

# How are patient-reported outcomes and symptoms being measured in adults with relapsed/refractory multiple myeloma? A Systematic Review

## *Quality of Life Research*

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**Table S1.** Full Search Strategy, Searched: 11/20/18

PubMED		
1	"multiple myeloma"[MeSH] OR myeloma[tiab] OR Myelomas[tiab] OR Myelomatosis[tiab] OR Myelomatoses[tiab] OR "Kahler Disease"[tiab]	56,468
2	"Recurrence"[Mesh] OR "Neoplasm Recurrence, Local"[Mesh] OR "Retreatment"[Mesh] OR relapse[tiab] OR relapses[tiab] OR "Relapsed"[TIAB] OR "refractory"[TIAB] OR "RRMM"[TIAB] OR recurrence[tiab] OR recurrences[tiab] OR recurred[tiab] OR retreatment[tiab] OR retreated[tiab]	667493
3	"quality of life"[MeSH] OR "quality of life"[tiab] OR "life quality"[tiab] OR "well being"[tiab] OR "well-being"[tiab] OR "health status"[mesh] OR "health status"[tiab] OR "function"[TIAB] OR "functional"[TIAB] OR "signs and symptoms"[Mesh] OR "symptoms"[tiab] OR symptom[TIAB] OR symptomatic[TIAB] OR "nausea"[tiab] OR "nauseous"[tiab] OR "vomiting"[tiab] OR "constipation"[tiab] OR "diarrhea"[tiab] OR "diarrhoea"[tiab] OR "shortness of breath"[TIAB] OR dyspnea[TIAB] OR "peripheral neuropathy"[tiab] OR "peripheral neuropathies"[tiab] OR "cognition"[MeSH] OR "cognition"[TIAB] OR cognitive[tiab] OR "memory"[MeSH] OR "memory"[TIAB] OR "pain"[tiab] OR "insomnia"[tiab] OR "sleep disturbance"[tiab] OR "Fatigue"[tiab] OR "anxiety"[Mesh] OR "anxiety"[tiab] OR "anxieties"[tiab] OR "anxious"[tiab] OR "nervousness"[tiab] OR "depression"[Mesh] OR "depression"[tiab] OR "depressions"[tiab] OR "depressive"[tiab] OR "depressed"[tiab] OR distress[tiab] OR burden[tiab] OR "stress, psychological"[Mesh] OR stress[tiab] OR stresses[tiab] OR suffering[tiab]	6950707
4	#1 AND #2 AND #3	1760
5	#4 NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh]) NOT ("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh]) NOT "Adult"[Mesh]) AND English[lang] AND ("2003/01/01"[PDAT] : "2018/12/31"[PDAT])	1033
CINAHL		
1	(MH "multiple myeloma") OR TI (myeloma OR Myelomas OR Myelomatosis OR Myelomatoses OR "Kahler Disease") OR AB (myeloma OR Myelomas OR Myelomatosis OR Myelomatoses OR "Kahler Disease")	7113
2	(MH "recurrence") OR (MH "Neoplasm Recurrence, Local") OR TI (relapse OR relapses OR Relapsed OR refractory OR RRMM OR recurrence OR recurrences OR recurred OR retreatment OR retreated) OR AB (relapse OR relapses OR Relapsed OR refractory OR RRMM OR recurrence OR recurrences OR recurred OR retreatment OR retreated)	108,471
