Cumulative complexity: a functional, patient-centered model of patient complexity can improve research and practice

Nathan D. Shippee[a,b,*], Nilay D. Shah[a,b], Carl R. May[c], Frances S. Mair[d], Victor M. Montori[a,b]

[a]Division of Health Care Policy & Research, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA
[b]Knowledge and Evaluation Research Unit, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA
[c]School of Health Sciences, University of Southampton, Building 67 (Nightingale), Highfield Campus, University Road, Southampton SO17 1BJ, UK
[d]General Practice and Primary Care, University of Glasgow, 1 Horselethill Road, Glasgow G12 9LX

Abstract

Objective: To design a functional, patient-centered model of patient complexity with practical applicability to analytic design and clinical practice. Existing literature on patient complexity has mainly identified its components descriptively and in isolation, lacking clarity as to their combined functions in disrupting care or to how complexity changes over time.

Study Design and Setting: The authors developed a *cumulative complexity model*, which integrates existing literature and emphasizes how clinical and social factors accumulate and interact to complicate patient care. A narrative literature review is used to explicate the model.

Results: The model emphasizes a core, patient-level mechanism whereby complicating factors impact care and outcomes: the balance between patient *workload* of demands and patient *capacity* to address demands. *Workload* encompasses the demands on the patient's time and energy, including demands of treatment, self-care, and life in general. *Capacity* concerns ability to handle work (e.g., functional morbidity, financial/social resources, literacy). Workload-capacity imbalances comprise the mechanism driving patient complexity. Treatment and illness burdens serve as feedback loops, linking negative outcomes to further imbalances, such that complexity may accumulate over time.

Conclusion: With its components largely supported by existing literature, the model has implications for analytic design, clinical epidemiology, and clinical practice.

1. Introduction

Multimorbidity and chronic conditions are increasingly [...] tinue to disrupt access, utilization, and self-care [6–8]. Consequently, there is a growing interest in studying patient complexity as a way of understanding these dilemmas [5,9–12]. However, prior conceptual work has yielded mainly descriptive explanations with limited practical applicability, and most empirical studies on patient complexity have lacked rigor and comprehensiveness [11].

We propose a model of patient complexity that integrates extant approaches and improves clarity and applicability by emphasizing *functional* mechanisms of complexity at the level of the patient. This practical, patient-centered model is intended to guide improvements in the analysis and evaluation of patient complexity and promote innovative care de[...]tions, we [...]ure in describing its components, and (3) discuss its implications for analytic design, clinical epidemiology, and practice.

1.1. A cumulative model of patient complexity

Complexity is inherently difficult to define, measure, or predict [11–15], which creates challenges for analysis and problem solving [16]. To get past this, we functionally define patient complexity as a dynamic state in which the personal, social, and clinical aspects of the patient's experience operate as complicating factors. We believe these factors appear and accumulate over time, interacting with each other in emergent, and even cyclical, ways. Our focus differs from work on complex interventions (which emphasizes organizational/systems processes and intervention

* Corresponding author. Tel.: 507-266-1832; fax: 507-538-0850.
E-mail address: shippee.nathan@mayo.edu (N.D. Shippee).

What is new?

- The authors outline a model of patient complexity that focuses on the balance between patient workload of demands and patient capacity.

- Patient workload-capacity imbalances are identified as the central mechanism driving patient complexity—a mechanism that is also affected by intensified treatment burden and worsened illness burden over time.

- This model's patient-centered, functional design makes it more amenable to testing and application than previous models, and offers a heuristic framework that is generalizable to numerous clinical and social circumstances.

- This paper indicates the need for cohesive, model-driven analyses that incorporate sufficient methodological and substantive rigor in studying patient complexity.

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design) and complex outcomes (which focuses more on biological/chemical processes). Although patient complexity may be evaluated via complex outcomes, and addressed through complex interventions, we emphasize care delivery, self-care, and health at the level of the patient.

Existing literature has identified several components of patient complexity, including clinical complications such as chronicity and comorbidity [17−19]; burdensome treatment and self-care regimens [20−22]; or environmental and social factors that influence access, use, self-care, and health [23−28]. Patients exist at the intersection of social, personal, and clinical circumstances [10], and so they may face multiple complicating factors [3,29−31].

However, conceptual literature remains focused on understanding complexity factors vis-à-vis their forms (clinical, socioeconomic, or cultural), rather than their functions in complicating care, a descriptive approach, which provides little analytic guidance. Perhaps reflecting this limitation, research has rarely comprehensively examined how combinations of complications interact to impact patients [11,31], which inhibits researchers' ability to track the clinical epidemiology of patient complexity or design practice interventions. Furthermore, authors have not emphasized how individuals adapt, or succumb, to complexity over time, which omits the accumulation of complicating factors and the possibility of patient resilience.

We posit a patient-centered model of patient complexity designed to address these issues by optimizing practical applicability. At the model's core is a functional mechanism by which medical, social, and personal factors translate into the patient's experience: namely, the balance between the *patient's workload of demands* (hereafter, patient workload)

and *patient capacity. Patient workload* represents all the tasks and responsibilities people grapple with on a day-to-day basis. This encompasses everyday life demands *plus* the responsibilities of patient-hood, including job/family, self-care, clinical appointments, and other priorities [29−34]. *Capacity* signifies abilities, resources, or readiness to address demands, including physical/mental functioning, socioeconomic resources, social support, literacy, and attitudes/beliefs [35−39]. Excessive workload or low capacity alone might challenge patients, causing poor access, nonadherence, low quality of life, or other problems. However, our central argument is that it is an *imbalance* between the two— a workload that exceeds capacity—which is the primary driver of disruptions in care, self-care, and outcomes. Meeting demands *require some level of functioning*; thus, limitations on capacity will necessarily impact how patients take part in, and experience, their lives and health care [40−42]. Additionally, facing burdensome demands with insufficient abilities/resources to respond represents a stress process, which may generate breakdowns in self-care and health [43−46]. Moreover, patients whose demands exceed capacity may experience care as burdensome, fragmented, or low quality [47−49], which may worsen adherence, engagement, quality of life, and health outcomes [50]. Fig. 1 displays this general pattern.

