

# A Concept Development for the Symptom Science Model 2.0

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**Background:** The National Institute of Nursing Research developed the National Institutes of Health symptom science model (SSM) in 2015 as a parsimonious conceptual model to guide symptom science research.

**Objectives:** This concept development paper synthesizes justifications to strengthen the original model.

**Methods:** A literature review was performed, discussions with symptom science content expert stakeholders were held, and opportunities for expanding the current model were identified. Concept elements for a revised conceptual model—the SSM 2.0—were developed.

**Results:** In addition to the four original concept elements (complex symptom presentation, phenotypic characterization, biobehavioral factors [previously biomarker discovery], and clinical applications), three new concept elements are proposed, including social determinants of health, patient-centered experience, and policy/population health.

**Discussion:** There have been several calls to revise the original SSM from the nursing scientific community to expand its utility to other healthcare settings. Incorporating three additional concept elements can facilitate a broader variety of translational nursing research symptom science collaborations and applications, support additional scientific domains for symptom science activities, and produce more translatable symptom science to a wider audience of nursing research scholars and stakeholders during recovery from the COVID-19 pandemic. The revised SSM 2.0 with newly incorporated social determinants of health, patient-centered experience, and policy/population health components now empowers nursing scientists and scholars to address specific symptom science public health challenges particularly faced by vulnerable and underserved populations.

**Key Words:** nursing research • social determinants of health • symptom management • Symptom Science Model 2.0 • symptom science research

*Nursing Research, November/December 2022, Vol 71, No 6, E48-E60*

Historically, the mission of the National Institute of Nursing Research (NINR) at the National Institutes of Health (NIH) was to promote and improve the health of individuals, families, and communities by conducting clinical, translational, and basic research to inform clinical practice in the areas of symptom science, wellness, self-management of chronic conditions, and end-of-life and palliative care (NINR, 2016). Symptom science uses clinical, basic, and translational research methods to understand the mechanisms and presence of patient symptoms and clusters, in conjunction with environ-

mental factors and health outcomes (Cashion & Grady, 2015; Saligan, 2019). Symptoms are signs of diseases or injuries noticed or experienced by individuals. Symptom presence, severity, complexity, and timing can affect physical, mental, and social functioning. Understanding their significance can assist in identifying and diagnosing illnesses or treatment modifications. Common symptom examples that profoundly affect a person's experience of health and well-being include—but are not limited to—fatigue, pain, unintentional weight loss or gain, exhaustion, anxiety, fever, and insomnia.

Description and management of complex symptoms in facilitating equitable healthcare treatment for acute and chronic health conditions is a key foundation of the nursing profession that spans the human life span and has gained prominence globally as a unique nursing specialty (Henly, 2015, Rosa, 2019). Improved understanding of patients' infectious and noncommunicable disease symptoms throughout an illness course, ensuring adequate access and healthcare provision for their resolution, and assisting patients to prevent and ameliorate their symptoms via self-management effectively can reduce human suffering, facilitate well-being, and decrease economic healthcare burdens (Centers for Medicare & Medicaid Services, 2020; Feldman et al., 2017; National

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DOI: 10.1097/NNR.0000000000000605

Academies of Sciences, Engineering, and Medicine [NASEM], 2021; Rosa et al., 2019). The purposes of this concept development paper are to summarize current symptom science and symptom management models used by the nursing research community, highlight areas where the original NIH SSM is working well, identify SSM gaps, and develop concepts for a revised SSM 2.0 to broaden its utility.

### Symptom Science and the Evolution of the Original SSM

Symptom science focuses on how an individual's symptoms (e.g., patient-reported descriptions, clinical documentation, physical assessment findings, laboratory tests, digital and wearable device sensor data, genetic test results, and -omics data) guide understanding of health and inform clinician decision-making for well-being, diagnosis, and tailored health care treatments (Dorsey et al., 2019). In 2015, the NIH SSM guided the conduct of basic and biobehavioral symptom science research for nurse scientists and—combined with the Nursing Science Precision Health Model—resulted in the integration of nursing symptom science with the precision health movement (Cashion & Grady, 2015; Hickey et al., 2019). Precision health is a broader interdisciplinary approach rooted in public health that makes use of “big data” (e.g., genetics/genomics, epigenetics, -omics, and microbiomics) to focus on targeted disease prevention and healthy well-being across the life span for different populations (Khoury et al., 2016). Both symptom science and precision health movements parallel broader scientific initiatives seeking to understand diagnosis, management, and treatment of patient illness and symptoms. In addition, the COVID-19 pandemic's “triple hit” on health, education, and income highlights a pressing need for integration of additional concepts including social determinant factors to reverse profound health equity disparities in local through global communities (United Nations Development Programme [UNDP], 2022). We propose this concept development paper to broaden the utility of the original NIH SSM and to help address wider public health concerns and health outcome disparities in symptom science.

### METHODS

We conducted a narrative literature review to evaluate the most commonly used symptom management theories and models, and to identify concept gaps in the original NIH SSM.

### Research Questions

The research questions were as follows:

**Question 1:** “What are the illness symptom theories and models being applied in acute and chronic illness in nursing research?”

**Question 2:** “What concept areas are needed to derive a more inclusive model of scientific inquiry for nursing symptom science research so it can be broadly applied to the healthcare system as a whole?”

**Question 3:** “What are the research methods, designs, and approaches that can, and should be used, to organize the conceptual model elements and inform a more inclusive SSM 2.0?” (Supplemental Digital Content [SDC] Table 1, <http://links.lww.com/NRES/A438>).

