Can Living Systematic Literature Reviews Reduce Research Wastage? An Evaluation of LiveSLR®

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Background

- Living systematic reviews (LSR) could enable timely health technology assessment (HTA) in rapidly evolving disease areas.
- LSRs can be supported by tools such as Cytel's web-based platform, LiveSLR®, an up-to-date Cochrane/National Institute for Health and Care Excellence (NICE)-compliant curated systematic literature reviews (SLR) library following PRISMA standards.

Objective

The aim was to assess the feasibility of utilising LiveSLR® to support HTAs via its ability to replicate SLRs registered on the International Prospective Register of Systematic Reviews (PROSPERO).

Methods

- Over a search period of database inception to May 24, 2024, medical subject heading terms were used to search PROSPERO for 26 regularly updated indications included in the LiveSLR® library.
- Records were screened for outcomes relevant to HTA (clinical efficacy/effectiveness, healthcare resource utilisation [HCRU]/costs, and health-related quality of life).
- SLRs including HTA-relevant outcomes were categorised according to their replicability using LiveSLR®:
  - 'Replicable': overlap with indication; research question answerable with existing data; or
  - 'Replicable with adaptation': overlap with indication; research question answerable by expanding the SLR.
- SLRs registered in PROSPERO not retrieved in the search were considered 'not replicable' (no overlap with indication).
- The LiveSLR® small-cell lung cancer (SCLC) SLR was used as a case study to identify SLRs conducted for HTA submissions that could be replicated using LiveSLR® from the independent Institute for Quality and Efficiency in Health Care (IQWiG), NICE, Canada's Drug Agency, and Scottish Medicines Consortium (SMC) databases.

Results

- Of 3,319 identified PROSPERO-registered SLRs, 2,902 were classified as 'replicable with adaptation' and 417 were classified as 'replicable' (**Table 1**).
- By indication and topic LiveSLR® was able to replicate more than 10 of each of the following SLR types:
  - Clinical efficacy and effectiveness in non-muscle invasive bladder cancer (NMIBC), severe asthma, ulcerative colitis (UC), non-small cell lung cancer, colorectal cancer, prostate cancer (PC), SCLC, and multiple myeloma
  - Humanistic burden of illness in NMIBC, UC, systemic lupus erythematosus (SLE), PC, and SCLC
  - HCRU/costs in NMIBC, UC, SLE, PC, and SCLC

Case study of SCLC SLRs

- The LiveSLR® SCLC library was able to replicate SLRs from nine HTAs (NICE [n=3], SMC [n=4], and IQWiG [n=2]) demonstrating the relevance of LiveSLR® for HTA submissions (**Figure 2**).

Strengths/limitations

- The LiveSLR® database was able to replicate SLRs for a range of diseases across three HTA bodies.
- As only SLR titles were screened, further investigation of the full-text articles would be required to determine overlapping SLR evidence types.
- Relevant SLRs not registered on PROSPERO were not included. Any relevant registered SLRs not completed and/or published at the time of the study were not included.

Conclusions

- Many PROPSPERO-registered SLR research questions can be answered using existing SLRs in LiveSLR®.
- The use of existing data from LiveSLR® is likely to create time efficiencies versus de novo SLRs for HTA submissions.
- For SLR questions that cannot be directly answered (e.g., for specific subpopulations), LSRs can be adapted using LiveSLR® SLR libraries.

References

1. NICE, technology appraisal guidance. 2020; TA638. **2.** SMR, Medicines advance. 2020; SMC2279. **3.** IQWiG, Drug Assessment. 2020; Addendum to Commission No. A20-81. **4.** IQWiG, Drug Assessment. 2019; Benefit assessment reports No. A19-86 **5.** NICE, technology appraisal guidance. 2020; TA662. **6.** SMR, Medicines advance. 2021; SMC2434. **7.** IQWiG, Drug Assessment. 2021; Addendum to Commission No. A21-19 **8.** IQWiG, Drug Assessment. 2020; Benefit assessment reports No. A20-87. **9.** NICE, technology appraisal guidance. 2009; TA184. **10.** SMR, Medicines advance. 2007; SMC545/09. **11.** SMR, Medicines advance. 2009; 366/07.

Disclosures

Conflict of interest: Rhiannon Campden, Jessica Agranat, Victoria Young were employees of Cytel Inc at the time of the study.