Health "outcomes" often are not final endpoints—especially in chronic care—but rather have ongoing consequences for patient care and well-being via their experiential impacts on patients: namely, the *burden of illness* (BOI) (e.g., pain, functional morbidity [51−53]) and *burden of treatment* (BOT) (intensification, added demands [33,54−56]). The model incorporates these burdens as feedback loops, connecting poor outcomes with further erosion of patient capacity (illness) and intensified demands (treatment), such that patient complexity may build through cumulative cycles.

In the following section, we use a narrative literature review to describe a cumulative model of patient complexity (hereafter, the *cumulative complexity model*, Fig. 2)—a patient-centered framework that emphasizes the workload-capacity balance and incorporates treatment and illness burdens.

1.2. Workload and capacity

Patient *workload* encompasses all the demands in patients' lives, including everyday responsibilities alongside the demands of patient-hood—all of which impact complexity through their toll on patients' time, effort, and attention. These demands include job, family, travel/transportation, childcare, scheduling and attending clinical appointments, preventive care, self-education, self-care, taking medications, health behaviors, caregiving, and paperwork [29,32,34,57−59]. Demands may vary in several quantifiable attributes, including:

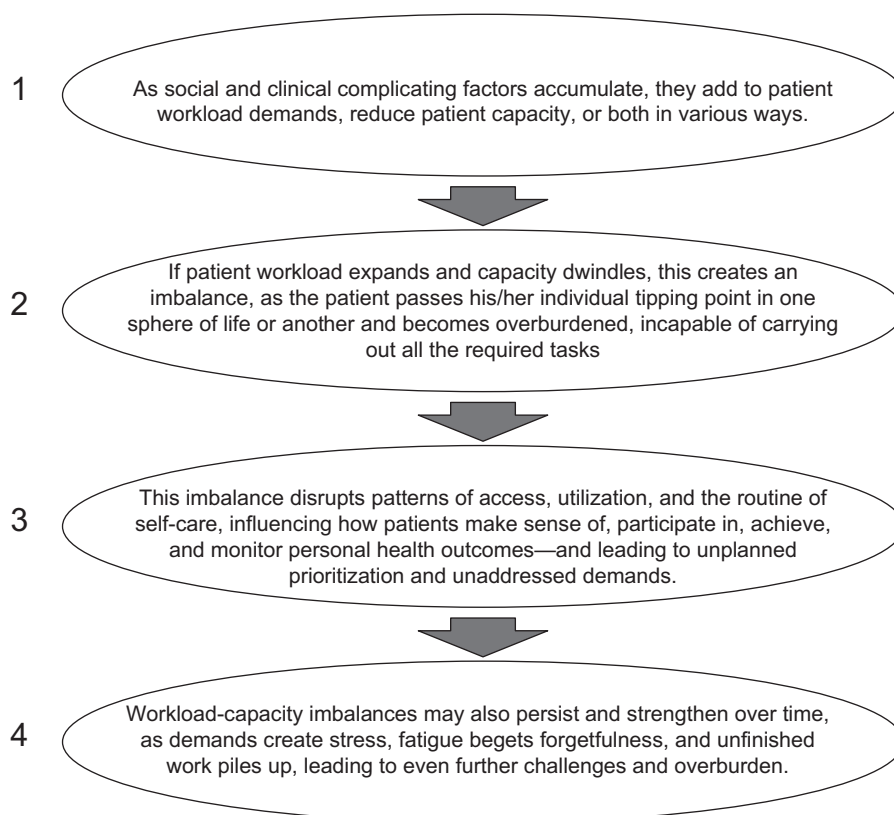- Number of demands
- Their difficulty

Fig. 1. Accumulation of patient workload demands and patient capacity factors.

- Their fit within patients' lives amidst other demands. Work on comorbidity [17] is informative here: demands may be *concordant* (e.g., monitoring a sick spouse while making phone calls), or *discordant* (job hours vs. clinical appointments).

Some patients persevere despite tremendous workloads; others falter even when relatively unencumbered. Accordingly, the model incorporates patient *capacity*, which denotes the resources and limitations affecting patients' ability or readiness to do work, such as mental/physical functioning [8,36,60–62]; unpleasant symptoms such as incontinence, psoriasis, or insomnia [63–65]; pain, stress, or fatigue [66–68]; and even problems secondary to the distinguishing features of a disease—for instance, the nonmotor complications of Parkinson's disease include genitourinary symptoms and depression [69]. Capacity also encompasses socioeconomic and psychological resources, literacy, language, and social support [26,29,35,70–72]. Disease and social factors may interact; for instance, nonvisible symptoms may fail to elicit empathy, legitimization, or social support [73–76], just when patients need it most. Attitudes and beliefs about health care [10,32] also shape individuals' readiness to perform patient-related work. Measurable attributes of capacity include the following:

- Amount/magnitude (e.g., greater/lesser symptoms, finances, or social support);

- Controllability (some factors, such as literacy, are more responsive to personal efforts than others, such as pain);
- Extensiveness or scope of impact (symptoms may have limited or widespread effects on functioning, self-efficacy may be global or domain specific [77], etc.).

1.3. Workload–capacity interactions

Patient workload and capacity are intertwined (path *a*), such that each affects the other. For instance, mental health disorders reduce capacity through functional morbidity [36,78–80], but also entail additional work in help seeking, appointments, or taking medications [81–83]. Likewise, demanding workloads, as in caregiving, may reduce capacity because of fatigue [84]. Analytically, this may confound causal effects and interactions: analyses may require disentangling ''chicken-or-the-egg'' questions in chronic disease management, nonlinear fluctuations in complicating factors, or situational tipping points. Given these complexities, multiple interactions may shape patient demands, capacity, and the interplay between them (Fig. 3). Operationalizations will differ depending on the study, but the extent to which these interactions are optimized is likely central to whether patients exhibit resiliency or worsened care and outcomes.

