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Development of a Set of Lupus-Specific Ambulatory Care Sensitive, Potentially Preventable Adverse Conditions: A Delphi Consensus Study

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Abstract

Objective: Individuals with systemic lupus erythematosus (SLE) are at high risk for infections, SLE- and medication-related complications. We defined a set of SLE-specific adverse outcomes that could be prevented, or their complications minimized, if timely, effective ambulatory care had been received.

Methods: We used a modified Delphi process beginning with a literature review and key informant interviews to select initial SLE-specific potentially preventable conditions. We assembled a panel of sixteen nationally-recognized U.S.-based experts from eight subspecialties. Guided by the RAND-UCLA Appropriateness Method, we held two survey rounds with controlled feedback and an interactive webinar to reach consensus regarding preventability and importance on a population level for a set of SLE-specific adverse conditions. In a final round, the panelists endorsed the potentially preventable conditions.

Results: Thirty-five potential conditions were initially proposed; 62 conditions were ultimately considered during the Delphi process. The response rate was 100% for both survey rounds, 88% for the webinar, and 94% for final approval. The 25 SLE-specific conditions meeting consensus as potentially preventable and important on a population level fell into four categories: vaccine-preventable illnesses (6 conditions), medication-related complications (8), reproductive health-related complications (6) and SLE-related complications (5).

Conclusions: We reached consensus on a diverse set of adverse outcomes relevant to SLE patients that may be preventable if patients received high quality ambulatory care. This set of outcomes may be studied at the health system level to determine how to best allocate resources and improve quality to reduce avoidable outcomes and disparities among those at highest risk.

Background

Systemic lupus erythematosus (SLE) is a chronic, heterogeneous autoimmune disease that often results in significant morbidity and mortality, frequent healthcare use, and high healthcare costs.(1–6) In the U.S., nearly 25% of individuals with SLE are hospitalized each year and SLE patients have the sixth highest readmission rate among all chronic medical conditions.(7) SLE management is complex and prior studies describe low quality, inconsistent subspecialty care and inadequate preventive services with significant racial/ethnic and socioeconomic (SES) disparities.(8–11) In the U.S. population, chronic disease burden and severity do not entirely explain frequent, costly and potentially avoidable acute care use (e.g. treat-and-release ED visits and certain hospitalizations and readmissions).(12–15) High resource-utilizing patients often have low SES and vulnerable social situations, are disproportionately black or Hispanic, and receive fragmented outpatient care.(12–14, 16) SLE patients have even higher rates of costly acute care use compared with non-SLE patients.(6, 7, 17, 18) SLE-related factors, specifically lupus nephritis and neuropsychiatric manifestations, are also associated with increased overall utilization and higher costs.(2, 19–21)

In 2001, the Agency for Healthcare Research & Quality (AHRQ) adopted a general population set of “ambulatory care sensitive conditions” based on avoidable hospital conditions defined by Weissman, et al. for which high quality outpatient care may prevent acute care use.(22, 23) Specifically, these are conditions that “should be treatable on an outpatient basis, or that could be less severe if treated early and appropriately” and for which there is a strong link between receipt of effective outpatient care and avoidance of hospitalization.(22, 23) These conditions included various infections, diabetes and related complications, cardiovascular and pulmonary disease exacerbations, and other complications such as ruptured appendix, dehydration, perforated or bleeding ulcer, and hypokalemia.(22, 23) In a past study, nearly 20% of SLE patients were hospitalized for one of these general population avoidable conditions over three years in New York.(24) However to date, while there are SLE quality indictors which were published in 2009 (25), we lack a set of SLE-specific potentially preventable, ambulatory care sensitive conditions that reflect the most recent SLE literature and expert consensus for best practices. Like the AHRQ initiative, we aimed to develop a set of SLE-specific conditions to allow researchers to identify vulnerable populations at risk of acute care use for avoidable illnesses and complications and to examine differences across racial/ethnic groups, geographic areas and health care systems. Further, they could be applied to assess the breakdown of health delivery and to measure the impact of preventive care and outpatient rheumatology services.

Methods

We used a modified Delphi process, guided by a health services researcher and Delphi expert (JSW) who published parts of the foundational research that informed the AHRQ general preventable conditions process. The Delphi process is designed to reach consensus among multidisciplinary experts using an iterative process of problem definition, feedback and revisions (Figure 1).(26, 27) The modified version of the Delphi method allows for expert input on a selected set of initial items with multiple rounds of anonymous feedback and revisions, without requiring face-to-face meetings.(26, 27)

We first conducted a literature review using PubMed searching “systemic lupus erythematosus (MeSH lupus terms) and “avoidable” (6 articles) “preventable” (39), “hospitalization” (483), “readmission” (14), “emergency department” (304), “quality indicators” (83), and “ambulatory” (143). The first author reviewed all peer-reviewed, published studies in English for which full articles were available with a specific focus on quality metrics, assessment of potentially preventable conditions and outcomes. This initial literature review served to determine the potential broad categories of interest and initial conditions to consider. Three key informant interviews were then conducted with rheumatologists with clinical and research expertise in SLE to review the initial categories and conditions abstracted from the literature.

We assembled a Delphi panel of 16 U.S.-based physicians and researchers across disciplines with expertise in clinical lupus management and lupus-related research. Our choice of expert panelists was guided by the categories of interest from the initial literature review and all 16 physicians who were invited agreed to participate. The panel included adult rheumatologists (7), pediatric rheumatologists (2), nephrologists (2), a neurologist, a cardiologist, an

obstetrician/gynecologist, an infectious disease physician, and a joint specialty dermatologist/rheumatologist. Expert panelists were geographically dispersed, from several different states including CA, IL, TX, OK, OH, MA, AK, and UT.