3	(MH "quality of life+") OR (MH "symptoms+") OR (MH cognition+) OR (MH memory+) OR (MH "Anxiety+") OR (MH "depression+") OR (MH "stress, psychological+") OR (MH "health status+") OR TI ("quality of life" OR "life quality" OR "well being" OR "well-being" OR "health status" OR function OR functional OR symptoms OR symptom OR symptomatic OR nausea OR "nauseous" OR "vomiting" OR "constipation" OR "diarrhea" OR "diarrhoea" OR dyspnea OR "shortness of breath" OR "peripheral neuropathy" OR "peripheral neuropathies" OR cognition OR cognitive OR memory OR "pain" OR "insomnia" OR "sleep disturbance" OR "Fatigue" OR "anxiety" OR "anxieties" OR "anxious" OR "nervousness" OR "depression" OR "depressions" OR "depressive" OR "depressed" OR distress OR "stress" OR "stresses" OR "suffering") OR AB ("quality of life" OR "life quality" OR "well being" OR "well-being" OR "health status" OR function OR functional OR symptoms OR symptom OR symptomatic OR nausea OR "nauseous" OR "vomiting" OR "constipation" OR "diarrhea" OR "diarrhoea" OR dyspnea OR "shortness of breath" OR "peripheral neuropathy" OR "peripheral neuropathies" OR cognition OR cognitive OR memory OR "Pain" OR "insomnia" OR "sleep disturbance" OR "Fatigue" OR "anxiety" OR "anxieties" OR "anxious" OR "nervousness" OR "depression" OR "depressions" OR "depressive" OR "depressed" OR distress OR "stress" OR "stresses" OR "suffering")	1,143,138
4	#1 AND #2 AND #3	299
5	2003 – 2018, English	289
PsycINFO		
1	TI (myeloma OR Myelomas OR Myelomatosis OR Myelomatoses OR "Kahler Disease") OR AB (myeloma OR Myelomas OR Myelomatosis OR Myelomatoses OR "Kahler Disease")	256
2	DE "Relapse (Disorders)" OR TI (relapse OR relapses OR Relapsed OR refractory OR RRMM OR recurrence OR recurrences OR recurred OR retreatment OR retreated) OR AB (relapse OR relapses OR Relapsed OR refractory OR RRMM OR recurrence OR recurrences OR recurred OR retreatment OR retreated)	41,485
3	DE "quality of life" OR DE "Symptoms" OR DE "Psychiatric Symptoms" OR DE "Mental Disorders due to General Medical Conditions" OR DE cognition OR DE memory OR DE Anxiety OR DE "Depression (Emotion)" OR DE stress OR TI ("quality of life" OR "life quality" OR "well being" OR "well-being" OR "health status" OR function OR functional OR symptoms OR symptom OR symptomatic OR nausea OR "nauseous" OR "vomiting" OR "constipation" OR "diarrhea" OR "diarrhoea" OR dyspnea OR shortness of breath OR "peripheral neuropathy" OR "peripheral neuropathies" OR cognition OR cognitive OR memory OR "Pain" OR "insomnia" OR "sleep disturbance" OR "Fatigue" OR "anxiety" OR "anxieties" OR "anxious" OR "nervousness" OR "depression" OR "depressions" OR "depressive" OR "depressed" OR distress OR "stress" OR "stresses" OR "suffering") OR AB ("quality of life" OR "life	1,630,394