Beyond the aforementioned attributes of demands (number/difficulty/fit), how patients *prioritize* based on time or other
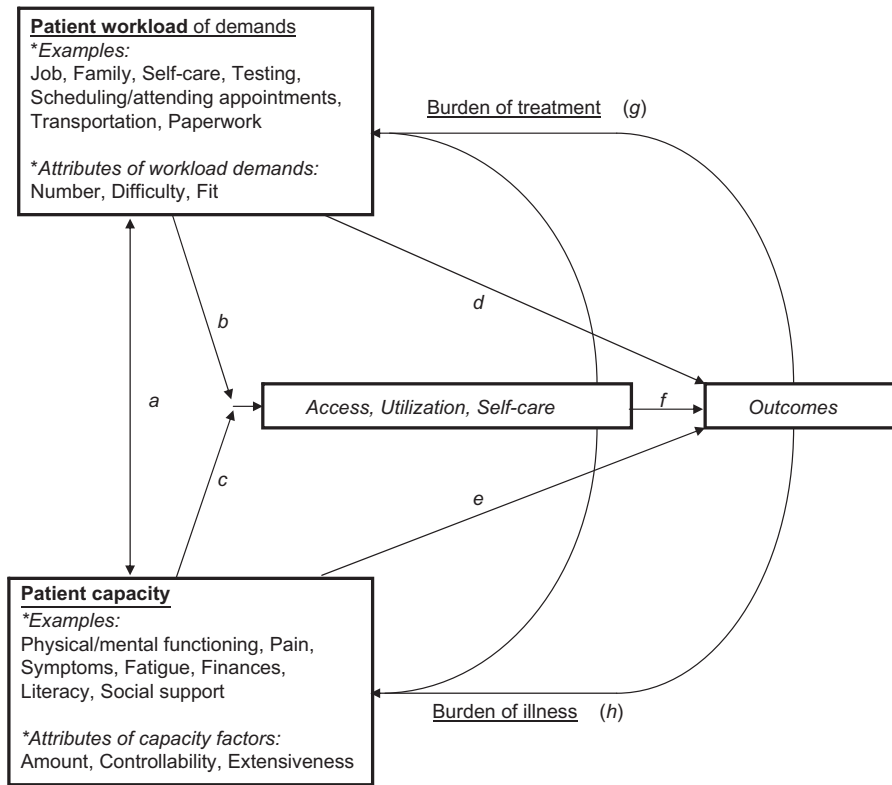
Fig. 2. The cumulative complexity model.

constraints, or alternatively *synchronize* demands to render them more manageable, may be crucial in balancing workloads [17,85]. Likewise, how patients *mobilize* resources [86], or *coordinate* resources, limitations, and their environments [87] while adapting to demands, will shape how capacity manifests. Finally, the ways in which patients *improvise* in these processes [88], *routinize* them into daily life [89,90], and the *timing* with which they match resources to demands, are vital yet virtually unexplored processes shaping care and outcomes.
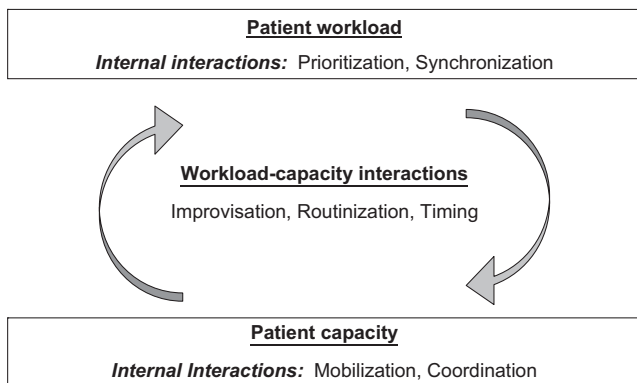

Fig. 3. Interaction processes between patient workload-related and patient capacity-related factors.

1.4. Access, utilization, and self-care: paths b and c

Workload and capacity both affect patients' experiences with care and self-management. Time and effort—as impacted by demands surrounding polypharmacy, transportation difficulties, planning/scheduling, job, family, etc. [29,57, 91−93]—are central in determining whether and how patients will effectively access, use, and enact care (Fig. 2, path *b*). Interventions to improve medication adherence—including lowering dosing frequency or providing reminders—have supported the usefulness of reducing or helping manage patients' medication demands [94−96], and government programs have tried alleviating other demands, including transportation assistance [97−99]. Thus, existing efforts generally have emphasized reducing workload and/or providing support (essentially, bolstering capacity). Comparative effectiveness examinations of these strategies would help optimize future interventions.

Capacity also shapes patterns of care and self-management (path *c*). Functionally limiting mental or physical conditions (depression, in particular) have well-established associations with access, self-care, and adherence [8,100−106]. However, there is relatively sparse evidence on cumbersome "secondary" symptoms, such as blurred vision or gastrointestinal problems, especially concerning treatments for which they are not side effects [107]. Additionally, language, literacy, and numeracy [41,57,108], and patients' backgrounds and environment [39], also shape their readiness to access and use care.

Although symptoms diminish individuals' capacity to access services, they also decrease quality of life, and so may *promote* help seeking in seemingly contradictory patterns. For instance, individuals with depression often do not opportunely seek help for it [109–111], yet depression also predicts higher utilization and costs [112–114]. In brief, depressed individuals may use services that are ill suited to their needs, exacerbated by a greater sensitivity to pain and somatic symptoms [35,115–117]. Therefore, capacity may be understood as *disrupting* effective care, rather than simply *reducing* quantity of care per se.

