

Synthesising Evidence for Complex Questions: the NICE Perspective

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NICE Guideline Portfolio (March 2021)

- Approx. 330 guidelines published since 2002 (includes new and updated topics)
 - Comprising ~4-5000 review questions and (since 2009) >16,000 recommendations
- Covers clinical (n~210), public health (n~70) and social care (n~70) topic areas.
- Approximately 60 guidelines currently being developed/updated, involving over 1000 people (most on a voluntary basis)

Challenges with ongoing maintenance

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NICE CHTE Portfolio (May 2022)

Currently active guidance:

- Technology appraisals: 605
- Medical technologies guidance: 63
- Diagnostics guidance: 41

What do people want from our guidance?

People are very clear they want two things from our guidance:

- It to be up to date and reflect the latest evidence in all areas, so people can be sure advice is not outdated.
- The guidance not to change too often, as each time the guidance in an area changes this comes with an implantation cost.

Differences between people's stated and revealed preferences – some particular data from our COVID guidance.

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Conclusion – people are terrible at telling you what they want, and are just reacting by suggesting the opposite of what the current situation is.

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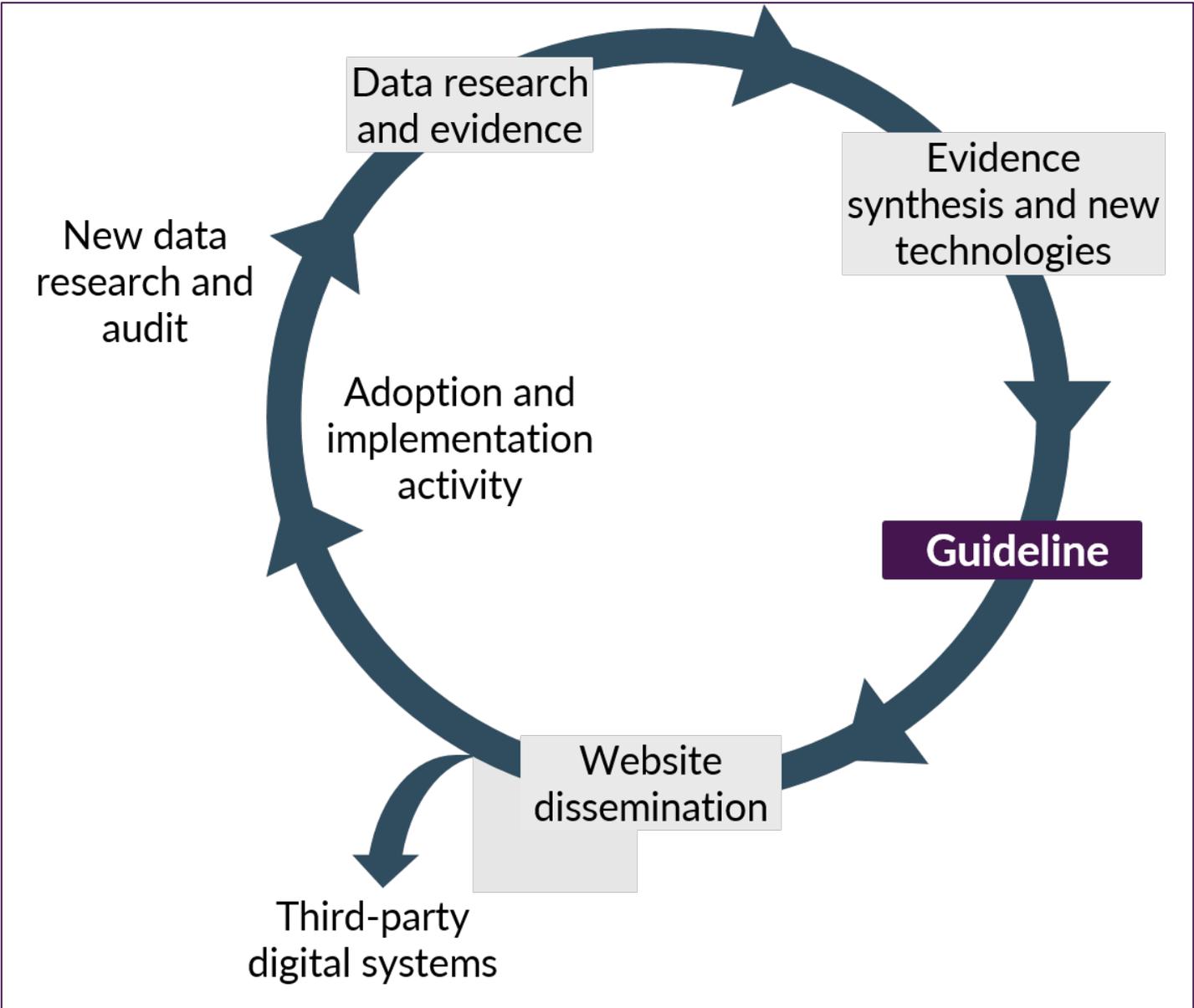
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Possibly more helpful conclusion – when people say they want up to date and reflect the latest evidence, they mean if anything substantive has changed in the conclusions.