We then developed a definition for the term “SLE-specific preventable conditions” and piloted this definition, our instructions for panelists, and the first survey iteration among four rheumatologists and incorporated their feedback. Delphi participants were then tasked with developing a set of SLE-specific preventable conditions, which we defined as “conditions for which high quality, sustained outpatient rheumatologic care can potentially a) prevent the need for hospitalization or emergency department visits ***or*** b) for which early intervention can prevent or minimize complications or the development of more severe disease.” Panelists were asked to rate the potential preventability of each condition on a scale of 1 (definitely preventable) to 9 (definitely not preventable) by considering the extent to which each condition may be prevented, or the complication minimized, if sustained, high quality rheumatology care was received. For each condition, panelists were also asked to rate the importance of each condition on a population level from A (extremely important) to D (not important) and were instructed to consider the population prevalence of the potential condition and how closely tied it is to the quality of rheumatologic care. In addition, participants were asked to write in specific comments for each condition as well as to suggest additional conditions for the group to consider.

Guided by the RAND/UCLA Appropriateness Method (28), we developed strict and lenient consensus criteria by which to evaluate panelists’ scoring of both preventability and importance for each condition (**See Table 2 footnote and** Supplemental Data 1). After removing one extreme high and one extreme low value from each condition’s preventability and importance scales, conditions meeting consensus criteria with scores below the prespecified lowest tertile cutoffs on both the preventability and importance scales were included as preventable and important; conditions meeting consensus criteria with scores above the highest tertile cutoffs, were removed from consideration as not preventable and/or not important on a population level.

Beginning in September 2017, for the first two Delphi rounds, experts were asked to provide private rankings to maintain anonymity between panelists and to prevent any one perspective from dominating. Following each round, we provided controlled feedback to each participant showing his/her rankings for each condition next to the distribution of the groups’ responses. Multiple rounds to allow for consensus building and for opinion change are inherent to the Delphi method. Therefore, following these first two private rounds each followed by personalized feedback, we held an interactive webinar (“round 3”) to discuss and vote on conditions that did not yet reach consensus. The webinar was recorded and transcribed verbatim to allow for re-review. Following this step, we updated the literature review for each condition that reached consensus and presented a table to all participants that included these conditions, the way in which each condition may be preventable or have complications minimized, and a summary of the published SLE-related literature for each condition regarding preventability and importance on a population level. We requested that the panelists review this table of all conditions reaching consensus from the Delphi process and provide any additional references and recommendations to include. In addition, we

solicited votes on the preventability and importance of one new condition that was thought to be relevant following the updated literature review, and the rephrasing of a prior condition that reached consensus suggested by a panelist ("round 4"). Finally, in February 2019, a summary of the group response was presented to the Delphi panelists for their final endorsement. The Partners Healthcare Human Research Committee approved this work.

Results

Based on the initial literature review and key informant interviews, 35 SLE-specific preventable conditions were presented to the 16 Delphi panelists and over the course of the Delphi process, 27 additional or rephrased conditions were elicited and considered (Table 1). The response rate was 100% for both survey rounds, 88% for the webinar, and 94% for the final approval round. Through the multiple iterations, additional candidate conditions were added for consideration and original conditions were reworded based on written feedback and webinar discussion with the expert panelists as well as from an updated literature review (Figure 2). Conditions discussed ultimately fell into four broad categories: vaccine-preventable illnesses, medication-related complications, reproductive health-related complications and SLE-associated comorbidities. After applying our consensus criteria, 25 conditions were included based on their preventability and importance ratings (Table 2) and the strategies to potentially prevent these conditions and their importance on a population level are outlined in Table 3 **and in** Supplemental Data 2.

Vaccine-Preventable Illnesses

The first category was vaccine preventable illnesses for which eight conditions were considered. One condition was re-worded during the process– pneumococcal pneumonia to pneumococcal disease to more broadly represent the sequelae of infection- and six of the eight conditions met consensus for inclusion. The Delphi process was initiated prior to clinical introduction of the recombinant, adjuvanted zoster vaccine (Shingrix) and therefore the panelists' thinking evolved over the rounds. Initially, herpes zoster was thought to not be preventable because immunosuppression often needs to be started quickly prior to the opportunity to vaccinate with the live attenuated vaccines (Zostavax). Challenges with insurance coverage particularly among younger individuals were also raised. With the newer Shingrix recombinant vaccine, there was some concern that we did not have extensive data yet as to how SLE patients would respond, however the consensus was that with the introduction of this new vaccine, herpes zoster should be considered a potentially preventable condition, particularly for individuals over age 50.

A concern raised for both influenza and pneumococcal disease was that while incidence and severity may be reduced with the vaccinations, the efficacy is imperfect. For encapsulated organism infections, concerns that led to the condition not reaching consensus included: a) the category was too broad and some encapsulated organism infections are not preventable with vaccinations, b) children are routinely receiving the *Haemophilus influenze* vaccine, and c) it is not clear that SLE patients who do not have anatomic or functional asplenia have significantly increased risk of this entire category of infection to warrant revaccination in adulthood. For meningococcal disease however, additional risk factors during young

adulthood (e.g. college students living in residential housing, challenges differentiating this from other SLE manifestations), and the existence of a safe and efficacious vaccine, led to inclusion of this condition. Several panelists recommended considering Hepatitis B in two separate categories – reactivation of chronic infection or prior exposure in the setting of immunosuppressive therapy, and prevention of initial infection with vaccination. While the panel ultimately considered the two together, the consensus was that both were potentially preventable particularly among the highest risk patients, specifically those with known risk factors for infection who should be vaccinated, and those with chronic infection who should receive antivirals in the setting of immunosuppressive therapy. It was also suggested that patients with lupus nephritis should be considered for vaccination as patients with chronic kidney disease are more likely to respond to the Hepatitis B vaccine if they are treated when they have higher levels of kidney function.(29)