Various multivariate relationships operate between paths *b* and *c*. For example, demands may increase stress or depression, which in turn reduce energy and cognitive functioning, leading to lower adherence (*mediation*). Alternatively, poor mental health may render some individuals especially vulnerable to heavy workloads (*moderation*). These and other relationships require careful testing, especially with longitudinal data, before making causal judgments.

1.5. Health outcomes: paths d–f

Workload and capacity may *directly* impact patient outcomes (paths *d* and *e*), regardless of experiences with care. This distinction highlights subtle but important causal processes: some interventions improve health outcomes but not adherence, and vice versa [94,118,119]. Workload's effect on health (*d*) may be mediated by capacity (*e*), though little research exists on the subject. Demands such as family responsibilities can affect self-rated health and psychosomatic symptoms, including trouble sleeping [120]. However, this may occur indirectly through capacity-related factors, such as depression, stress, fatigue, and socioeconomic resources, and their direct effects on hypertension, mortality, and other outcomes [121–123].

Of course, disruptions in care are themselves well-known contributors to poorer health (path *f*). Access, self-care, and unmet need are all associated with health, quality of life, and mortality [7,124–127]; particularly direct examples include highly active antiretroviral therapy [128–132] and postmyocardial infarction care [133,134]. Unmet need stemming from causes such as access problems, nontreatment, or nonadherence can also contribute to clinical complications [135–137] (e.g., low insulin adherence triggering poor glycemic control and subsequent ketoacidosis [138]), further driving costs, avoidable health events and hospitalizations, and mortality [139–143].

1.6. Patient burdens: paths g and h

Poor outcomes may lead clinicians to intensify treatment [144,145], creating a BOT linking care and outcomes back to increased demands. This is partially outlined in normalization process theory [146,147], which focuses on the implementation of new demands into existing routines. Because of BOT, patients whose workloads already exceed their capacity may be expected to insert further demands into their lives, increasing the potential for overburden. However, although poor outcomes will, intuitively, lead to intensified care demands [148,149], some studies find otherwise [144,150]. Such inconsistency may reflect the lack of sufficient evidence with proper controls for the adherence–intensification relationship [42,151], which illustrates a need for more comprehensive analyses of care *following* health outcomes, particularly in chronic care.

If BOT is a feedback loop, then preventive care should curb future demands: a benefit rarely addressed in existing literature. For example, insufficient diabetes management hinders glycemic control and can create complications—complications that require escalating treatments and self-care (in patients with reduced capacity, no less, given their worsened health/functional status). Unfortunately, BOT's impact is elusive: clinicians have trouble recognizing nonadherence [152], and may mistakenly raise doses rather than address the underlying difficulties. Consequently, intensified treatment to clinical targets, with little regard for BOT, may prove unsustainable because overburdened patients may not adhere. Therefore, minimally disruptive medicine [153], which accounts for patients' finite time and energy with careful attention to treatment demands, is vital alongside evidence-based guidelines in caring for complex patients.

Parallel to BOT is the BOI. Elements of BOI—the aspects of poor health that impact patients' functioning and quality of life [51–53]—link poor outcomes and/or disease progression to further decreased capacity. Unlike strictly clinical measures (e.g., lab numbers), BOI's manifestation in patients' functioning and well-being may further disrupt their ability to manage demands. Thus, BOI is a feedback mechanism driving patient complexity through capacity erosion. It also embodies the lost potential of unsuccessful treatments and self-care, which impose workloads but fail to improve symptoms or capacity. This may reflect resistant diseases, inadequate dosing/adherence, or ineffective treatment [154–156], but the consequences are the same: continued, capacity-related vulnerabilities.

2. Implications

The cumulative complexity model integrates existing literature into a practical, patient-centered framework. With the workload-capacity balance at its core, and by incorporating patient burdens, the model emphasizes the longitudinal, patient-level interplay of complicating factors. Here, we outline its implications for analytic design, clinical epidemiology, and practice (see Fig. 4 for proposed approaches to implementation).

2.1. Analytic design

First, this model indicates how to identify complicating factors that remain understudied by asking questions about
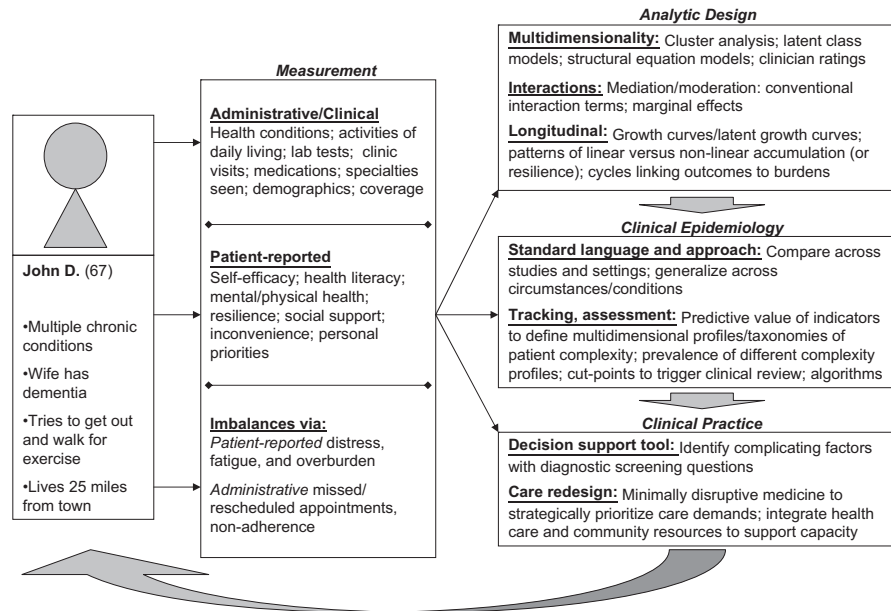
Fig. 4. Proposed implementation of model-based analyses, clinical research, and practice interventions.

workload-capacity challenges: what is consuming patients' time, energy, and attention, and what is limiting their ability to manage demands? As noted, understudied factors include the capacity-limiting impacts of often-"secondary" symptoms such as gastrointestinal problems, workload's impact on health (via stress processes vs. resultant poor health behaviors), and BOT. However, if factors *interact* to shape patient complexity (a key assertion here), then assessing them singly is of limited usefulness.

