eTable 2: Review questions, inclusion and exclusion criteria

PIRO questions	Inclusion criteria	Exclusion criteria
Population	• has to reflect the real-world referral setting of a specialised care centre, i.e., patients with rapid progressive neurodegeneration who are suspected of sCJD, but have no final diagnosis yet • has to described in sufficient detail to allow for replication, validation, and generalization of the study, i.e., two of the following characteristics are described: age of patients, female to male ratio, or distribution of symptoms	criterion "*inappropriate / not well-defined population*" is met if • the non-CJD group consists of healthy individuals or does not focus on patients representing true differential diagnoses of sCJD • the samples are selected from biorepositories based on already known diagnoses • the population is not sufficiently described
Target condition	• sCJD according to ICD-10[1] and CJD 2010[2,3]	criterion "*inappropriate target condition*" is met if • patients represent a mixture of sporadic CJD with genetic or other types of CJD that cannot be disentangled • the cases are reported to have CJD without further specification
Index test	• has to be performed during the patient's first diagnostic workup for her/his symptoms without a pre-defined diagnosis • has to be based on the measurement of biomarkers in blood or CSF • has to be described in sufficient detail to allow for replication, validation, and generalization of the study	criterion "*insufficient information on index test*" is met if • the index test is not sufficiently described
Reference test	• has to use established diagnostic criteria of sCJD[3,4] • has to be described in sufficient detail to allow for replication, validation, and generalization of the study	criterion "*insufficient information on reference test*" is met if • the reference test is not sufficiently described
Outcome	• numbers of true positives, false negatives, false positives, and true negatives • alternatively, sensitivity, specificity and the numbers of patients with and without sCJD to be able to calculate true positives, false negatives, false positives, and true negatives	criterion "*insufficient information on outcome*" is met if • the outcome cannot be calculated from the information in the publication
	Further exclusion criteria to ensure that the included studies adequately answer the review question	• duplicated data • samples not from living humans • no diagnostic test accuracy study / study design cannot be determined

References:
1. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders. 1993.
2. World Health Organization. Global surveillance, diagnosis, and therapy of human transmissible spongiform encephalopathies: report of WHO consultation (WHO/EMC/ZDI/98/9). Geneva; 1998.

3. Zerr I, Kallenberg K, Summers DM, et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain. 2009;132:2659–2668.
4. Mackenzie G, Will R. Creutzfeldt-Jakob disease: recent developments. F1000Research. 2017;6:2053.