

Appendix A: Protocol of the SLR

Table A1: In/exclusion Criteria for the SLR on the burden of illness associated with SAP and non-severe AP

Criteria	Inclusion Criteria	Exclusion criteria
Population	Adults with SAP or non-severe AP Note: definitions will be further defined with clinical experts, if necessary	<ul style="list-style-type: none"> • Studies not on adult patients with AP or SAP • Studies with fewer than 50 patients per arm or 100 patients total for non-severe AP studies
Intervention/comparators	N/A	N/A
Outcomes	<p><u>Demographic information:</u></p> <ul style="list-style-type: none"> • Demographic characteristics of SAP and AP patients (e.g., age, gender) • Predictive risk factors of SAP and AP • Comorbidities of SAP and AP survivors • Enrolment time since symptom onset: (ideally within 48 hours or less than 72 hours) <p><u>Epidemiology:</u></p> <ul style="list-style-type: none"> • Incidence of SAP • Prevalence of SAP • Incidence of SIRS onset among non-severe AP patients • Predictors of SIRS among non-severe AP patients • Prevalence of moderate-severe AP patients remaining unresolved and/or progressing to late phase <p><u>Mortality and morbidity:</u></p> <ul style="list-style-type: none"> • Prevalence of SAP survivors • SAP-related morbidity and comorbidities • AP-related comorbidities among survivors of non-severe AP • Mortality/death rate of SAP survivors • Mortality/death rate of non-severe AP survivors <p><u>Clinical outcome</u></p> <ul style="list-style-type: none"> • Short-term outcomes occurring soon after onset of SAP • Long-term outcomes of SAP patients surviving the case-fatality window • Early onset of SIRS • Multi- or single-organ failure • Transient or persistent organ failure 	Study does not report outcomes of interest

Criteria	Inclusion Criteria	Exclusion criteria
	<ul style="list-style-type: none"> ● Infected pancreatic necrosis ● Need for surgery due to pancreatic necrosis ● Complications caused by SAP <ul style="list-style-type: none"> ○ Pancreatic pseudocysts ○ Pancreatic exocrine insufficiency ○ Pancreatic endocrine insufficiency ● Where data are available, complications caused by non-severe AP compared with complications caused by SAP ● Treatment patterns and guidelines in the US and EU-5 countries <p><u>Humanistic burden</u></p> <ul style="list-style-type: none"> ● HRQoL following SAP vs. following AP ● EQ-5D ● Other QoL-validated instruments as reported <p><u>Economic burden</u></p> <ul style="list-style-type: none"> ● Resource utilisation ● Length of hospital, high-dependency unit, or ICU stay ● Number and type of hospital procedures used during the SAP-related hospitalisation ● Number and type of medication administered in hospital ● Number of primary care consultations during first year since SAP onset ● Total prescriptions/follow-up visits following hospital discharge issued in primary care ● Number of specialist care consultations during first year since SAP onset ● Total prescriptions issued in secondary care ● Number of hospitalisations during first year since SAP inset <p><u>SAP-related hospital costs</u></p> <ul style="list-style-type: none"> ● Total direct and indirect costs ● Direct costs by component (e.g., medication, hospital stays, physician visits) 	
Study design	<ul style="list-style-type: none"> ● Observational studies (prospective and retrospective) ● Registry and database analyses ● Cross-sectional studies 	<ul style="list-style-type: none"> ● RCTs, interventional studies ● Animal, in vitro, or genetic studies, ● Not systematic reviews, editorials, news

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Criteria	Inclusion Criteria	Exclusion criteria
		<ul style="list-style-type: none"> Case reports, editorials
Time period	<ul style="list-style-type: none"> Studies published between January 1, 1999 and June 2017* for SAP; and between January 1, 2006 to June 2017 for AP Conference abstracts/posters: 2015–2017 	Studies published outside of the search period defined in the inclusion criteria
Language	English language	Non-English language publications
Geographic location	US, EU-5	Evidence not from the countries of interest