	quality" OR "well being" OR "well-being" OR "health status" OR function OR functional OR symptoms OR symptom OR symptomatic OR nausea OR "nauseous" OR "vomiting" OR "constipation" OR "diarrhea" OR "diarrhoea" OR dyspnea OR shortness of breath OR "peripheral neuropathy" OR "peripheral neuropathies" OR cognition OR cognitive OR memory OR "Pain" OR "insomnia" OR "sleep disturbance" OR "Fatigue" OR "anxiety" OR "anxieties" OR "anxious" OR "nervousness" OR "depression" OR "depressions" OR "depressive" OR "depressed" OR distress OR "stress" OR "stresses" OR "suffering")	
4	#1 AND #2 AND #3	10
5	#4 AND 2003 – 2018, English	10
EMBASE		
1	'multiple myeloma'/exp OR myeloma:ti,ab OR Myelomas:ti,ab OR Myelomatosis:ti,ab OR Myelomatoses:ti,ab OR 'Kahler Disease':ti,ab	95,727
2	relapse/exp OR relapse:ti,ab OR relapses:ti,ab OR relapsed:ti,ab OR 'recurrence'/exp OR recurrence:ti,ab OR refractory:ti,ab OR RRMM:ti,ab OR recurrence:ti,ab OR recurrences:ti,ab OR recurred:ti,ab OR retreatment:ti,ab OR retreated:ti,ab	935099
3	'quality of life'/exp OR 'symptoms'/exp OR 'nausea'/exp OR 'vomiting'/exp OR 'diarrhea'/exp OR 'constipation'/exp OR 'pain'/exp OR 'peripheral neuropathy'/exp OR 'cognition'/exp OR 'memory'/exp OR 'dyspnea'/exp OR 'insomnia'/exp OR 'sleep disorder'/exp OR 'fatigue'/exp OR 'anxiety'/exp OR 'depression'/exp OR 'distress syndrome'/exp OR 'health status'/exp OR 'quality of life':ti,ab OR 'life quality':ti,ab OR 'well being':ti,ab OR 'well-being':ti,ab OR 'health status':ti,ab OR 'function':ti,ab OR 'functional':ti,ab OR 'symptoms':ti,ab OR symptom:ti,ab OR symptomatic:ti,ab OR 'nausea':ti,ab OR 'nauseous':ti,ab OR 'vomiting':ti,ab OR 'constipation':ti,ab OR 'diarrhea':ti,ab OR 'diarrhoea':ti,ab OR 'dyspnea':ti,ab OR 'shortness of breath':ti,ab OR 'peripheral neuropathy':ti,ab OR 'peripheral neuropathies':ti,ab OR 'cognition':ti,ab OR cognitive:ti,ab OR 'memory':ti,ab OR 'Pain':ti,ab OR 'insomnia':ti,ab OR 'sleep disturbance':ti,ab OR 'sleep disorder':ti,ab OR 'Fatigue':ti,ab OR 'anxiety':ti,ab OR 'anxieties':ti,ab OR 'anxious':ti,ab OR 'nervousness':ti,ab OR 'depression':ti,ab OR 'depressions':ti,ab OR 'depressive':ti,ab OR 'depressed':ti,ab OR 'distress':ti,ab OR 'stress':ti,ab OR 'stresses':ti,ab OR 'suffering':ti,ab	9,392,792
4	#1 AND #2 AND #3	6,510
5	#4 AND (2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py) AND ('article'/it OR 'article in press'/it OR 'chapter'/it OR 'conference paper'/it OR 'erratum'/it OR 'note'/it OR 'short survey'/it)	1,891
SCOPUS		
1	<p>myeloma OR Myelomas OR "Myelomatosis" OR "Myelomatoses" OR "Kahler Disease" 78,182</p> <p>Recurrence OR Retreatment OR relapse OR relapses OR Relapsed OR refractory OR RRMM OR recurrences OR recurred OR retreated 890,612</p> <p>"quality of life" OR "life quality" OR "well being" OR OR "health status" OR "function" OR "functional" OR symptoms OR symptom OR symptomatic OR nausea OR nauseous OR vomiting OR constipation OR diarrhea OR diarrhoea OR "shortness of breath" OR dyspnea OR "peripheral neuropathy" OR "peripheral neuropathies" OR cognition OR cognitive OR memory OR pain OR insomnia OR "sleep disturbance" OR fatigue OR anxiety OR anxieties OR anxious OR nervousness OR depression OR depressions OR depressive OR depressed OR distress OR burden OR "stress, psychological" OR stress OR stresses OR suffering 13,959,874</p> <p>1 &amp; 2 &amp; 3 3,978</p> <p>( LIMIT-TO ( PUBYEAR , 2018 ) OR LIMIT-TO ( PUBYEAR , 2017 ) OR LIMIT-TO ( PUBYEAR , 2016 ) OR LIMIT-TO ( PUBYEAR , 2015 ) OR LIMIT-TO ( PUBYEAR , 2014 ) OR LIMIT-TO ( PUBYEAR , 2013 ) OR LIMIT-TO ( PUBYEAR , 2012 ) OR LIMIT-TO ( PUBYEAR , 2011 ) OR LIMIT-TO ( PUBYEAR , 2010 ) OR LIMIT-TO ( PUBYEAR , 2009 ) OR LIMIT-TO ( PUBYEAR , 2008 ) OR LIMIT-TO ( PUBYEAR , 2007 ) OR LIMIT-TO ( PUBYEAR , 2006 ) OR LIMIT-TO ( PUBYEAR , 2005 ) OR LIMIT-TO ( PUBYEAR , 2004 ) OR LIMIT-TO ( PUBYEAR , 2003 ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) OR LIMIT-TO ( DOCTYPE , "cp" ) OR LIMIT-TO ( DOCTYPE , "sh" ) OR LIMIT-TO ( DOCTYPE , "no" ) OR LIMIT-TO ( DOCTYPE , "ch" ) OR LIMIT-TO ( DOCTYPE , "ip" ) OR LIMIT-TO ( DOCTYPE , "er" ) ) 2,203</p>	2,203