A second, more relevant implication is that in highlighting functional relationships, the model promotes investigations into *how* complicating factors interact. Based on reasoning and literature above, workload-capacity imbalances will create compounded risks in care and outcomes. Operationalizations must be addressed empirically by each study individually, but Fig. 3 above outlines several interactions, and previous literature on cumulative processes suggests other possibilities. For instance, socioeconomic disadvantages may have concurrent direct and indirect effects on care and outcomes (e.g., inability to pay alongside chronic stress), reflecting *structural amplification* [157]. Alternatively, capacity-limiting circumstances may *sensitize* [158] patients, leaving them especially vulnerable to heavy workloads. Ascertaining these processes could entail various methods, including structural equation models, formal mediation/ moderation analyses, simulations, or qualitative approaches.

Third is the combination of BOT and BOI, particularly for already-complex patients. Patients can integrate burdens into their daily lives [146,159], but how do they experience BOT *alongside* BOI and other factors? After all, comorbidity, pent-up need, or other problems will likely create high burdens on all sides [139,140,160,161]. Prior work has highlighted the problem of balancing concurrent treatment demands [17]; we propose studying how patients balance

self-care and *functional limitations*. Furthermore, what happens when asymptomatic but treatment-intensive conditions (high BOT, low BOI) collide with bothersome but clinically minor symptoms (low BOT, high BOI)—do people prioritize clinical targets or subjective comfort? Patients may attempt, above all, to maintain workload-capacity balances (i.e., do whatever keeps them functioning from day to day). If so, then studying patients with chronic conditions entails assessing whether treatment demands fit within their daily lives: disruptive tasks may be ignored.

A fourth implication is the cyclical, ongoing nature of complexity. Patients may become more complex over time because of accumulation and feedback between factors. Thus, linking early workload-capacity imbalances to later burdens—whether through worsened symptoms, pent-up demand, or intensification—is essential in mapping health and self-care. This is especially pertinent for patients with chronic conditions, for whom fatigue, demands, and other issues can have lifelong importance. Studying such patterns requires longitudinal data and, for instance, growth curves for assessing individual trajectories.

A final implication is the possibility of resilience. During continued experiences with patient-hood over time, some individuals may be particularly successful at normalizing burdens [33]. Literature elsewhere has identified some patterns of resilience, including "desensitization" and "acquired immunity" [158,162], in which early adversity toughens individuals against future hardship (e.g., an early chronic disease diagnosis may spark patient engagement). Resilience also can be seen as an aspect of capacity: self-efficacy or other psychological resources may help some patients resist overburden. Finally, resilient adaptations may reflect patients' success in optimizing the interactions outlined in Fig. 3.

2.2. Clinical epidemiology

The present model has implications for the clinical epidemiology of patient complexity: it suggests an approach to the measurement, evaluation, and tracking of patient complexity itself as a dynamic state with ongoing clinical and personal consequences. Currently, no common language or framework exist for doing so, which prevents comprehensive estimates and risk assessment. The cumulative complexity model addresses this by providing a unifying language and generalizable approach that capture the multidimensional variability and accumulation potential of complexity.

Studying how complicating factors affect care and outcomes would generate estimates of their *predictive value* for prognostic/risk assessment of complex patients. Those with the greatest analytic utility could then be combined to efficiently assess patient complexity as multidimensionally, using approaches such as cluster analysis. This would produce efficient, clinically relevant taxonomies of patient complexity, based on common patient *phenotypes* (we currently have one such proposal under review). Studies could then develop *prevalence estimates* of these phenotypes, including estimates of their distributions across groups.

As evidence grows, researchers could exploit the repeated use of standard assessments and studies of prognostic value to determine *cut points* for when combinations of patient complexity will result in measurable problems for care. This would, furthermore, facilitate development of *diagnostic criteria* or *decision trees/algorithms* for managing complexity in practice.

2.3. Clinical practice

Beyond the possibilities listed above, the proposed model has immediate implications for clinical practice. Treatment and self-care demands partially result from clinical action, and are thus amenable to change. If care enlists multiple specialties or targets clinical outcomes without considering burden, patients may become overwhelmed by fragmented, demanding care [21]. Facing other demands and limitations, they may resort to self-initiated prioritization rather than alerting providers. Thus, there is a need to embed treatment strategies into patients' lives to minimize burden and ensure adherence—a minimally disruptive medicine approach [153] toward preventing workload-capacity imbalances.

Clinicians can begin by working with patients to identify workload-capacity difficulties. As such, the model can inform development of a decision-support tool to help ascertain problems during clinical encounters and suggest solutions for minimizing patient burdens, similar to other decision aids and shared decision-making approaches [163,164]. Complications include finding the correct terminology: patients may dislike notions of "burden" or limited "capacity." However, such a tool could improve communication, patient experiences, and self-care, and uncover otherwise-missed complexity within the limited clinical encounter timeframe.

Patient-centered medical homes [160] represent one site for improved workload-capacity balances in practice. Yet, if coordinated care still necessitates intensive treatment and self-care, practices will need to include capacity support (via care managers or community services), or work to carefully minimize demands. Our team currently is developing a model-based intervention (currently in prototype-testing stages) to help reduce the footprint of health care in the lives of patients with multiple chronic conditions. However, more needs to be done in this area to ensure that providers and patients can meet the increasingly salient challenges of patient complexity.