**Question 1** To address Question 1, we conducted a narrative literature search with an NIH biomedical librarian across the following biomedical literature databases: CINAHL, EMBASE, PsychInfo, Scopus, and Web of Science. The timeline used was for articles published from January 1, 2009, to November 1, 2019, with key words including illness symptom models and/or theories applied to acute and chronic illnesses, organ system involvement (e.g., psychiatric, diabetes, renal, cardiac, and neuro), life span (e.g., pediatric and older adult), and health setting (e.g., community health, public health, and population health). Specific key words included nursing models, nursing theory and philosophy, nursing research, symptom clusters, symptom models, nursing methodology, symptom science and symptom management, self-management, and precision health nursing theory. From 148 total articles (Embase, Scopus, WoS, CINAHL, PsychInfo), 63 articles were identified as containing concepts and elements to inform a more inclusive SSM for nursing research and 24 are included in this synthesis (SDC Figure 1, <http://links.lww.com/NRES/A445>).

**Question 2** To address Question 2, we performed complementary narrative literature searches in PubMed and Google Scholar using the following search terms: social determinants of health (SDOH), machine learning and artificial intelligence, health systems integration, policy and population health, patient-centered experience and patient-reported outcomes, and engaged in conversations with nursing policy and symptom science stakeholders. From 80 total articles (PubMed, Google Scholar) and 23 other records (thought leader statements and organization websites); 27 relevant peer-reviewed articles, government agency reports, nonprofit foundation consensus study research reports, and thought leader statements were identified, including SDOH-related changes emerging during the COVID-19 pandemic (SDC Figure 1, <http://links.lww.com/NRES/A445>).

**Question 3** To address Question 3, we facilitated an expert stakeholder review and received critical input to confirm developed concepts for the revised SSM 2.0. Expert stakeholders included nurse scientist leaders who performed symptom science research, a nurse scientist academic consultant, and an internationally renowned nurse scientist theorist and methodologist. We received input on a broader symptom science research agenda comprising qualitative and quantitative research method elements, mixed methodology research designs, content emphases, symptom science research applications and concept development fields, nursing

practice domains, patient experiences, population science, and health policy applications (SDC Table 1, <http://links.lww.com/NRES/A438>).

## RESULTS

The results are presented by order of research question. For question 1, nursing philosophy results identified various frames for guiding development of symptom science nursing theories and models and are presented in SDC Supplemental Data at: <http://links.lww.com/NRES/A440>. Due to space limitations, we highlight only currently used symptom science nursing theories and models relevant to informing the SSM 2.0 revision. Question 2 results highlight current symptom science advances, concepts, and applications needed to inform wider healthcare system use. For Question 3, we reviewed and synthesized stakeholder feedback with our literature reviews to draft a revised SSM 2.0.

### Question 1

**Commonly Utilized Symptom Management Theories and Models** Commonly used nursing theories and models are often disease agnostic so that they can apply to a broad range of conditions, environmental settings, and patient populations. Comparatively, other theories may be developed for application to a specific disease, patient, or caregiver group. Table 1 presents several nursing theories or models of symptom science and symptom management used in nursing research and practice. Themes across articles from our literature search were categorized as follows: (a) models and theories focused on defining and characterizing the experience of a symptom or symptom cluster in a specific disease or condition, (b) models aimed at specific characterization of symptoms of specific conditions/diseases, and (c) reviews/critiques with the charge of developing new symptom management models.

More than half of the articles fell into the theme of symptom experience and/or symptom clusters. A significant gap identified in most articles was the lack of longitudinal study of symptoms that could define complex symptom origination through their resolution. This would allow for the development of models to target the sources of symptoms before their severity peaks (Brant et al., 2010). Among the most cited symptom management theories were the University of California San Francisco (UCSF) Symptom Management Model (SMM) and the theory of unpleasant symptoms (TOUS), which focus on patients' symptom experiences and symptom outcomes (Lenz et al., 1995; UCSF School of Nursing Symptom Management Faculty Group, 1994). Other theories focused on integrating symptoms with self-care behaviors in the management of chronic illnesses (Riegel et al., 2019). Lastly, many nursing and nonnursing research models and theories aimed to characterize symptoms through organ systems, condition-specific lenses, and evaluate symptom variability across disease pathologies and patient subpopulations.

### Questions 2 and 3

#### **Strengths and Weaknesses of the Original NIH SSM**

The original NIH SSM is a well-cited conceptual model used by nurse scientists to evaluate biological correlates of symptoms (Cashion & Grady, 2015; NINR, 2016). The NIH SSM advanced the field of symptom science and recently facilitated development of a national collaborative research consortium to better understand biological underpinnings of the symptom experience (Saligan, 2019). Table 2 highlights recent symptom science advances conducted by nurse scientists using the original NIH SSM, as well as key strengths and weaknesses identified in the literature review.

**The Revised SSM 2.0** Concurrent with this revision process, NINR developed larger intra- and interinstitute/center collaborations, broadened global nursing research training opportunities with a richer diversity of collaborators, and developed a biosample repository. During the open portion of the September 17, 2019, NINR National Advisory Council for Nursing Research (NACNR) meeting, recommendations were made to revise the original SSM and incorporate additional concept elements and themes to make it more broadly applicable (NACNR 2019). There was consensus that symptom science be expanded to: ensure relevance to the wider nursing community; ensure consistency with emerging healthcare trends and scientific movements including artificial intelligence and machine learning platforms supporting big data analyses; include SDOH; include patient and family-centered symptom experiences to better guide symptom self-management; and ensure relevance to population health and policy frameworks (Dorsey et al., 2019; Hickey et al., 2019).

Figure 1 presents the revised SSM 2.0 with a total of seven concept elements:

1. SDOH,
2. patient-centered experience,
3. biobehavioral factors,
4. complex symptoms,
5. phenotype characterization,
6. clinical application, and
7. policy and population health.