**Table S2.** CONSORT PRO Extension checklist scoring rubric

	CONSORT 2010	PRO ADDENDUMS (Calvert 2013)	SCORING RUBRIC (1 if met, 0 if not met)	NOTES
ABSTRACT	1b Structured summary of trial design, methods, results and conclusions	EXTENSION: The PRO should be identified in the abstract as a primary or secondary outcome	1. PRO identified in abstract as primary or secondary outcome	Mention of PRO instrument or concept only assessable by PRO e.g. pain, or QoL. CIPN doesn't count as it is frequently assessed by clinician report
INTRODUCTION	2a Scientific background and explanation of rationale	ELABORATION: The relevant background and rationale for why PROs were assessed in the RCT should be briefly described	2. Background and rationale for PRO assessment	Mere mention of PRO or concept doesn't count. Must be justified in the context of the study.
	2b Specific Objectives and hypotheses.	EXTENSION: The PROs hypothesis should be stated, and relevant domains identified if applicable	3. PRO hypothesis stated	
METHODS	6a Completely define prescribed primary and secondary outcome measures, including how and when they were assessed	EXTENSION: Evidence of PRO validity and reliability should be provided or cited if available	5. Present evidence and/or reference of reliability and validity for PRO instruments	Evidence provided in text w/ reference and/or validity/ reliability mentioned and referenced and/or instrument referenced and reference details validity/reliability
		ELABORATION: Details of the mode of PRO completion (who completes PRO) and the method of data collection	6. Person completing PRO specified	Participant or proxy
			7. Mode of administration specified	Paper, interview, telephone, electronic device etc.
	12a Statistical methods used to compare groups for primary and secondary outcomes	EXTENSION: Statistical approaches for dealing with missing data should be explicitly stated for PROs prespecified as primary or important secondary outcomes	8. Assessment timepoints specified	Cross-sectional studies awarded 1 point, if met for the single timepoint
			9. Statistical methods for analyzing PRO data specified	
			10. Statistical approaches for missing data specified	
13a For each group the numbers of participants who were randomly assigned, received intended treatment and were analyzed for primary outcome	ELABORATION: The number of participants reported PRO data at baseline and at subsequent timepoints should be made transparent	11. Number of PRO participants at each timepoint reported	Cross-sectional studies awarded 1 point, if met for the single timepoint	
RESULTS	15 A table showing baseline demographic and clinical characteristics for each group	ELABORATION: Included baseline data when collected	12. Baseline PRO data reported	In text, table or figure.
	17a For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	ELABORATION: For multidimensional PROs results from each domain and timepoint	13. PRO results for all domains reported	May not be every domain in the instrument if a subset was identified as domains of interest
DISCUSSION	20 Trial limitations, addressing sources of bias, imprecision, and, if relevant, multiplicity of analyses. 21 Generalizability of trial findings	EXTENSION: PRO-specific limitations and implications for generalizability of study findings and clinical practice	14. PRO specific limitations and implications for generalizability and clinical practice	Potential sources of bias in PRO: High levels of missing data, Knowledge of tx arm in open label studies.
	22 Interpretation Consistent with results, balancing benefits, and harms, and considering other relevant evidence	ELABORATION: Patient reported outcome data should be interpreted in relation to clinical outcomes including survival data where relevant	15. Patient reported outcome data is interpreted in relation to clinical outcomes including survival data where relevant	