Medication-Related Complications

The second category was medication-related complications for which twelve conditions were considered and one was reworded (*Pneumocystis jirovecii* pneumonia (PJP) while on moderate-to-high doses of glucocorticoids, compared to the original wording of PJP not in the setting of immunosuppression, or while receiving any dose glucocorticoids). Eight of the twelve conditions considered in this category reached consensus for inclusion. We engaged in a discussion around the preventability of PJP, the potentially low prevalence among SLE patients, and concerns about adverse effects from prophylactic antibiotics. Some prior literature suggests SLE flare risk as well as increased cutaneous reactions associated with sulfonamides.(30–32) Consensus was reached to include the condition in the final list with the caveat that the decision regarding PJP prophylaxis should be made on a case-by-case basis, and in the setting of moderate-to-high doses of glucocorticoids. Avascular necrosis (AVN) among patients with SLE receiving prolonged glucocorticoids ultimately reached consensus for inclusion based on the premise that minimizing the dose and duration of glucocorticoids would potentially reduce the incidence of AVN. However, several panelists did note that this is not always preventable as prolonged moderate-to-high dose steroids may be required for organ preservation, and at times, SLE patients may develop AVN even with minimal or no glucocorticoid exposure.

Azathioprine toxicity without prior assessment of thiopurine methyltransferase (TMPT) activity was voted on both in rounds 1 and 2 and then discussed during the webinar after failing to reach consensus. Ultimately this condition did not reach consensus for inclusion as: 1) azathioprine toxicity may occur even with normal TMPT activity, 2) the cost of the test may be prohibitive and not covered by insurance, and 3) other strategies (e.g. monitoring blood counts 1–2 weeks following initiation) may be reasonable and more cost-effective. One participant did feel that if an individual has a homozygous TMPT deficiency and was prescribed azathioprine and develops toxicity, this would have been potentially preventable. However overall, the panelists did not feel that this scenario had high enough prevalence considering the other concerns raised to be considered important on a population level. Progressive multifocal leukoencephalopathy was thought to be exceptionally rare and at this point, not preventable as nearly all SLE-related immunosuppressive medications have been implicated and JC virus is not routinely screened for in SLE patients.

Reproductive Health-Related Complications

We considered fifteen reproductive health-related conditions, several of which involved terminology changes (e.g. premature ovarian failure to premature ovarian insufficiency/infertility) led by the obstetrics/gynecology expert panelist and rheumatologists with reproductive health expertise. Six of the fifteen conditions considered reached consensus. While premature ovarian insufficiency/failure was not thought to be preventable overall among SLE patients, in the specific case of receipt of *standard dose* cyclophosphamide (not the Euro-Lupus nephritis protocol) the risk was thought to be mitigated by administration of a gonadotropin-releasing hormone analog.(33) Particularly among SLE patients with a prior pregnancy complicated by congenital heart block, panelists felt that hydroxychloroquine use, and close fetal cardiac monitoring may prevent disease in a subsequent pregnancy. Preconception counseling, discussion regarding contraception, and evaluation of potential risk factors both related to exogenous estrogen and to teratogenic medications were thought to be critical. Therefore, related adverse outcomes (e.g. fetal abnormalities and spontaneous abortion in a SLE patient receiving teratogenic medications, vascular thrombosis among SLE patients with positive antiphospholipid antibodies receiving estrogen-based contraception), were deemed to be preventable if reproductive health factors were appropriately assessed and discussed. Similarly, obstetrical complications among patients with SLE who have known antiphospholipid syndrome (APS), particularly in the second and third trimesters, were thought to be minimized with appropriate high-risk pregnancy supervision, aspirin, anticoagulation and hydroxychloroquine use. Preeclampsia among patients with SLE was not thought to be preventable as aspirin may diminish but not eliminate risk and the number of SLE patients included in studies to date is very small.(34–36)

SLE-Associated Comorbidities

We considered twenty-seven conditions and after terminology changes, five reached consensus for inclusion. We considered different permutations of acute and chronic kidney disease both in the context of known lupus nephritis and among all SLE patients. Ultimately the groups' consensus was that while an initial episode of renal failure or acute flares in the setting of known nephritis were not preventable, the progression to chronic kidney disease or end-stage renal disease (ESRD) had the potential to be minimized if patients received timely, high quality ambulatory care. This included initial renal biopsy to confirm the diagnosis, immunosuppression, angiotensin-converting-enzyme inhibitor therapy, hydroxychloroquine, and regular monitoring of renal function, urinary protein, blood pressure and SLE disease activity (Table 3).

Discussions regarding myocardial infarction included lack of preventability of first presentation, particularly if it is an early manifestation of SLE. However, consensus was reached regarding the potential preventability of recurrent myocardial infarction through patient engagement in secondary prevention strategies (e.g. smoking cessation, exercise, diet), consideration of statins, avoidance of oral contraceptives if lupus anticoagulant positive (37), and possibly, use of low-dose aspirin and hydroxychloroquine, although panelists noted that randomized controlled trial data in SLE patients are lacking. A first episode of pericarditis or cardiac tamponade was thought to not be preventable and, while

subsequent episodes of tamponade may be reduced with adequate treatment, recurrence was thought to be rare, and overall, hard to prevent even with optimal therapy.

Ischemic tissue injury associated with Raynaud's was thought to be rare among patients with SLE and more of a concern for those with overlap syndromes with features of scleroderma. For patients with SLE, severe refractory Raynaud's was thought to be difficult to manage and at times, not preventable even with the highest quality care. Vascular thrombosis in all SLE patients or in those with positive antiphospholipid antibodies was not thought to be preventable due to a lack of data regarding prevention in the absence of known APS. However, in a patient with known APS who is appropriately anticoagulated, vascular thrombosis, as well as embolic stroke, should be preventable. Most other neurologic manifestations were thought to either be challenging to prevent, or not prevalent enough among SLE patients to reach importance on a population level. Posterior reversible encephalopathy syndrome either as first presentation, or in a person with known hypertension, was thought to be hard to prevent even with close blood pressure monitoring and control, and not prevalent enough among SLE patients to be considered highly important on a population level.