Three concepts are unchanged, and one is revised from the original NIH SSM (now biobehavioral factors instead of biomarkers). Three new concepts are included (SDOH, patient-centered experience, and policy and population health). The final policy and population health concept in Figure 1 is shown as encompassing all other concepts in the proposed model to help inform broader applications of symptom science. Table 3 presents concept definitions for use in meta-analysis and systematic reviews and offers a range of example research applications for the revised SSM 2.0 to expand the scope of symptom science in acute and chronic illnesses (i.e., nursing research designs, methods, techniques, populations, settings, emphases, tools, etc.).

**TABLE 1. Commonly Utilized Symptom Theories and Models**

Theory	Study	Purpose	Condition, application	Limitations
Symptom management model	UCSF SON Symptom Management Faculty Group (1994)	Depicts single or multiple symptoms expressed within an intervention framework. Three underlying dimensions: symptoms experience, symptom management, symptom outcomes.	Pain (OA) Gerontology Critical care/ICU Postpartum pain Postpartum thirst Neurological disorders/disease Sleep + pregnancy GI surgery Peds + hyperactivity Cancer (peds + adults) Thoracic surgery CF Telemedicine/health	(1) Variables fit into multiple categories (i.e., physical and cultural). (2) Lack of evaluation of multiple symptoms; interactive relationships among symptoms. (3) How temporal components of a symptom are evaluated (i.e., resolution, exacerbation).
Theory of unpleasant symptoms	Lenz et al. (1995)	Depicts three antecedent factors that influence the symptoms experience: physiological, psychological, situational. May include single or multiple symptoms and clusters.	CKD—as symptom clusters	(1) Antecedent and outcome categories are not well-defined. (2) Lack of consideration for resolution or exacerbation of symptoms. (3) No intervention component.
Symptom experience model	Armstrong (2003)	Integrated model incorporating concepts from other symptom models/theories. Takes multiple symptoms into account and their influence and interactions on outcomes.	Provide input into the symptom experience and produce the symptom perception. Included in this model are demographic, disease, and individual characteristics.	(1) Does not address changes over time. (2) No interventions were included.
Symptom experience model	Armstrong (2014)	Updates to this model include the assessment of changes in symptoms over time and self-management approaches.	Application is universal wherever symptoms occur, examining longitudinal data related to the occurrence and severity of symptoms over the disease/treatment.	(1) Does not address patient–family–provider/nurse interaction
Symptoms experience in time	Henly et al. (2003)	Integrated model incorporating concepts from other symptom models/theories.	Considers symptom experience in the context of time, with four temporal assumptions, clock/calendar time, biological/social time, perceived time, and transcendence.	(1) Conceptual definitions of time remain abstract. (2) Does not examine symptoms interactions/clusters.
NIH symptom science model	Cashion & Grady (2015)	Developed to guide symptom science researchers in identifying biological correlates of symptoms using -omics and bioinformatic strategies.	Applies -omics focusing on the symptom or symptoms through a disease agnostic lens, although it has been applied to symptoms associated with various conditions/diseases.	(1) Is not easily adjustable for researchers not examining symptom biology. (2) Difficult for clinical translation, healthcare system implementation in the absence of validated biomarkers.
Dynamic symptoms model	Brant et al. (2010)	Developed to address the complex nature of symptoms, co-occurring symptoms, symptom interaction, and longitudinal trajectories of symptoms over time.	Commonly used: – in cancer populations – to inform symptom trajectories – for symptom clusters	(1) Does not consider the patient–family–provider/nurse interaction.
Revised dynamic symptoms model	Brant et al. (2016)	Revised to incorporate changes in symptoms over time.	Commonly used: – in cancer populations – to inform symptom trajectories – for symptom clusters	(1) Does not consider the patient–family–provider/nurse interaction.

Note. UCSF SON = University of California San Francisco, School of Nursing; OA = osteoarthritis; ICU = intensive care unit; GI = gastrointestinal; Peds = pediatric; CF = cystic fibrosis; CKD = chronic kidney disease.

The revised SSM 2.0 now proposes examining a complex symptom, as it leads to phenotype characterization, which is informed and affected by an individual's SDOH and patient-centered illness experience. Symptoms can be

analyzed quantitatively and qualitatively with methods that include philosophical- and theoretical-based inquiries or integrated mixed methods research designs. Examination of biobehavioral factors in addition to the biology associated



**TABLE 2. Symptom Science Research Highlights From the Original National Institutes of Health Symptom Science Model (NIH SSM)****SSM summary and research highlights****Strengths of NIH SSM**

- Documented support emphasizes symptom science's importance and utility for the nursing profession (Henly, 2015).
- Elegant, simple, and straightforward and allows for a sequential process of symptom inquiry (Castner et al., 2019; Dorsey et al., 2019).

**Weaknesses of NIH SSM**

- Recent commentaries on thought leader statements and regional and national collaborative workgroups requested inclusions of environmental health, social, societal, and health policy perspectives to better complement -omics methodologies and research designs (Castner et al., 2019; Dorsey et al., 2019).
- There is a noticeable gap for nurse researchers who aspire to perform and expand symptom science research beyond the preclinical -omics or molecular biology of symptoms, including environmental health, health policy, social justice, and societal factors content areas (Castner et al., 2019).
- Local through global COVID-19 healthcare disparities results in a profound need for broader applications into community health settings, underserved and vulnerable populations, and healthcare system applications to ensure access to adequate treatment.
- SDOH and centering on the patient experience are not explicitly stated in the model.

**Complex symptom**

Miaskowski et al. (2017) describe what makes symptoms complex as the characteristics that feed into them, such as (a) subjective perception, (b) temporal changes, (c) underlying mechanisms, (d) co-occurrence of symptoms, and (e) how they are measured. Leading these discussions around symptoms and their complexities has been the Symptom Management Research Group of the University of California San Francisco. They were the first to present the concept of symptom clusters, recognizing that patients rarely present with one symptom but generally have multiple symptoms that may or may not interact with each other, or synergize other symptoms when co-occurring.