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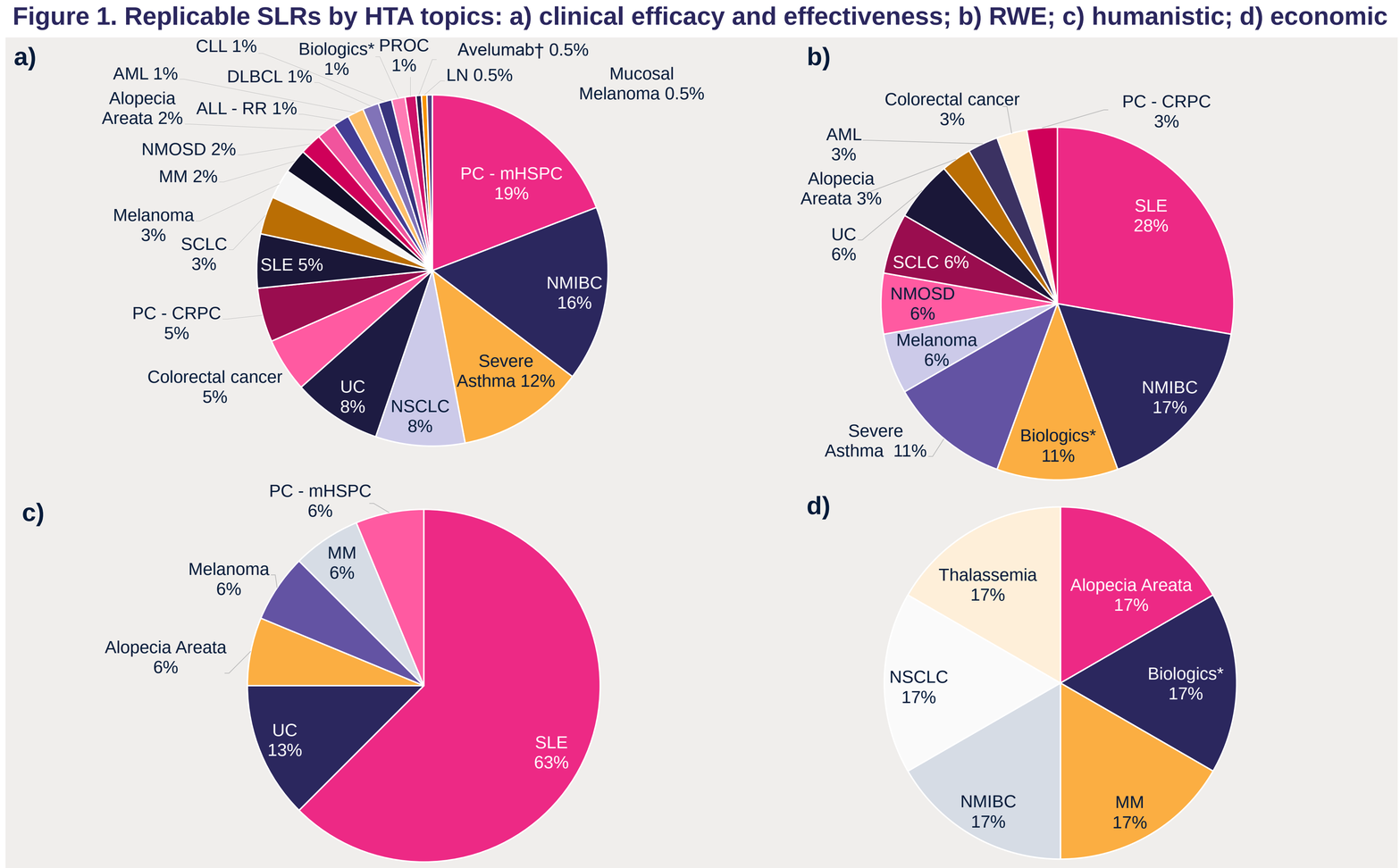
Results (cont.)

Table 1. Identified 'replicable' SLRs in LiveSLR® and evidence types

Topic*	Subpopulation	Clinical	RWE	Humanistic	Economic	PROSPERO SLR (N)	Replicable SLR (n)
Prostate cancer	CRPC	Yes	-	Yes	Yes	139	98
	mCRPC	Yes	-	Yes	Yes		
	mHSPC	Yes	-	Yes	Yes		
NMIBC	-	Yes	Yes	Yes	Yes	131	66
Severe asthma	-	Yes	Yes	-	-	716	47
UC	-	Yes	-	Yes	Yes	119	35
NSCLC	-	Yes	-	-	-	277	34
	EGFR Exon20	Yes	Yes	Yes	Yes		
	METex14	Yes	Yes	Yes	Yes		
SLE	-	-	-	Yes	Yes	107	30
Colorectal cancer	-	Yes	-	-	-	712	20
SCLC	-	Yes	Yes	Yes	Yes	28	14
	First line	Yes	-	-	-		
	Second line	Yes	-	-	-		
Multiple myeloma	-	Yes	Yes	-	-	59	10
	Maintenance	Yes	Yes	Yes	Yes		
	Newly diagnosed	Yes	Yes	Yes	Yes		
	RR	Yes	Yes	Yes	Yes		
	Triple class exposed	Yes	-	-	-		
	WII/TIE	Yes	Yes	Yes	Yes		
Melanoma	-	Yes	-	Yes	Yes	158	11
	Mucosal melanoma	Yes	Yes	-	-		
NMOSD	-	Yes	Yes	-	-	12	8
Alopecia areata	-	Yes	Yes	Yes	Yes	16	7
AML	-	Yes	Yes	-	-	33	6
	IC NIC	Yes	Yes	Yes	Yes		
	Newly diagnosed NIC	Yes	Yes	Yes	Yes		
Diffuse large B cell lymphoma	-	Yes	Yes	Yes	Yes	14	6
RR acute lymphoblastic leukemia	-	Yes	-	Yes	Yes	45	6
CLL	-	Yes	-	-	-	8	5
LT safety of respiratory biologics	CRSwNP, EGPA, and HES	-	Yes	-	-	95	5
Platinum-resistant ovarian cancer	-	Yes	-	Yes	Yes	6	4
Avelumab	MCC, RCC, UC, other	Yes	Yes	Yes	Yes	347	2
Lupus nephritis	-	-	Yes	Yes	Yes	16	2
Thalassemia	-	-	-	Yes	Yes	26	1