Discussion

Utilizing a modified Delphi process, a multidisciplinary panel of experts endorsed twenty-five ambulatory care sensitive, potentially preventable SLE-specific adverse conditions. Through multiple rounds with controlled feedback, re-review of the literature, and a webinar with active discussion, conditions that reached consensus spanned SLE-associated comorbidities, reproductive health issues, vaccine-preventable illnesses and medication-related complications. This broad range of conditions reflects the heterogeneity of the disease and the heightened vulnerability of SLE patients to certain conditions such as infectious diseases, reproductive health issues, and organ-threatening complications, which may be avoided if sustained, high quality ambulatory care is provided.

We found that vaccine-preventable illnesses and medication- and reproductive health-related complications with evidence-based strategies for risk reduction readily reached consensus. Of the conditions considered, the lowest percentage reaching consensus were among SLE-specific complications. One possible contributing factor was the rarity of several of the conditions discussed (e.g. lupus pneumonitis, transverse myelitis, posterior reversible encephalopathy syndrome) and the lack of studies regarding population-based prevalence to determine importance on a broader, public health scale. In addition, particularly for this category, but also noted for other categories as well, participants highlighted a paucity of randomized controlled trials that examine the effectiveness of prevention strategies among SLE patients (e.g. for cardiovascular risk reduction). Overall, the challenges of the limited medications options, the unpredictability of flares, and first-time SLE manifestations such as cardiac tamponade and acute renal failure, made it particularly difficult to consider certain conditions to be preventable even with optimal SLE care. In general, recurrence or progression of preexisting conditions, including recurrent myocardial infarction, vascular thrombosis in the setting of a prior APS diagnosis, and development of chronic kidney disease or ESRD in a patient with known nephritis, were felt to be more preventable than

initial, acute presentations. Certain adverse outcomes were also thought to be potentially avoidable if rheumatologist-patient communication was improved. These included assessments of reproductive health preferences and counseling regarding teratogenic medications, conversations regarding flares in the setting of UV exposure, and advice regarding lifestyle modifications to reduce cardiovascular risk.

To date, a set of general conditions that may result in avoidable hospitalizations was developed in 2001 and included some vaccine-preventable illnesses, cellulitis, complications from diabetes, heart failure, asthma and chronic obstructive pulmonary disease exacerbations, ruptured appendix, dehydration, malignant hypertension, pyelonephritis, pneumonia, perforated or bleeding ulcer, and hypokalemia.(22, 23) Over a three year period in New York, nearly 20% of SLE patients were hospitalized for one of these general avoidable conditions.(24) Several SLE-specific conditions, including certain vaccine-preventable illnesses, uncontrolled diabetes (in the setting of glucocorticoid use in the SLE population), and gastrointestinal bleed (in the setting of glucocorticoids, NSAIDs or anticoagulants), overlapped with general population conditions and highlight the increased susceptibility among SLE patients due to risk factors from the disease and its treatments. SLE patients suffer from a high burden of the serious infections identified as resulting in avoidable hospitalizations in the general population, including pneumonia, cellulitis and pyelonephritis.(38) Similarly, SLE patients have an increased burden of cardiovascular disease and heart failure-related hospitalizations compared to the general population, as well as lower rates of lipid testing and statin prescriptions.(39–41) In a final list for future research purposes, the new twenty-five SLE-specific conditions could be assessed in addition to the general conditions, which will likely reveal substantially more potentially avoidable hospitalizations in this high risk population.

Strengths of this work include the engagement of a multidisciplinary panel of SLE experts across the U.S. in a rigorous modified Delphi process to define a set of SLE-specific conditions in the context of the most recent literature that are potentially preventable if patients received high quality ambulatory, and specifically rheumatologic care. A 2009 study comprehensively outlined a set of SLE-related quality metrics (25). This endeavor updates past work based on advances in knowledge and endorses a set of potentially measurable, potentially avoidable outcomes if these quality metrics are not achieved. In addition, the current Delphi panel results are presented in the setting of the 2019 update of the EULAR recommendations for SLE management.(42) Adherence to many of the recommended strategies including ophthalmologic screening and hydroxychloroquine dose reduction, minimizing glucocorticoid use, encouraging vaccinations, early and aggressive diagnosis and management of lupus nephritis, and cardiovascular risk assessments, will hopefully minimize many of the SLE-specific avoidable complications included.(42) By defining these adverse conditions, we also have developed a framework that can be used to describe and compare outcomes across health systems and populations to define high quality SLE care, to recognize gaps in the care patients are receiving, and to elucidate key issues in the care of SLE patients that may require randomized controlled trials to ultimately improve SLE-related outcomes.