Abbreviations: AP = acute pancreatitis; BOI = burden of illness; EQ-5D = EuroQol Five Dimensions Questionnaire; EU-5 = European Union Five (France, Germany, Italy, Spain, the United Kingdom) HRQoL = health-related quality of life; ICU = intensive care unit; N/A = not applicable; PICOS = population, interventions, comparators, outcomes, and study design; QoL = quality of life; RCT = randomised controlled trial; SAP = severe acute pancreatitis; SIRS = systemic inflammatory response syndrome; US = United States

Table A2: Embase Search Strategies for the burden of illness associated with of SAP (with search conducted in May 2017):

Search Number	Search String	Search Yield
Patient population		
1	'severe acute pancreatitis'/exp OR 'severe acute pancreatitis' OR 'severe acute pancreatiti*':ab,ti	4,256
2	'acute pancreatit*' AND ('severe' OR 'advanced')	9,534
3	'systemic inflammatory response syndrome*' OR 'sirs' AND ('severe acute pancreatitis' OR 'acute pancreatitis')	813
4	#1 or #2 or #3	9,865
Epidemiology, risk factors, and disease outcomes		
5	'epidemiology'/exp OR epidemiol*':ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR 'risk factor' OR risk*':ti OR 'risk factor*':ab OR 'prognosis'/exp OR prognosis OR 'mortality'/exp OR mortalit* OR mortalit*':ab,ti OR 'comorbidity'/exp OR comorbidity:ti,ab OR 'morbidity'/exp OR morbidity:ti,ab	4,974,503
Clinical burden		
6	'systemic inflammatory response syndrome'/exp OR (inflam* AND pancrea*) OR 'multiple organ failure'/exp OR 'multiple organ failure' OR 'organ failure' OR 'pancreas necrosis'/exp OR 'pancrea* necro*' OR 'infectious pancreatic necrosis'/exp OR 'infectious pancreatic necrosis' OR 'infectious pancreatic necrosis virus'/exp OR 'infectious pancreatic necrosis virus' OR 'pancreas pseudocyst'/exp OR 'pancrea* pseudocyst' OR 'pancreatic insufficiency'/exp OR 'pancreatic insufficiency' OR 'pancreatic exocrine insufficiency' OR 'pancreatic endocrine insufficiency'	297,366
Health-related quality of life (humanistic burden and utilities)		
7	'quality of life'/exp OR 'quality of life' OR qol OR 'qaly':ab,ti OR 'qalys':ab,ti OR 'quality adjusted life year'/exp OR 'quality adjusted life year':ab,ti OR 'quality adjusted life years':ab,ti OR 'quality of life':ab,ti OR (utilit*':ab,ti AND health:ab,ti) OR (utilit*':ab,ti AND scor*':ab,ti) OR (utilit*':ab,ti AND valu*':ab,ti) OR (disutilit*':ab,ti AND 'health':ab,ti) OR (disutilit*':ab,ti AND scor*':ab,ti) OR (disutilit*':ab,ti AND valu*':ab,ti) OR disutili* OR utility* OR 'daly':ab,ti OR 'dalys':ab,ti OR 'disability adjusted life year':ab,ti OR 'disability adjusted life years':ab,ti OR 'sf 36':ab,ti OR 'short form 36':ab,ti OR 'sf 6d':ab,ti OR 'short form 6d':ab,ti OR 'sf 20':ab,ti OR 'short form 20':ab,ti OR 'eq 5d':ab,ti OR 'eq5d':ab,ti OR 'eq-5d':ab,ti OR 'euroqol':ab,ti OR 'euro qol':ab,ti OR hql OR hqol OR 'h qol' OR hrqol OR 'hr qol' OR 'euroqol 5d':ab,ti OR 'eortc':ab,ti OR 'qlq':ab,ti OR 'patient report* outcome*' OR 'fatigue':ab,ti OR 'physical function':ab,ti OR 'pain':ab,ti OR 'general health':ab,ti OR 'vitality':ab,ti OR 'mental health':ab,ti OR 'social	2,468,287