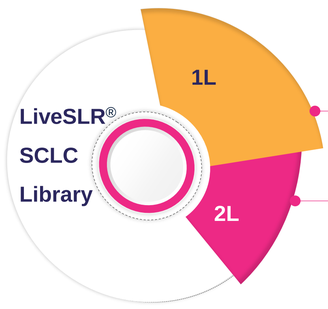
*Acute graft-versus-host disease, Leber hereditary optic neuropathy, low-risk myelodysplastic syndromes, and non–cystic fibrosis bronchiectasis had 0 replicable SLRs using the LiveSLR® dataset. Abbreviations: AML, acute myeloid leukaemia; CLL, chronic lymphocytic leukaemia; CRPC, castration-resistant prostate cancer; CRSwNP, chronic rhinosinusitis with nasal polyps; EGFR, epidermal growth factor receptor; EGPA, eosinophilic granulomatosis with polyangiitis; HES, hypereosinophilic syndrome; HSPC, hormone-sensitive prostate cancer; IC, suitable for intensive chemotherapy; LT, long term; m, metastatic; MCC, Merkel cell carcinoma; METex14, MET exon 14; NIC, non-intensive chemotherapy treated; NMIBC, non-muscle invasive bladder cancer; NMOSD, neuromyelitis optica spectrum disorder; NSCLC, non-small cell lung cancer; PROSPERO, The International Prospective Register of Systematic Reviews; RCC, renal cell carcinoma; RR, relapsed and/or refractory; RWE, real-world evidence; SCLC, small cell lung cancer; SLE, systemic lupus erythematosus; SLR, systematic literature review; UC, ulcerative colitis; WII/TIE, for whom haematopoietic stem cell transplant is not planned as initial therapy.

Figure 1. Replicable SLRs by HTA topics: a) clinical efficacy and effectiveness; b) RWE; c) humanistic; d) economic



*Long-term safety of respiratory biologics (CRSwNP, EGPA, and HES). †Avelumab treatment of MCC, RCC, UC, other. Abbreviations: ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; CLL, chronic lymphocytic leukaemia; CRPC, castration-resistant prostate cancer; CRSwNP, chronic rhinosinusitis with nasal polyps; DLBCL, diffuse large B cell lymphoma; EGPA, eosinophilic granulomatosis with polyangiitis; HES, hypereosinophilic syndrome; HSPC, hormone-sensitive prostate cancer; HTA, health technology assessment; LN, lupus nephritis; m, metastatic; MCC, Merkel cell carcinoma; MM, multiple myeloma; NMIBC, non-muscle invasive bladder cancer; NMOSD, neuromyelitis optica spectrum disorder; NSCLC, non-small cell lung cancer; PC, prostate cancer; PROC, platinum-resistant ovarian cancer; RCC, renal cell carcinoma; RR, relapsed and/or refractory; RWE, real-world evidence; SCLC, small cell lung cancer; SLE, systemic lupus erythematosus; SLR, systematic literature review; UC, ulcerative colitis

Figure 2. SCLC LiveSLR® replication example



Six HTAs identified from NICE (n=2), SMC (n=2), and IQWiG (n=2)
Atezolizumab with carboplatin and etoposide for untreated extensive-stage SCLC[1-4]
Durvalumab in combination for untreated extensive-stage SCLC[5-8]

Three HTAs identified from NICE (n=1) and SMC (n=2)
Topotecan p.o. for relapsed SCLC for whom re-treatment with 1L regimen is not deemed appropriate[9,10]
Topotecan infusion for relapsed SCLC for whom re-treatment with 1L regimen is not deemed appropriate[11]

Abbreviations: 1L, first line; 2L, second line; HTA, health technology assessment; IQWiG, the independent Institute for Quality and Efficiency in Health Care; NICE, National Institute for Health and Care Excellence; p.o., per os, by mouth; SCLC, small cell lung cancer; SMC, Scottish Medicines Consortium.