There are several limitations to this work. Throughout this process, we updated the conditions we considered to remain consistent with the growing body of literature. It is possible that certain conditions might have been missed or conditions may have been included or excluded based on the knowledge, experiences and perspectives of our panelists, which may not be shared across all providers caring for SLE patients. While our panelists included providers across the U.S., we did not have international representation. Our current conditions were considered and endorsed within the context and constraints of the U.S. health care system with the goal of applying them to better understand domestic gaps, disparities and strategies for improvement. Next steps should include additional considerations of these conditions in the context of other countries' health care systems. Finally, several of the conditions that ultimately reached consensus have specific caveats (e.g. in the setting of glucocorticoid use, in the setting of APS, in a person with positive antiphospholipid antibodies, recurrent but not primary episode), which may make it challenging to study these outcomes as a single set of administrative claims/billing codes without an understanding of laboratory values, medication use and clinical context. However, with the rapidly developing field of big data analytics, the use of natural language processing to understand unstructured as well as structured data, and the linking of electronic health records with claims data, ongoing research using these conditions as outcomes is tenable.(43)

In this study, we defined a set of twenty-five ambulatory care sensitive potentially avoidable SLE-specific adverse conditions to allow for population-level studies of health system gaps and racial/ethnic and socioeconomic disparities in SLE-related care and outcomes. SLE patients enrolled in Medicaid, the U.S. public insurance predominately for low income individuals, have a high burden of infections (38), low rates of baseline hydroxychloroquine eye examinations (44), inadequate receipt of high-quality lupus nephritis care, and insufficient lipid testing.(41) Studies in other populations of SLE patients have revealed low rates of vaccine uptake and general preventive care.(10) With this comprehensive list of potentially avoidable conditions, we can further define at-risk populations and the evidence-based preventability of each of these conditions allows for the design of interventions to concretely address the gaps uncovered. This process also allowed us to examine many SLE-related complications that are not yet preventable, suggesting that we must continue to work to improve and evaluate SLE treatments, the early detection of complications, and the ability to risk-stratify patients to intervene to help those at highest risk of adverse outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- SLE patients suffer from a high burden of adverse outcomes many of which may be prevented, or their complications minimized if patients had access to high quality, sustained ambulatory care. Racial/ethnic minorities and lower socioeconomic status individuals disproportionately experience adverse outcomes.
- We used a Delphi process with sixteen national experts to rigorously identify a set of twenty-five conditions relevant to SLE patients that are potentially preventable. These conditions fall into four categories: vaccine-preventable illnesses, medication-related complications, reproductive health-related complications and SLE-related complications.
- These potentially preventable adverse conditions can now be studied on the health system level to better understand and address health disparities to improve health care delivery for the most vulnerable patients.

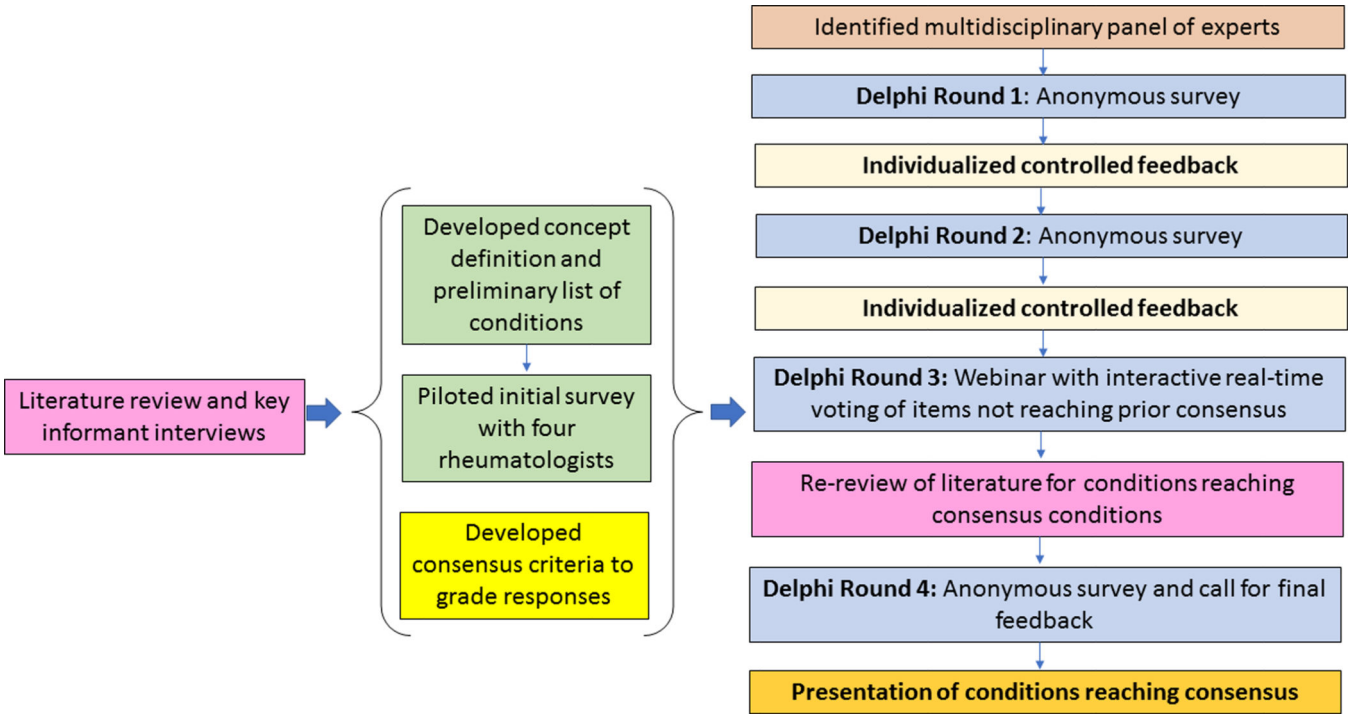

Figure 1.