3. Conclusions

This article proposes a patient-centered model of patient complexity in which clinical and social factors accumulate and interact to shape access, utilization, self-care, and health. Integrating prior literature, this cumulative complexity model emphasizes patient-level functions whereby complicating factors influence outcomes: workload, capacity, and treatment and illness burdens. This focus on function facilitates a cohesive, generalizable framework with practical applicability. The model also suggests advances in analytic design, clinical epidemiology, and practice.

This model is neither final nor static. It is meant to drive empirical and practice-based applications, and therefore is subject to clarification, falsification, and critique. Moreover, it cannot irrefutably specify all the methodological decisions implied by its paths, because these will differ for each study.

Overall, the cumulative complexity model is intended to stimulate innovations in research and practice that respect the clinical importance of workload-capacity imbalances. This implies a need for improvement in areas from access barriers to treatment burden. It also highlights the need to move from disease-centered to patient-centered paradigms in care delivery. As such, it speaks to a broad array of patient experiences and difficulties, and illustrates possibilities for improved analysis and care in the patient-provider interface and beyond.

References

[1] Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;162:2269–76.

[2] Paez KA, Zhao L, Hwang W. Rising out-of-pocket spending for chronic conditions: a ten-year trend. Health Aff 2009;28:15–25.

[3] Anderson GF. Medicare and chronic conditions. N Engl J Med 2005;353:305—9.

[4] Naessens JM, Leibson CL, Krishan I, Ballard DJ. Contribution of a measure of disease complexity (COMPLEX) to prediction of outcome and charges among hospitalized patients. Mayo Clin Proc 1992;67:1140—9.

[5] Taheri PA, Butz DA, Greenfield LJ. Paying a premium: how patient complexity affects costs and profit margins. Ann Surg 1999; 229:807.

[6] Pollock DL, Rainer NE. Healthcare access: a review of major barriers to health care services for women. Georgetown J Gend Law 2005;6: 825—58.

[7] Arora NK, Johnson P, Gustafson DH, McTavish F, Hawkins RP, Pingree S. Barriers to information access, perceived health competence, and psychosocial health outcomes: test of a mediation model in a breast cancer sample. Patient Educ Couns 2002;47:37—46.

[8] Kroll T, Jones GC, Kehn M, Neri MT. Barriers and strategies affecting the utilisation of primary preventive services for people with physical disabilities: a qualitative inquiry. Health Soc Care Community 2006;14:284—93.

[9] Peek CJ, Baird MA, Coleman E. Primary care for patient complexity, not only disease. Fam Syst Health 2009;27:287—302.

[10] Safford M, Allison J, Kiefe C. Patient complexity: more than comorbidity. The vector model of complexity. J Gen Intern Med 2007;22:382—90.

[11] Whittle J, Bosworth H. Studying complexity is complex. J Gen Intern Med 2007;22:379—81.

[12] Grant RW, Ashburner JM, Hong CC, Chang Y, Barry MJ, Atlas SJ. Defining patient complexity from the primary care physician's perspective: a cohort study. Ann Intern Med 2011;155:797—804.

[13] Plsek PE, Greenhalgh T. The challenge of complexity in health care. BMJ 2001;323:625—8.

[14] Kurtz CF, Snowden DJ. The new dynamics of strategy: sense-making in a complex and complicated world. IBM Syst J 2003;42:462—83.

[15] Nardi R, Scanelli G, Corrao S, Iori I, Mathieu G, Cataldi Amatrian R. Co-morbidity does not reflect complexity in internal medicine patients. Eur J Intern Med 2007;18:359—68.

[16] May C. A rational model for assessing and evaluating complex interventions in health care. BMC Health Serv Res 2006;6:86.

[17] Piette JD, Kerr EA. The impact of comorbid chronic conditions on diabetes care. Diabetes Care 2006;29:725—31.

[18] Piette JD, Richardson C, Valenstein M. Addressing the needs of patients with multiple chronic illnesses: the case of diabetes and depression. Am J Manag Care 2004;10:152—62.

[19] Turner BJ, Cuttler L. The complexity of measuring clinical complexity. Ann Intern Med 2011;155:851—2.

[20] DeRubertis BG, Pierce M, Chaer RA, Rhee SJ, Benjeloun R, Ryer EJ, et al. Lesion severity and treatment complexity are associated with outcome after percutaneous infra-inguinal intervention. J Vasc Surg 2007;46:709—16.

[21] Bohlen K, Scoville E, Shippee ND, May CR, Montori VM. Overwhelmed patients: a videographic analysis of how patients with type 2 diabetes and clinicians articulate and address treatment burden during clinical encounters. Diabetes Care 2012;35:47—9.

[22] Bayliss EA, Steiner JF, Fernald DH, Crane LA, Main DS. Descriptions of barriers to self-care by persons with comorbid chronic diseases. Ann Fam Med 2003;1:15—21.

[23] Boulware LE, Cooper LA, Ratner LE, LaVeist TA, Powe NR. Race and trust in the health care system. Public Health Rep 2003;118: 358—65.

[24] Friedman E. Money isn't everything: nonfinancial barriers to access. JAMA 1994;271:1535—8.

[25] Johnson SK. Hmong health beliefs and experiences in the western health care system. J Transcult Nurs 2002;13:126—32.

[26] Williams MV, Parker RM, Baker DW, Parikh NS, Pitkin K, Coates WC, et al. Inadequate functional health literacy among patients at two public hospitals. JAMA 1995;274:1677—82.

[27] Love D, Lindquist P. The geographical accessibility of hospitals to the aged: a geographic information systems analysis within Illinois. Health Serv Res 1995;29:629—51.

[28] Brown AF, Ettner SL, Piette J, Weinberger M, Gregg E, Shapiro MF, et al. Socioeconomic position and health among persons with diabetes mellitus: a conceptual framework and review of the literature. Epidemiol Rev 2004;26:63—77.

