| **12. Feasibility** | ☐ No ☐ Probably no X Probably Yes ☐ Yes ☐ Varies ☐ Don't know |

**PICO-8: GRADE Evidence-to-Decisions Framework**

**TYPE OF RECOMMENDATION:** **In adult patients with recurrent low-risk chest pain, we suggest referral for anxiety/depression management, as this might have an impact on healthcare use/return ED visits. (Conditional/Either).**

***Implications for Strength of Recommendations:***

| Stakeholder | Strong Recommendation | Weak Recommendation |
|---|---|---|
| Policy makers | The recommendation could be adapted as a "policy" in most situations.<br>The recommendation could be operationalized into a performance indicator for audit/feedback and quality improvement. | There is a need for substantial debate and involvement of stakeholders.<br>The recommendations should not be used as a performance indicator for audit/feedback and quality improvement. |
| Patients | Most patients in this situation would want the recommended course of action (only a few may not) | A majority of patients may want the recommended action, but many would not |
| Clinicians | Most patients should receive the recommended course of action | Prepare to have a more individualized shared-decision making process with patients based on their own values/preferences |

**FOR THIS RECOMMENDATION?**

| | |
|---|---|
| **Strength of Recommendation** | ☐ Strong ☒ Conditional |
| **Direction of Recommendation** | ☐ For X Either (neither) ☐ Against |

## PICO-8: GRADE Evidence-to-Decisions Framework

| **Recommendation:** **In adult patients with recurrent low-risk chest pain, we suggest referral for anxiety/depression management, as this might have an impact on healthcare use/return ED visits. (Conditional/Either).** | | | | | |
|---|---|---|---|---|---|
| **Balance of consequences** | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
| | ○ | ○ | X | ○ | ○ |

| **Type of recommendation** | We recommend against this option | We suggest not this option | We suggest this option | We recommend this option |
|---|---|---|---|---|
| | ○ | ○ | X | ○ |
| **Recommendation** | *Clear statement of the recommendation, with clear language "Suggest vs recommend" and "For vs against"* | | | |
| **Justification** | ??? | | | |
| **Subgroup considerations** | Are there specific risk groups that need to be considered differentially? | | | |
| **Implementation considerations** | Provide a care pathway/protocol/algorithm if relevant.<br>Include key performance indicators for future QI/PDSA cycles.<br><br>What is the dissemination/education plan for these recommendations? | | | |
| **Monitoring and evaluation** | Assessment of key performance indicators as outlined above.<br>Specify measurement schedule. | | | |
| **Research possibilities** | Where are the current gaps in care/management of your population of interest?<br>What are the next steps needed for research (short/middle/long-term)? | | | |