**Biomarker**

McCall et al. (2018) used the NIH SSM to perform a systematic review of published symptom science research to investigate -omics based approaches for five exemplar disease-agnostic symptom phenotypes: sleep disruption, cognitive impairment, fatigue, GI distress, and pain. The authors focused on published quantitative reports of selected symptom phenotypes using genomic, transcriptomic, and epigenomic approaches and formal statistical analyses that generated significant results. McCall et al. identified 27 genes present in more than symptom phenotype involving immune, inflammatory, and cell signaling canonical pathways. Ingenuity pathway analysis (QIAGEN) of these -omics associations produced a 15-gene model that informs shared biological underpinnings and mechanistic pathways of co-occurring symptoms. These approaches advance our knowledge of co-occurring symptoms and genetic regulation that can better inform precision treatments for acute and chronic treatments in a disease-agnostic manner.

**Phenotypic characterization**

Phenotype describes an organism's observable characteristics and physical and behavioral traits. This may or may not include a symptom related to the observed phenomenon. Fu et al. (2016) prospectively examined the phenotype of arm lymphedema, where symptoms and other measures were used to characterize different traits associated with lymphedema, including discomfort, fluid accumulation, and limb mobility. Phenotyping and defining a complex symptom may overlap in their characterization, however, represent distinct components of the current symptom science model sequence. There may exist tiers or hierarchies within symptoms or illness in which the presentation of certain traits represents associated change; these may be the result of symptoms or contribute to symptom development. The ability to characterize and group what is being observed provides precision in assessment as well as how to best approach management.

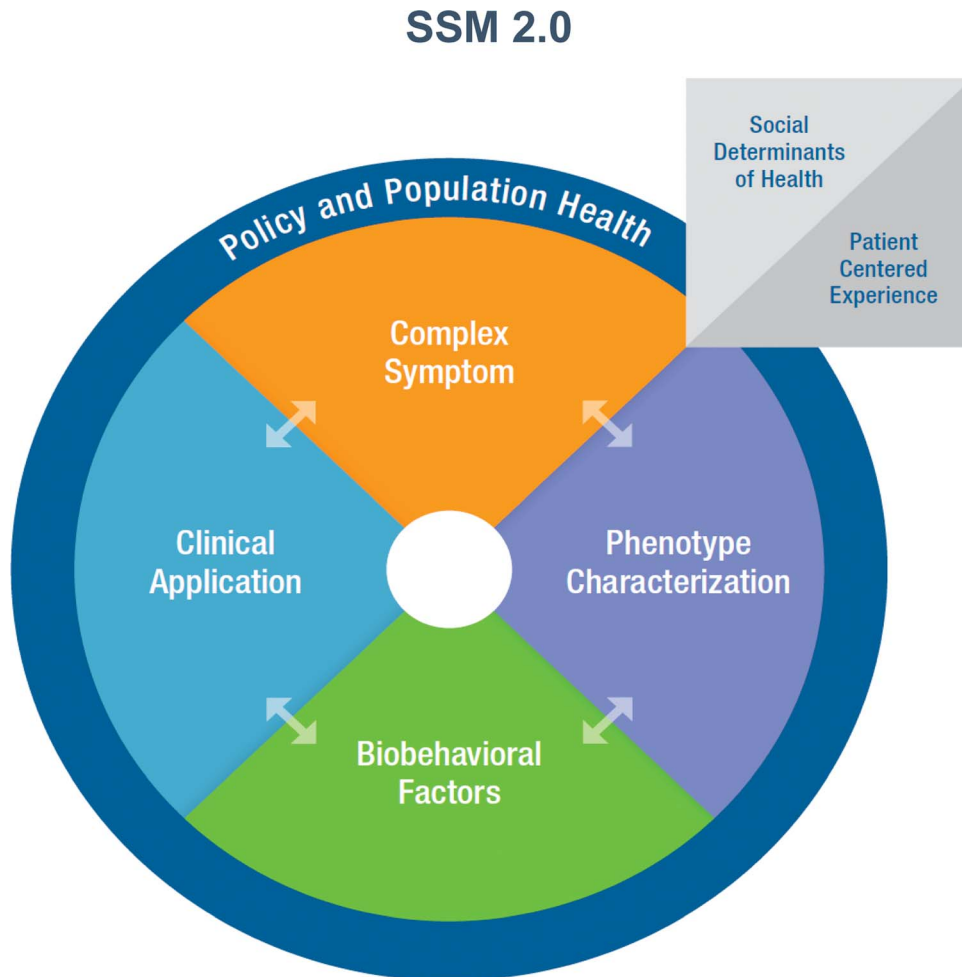
**Clinical application**

Saligan et al. (2016) conducted an exploratory analysis of ketamine versus placebo use on fatigue symptoms in two double-blind, randomized crossover trials for 36 patients with treatment-resistant bipolar 1 or 2 disorder. After controlling for depressive symptoms, significantly lower NIH Brief Fatigue Inventory scores were observed in the ketamine treatment group from 40 minutes posttreatment to Day 14 (except Day 7), with Day 2 demonstrating greatest improvement effect.

Note. Abbreviations: SSM=Symptom Science Model; GI=gastrointestinal.

with or contributing to a person's symptoms allows for the development of personalized prevention approaches and targeted treatments. However, policy and population health levers are needed to accomplish clinical translation in a systematic and structured way. Integration examples of clinical and research symptom science infrastructure into broader health system use may include: robust data col-

lection mechanisms and interoperability standards; symptom analytics for defined clinical patient populations and subpopulations (i.e., by age, gender, race, income level, disease type, clinical subspecialty, SDOH component, and others); inclusion of marginalized and vulnerable individuals in underserved geographical locations (i.e., rural and urban areas of poverty); and/or methods of defining clinical subtypes of



**FIGURE 1.** Symptom Science Model 2.0 (SSM 2.0). The revised SSM 2.0 features three additional concepts: social determinants of health, patient-centered experience, and policy and population health. Biomarkers are modified to biobehavioral factors.

disease such as biomarker status (NASEM, 2018). The modified and newly developed concepts are described below.