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Search Number	Search String	Search Yield
	behavi*':ab,ti OR 'stress':ab,ti OR 'role emotional':ab,ti OR 'adaptation':ab,ti OR 'survey and questionnaires' OR 'patient satisfaction' OR 'patient report outcome*' OR 'functional impairment' OR 'visual analogue scale'/exp OR 'visual analogue scale' OR vas	
<i>Economic burden/resource utilisation</i>		
8	'cost of illness'/exp OR 'cost of illness' OR 'illness cost' OR 'illness costs' OR 'cost of disease' OR 'costs of disease' OR 'sickness cost' OR 'disease cost' OR 'disease costs' OR 'cost of sickness' OR 'sickness costs' OR 'health care cost'/exp OR 'drug cost'/exp OR 'hospital cost'/exp OR 'nursing cost'/exp OR 'direct costs' OR 'indirect costs' OR 'medical care cost' OR 'medical care costs' OR 'cost of treatment' OR 'economic burden' OR 'cost':ti,ab OR 'costs':ti,ab OR 'economic':ti,ab OR 'economics':ti,ab OR 'cost-benefit-analysis' OR 'cost effectiveness' OR resource OR utili*':ab,ti OR model*':ab,ti OR cost*':ab,ti OR econom*':ab,ti OR 'health care use':ab,ti OR 'healthcare use':ab,ti OR 'health service use':ab,ti OR 'health services use':ab,ti OR 'health care utilisation':ab,ti OR 'healthcare utilisation':ab,ti OR 'healthcare utilization':ab,ti OR 'health care utilization':ab,ti OR 'health resource utilization':ab,ti OR 'health resource utilisation':ab,ti OR 'health service utilisation':ab,ti OR 'health service utilization':ab,ti OR 'health services utilisation':ab,ti OR 'health services utilization':ab,ti OR 'resource use':ab,ti	4,383,949
<i>Limit to relevant publication types</i>		
9	'case study'/exp OR 'letter'/exp OR 'editorial'/exp OR (review:it NOT (systematic OR meta AND analy* OR (indirect OR mixed AND 'treatment comparison')) OR ('animal'/exp NOT 'human'/exp))	8,410,800
10	[humans]/lim AND [english]/lim AND [abstracts]/lim AND [1999-2017]/py	8,826,818
11	registry OR (retrospective* AND registry) OR database OR cohort OR prospective* OR retrospective* OR observational OR longitudinal* OR 'population based' OR 'population-based' OR 'cohort study':ab,ti OR 'cohort studies':ab,ti OR 'case control study':ab,ti OR 'case control studies':ab,ti OR 'cross sectional study':ab,ti OR 'cross sectional studies':ab,ti OR (real AND ('world'/exp OR world) AND evidence)	3,017,047
<i>Combined for epidemiology/risk factors limited by study design and adults</i>		
	#4 AND #5 AND #10 AND #11 AND ([young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #9	737
<i>Combined for clinical outcomes limited by study design</i>		
	#4 AND #6 AND #10 AND #11 NOT #9	993
<i>Combined for humanistic outcomes/utilities not limited by study design, limited by adults</i>		
	#4 AND #7 AND #10 AND ([young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #9	539
<i>Combined for economic outcomes/costs not limited by study design, limited by adults</i>		
	#4 AND #8 AND #10 AND ([young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #9	271

Table A3: Embase Search Strategy for the burden of illness associated with AP (with search conducted in May, 2017)

Search Number	Search String	Search Yield
1	'acute pancreatitis'/exp OR 'acute pancreatitis':ab,ti OR 'acute pancrea*' OR 'necro* pancrea*' OR 'inflam* pancrea*'	36,917
2	'systemic inflammatory response syndromes' OR 'sirs' AND 'acute pancrea*'	414
3	#1 OR #2	36,917
4	'epidemiology'/exp OR epidemiol*':ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR 'risk factor' OR risk*':ti OR 'risk factor*':ab OR 'prognosis'/exp OR prognosis OR 'mortality'/exp OR mortalit* OR mortalit*':ab,ti OR 'comorbidity'/exp OR comorbidity:ti,ab OR 'morbidity'/exp OR morbidity:ti,ab	4,974,503