Illustration of the modified Delphi process used to reach consensus on SLE-specific potentially preventable adverse conditions

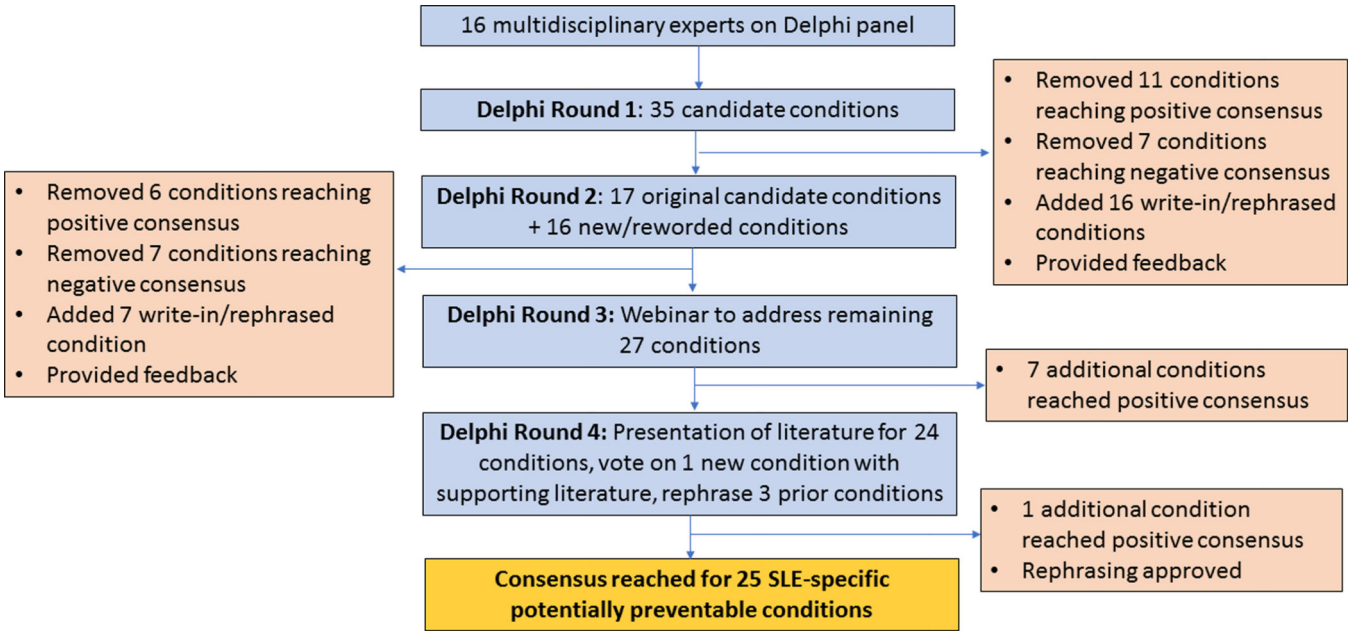

Figure 2.
Flowchart of the candidate condition consideration process

Table 1.

Conditions considered by the Delphi panelists during the four rounds*

Conditions	Round 1	Round 2	Round 3	Round 4	Final List
Vaccine-preventable illnesses					
Herpes zoster					
High-grade cervical dysplasia or cervical cancer					
Influenza					
Meningococcal disease					
Pneumococcal pneumonia					
**Pneumococcal disease					
Hepatitis B					
Encapsulated organism infections					
Medication-related complications					
Avascular necrosis (osteonecrosis) among patients with SLE receiving prolonged glucocorticoids					
Complications from uncontrolled glucocorticoid-induced diabetes					
Chronic opioid use					
Opioid overdose					
Gastrointestinal bleed on glucocorticoids, NSAIDs or anticoagulants					
Osteoporotic fracture among patients with SLE receiving glucocorticoids					
Vision loss secondary to hydroxychloroquine toxicity					
Azathioprine toxicity without TMPT activity assessed					
Pneumocystis pneumonia					
Pneumocystis pneumonia among patients with SLE receiving glucocorticoids					
***Pneumocystis jirovecii* pneumonia (PJP) on moderate to high doses of glucocorticoids					
Progressive multifocal leukoencephalopathy					
Reproductive health-related complications					
Premature ovarian failure					
Premature ovarian insufficiency/infertility in a patient with SLE who received cyclophosphamide without Lupron					
**Premature ovarian insufficiency/infertility following standard dose cyclophosphamide					
Spontaneous abortion among all SLE patients without known positive antiphospholipid antibodies					
Spontaneous abortion in a SLE patient with antiphospholipid antibody syndrome (APS)					
**Obstetrical complications among SLE patients with APS					
Neonatal lupus or congenital heart block among all newborns of mothers with SLE and without known Ro/La status					
Neonatal lupus/complete heart block in a patient with subacute cutaneous lupus without Ro/La antibodies checked					

Conditions	Round 1	Round 2	Round 3	Round 4	Final List
Neonatal lupus/congenital heart block with maternal anti-Ro/La antibodies					
Intrauterine growth restriction					
Preeclampsia					
Spontaneous abortion in a SLE patient receiving teratogenic medications					
Fetal anomalies on teratogenic medications					
Vascular thrombosis among SLE patients receiving estrogen-based contraception					
Vascular thrombosis among SLE patients with positive antiphospholipid antibodies receiving estrogen-based contraception					
SLE-associated comorbidities					
Acute renal failure					
Acute renal failure (initial episode)					
Acute renal failure among patients with known lupus nephritis					
**Chronic kidney disease or end-stage renal disease (ESRD) in patients with known lupus nephritis					
Chronic kidney disease					
Myocardial infarction					
Myocardial infarction (presenting episode)					
Recurrent myocardial infarction					
Cardiac tamponade (presenting episode)					
Cardiac tamponade (recurrence)					
Avascular necrosis (osteonecrosis)					
Embolic stroke among all SLE patients without known positive antiphospholipid antibodies					
Embolic stroke among patients with SLE and APS					
Ischemic stroke					
Interstitial lung disease					
Ischemic tissue injury associated with Raynaud's phenomenon					
Lupus flare in the absence of UV-protection					
Lupus pneumonitis					
Osteoporotic fracture					
Pericarditis					
Posterior reversible encephalopathy among patients with SLE with known hypertension					
Posterior reversible encephalopathy syndrome					
Seizures					
Transverse myelitis					
Vascular thrombosis among all SLE patients without known positive antiphospholipid antibodies					
Vascular thrombosis among SLE patients with positive antiphospholipid antibodies					
Vascular thrombosis among SLE patients with APS					

*Conditions that reached consensus (either positive consensus for inclusion, or negative consensus for removal), were not considered again until Round 4 when final approval was solicited

**Condition is reworded based on feedback from the prior round

Table 2.