**Social Determinants of Health** Nurses play vital roles in health improvement and health equity and need to address SDOH to improve health outcomes for marginalized and disadvantaged patients and citizens. Researchers have examined SDOH closely for decades, and SDOH are gaining greater prominence as social science methods have evolved and evidence accumulates (Taylor et al., 2016). Presently, a dilemma exists about incorporating SDOH in a structured way to augment clinical care goals to deliver improved patient outcomes at lower costs (Hammond & Maddox, 2019). The World Health Organization defines SDOH as “the conditions in which people are born, grow, live, work, and age, including the health system”, (Dahlgren & Whitehead, 2007). And although SDOH models and definitions vary, a well-recognized model classifies SDOH factors into four tiers: general socioeconomic, cultural, and environmental conditions (food availability, education

level, work environment, living and working conditions, unemployment, water and sanitation, healthcare services such as insurance, access to hospitals and clinicians, and housing); social, community influences and networks (economic conditions of neighborhood such as poverty, witnessing violence, marital status, and urban and rural geography); individual lifestyle factors (chronic diseases, health maintenance, and wellness behavior choices such as diet, alcohol, and drug use); and age, sex, and constitutional factors (biological factors, genetics, gender, and race; Dahlgren & Whitehead, 2007). It is estimated that ~80%–90% of health outcomes at the population level are attributable to SDOH (Magan, 2017).

SDOH advances applied to symptom science can improve understanding of a patient’s situational context in symptom self-management, contribute to improved health equity, and advance accuracy of artificial intelligence algorithms that integrate molecular -omics data with electronic health records (EHRs), medical imaging data, text fields, and other clinical and social determinant factors (Emengo et al., 2020; Raza,

**TABLE 3. Concept Headings and Example Research Applications for the Revised Symptom Science Model 2.0**

Concept heading	Concept definitions and example research designs, methods, techniques, populations, settings, tools, and applications
Patient-centered experience	<p><u>Concept definition:</u> During the range of interactions that patients have with the healthcare system, providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>Patient context in community, family, group, clinic, healthcare system</li> <li>Patient goals, beliefs, perspectives, values, and principles (patient, family satisfaction)</li> <li>Dialogue and encounter with the patient and family; patient-centered and family-centered care</li> <li>Symptom self-management, self-efficacy, individual health care decision-making</li> <li>Patient context in community, family, group, clinic, healthcare system</li> <li>Nursing philosophy, nursing theory, qualitative methodologies, mixed-methods inquiry</li> <li>Psychometric Patient-Reported Outcome measures development for precision health</li> </ul>
Social determinants of health	<p><u>Concept definition:</u> The conditions in which people are born, grow, live, work, and age, including the health system.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>General socioeconomic cultural environment and context</li> <li>Support system(s), access to culturally relevant support at community level, including worship</li> <li>Education level, health literacy, language barriers</li> <li>Food quality and availability</li> <li>Employment and work environment</li> <li>Clean water and sanitation access, sustainable development</li> <li>Integral ecology</li> <li>Sustainable development goals, United Nations (i.e., Goal #3, good health and well-being)</li> <li>Healthcare services, access, health equity</li> <li>Housing</li> <li>Environmental health, harmful environmental exposure reduction, climate effects, environmental justice</li> <li>Social justice for vulnerable groups: gender, sex, and/or pregnancy, disability, race, color, ethnicity, age, socioeconomic status, LGBTQ+, religion, genetic information, etc.; rural, urban poverty; domestic, global</li> </ul>
Biobehavioral factors	<p><u>Concept definition:</u> The use of biological, genomic, -omic, physiological, and other clinical laboratory data to identify and refine reliable, valid biomarkers for the detection and monitoring of physical and behavioral symptoms to understand correlative relationships with human disease.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>Biomarker discovery and bio-sample repositories</li> <li>Clinical, physiological, biological factors and findings; psychological, behavioral, and cognitive factors</li> <li>Artificial intelligence, machine learning, and big data</li> <li>Genetics, genomics, epigenetics, and -omics</li> <li>Preclinical studies for patient safety and accuracy</li> <li>Basic science and biology, functional validation, in vitro and ex vivo experiments</li> </ul>
Complex symptom	<p><u>Concept definition:</u> Signs of acute or chronic disease and injury that are noticed or experienced by individuals and have a measurable effect on physical, mental, and social functioning. Symptoms are complex when multiple symptoms co-occur, demonstrate synergy with other symptoms, and/or involve mediating phenomena such as triggers, predictability, clustering, and timing components.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>Impacted organ systems</li> <li>Defining the quality, nature, mechanism, and severity of symptoms</li> <li>Onset and predictability triggers</li> <li>Functional status</li> <li>Clustering of symptoms</li> <li>Co-occurrence of symptoms</li> <li>Symptom burden, symptom resolution</li> <li>Clinical and psychometric measurement assessments of symptoms</li> <li>Longitudinal studies, cross-sectional studies, case-control studies, natural history studies</li> </ul>
Phenotype characterization	<p><u>Concept definition:</u> Characterization of symptom phenotype (an individual's observable traits, such as height, weight), which is influenced by genotype and environmental components including lifestyle factors including diet, culture, exercise, etc.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>Patient symptoms and behaviors observed by the nurse, nurse practitioner, care provider, caregiver</li> <li>Self-reported symptoms</li> <li>Clinical documentation and care coordination (instrument development, questionnaires, and interview checklists)</li> <li>Common data elements</li> <li>Environmental choices and exposures; lifestyle habits; wellness homeostasis</li> <li>Quality of life</li> <li>Functional status and performance</li> <li>Observational studies, observational comparison studies, natural history studies</li> </ul>