[29] Ahmed SM, Lemkau JP, Nealeigh N, Mann B. Barriers to healthcare access in a non-elderly urban poor American population. Health Soc Care Community 2001;9:445—53.

[30] Kullgren JT, McLaughlin CG. Beyond affordability: the impact of nonfinancial barriers on access for uninsured adults in three diverse communities. J Community Health 2010;35:240—8.

[31] Shi L, Stevens GD. Vulnerability and unmet health care needs. J Gen Intern Med 2005;20:148—54.

[32] Davis K, Collins KS, Schoen C, Morris C. Choice matters: enrollees' views of their health plans. Health Aff 1995;14:99—112.

[33] Gallacher K, May CR, Montori VM, Mair FS. Understanding patients' experiences of treatment burden in chronic heart failure using normalization process theory. Ann Fam Med 2011;9:235—43.

[34] Joseph AE, Hallman BC. Over the hill and far away: distance as a barrier to the provision of assistance to elderly relatives. Soc Sci Med 1998;46:631—9.

[35] Bair MJ, Matthias MS, Nyland KA, Huffman MA, Stubbs DL, Kroenke K, et al. Barriers and facilitators to chronic pain self-management: a qualitative study of primary care patients with comorbid musculoskeletal pain and depression. Pain Med 2009;10:1280—90.

[36] Burdick KE, Gunawardane N, Goldberg JF, Halperin JM, Garno JL, Malhotra AK. Attention and psychomotor functioning in bipolar depression. Psychiatry Res 2009;166:192—200.

[37] Hartnett ME, Key IJ, Loyacano NM, Horswell RL, DeSalvo KB. Perceived barriers to diabetic eye care: qualitative study of patients and physicians. Arch Ophthalmol 2005;123:387—91.

[38] Siegel K, Raveis VH, Houts P, Mor V. Caregiver burden and unmet patient needs. Cancer 1991;68:1131—40.

[39] Mackenzie CS, Gekoski WL, Knox VJ. Age, gender, and the under-utilization of mental health services: the influence of help-seeking attitudes. Aging Ment Health 2006;10:574—82.

[40] McKellar JD, Humphreys K, Piette JD. Depression increases diabetes symptoms by complicating patients' self-care adherence. Diabetes Educ 2004;30:485—92.

[41] Kalichman SC, Ramachandran B, Catz S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. J Gen Intern Med 1999;14:267—73.

[42] Katon W, Russo J, Lin EHB, Heckbert SR, Karter AJ, Williams LH, et al. Diabetes and poor disease control: is comorbid depression associated with poor medication adherence or lack of treatment intensification? Psychosom Med 2009;71:965—72.

[43] Gallant MP, Connell CM. Predictors of decreased self-care among spouse caregivers of older adults with dementing illnesses. J Aging Health 1997;9:373—95.

[44] Norbeck JS, Tilden VP. Life stress, social support, and emotional disequilibrium in complications of pregnancy: a prospective, multivariate study. J Health Soc Behav 1983;24:30—46.

[45] Murphy DA, Greenwell L, Hoffman D. Factors associated with antiretroviral adherence among HIV-infected women with children. Women Health 2002;36:97—111.

[46] Son J, Erno A, Shea DG, Femia EE, Zarit SH, Parris Stephens MA. The caregiver stress process and health outcomes. J Aging Health 2007;19:871—87.

[47] Shi L. Type of health insurance and the quality of primary care experience. Am J Public Health 2000;90:1848—55.

[48] Shi L. Experience of primary care by racial and ethnic groups in the United States. Med Care 1999;37:1068—77.

[49] Oberst MT, Hughes SH, Chang AS, McCubbin MA. Self-care burden, stress appraisal, and mood among persons receiving radiotherapy. Cancer Nurs 1991;14:71—8.

[50] Beach MC, Keruly J, Moore RD. Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? J Gen Intern Med 2006;21:661—5.

[51] McGuire T, Wells KB, Bruce ML, Miranda J, Scheffler R, Durham M, et al. Burden of illness. Ment Health Serv Res 2002;4:179—85.

[52] Waern M, Rubenowitz E, Runeson B, Skoog I, Wilhelmson K, Allebeck P. Burden of illness and suicide in elderly people: case-control study. BMJ 2002;324:1355.

[53] Gore M, Brandenburg NA, Hoffman DL, Tai K-S, Stacey B. Burden of illness in painful diabetic peripheral neuropathy: the patients' perspectives. J Pain 2006;7:892—900.

[54] Oude Elberink JNG, van der Heide S, Guyatt GH, Dubois AEJ. Analysis of the burden of treatment in patients receiving an EpiPen for yellow jacket anaphylaxis. J Allergy Clin Immunol 2006;118: 699—704.

[55] Carlsson S, Aus G, Bergdahl S, Khatami A, Lodding P, Stranne J, et al. The excess burden of side-effects from treatment in men allocated to screening for prostate cancer. The Göteborg randomised population-based prostate cancer screening trial. Eur J Cancer 2011;47:545—53.

[56] Anderson RT, Girman CJ, Pawaskar MD, Camacho FT, Calles J, Kelly WS, et al. Diabetes medication satisfaction tool. Diabetes Care 2009;32:51—3.

[57] Flores G, Abreu M, Olivar MA, Kastner B. Access barriers to health care for Latino children. Arch Pediatr Adolesc Med 1998;152: 1119—25.

[58] Yang S, Zarr RL, Kass-Hout TA, Kourosh A, Kelly NR. Transportation barriers to accessing health care for urban children. J Health Care Poor Underserved 2006;17:928—43.

[59] Kelly SE, Binkley CJ, Neace WP, Gale BS. Barriers to care-seeking for children's oral health among low-income caregivers. Am J Public Health 2005;95:1345—51.

[60] Saunders DG. Posttraumatic stress symptom profiles of battered women: a comparison of survivors in two settings. Violence Vict 1994;9:31—44.