Ratings of preventability and importance on a population level for final conditions reaching consensus, ordered by lowest (most preventable) to highest (least preventable) mean rating

SLE-Specific Potentially Preventable Conditions	Preventability Rating*		Importance Rating** N (%)			
	Mean (SD)	Median (range)	A	B	C	D
Vaccine-preventable illnesses						
Hepatitis B (N=15)	2.0 (1.1)	2 (1–5)	9 (60)	4 (27)	1 (7)	1 (7)
Influenza (N=15)	2.4 (0.5)	2 (2–3)	9 (60)	5 (33)	1 (7)	--
High-grade cervical dysplasia/cervical cancer (N=14)	2.6 (1.3)	2 (1–5)	12 (86)	2 (14)	--	--
Pneumococcal disease (N=14)	3 (1)	3 (2–5)	9 (64)	4 (29)	1 (7)	--
Herpes zoster (N=11)	2.9 (1.2)	2.5 (2–5)	6 (55)	5 (45)	--	--
Meningococcal disease (N=11)++	3.5 (1.7)	3 (2–6)	4 (36)	4 (36)	3 (27)	--
Medication-related complications						
Vision loss from hydroxychloroquine toxicity (N=15)	1.6 (0.7)	1.5 (1–3)	13 (87)	1 (7)	--	1 (7)
Pneumocystis pneumonia in a patient receiving prolonged moderate-to-high dose glucocorticoids (N=15)	2.1 (0.9)	2 (1–4)	8 (53)	4 (27)	2 (13)	1 (7)
Chronic opioid use (N=13)	2.5 (0.9)	2 (1–4)	7 (54)	6 (46)	--	--
Opioid overdose (N=13)	2.6 (0.9)	2.5 (1–4)	9 (69)	4 (31)	--	--
Gastrointestinal bleed on glucocorticoids, NSAIDs or anticoagulation (N=12)	2.6 (0.7)	3 (2–4)	3 (25)	9 (75)	--	--
Complications from uncontrolled glucocorticoid-induced diabetes (N=15)	3.1 (1.4)	3 (1–6)	10 (67)	4 (27)	1 (7)	--
Osteoporotic fracture among patients with SLE receiving glucocorticoids (N=15)	3.2 (1.3)	3 (2–6)	9 (60)	6 (40)	--	--
Avascular necrosis among patients with SLE receiving prolonged glucocorticoids (N=10)	3.7 (1.3)	3 (3–6)	3 (30)	6 (60)	1 (10)	--
Reproductive health-related complications						
Fetal anomalies on teratogenic medications (N=16)	1.8 (0.9)	1.5 (1–3)	16 (100)	--	--	--
Vascular thrombosis among SLE patients with positive antiphospholipid antibodies receiving estrogen-based contraception (N=14)	2.6 (0.9)	3 (1–4)	9 (64)	5 (36)	--	--
Premature ovarian insufficiency/infertility in a patient following standard dose cyclophosphamide (N=13)	3.0 (1.0)	3 (1–5)	8 (62)	5 (38)	--	--
Obstetrical complications among SLE patients with antiphospholipid syndrome (N=12)	3.0 (0.6)	3 (1–4)	8 (67)	4 (33)	--	--
Neonatal lupus/congenital heart block in a patient with positive anti-Ro or anti-La antibodies (N=11)	3.1 (0.9)	3 (2–5)	7 (64)	4 (36)	--	--
Spontaneous abortion in a SLE patient receiving teratogenic medications (N=15)#	3.3 (2.0)	3 (1–7)	8 (53)	5 (33)	1 (7)	--
SLE-related complications						
Vascular thrombosis among SLE patients with antiphospholipid syndrome (N=15)	2.4 (0.7)	2 (1–4)	12 (80)	3 (20)	--	--
Embolic stroke among SLE patients with antiphospholipid syndrome (N=15)	2.8 (0.9)	3 (2–5)	10 (67)	5 (33)	--	--

SLE-Specific Potentially Preventable Conditions	Preventability Rating*		Importance Rating** N (%)			
	Mean (SD)	Median (range)	A	B	C	D
Chronic kidney disease or ESRD among patients with known lupus nephritis (N=9)	2.9 (1.0)	3 (2–5)	8 (89)	1 (11)	--	--
Lupus flare in the absence of UV protection (N=12)++	3.2 (1.9)	3 (1–6)	5 (42)	7 (58)	--	--
Recurrent myocardial infarction (N=11)	3.9 (1.4)	3 (3–7)	9 (82)	2 (18)	--	--

+Panelists with specific expertise could opt-out of rating conditions outside of their area; results presented for the final round for which consensus for inclusion was reached

*Preventability scale is 1 (definitely preventable) to 9 (not preventable); mean and median scores reflect removal, when applicable, of 1 extreme high (8–9) and/or 1 extreme low (1–2) per a priori consensus criteria

**Importance was defined on the population level, including consideration of the prevalence of the outcome in the SLE population; range was A (very important) to D (not important). Importance consensus, after removing 1 extreme high (D) and 1 extreme low (A), required >9 remaining rates to be A or B and <3 ratings of D or N/A. For items with fewer responses, >60% with ratings of A or B were required.

++Met lenient but not strict consensus criteria. Lenient preventability consensus criteria for inclusion defined as median <3 and no more than 4 panelists providing a rating in the highest tertile (7–9), after removal of 1 extreme high (7–8) and one extreme low (1–2). Strict preventability consensus criteria for inclusion, after removal of one extreme high and one extreme low, defined as >9 remaining ratings <3 and <2 ratings >7. For items with fewer responses, >60% with ratings <3 were required.