(continues)

**TABLE 3. Concept Headings and Example Research Applications for the Revised Symptom Science Model 2.0, Continued**

Concept heading	Concept definitions and example research designs, methods, techniques, populations, settings, tools, and applications
Clinical application	<p><u>Concept definition:</u> Use symptom science applications in clinical research and practice settings with defined patient populations to examine therapeutic clinical intervention(s), meaning, and treatment efficacy outcomes.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>Translational research and translational nursing science</li> <li>Precision health and clinical data privacy and confidentiality</li> <li>Adverse events evaluation and reporting; intervention treatment patient safety and efficacy</li> <li>Regulatory review and approvals using evidence from structured symptom science outcome measures</li> <li>Interventions and intervention targets</li> <li>Symptom management; health care outcomes</li> <li>Clinical decision support; mHealth and digital monitoring; telehealth and virtual health care visits</li> <li>Proof-of-concept clinical trial</li> <li>Randomized controlled trials (RCTs) and longitudinal studies; real world data (RWD) and real world evidence (RWE)</li> <li>Dissemination and implementation science: evidence-based practice and healthcare quality improvement</li> <li>Nursing administration: clinical practice guidelines, staffing, workforce training, and development</li> </ul>
Policy and population health	<p><u>Concept definition:</u> An approach that treats the population as a whole (including the environmental and community health contexts) as the patient.</p> <p><u>Examples:</u></p> <ul style="list-style-type: none"> <li>U.S. and global health system applications, policy levers, regulations, and regulatory</li> <li>Policy interventions, levers, policy reform, advocacy, ethics</li> <li>Data sciences for predictive analytic modeling; computer science; interoperability standards</li> <li>Population health studies; population health; public health outcomes</li> <li>Service delivery models (i.e., high need-high cost)</li> <li>Vulnerable, marginalized, and underserved populations</li> <li>Community engagement, community health care, community-based participatory research</li> <li>Economic outcomes; resource utilization</li> <li>Claims data and cost/benefit/value analyses</li> <li>Performance benchmarking, patient safety and healthcare quality</li> <li>Publicly reported healthcare quality metrics for effective symptom treatment outcomes</li> <li>Multidata set combinations; secondary data analyses; population databases, data mining, integrated care program evaluations (see also artificial intelligence, machine learning, big data)</li> </ul>

2020; Troseth, 2017; Yurkovic et al., 2019). The nursing profession is poised to embrace SDOH as a critical foundation for rebuilding the U.S. healthcare system from COVID-19 to achieve health equity (NASEM, 2021). An improved SDOH focus ensures symptom science can integrate population health and policy to improve health equity outcomes in local contexts (UNDP, 2022).

**Patient-Centered Experience** In order to achieve high-quality health care patients must receive care that is respectful of and responsive to their individual preferences, needs, and values during the range of interactions with the health system (NASEM, 2021). To understand an illness and its symptoms through the eyes of the patient, the SSM 2.0 must ensure that greater priority is given to patient- and family-centered care experiences. This cannot be achieved without deriving full meaning from the context of the patient's individual experiences, which are multidimensional and include economic, sociocultural, motivational, and psychological factors (Mead & Bower, 2000). Without a full understanding of the patient experience through all aspects of the symptom-illness trajectory, clinical interventions derived from these works will lack validity, utility, relevance, and accuracy. In-depth, open-ended interviews and focus group discussions using grounded theory, ethnography, phenomenology, and other qualitative research and mixed-methods approaches help nurse scientists place biological and molecular correlates into context

to understand the complex social and environmental phenomena underlying illnesses and provide holistic and truthful interpretation of objective evidence (Cobb & Forbes, 2002; Polit & Beck, 2021). Findings from these efforts assist with the development and refinement of standardized psychometric instruments, health surveys, and implementation tools for the evaluation of patient-reported outcome measures across many complex symptom experiences (e.g., functional status, pain, quality of life, fatigue, and anxiety) to build health-monitoring platforms in a wide variety of clinical, health care research, and integrated health policy arenas (Capella-Peris et al., 2020; FDA-NIH Biomarker Working Group, 2021; NIH, 2019; UNDP, 2022).

**Biobehavioral Factors** Biobehavioral factors are a modification and expansion of the original SSM "biomarker discovery" concept. These are defined as the use of biological, genomic, -omic physiological, and other clinical laboratory data to identify and refine reliable, valid biomarkers for the detection and monitoring of physical and behavioral symptoms and understand correlative relationships with human disease (Cashion & Grady, 2015; FDA-NIH Biomarker Working Group, 2021; Hickey et al., 2019; Saligan, 2019). Research that independently examines biological and patient behavioral factors can more fully consider the complexity of influences driving the development of a particular disease, symptom, or symptom cluster.



**TABLE 4. National Institutes of Health (NIH) Scientific Initiatives Where Interested Nurses Can Help Advance Symptom Science****NIH initiative title and program summary****“All of Us” Initiative**

Precision medicine is an “emerging approach for disease treatment and prevention that considers individual variability in genes, environment, and lifestyle for each person” and is fueled by the “All of Us” longitudinal research cohort (The All of Us Research Program Investigators et al., 2019). The Precision Medicine Initiative is a 10-year (\$1.5 billion) longitudinal research effort that will recruit and enroll a diverse cohort of ~1 million U.S. adults, including marginalized and vulnerable populations, and engagement with American Indians/Alaska Natives. As of December 2021, 264,000 participants consented to access their electronic health record clinical data, and 332,000 participants provided a biospecimen sample. Nurse scientists can perform symptom science research using the “All of Us” data browser and researcher workbench resources to identify genetic, environmental, and lifestyle contributions to a wide range of symptoms and multifactorial conditions from this socially diverse sample (The All of Us Research Program Investigators et al., 2019).

