Background Adherence to current monomorbidity-focused, mono-disciplinary guidelines may result in undesirable effects for persons with several comorbidities, in adverse interactions between drugs and diseases, conflicting management strategies, and polypharmacy. As yet no satisfactory approaches exist to address multimorbidity (MM) in clinical guidelines since this patient group is too heterogeneous as to be met by guideline recommendations.

Objectives To develop a set of case-based (N=1) guidelines for common disease combinations identified through epidemiological research and expert (GP) consultations.

Methods We followed a new 5-step, mixed methods approach comprising: (1) review of epidemiological data on MM patterns; (2) interdisciplinary focus groups developed case vignettes according to the new 5-step-process. We present a new approach to capture the complex and heterogeneous problems of MM through evidence-based recommendations. This set of N-of-one-guidelines may serve as a framework of evidence-based recommendations for MM patients as the base for the development of meta-tools for both guideline developers and clinicians.

Results Fifteen guidelines were included: 1 Japanese, 1 Danish, 2 Finnish, 2 South-Korean, 2 British and 7 Dutch. The quality of the guidelines varied. Barriers and facilitators for implementation (Applicability), competing interests (Editorial independences), and the process to gather and synthesise evidence (Rigour of Development) were poorest described. The domain Scope and Purpose scored highest. Recommendations concerning assessment refer to diagnostic classification, inventory of performance problems, causal factors and barriers for recovery. Specific workplace factors are often mentioned. Guidelines agree on work adaptation if necessary, psychological treatment and communication about treatment plan between involved actors.

Discussion Guidelines are difficult to find since they are commonly exclusively available in local languages. Therefore probably more guidelines exist then found. To learn from each other, guidelines should be translated into world languages and be accessible via international databases.

Implications Guideline developers can use AGREEII to increase quality. Although social context may differ among countries and can influence guideline recommendations, developers can learn from each other through reviews of this kind.