#One response of “not applicable” for the importance rating

Table 3:

List of SLE-specific ambulatory care sensitive potentially preventable conditions reaching consensus and the strategy for prevention or reduction of adverse outcomes*

SLE-Specific Ambulatory Care Sensitive Condition	Strategy for Prevention or Reduction of Adverse Outcomes
Vaccine-preventable illnesses	
High-grade cervical dysplasia/cervical cancer	HPV vaccination and regular pap screening with HPV cotesting per 2018 American College of Obstetricians and Gynecologists, American Society for Colposcopy and Cervical Pathology and the Society of Gynecologic Oncology
Influenza	Yearly influenza vaccine
Herpes zoster	Live attenuated herpes zoster vaccine (Zostavax) and HZ/su adjuvanted herpes zoster subunit vaccine (Shingrix)
Meningococcal disease	Meningococcal vaccines (quadrivalent vaccine approved for ages 11–18, and for ages ≤10 and ≥19 who are at increased risk for invasive meningococcal disease, and serogroup B vaccine FDA approved for individuals 10–25, also supported for anyone >10 by the Advisory Committee on Immunization Practices)
Pneumococcal disease	Pneumococcal vaccines (PCV13 and PPSV23)
Hepatitis B (HBV)	HBV vaccination and screening for chronic infection or prior exposure (Hepatitis B core antibody and Hepatitis surface antigen) prior to initiation of immunosuppressive medications and consideration of antiviral treatment when indicated
Medication-related complications	
Vision loss from hydroxychloroquine toxicity	Dose adjustment (≤5mg/kg real weight) and baseline fundus exam and then after 5 years, yearly optical coherence tomography (OCT) plus automated visual field examinations per the American Academy of Ophthalmology
Opioid overdose	Opioid agonist therapy prescribing and overdose education and identification of high-risk patients for close monitoring
Chronic opioid use	Pain management alternatives for SLE patients and treatment of concomitant fibromyalgia diagnoses
Pneumocystis jirovecii pneumonia (PJP) on moderate to high doses of glucocorticoids +	PJP prophylaxis (trimethoprim-sulfamethoxazole, atovaquone, dapsone)
Gastrointestinal bleed on glucocorticoids, NSAIDs, or anticoagulants	Proton pump inhibitors
Complications from uncontrolled glucocorticoid-induced diabetes	Minimization of glucocorticoids, glucose monitoring and intervention when appropriate
Osteoporotic fracture on glucocorticoids	Following the American College of Rheumatology guidelines regarding osteoporosis screening, prevention and treatment depending on age and level of fracture risk
Avascular necrosis (osteonecrosis) on prolonged glucocorticoid therapy	Minimizing glucocorticoid use (e.g. early consideration of steroid-sparing agents), and early recognition of avascular necrosis as prognosis and potential for native joint preservation are affected by disease stage
Reproductive health-related complications	
Fetal anomalies on teratogenic medications	Assessment of reproductive health preferences, offering appropriate, effective contraception or prescribing of pregnancy-compatible medications for women planning to conceive
Vascular thrombosis with estrogen-containing contraception and positive antiphospholipid antibodies	Avoiding estrogen-based contraception in the setting of antiphospholipid antibody positivity

SLE-Specific Ambulatory Care Sensitive Condition	Strategy for Prevention or Reduction of Adverse Outcomes
Premature ovarian insufficiency/infertility following standard dose cyclophosphamide	Use of gonadotropin-releasing hormone analog
Spontaneous abortion while on teratogenic medications	Discussion about potential teratogenic risks and offering effective contraception
Obstetrical complications in SLE patients with antiphospholipid syndrome (APS)	Recognition of APS and appropriate treatment with low dose aspirin and prophylactic-dose low molecular weight heparin or unfractionated heparin, and consideration of hydroxychloroquine use
Neonatal lupus/congenital heart block with maternal anti-Ro/La antibodies	Appropriate testing for anti-Ro/La antibodies, hydroxychloroquine use, and fetal cardiac monitoring
SLE-related comorbidities	
Vascular thrombosis in SLE patients with known APS	Anticoagulation with appropriate monitoring of INR. Consideration of hydroxychloroquine use.
Embolic stroke in SLE patients with known APS	APS management with anticoagulation with appropriate monitoring of INR, control of active SLE with prednisone and/or immunosuppressives as appropriate, and consideration of echocardiographic evaluation for valvular disease. Consideration of hydroxychloroquine use.
Lupus flare in the absence of ultraviolet (UV) protection	UV protection and sun avoidance counseling
Chronic kidney disease or end-stage renal disease (ESRD) in patients with known lupus nephritis	Renal biopsy to diagnose lupus nephritis, then monitoring of renal function, urinary protein, blood pressure and SLE disease activity labs per ACR guidelines and SLE quality indicators, as well as appropriate treatment for lupus nephritis (immunosuppressives, glucocorticoids, ACE inhibitor/ARB, hydroxychloroquine)
Recurrent myocardial infarction	Secondary prevention strategies (e.g. diet, weight loss, smoking cessation, exercise), aspirin, statin therapy, hypertension management and consideration of certain antihypertensives based on risk factors. If lupus anticoagulant positive, avoidance of oral contraceptives. Consideration of hydroxychloroquine use.

*Please see Supplemental Data 2 for further details and for a review of preventability and importance data by condition and applicable references

+The expert panel concluded in their final recommendations that while PJP should be included in this list of potentially preventable conditions, the decision for use of prophylaxis should be made on a case-by-case basis weighing the population-based prevalence of the condition, the risks associated with the prophylactic antibiotics, the severity of the patient's SLE, the patient's comorbidities, and the concomitant use of other immunosuppressive agents.