**Centers for AIDS Research (CFAR)**

To support independent multidisciplinary research to reduce domestic and global burdens of HIV, the National Institute of Allergy and Infectious Diseases oversees 11 NIH Institutes to operate 17 academic, research CFARs and affiliated coalition collaborative working groups. CFAR leverages robust data and scientific tools to support extension of research infrastructure to minority institutions and local health departments, thus strengthening innovative HIV prevention and AIDS treatment solutions. U.S. goals are to reduce new HIV infections by 75% in 5 years and 90% by 2030. Interested nurse scientists can contribute to the prevention and management of symptoms associated with HIV and AIDS through the collaborative conduct of basic, clinical, epidemiological, behavioral, and translational research and improve the prevention, detection, treatment, and cure/remission of HIV infection and its associated complications/comorbidities.

**Helping to End Addiction Long-term (HEAL) Initiative**

As of December 2021, the NIH HEAL Initiative (\$1.5 billion) aims to provide rapid scientific and evidence-based solutions to the U.S. opioid epidemic crisis, which is profoundly exacerbated by the COVID-19 pandemic. NIH HEAL comprised ~500 research projects spanning pain management and opioid misuse and addiction domains spanning 12 NIH Institutes and Centers. NIH HEAL comprised six scientific workgroups supporting the full spectrum of basic science to dissemination and implementation research, including (a) translation of research to practice for the treatment of opioid addiction, (b) new strategies to prevent and treat opioid addiction, (c) enhanced outcomes for infants and children exposed to opioids, (d) novel medication options for opioid use disorder and overdose, (e) clinical research in pain management, and (f) preclinical and translational research in pain management. Interested nurse scientists can contribute to NIH HEAL and advance symptom science by performing nursing research that enhances acute/chronic pain management and improves treatments for opioid misuse and addiction.

**Post-Acute Sequelae of SARS-CoV-2 (PASC) Infection Initiative**

The PASC Initiative (\$1.15 billion over 4 years) aims to perform research that will advance understanding of individuals who were sickened by COVID-19 and continue to be affected by debilitating, long-term symptoms and sequelae long after the acute infection period resolves. Interested nurses can advance symptom science by performing research to identify the biological underpinnings of these symptoms and assist in developing treatments to improve health outcomes of those affected by an extended COVID-19 recovery period.

**Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) Program**

The RADx-UP Program (\$500 million) facilitates rapid development and commercialization of innovative point-of-care, laboratory, and home-based SARS-CoV-2 diagnostic tests. RADx-UP will bring SARS-CoV-2 diagnostic testing to a broad range of vulnerable health disparity populations, including but not limited to African American, Latino, American Indian/Alaska Native, AAPI, and other vulnerable, underserved, marginalized ethnic populations, nursing homes, jails, rural areas, underserved urban areas, pregnant women, the homeless, LGBTQ+, poor and/or low socioeconomic status (Tromberg et al., 2020). Nurse scientists can help advance symptom science by encouraging and participating in collaborations to bring these valuable technologies to marginalized testing sites and overcome hesitancy and ensure optimization of their use in frontline community settings (i.e., tribal health centers, houses of worship, homeless shelters, prisons, etc.).

The exponential growth of genetic, genomic, and -omics technologies allows nurse scientists to achieve more sophisticated understandings and approaches to identify, manage, and understand patients' symptoms for various health and illness states. While not explicitly stated in the original NIH SSM components, biobehavioral approaches were an expected emphasis of symptom science inquiry. A primary aim of the biobehavioral science concept is to identify therapeutic biomarker targets based on a patient's molecular signatures to tailor a patient treatment option based

on specific behavioral, diet, and lifestyle choices (Table 2). Presently, nurses conduct biobehavioral symptom science by performing molecular and preclinical laboratory basic science, validation studies, and advancing -omics initiatives by developing biosample repositories (Saligan, 2019; SDC Table 1, <http://links.lww.com/NRES/A438>).

**Policy and Population Health** Population health has many definitions, but a common interdisciplinary definition is “an approach that treats the population as a whole (including the

environmental and community health contexts) as the patient” (Institute of Medicine, 2014). Populations can be defined by race, geography, sex/gender, health status, disability, religion, education, genetic composition, etc. Example performance and health outcomes used in this type of research include utilization and costs, workforce metrics, symptom occurrence, disability and diagnosis rates, mortality, and morbidity in a defined population of interest (preterm births, 30-day readmission rates, obesity, deaths at 12-month follow-up post-discharge etc.).

Nurse scientist examination of symptom questions through a population health lens informs improvement in care-coordination interventions and program management approaches; it is also a recommended focus of federal nursing science as a mechanism to reach rural and underserved patient populations (National Advisory Council on Nurse Education and Practice, 2016). Research examples of this approach include examining patient symptoms using national population survey data (utilization, surveys, physical examination, clinical and laboratory, social demographic information) or data from larger cross-sectional and longitudinal research designs to understand associations and causes of symptoms. However, newer genomics-based population health approaches are currently revolutionizing health care delivery. For example, several health systems (i.e., Geisinger Health) implement genomic screening programs directly into routine health care for conditions including familial hypercholesterolemia and hereditary cancer prevention (NASEM, 2018). Nurse scientists can also apply population health trends in innovative ways in community health care to better understand, prevent, and treat complex, debilitating symptoms and integrate maintenance and prevention mechanisms in conjunction with SDOH factors (NASEM, 2019).