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Search Number	Search String	Search Yield
5	'systemic inflammatory response syndrome'/exp OR (inflam* AND pancrea*) OR 'multiple organ failure'/exp OR 'multiple organ failure' OR 'organ failure' OR 'pancreas necrosis'/exp OR 'pancrea* necro*' OR 'infectious pancreatic necrosis'/exp OR 'infectious pancreatic necrosis' OR 'infectious pancreatic necrosis virus'/exp OR 'infectious pancreatic necrosis virus' OR 'pancreas pseudocyst'/exp OR 'pancrea* pseudocyst' OR 'pancreatic insufficiency'/exp OR 'pancreatic insufficiency' OR 'pancreatic exocrine insufficiency' OR 'pancreatic endocrine insufficiency'	297,366
6	'quality of life'/exp OR 'quality of life' OR qol OR 'qaly':ab,ti OR 'qalys':ab,ti OR 'quality adjusted life year'/exp OR 'quality adjusted life year':ab,ti OR 'quality adjusted life years':ab,ti OR 'quality of life':ab,ti OR (utilit*:ab,ti AND health:ab,ti) OR (utilit*:ab,ti AND scor*:ab,ti) OR (utilit*:ab,ti AND valu*:ab,ti) OR (disutilit*:ab,ti AND 'health':ab,ti) OR (disutilit*:ab,ti AND scor*:ab,ti) OR (disutilit*:ab,ti AND valu*:ab,ti) OR disutili* OR utility* OR 'daly':ab,ti OR 'dalys':ab,ti OR 'disability adjusted life year':ab,ti OR 'disability adjusted life years':ab,ti OR 'sf 36':ab,ti OR 'short form 36':ab,ti OR 'sf 6d':ab,ti OR 'short form 6d':ab,ti OR 'sf 20':ab,ti OR 'short form 20':ab,ti OR 'eq 5d':ab,ti OR 'eq5d':ab,ti OR 'eq-5d':ab,ti OR 'euroqol':ab,ti OR 'euro qol':ab,ti OR hqol OR hqol OR 'h qol' OR hrqol OR 'hr qol' OR 'euroqol 5d':ab,ti OR 'eortc':ab,ti OR 'qlq':ab,ti OR 'patient report* outcome*'	674,254
7	'cost of illness'/exp OR 'cost of illness' OR 'illness cost' OR 'illness costs' OR 'cost of disease' OR 'costs of disease' OR 'sickness cost' OR 'disease cost' OR 'disease costs' OR 'cost of sickness' OR 'sickness costs' OR 'health care cost'/exp OR 'drug cost'/exp OR 'hospital cost'/exp OR 'nursing cost'/exp OR 'direct costs' OR 'indirect costs' OR 'medical care cost' OR 'medical care costs' OR 'cost of treatment' OR 'economic burden' OR 'cost':ti,ab OR 'costs':ti,ab OR 'economic':ti,ab OR 'economics':ti,ab OR 'cost-benefit-analysis' OR 'cost effectiveness' OR resource OR utili*:ab,ti OR model*:ab,ti OR cost*:ab,ti OR econom*:ab,ti OR 'health care use':ab,ti OR 'healthcare use':ab,ti OR 'health service use':ab,ti OR 'health services use':ab,ti OR 'health care utilisation':ab,ti OR 'healthcare utilisation':ab,ti OR 'healthcare utilization':ab,ti OR 'health care utilization':ab,ti OR 'health resource utilization':ab,ti OR 'health resource utilisation':ab,ti OR 'health service utilisation':ab,ti OR 'health service utilization':ab,ti OR 'health services utilisation':ab,ti OR 'health services utilization':ab,ti OR 'resource use':ab,ti	4,383,949
8	'case study'/exp OR 'letter'/exp OR 'editorial'/exp OR (review:it NOT (systematic OR meta AND analy* OR (indirect OR mixed AND 'treatment comparison'))) OR ('animal'/exp NOT 'human'/exp)	8,410,800
9	[humans]/lim AND [english]/lim AND [abstracts]/lim AND [2006-2017]/py	7,068,891
10	cohort OR prospective* OR longitudinal* OR 'population based' OR 'population-based' OR 'cohort study':ab,ti OR 'cohort studies':ab,ti	1,705,522
Combined for epidemiology/risk factors limited by study design and adults		
	#3 AND #4 AND #9 AND #10 AND ([young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #8	839
	#3 AND #5 AND #9 AND #10 AND ([adolescent]/lim OR [young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #8	543
	#3 AND #6 AND #9 NOT #8 AND ([young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim)	132
	#3 AND #7 AND #9 AND ([adolescent]/lim OR [young adult]/lim OR [adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) NOT #8	596