How does one identify such situations, without having to conduct the whole review and look at the changes in results/conclusions?

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Traditional guideline surveillance

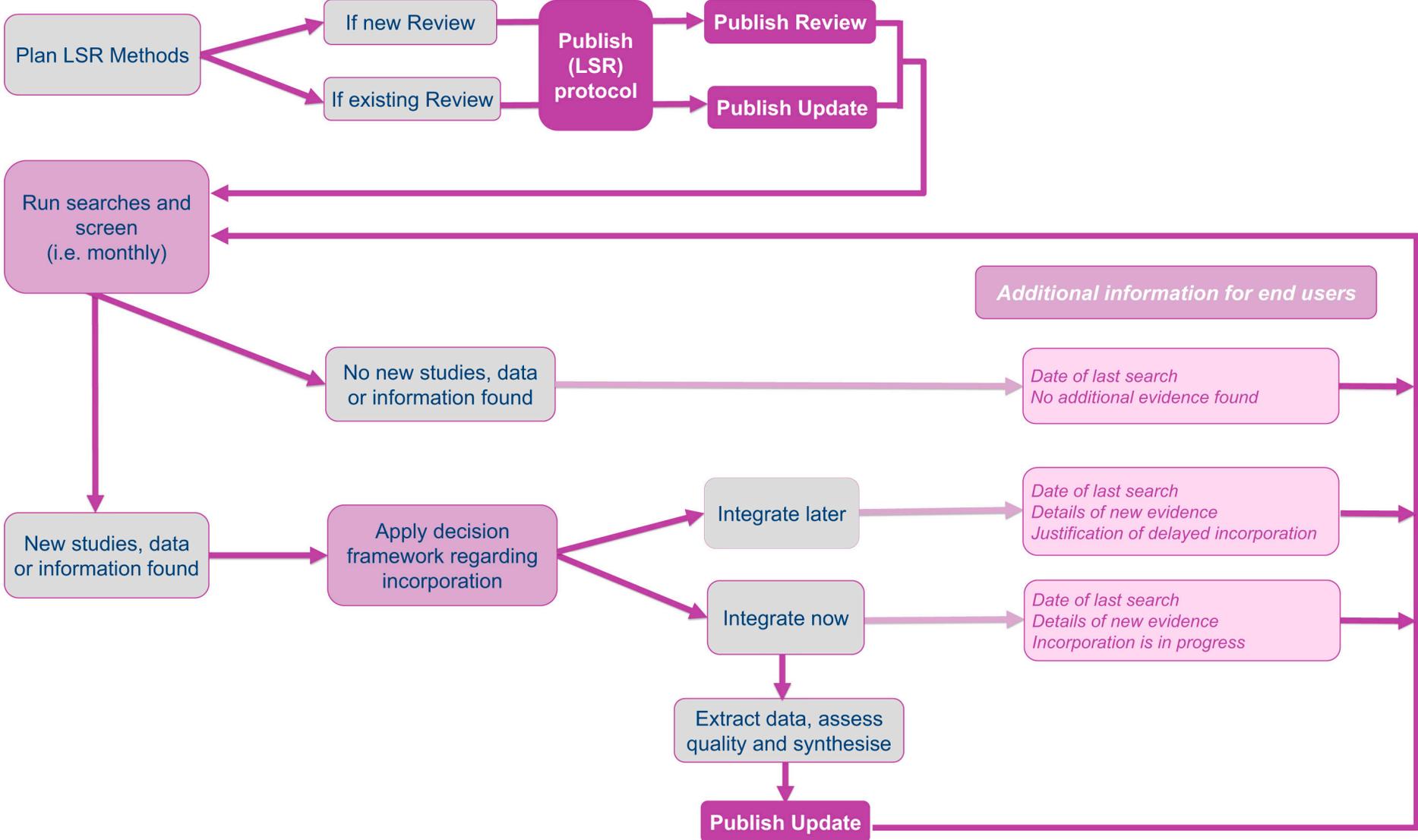
Reasons that an update might be triggered in a world of classical guideline surveillance:

- A large volume of new published evidence.
- New evidence that seems to contradict previous results.
- New evidence that is particularly more methodologically robust or applicable than previous evidence.
- People telling us our guidance doesn't reflect what the evidence base now says.

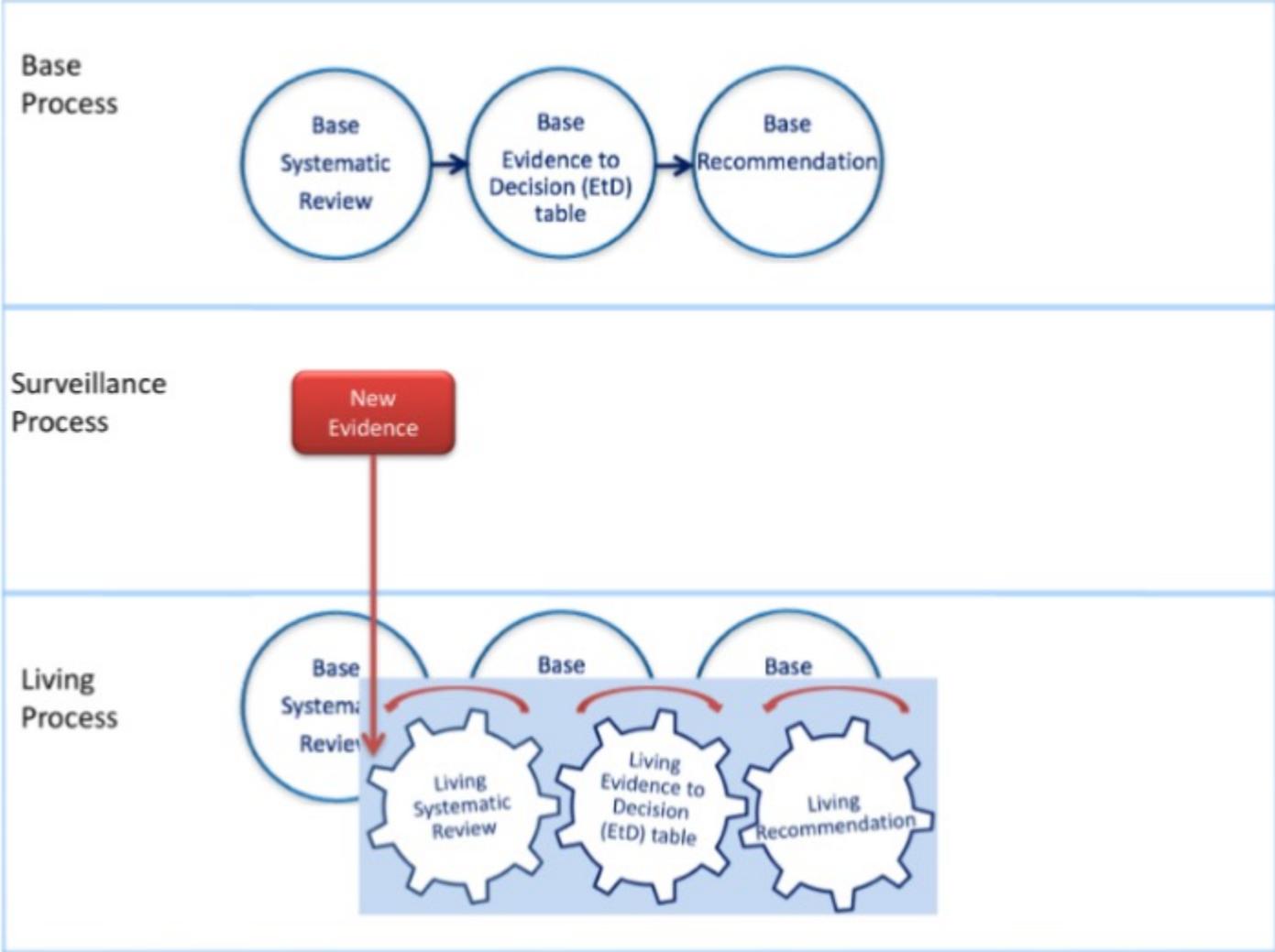
None of these things guarantees (or even really makes it that likely) that meaningful changes to our guidance will result.