Moving forward, ethical application of research advances from machine learning, artificial intelligence, cloud scaling for big data storage, and other advanced computational data science methodologies will be critical to harnessing insights when combining -omics and population-level analytics for symptom assessment at scale. This may include but is not limited to using information from patient EHR, clinical registry information, mobile devices, smartphones, wearable technologies, genomic and -omics data from biobanks, originating from within healthcare systems or from community sites external to hospitals and clinics (Aggarwal et al., 2020; Matheny et al., 2020). Ultimately, use of data generated from population health analyses can be used to inform, develop, and revise interdisciplinary, evidence-based policies at institutional, community, regional/state, national, and international levels (Ellenbecker & Edward, 2016).

**COVID-19 and Symptom Science Applications Using the Revised SSM 2.0** The COVID-19 pandemic has highlighted the disproportionate effect of SDOH contributions on poor patient-centered experiences nationally and globally

(NASEM, 2021; UNDP, 2022). There is a need for community and population health-based policy solutions to deliver effective clinical interventions for vulnerable and underserved populations to recover from COVID-19 (Bakken, 2020; NASEM, 2021; UNDP, 2022). For example, a key study demonstrated 20% of U.S. counties that were primarily African American disproportionately accounted for 52% of COVID-19 cases and 58% of COVID-19 related deaths (Millett et al., 2020). In addition, there is a lack of Hispanic/Latino surveillance data on COVID-19 test results and fatalities; the true magnitude of the pandemic for this group cannot be accurately identified. Still, it is estimated at approximately double the national overall rate (American Medical Association, 2020).

Using the revised SSM 2.0, nurses can conduct symptom science research to: support ethnic minority, underserved and vulnerable communities’ hesitancy to use life-saving vaccines; understand long-term symptom management of persistent COVID-19 illness following acute infection; understand crisis intersection points of acute and chronic pain management with opioid misuse and addiction; understand impacts of COVID-19 on precision medicine/health through a population health lens; and ensure dissemination and implementation of symptom science advances into at-risk domestic and global geographical locales (Table 4). Nurses can also use SSM 2.0 to facilitate social justice through use of patient-centered experience symptom management approaches and treatments. By incorporating SDOH factors nurses can also develop broader community and policy interventions to ensure equitable vaccine distribution to vulnerable and ethnic minority populations across the world.

## Conclusion

We presented a concept development revising the SSM 2.0 that broadens symptom science for nursing research, practice, education, and policy. Newly developed concepts include SDOH, patient-centered experience, and policy and population health. The revised SSM 2.0 facilitates expansion into broader domains of nursing research, expands use of symptom science to better support local communities and global health initiatives, and builds a stronger foundation for healthcare system implementation. Anchoring the revised SSM 2.0 to nursing theory serves as a powerful reminder for nursing’s application of data science and genomics to remain rooted in the spirit of holistic nursing practice and caring for patients, families, communities, and populations. Nurse and symptom scientists, nurse administrators, policy leaders, doctors of nursing practice, advanced practice nurses, clinical nurse leaders, nurse educators, and frontline workers can use the revised SSM 2.0 regardless of institutional affiliation or funding mechanism. Alternatively, nurse scientists can use the SSM 2.0 to expand into broader NIH and international scientific priorities and conduct secondary data analyses to better inform Precision Health, guide clinical implementation of symptom science in acute and chronic care settings at the global level, or understand factors

associated with disproportionate COVID-19 health disparities in underserved populations for a wide range of scientific challenges (Table 4). Thus, the revised SSM 2.0 can help support at-risk communities and healthcare workers to ensure innovative models of symptom evaluation and management are available for a wide range of acute and chronic illnesses regardless of a community's monetary resources. Demonstrating commitment to distributing these frameworks and tools during a time of extraordinary public health crisis ensures the nursing profession remains committed to and rooted in social justice to care for the most vulnerable among us (Rosa, 2019).

Accepted for publication April 9, 2022.

Acknowledgement is warmly extended to the following individuals for their time, mentorship, and supportive feedback on this manuscript: Leorey N. Saligan, PhD, RN, CRNP, FAAN, Acting Chief, Symptom Science Center, Principal Investigator, Symptom Biology Unit, Division of Intramural Research, National Institute of Nursing Research (NINR), National Institutes of Health (NIH); Joan Austin, PhD, RN, FAAN, Distinguished Professor Emerita, Indiana University School of Nursing; Terri Armstrong, PhD, ANP-BC, FAAN, FAANP, Deputy Chief, Neuro-Oncology Branch, Senior Investigator, National Cancer Institute, NIH; and Eun-Ok Im, PhD, MPH, RN, CNS, FAAN, Senior Associate Dean for Research and Innovation, Professor and Edith Folsom Honeycutt Endowed Chair, Emory University Nell Hodgson Woodruff School of Nursing, Council Member, National Advisory Council for Nursing Research, NINR, and President, Asian American/Pacific Islander Nurses Association, Inc.

This article has been exclusively prepared for and submitted to *Nursing Research* for publication consideration and has not been offered elsewhere. This article does not contain any studies involving animal or human participants performed by any authors. This is not a clinical trial; no registration is needed at this time.

Drs. Kurnat-Thoma, Graves, and Billones were supported by an NIH/NINR Clinical and Translational Intramural Research Training Awards. Dr. Emma L. Kurnat-Thoma was funded in part by a Tau Chapter small research grant, Sigma Theta Tau, School of Nursing and Health Studies, Georgetown University. Dr. Kurnat-Thoma performed this work in partial satisfaction of requirements in service as a Science Policy Detailee for the \$1.5B NIH Helping End Addiction Long-term (HEAL) Initiative. Dr. Letitia Y. Graves was funded in part by the Robert Wood Johnson Foundation. Dr. Billones performed this work in service as a Clinical Health Psychology Fellow for the Department of Intramural Research, NINR and was funded in part by Thrive Behavioral Sciences.

The authors have no conflicts of interest to report.


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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site ([www.nursingresearchonline.com](http://www.nursingresearchonline.com)).

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