Overdiagnosis

CHECKLIST OF ITEMS TO CONSIDER WHEN MODIFYING A DISEASE DEFINITION

CHECKLIST ITEM	COMMENTS
1. **Definition:** What are the differences between the previous and the new definition?	
2. **Number of people affected:** How will the new disease definition change the incidence and prevalence of the disease?	
3. **Trigger:** What is the trigger for considering the modification of the disease definition?	
4. **Prognostic ability:** How well does the new definition of disease predict clinically important outcomes compared with the previous definition?	
5. **Disease definition precision and accuracy:** What is the repeatability, reproducibility, and accuracy (when estimations are possible) of the new disease definition?	
6. **Benefit:** What is the incremental benefit for patients classified by the new definition vs the previous definition?	
7. **Harm:** What is the incremental harm for patients classified by the new definition vs the previous definition?	
8. **Net benefit and harms:** What is the net benefit and harm for patients classified by the new definition vs the previous definition?	

Reference: Doust J, Vandvik PO, Qaseem A, Mustafa RA, Horvath AR, Frances A, Al-Ansary L, Bossuyt P, Ward RL, Kopp I, Gollogly L, Schunemann H, Glasziou P, for the Guidelines International Network (G-I-N) Preventing Overdiagnosis Working Group. Guidance for Modifying the Definition of Diseases: A Checklist. *JAMA Intern Med.* 2017;177(7):1020-1025.

NOTES ON CHECKLIST ITEMS

1. **Definition: What are the differences between the previous and the new definition?**
   The panel needs to clearly describe the new and previous definitions of disease and how they differ. Previous definitions may not have been standardised, and if so, versions of the previous definition in widespread use should be outlined.

2. **Number of people affected: How will the new disease definition change the incidence and prevalence of the disease?**
   The panel should describe the expected effect of proposed changes on incidence and/or prevalence of disease. Where there is a change in the method of defining disease and not just a change in threshold, studies of prevalence need to cross-classify patients, showing where the definitions agree or are discordant. A change in testing methods can cause changes in the type of patients being diagnosed with a decrease or no change in incidence but most commonly will increase the incidence of disease. Studies estimating changes in incidence or prevalence should be conducted in their respective clinical contexts using the methods of measurement that will be used in clinical practice.

3. **Trigger: What is the trigger for considering the modification of the disease definition?**
   Outlining the trigger for the modification allows greater understanding for the need of a new disease definition. A panel might have 1 or several reasons for considering modifying a disease definition. Examples include the emergence of new treatments with clear benefits for patients identified by a new definition of disease, the development of a new test, new evidence on prognosis, a need to standardise definitions across clinical settings or for research purposes, or to improve the clarity or precision of a disease definition.

4. **Prognostic ability: How well does the new definition of disease predict clinically important outcomes compared with the previous definition?**
   Being diagnosed with a disease only benefits a patient if the diagnosis assists in understanding current symptoms or the risk of future clinically important events, or if the patient can benefit from specific treatment. To appreciate potential harms and benefits of the change in definition, it is necessary to understand the natural history for those patients labeled by the new definition but not by the previous definition. Where the prognosis of the additional patients is better than those classified with the previous definition, the average prognosis of all patients classified with the new definition will improve

5. **Disease definition precision and accuracy: What is the repeatability, reproducibility, and accuracy (when estimations are possible) of the new disease definition?**
   Disease definitions with poor precision result in inconsistent diagnoses in patients and have poor clinical utility. Measures of precision include repeatability (agreement in identical conditions) and reproducibility (agreement across comparable conditions). The variation observed around the threshold for the disease is of the most relevance. Precision is ideally tested in the clinical context using the measurement methods that will be used in clinical practice.

6. **Benefit: What is the incremental benefit for patients classified by the new definition vs the previous definition?**
   Wherever changes in disease definitions will alter which patients receive treatment, it is essential to assess treatment benefits and harms, focusing on the balance of benefits and harms for those diagnosed by the new definition and not diagnosed by the previous definition. Guideline panels may need to consider a wide variety of benefits, including non health outcomes.

7. **Harm: What is the incremental harm for patients classified by the new definition vs the previous definition?**
   The potential harms from diagnosis include the physical harms of diagnosis and treatment; psychological effects, such as anxiety; social effects, such as stigma and discrimination; and financial consequences, such as effects on employment. In the case of genetic diseases, harms may extend to family members. Changes in resource usage can result in harm by reducing access to care for some patients and by diversion and distraction of clinical care. This can happen at both the societal level, with resources taken from areas more important to health, and at the individual level, by distracting individuals from activities more important to their well-being.

8. **Net benefit and harms: What is the net benefit and harm for patients classified by the new definition vs the previous definition?**
   Modifying a disease definition should be guided by a balanced assessment of the anticipated benefits and harms, using the best evidence available. The definition should reflect the values and preferences of patients and the wider community and include the impact on resource usage. We recommend a transparent and explicit process, such as the approach developed by GRADE, using structured evidence summaries to tabulate anticipated absolute effects across important patient outcomes.