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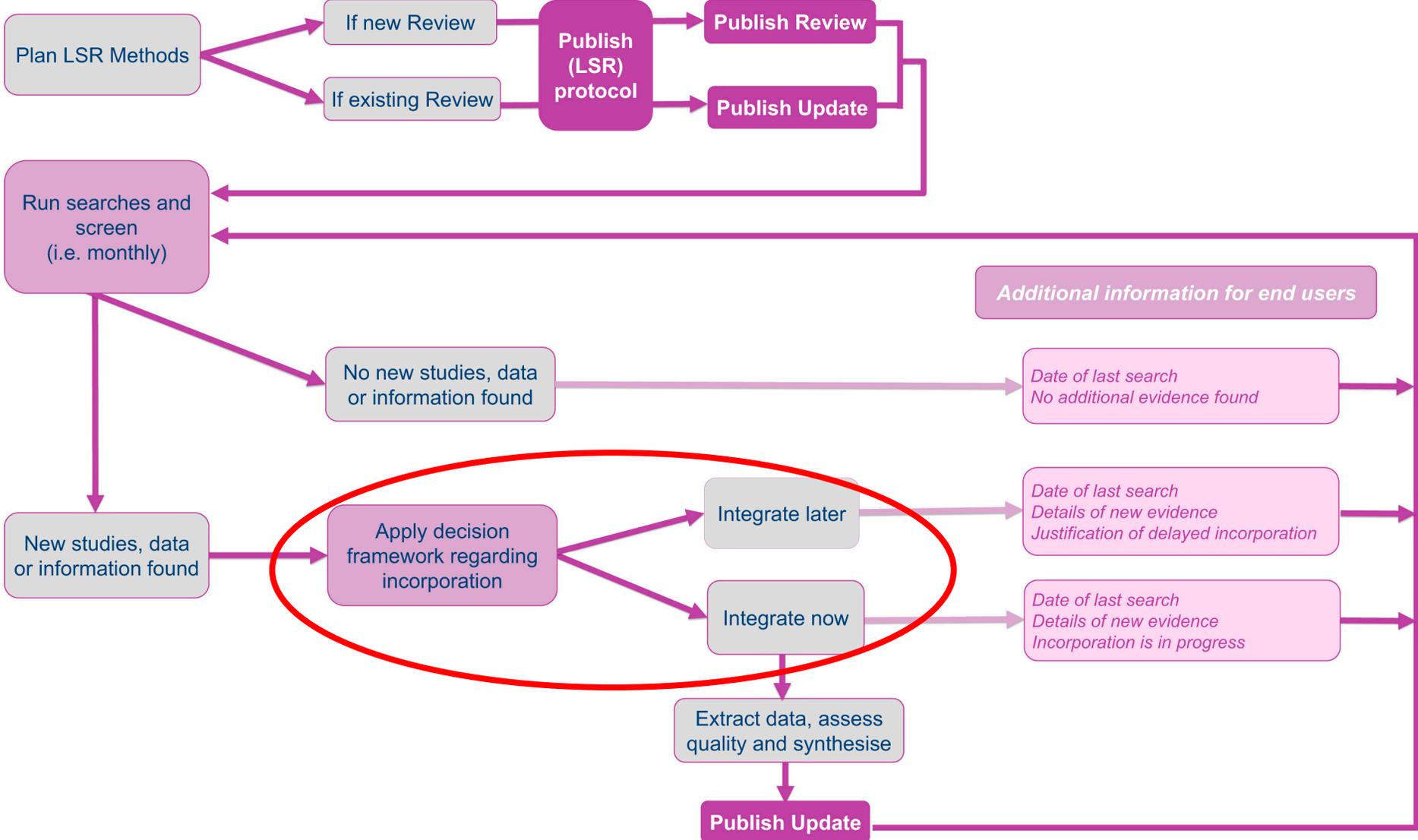
Living systematic reviews (Elliott 2017)



Living guidelines/recommendations (Akl 2017)



Living systematic reviews (Elliott 2017)



Increasing review complexity

- In 2016, approximately 12% of reviews in NICE guidelines were “complex.”
- In 2021, approximately 29% of (non-COVID) reviews in NICE guidelines were complex.

Complex in this case is defined as including more than one analytical method within how a question is addressed.

Reasons for this change

- Increasingly routine uptake of particular quantitative analytical techniques (for example network meta-analysis and meta-regression).

Probably doesn't have broader implications than the need to ensure software and advice documents reflect the broadening range of people who are not involved in such analyses.

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Example:

- Many interventions require a specific diagnosis to be eligible (or at least the research studies specified a particular diagnosis).
- Often that is not the way the condition is diagnosed in practice in the NHS.
- Therefore, it is not possible to accurately estimate the effectiveness of the intervention without considering the accuracy of the diagnostic tests.

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- A desire to create more complete treatment pathways, rather than considering individual interventions in isolation.

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- **An increased focus on the need to address health inequalities in a systematic and evidence based way.**

Given the lack of direct evidence that usually exists for many populations, it is hard to address such questions without considering the mechanisms by which an intervention works, and linking that to other information on how that may therefore lead to differential effectiveness.

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NICE has consulted on and is soon to publish a real-world evidence framework document. Aims:

- clearly describe best-practices for the planning, conduct, and reporting of real-world evidence studies
- improve the transparency and quality of real-world evidence used to inform NICE guidance
- improve committee trust in real-world evidence studies
- ensure real-world evidence is used where it helps to:
 - reduce uncertainties
 - improve recommendations
 - speed up access of patients to new effective interventions

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Real-world evidence framework

Two very broad use cases:

- Instead of RCTs when good evidence from them is not available.
- As well as RCTs when they can provide extra important contextual information:
 - Differences in patient populations.
 - Differences in adherence.
 - Differences in the context of how and where the interventions are used.

There will be an increasing need for advice on how such data are best analysed, and whether and how they can be integrated with more traditional research data.

Consequences of increased complexity

The more complex a review, the harder it is to identify how a change in the underlying evidence base will affect the conclusions of a review.

Simple comparison (pairwise meta-analysis versus network meta-analysis):

- An update of an NMA is likely to find a larger number of new studies than the update of a pairwise meta-analysis.
- The consequences of a new study with is different to the existence evidence base can be harder to predict:
 - Effects through indirect comparisons.
 - Effects through heterogeneity estimation.

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There currently aren't good techniques (I assert, or at least that are commonly applied) to understand how sensitive the results of an analysis are likely to be to future changes in the evidence base.

Can draw an analogy to value of information analysis which, whilst not that commonly used, does at least provide a framework to consider these issues in a health economic context.

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At the same time, the more complex a review, the harder it is to make modifications to that review as someone outside the original team:

- Complexity of analysis
- Access to data

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Most guidelines may become living guidelines, but most reviews won't become living reviews

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When planning a living evidence review, the more complex the review, the more upfront decisions that need to be made, and the higher the time investment in subsequently modifying those choices.

What do we think we need

- To respond to the change in certain analytical techniques from specialist and uncommon to much more routine.
- To find ways to define triggers for what new evidence has the highest chance of meaningfully changing the conclusions of a review.
- To understand how best to integrate data collected from research studies and that collected routinely in practice.
- To work out how best to collaborate better in the future on more complex reviews (in particular because of the differences in funding incentives between producers and users of a review).