[61] Huber SJ, Paulson GW, Shuttleworth EC. Relationship of motor symptoms, intellectual impairment, and depression in Parkinson's disease. J Neurol Neurosurg Psychiatry 1988;51:855—8.

[62] Gregg EW, Mangione CM, Cauley JA, Thompson TJ, Schwartz AV, Ensrud KE, et al. Diabetes and incidence of functional disability in older women. Diabetes Care 2002;25:61—7.

[63] Hilton P, Stanton SL. Urethral pressure measurement by microtransducer: the results in symptom-free women and in those with genuine stress incontinence. Br J Obstet Gynaecol 1983;90:919—33.

[64] Simon G, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417—23.

[65] Stern RS, Nijsten T, Feldman SR, Margolis DJ, Rolstad T. Psoriasis is common, carries a substantial burden even when not extensive, and is associated with widespread treatment dissatisfaction. J Investig Dermatol Symp Proc 2004;9:136—9.

[66] Bennett EJ, Tennant CC, Piesse C, Badcock C-A, Kellow JE. Level of chronic life stress predicts clinical outcome in irritable bowel syndrome. Gut 1998;43:256—61.

[67] Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A, Group. ICFSS. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med 1994;121:953—9.

[68] Swain MG. Fatigue in chronic disease. Clin Sci 2000;99:1—8.

[69] Chaudhuri KR, Healy DG, Schapira AHV. Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol 2006;5:235—45.

[70] Glasgow RE, Toobert DJ, Gillette CD. Psychosocial barriers to diabetes self-management and quality of life. Diabetes Spectr 2001;14:33—41.

[71] DeVoe JE, Baez A, Angier H, Krois L, Edlund C, Carney PA. Insurance + access? Health care: typology of barriers to health care access for low-income families. Ann Fam Med 2007;5:511—8.

[72] Timmins CL. The impact of language barriers on the health care of Latinos in the United States: a review of the literature and guidelines for practice. J Midwifery Womens Health 2002;47: 80—96.

[73] Glenton C. Chronic back pain sufferers—striving for the sick role. Soc Sci Med 2003;57:2243—52.

[74] Richardson JC, Ong BN, Sim J. Experiencing chronic widespread pain in a family context: giving and receiving practical and emotional support. Sociol Health Illn 2007;29:347—65.

[75] Stone SD. Reactions to invisible disability: the experiences of young women survivors of hemorrhagic stroke. Disabil Rehabil 2005;27: 293—304.

[76] Parsons T. The Social System. London, UK: Taylor & Francis; 1991 [1951].

[77] Leganger A, Kraft P, R⊘ysamb E. Perceived self-efficacy in health behaviour research: conceptualisation, measurement and correlates. Psychol Health 2000;15:51—69.

[78] Wagner HR, Burns BJ, Broadhead WE, Yarnall KSH, Sigmon A, Gaynes BN. Minor depression in family practice: functional morbidity, co-morbidity, service utilization and outcomes. Psychol Med 2000;30:1377—90.

[79] Shippee N, Shah N, Williams M, Moriarty J, Frye M, Ziegenfuss J. Differences in demographic composition and in work, social, and functional limitations among the populations with unipolar depression and bipolar disorder: results from a nationally representative sample. Health Qual Life Outcomes 2011;9:90.

[80] Borkowska A, Rybakowski JK. Neuropsychological frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. Bipolar Disord 2001;3:88—94.

[81] Horberg MA, Silverberg MJ, Hurley LB, Towner WJ, Klein DB, Bersoff-Matcha S, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. J Acquir Immune Defic Syndr 2008;47:384—90.

[82] Katon W, Cantrell CR, Sokol MC, Chiao E, Gdovin JM. Impact of antidepressant drug adherence on comorbid medication use and resource utilization. Arch Intern Med 2005;165:2497—503.

[83] Lin EHB, Katon W, Rutter C, Simon GE, Ludman EJ, Von Korff M, et al. Effects of enhanced depression treatment on diabetes self-care. Ann Fam Med 2006;4:46—53.

[84] Clark PC. Effects of individual and family hardiness on caregiver depression and fatigue. Res Nurs Health 2002;25:37—48.

[85] Golin C, Isasi F, Bontempi JB, Eng E. Secret pills: HIV-positive patients' experiences taking antiretroviral therapy in North Carolina. AIDS Educ Prev 2002;14:318—29.

[86] Gibson CH. A concept analysis of empowerment. J Adv Nurs 1991;16:354—61.

[87] Riegel B, Carlson B. Facilitators and barriers to heart failure self-care. Patient Educ Couns 2002;46:287—95.

[88] Wdowik MJ, Kendall PA, Harris MA. College students with diabetes: using focus groups and interviews to determine psychosocial issues and barriers to control. Diabetes Educ 1997;23: 558—62.

[89] Lundman B, Norberg A. Coping strategies in people with insulin-dependent diabetes mellitus. Diabetes Educ 1993;19:198—204.

[90] Roberts KJ. Barriers to and facilitators of HIV-positive patients' adherence to antiretroviral treatment regimens. AIDS Patient Care STDS 2000;14:155—68.

[91] Diamant AL, Hays RD, Morales LS, Ford W, Calmes D, Asch S, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;94:783—9.

[92] Stein M, Crystal S, Cunningham W, Ananthanarayanan A, Andersen R, Turner B, et al. Delays in seeking HIV care due to competing caregiver responsibilities. Am J Public Health 2000;90:1138—40.

[93] Emslie-Smith A, Dowall J, Morris A. The problem of polypharmacy in type 2 diabetes. Br J Diabetes Vasc Dis 2003;3:54—6.

[94] McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. JAMA 2002;288:2868−79.

[95] Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007;167:540−9.

[96] Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. Clin Ther 2001;23:1296−310.

[97] Minnesota Department of Human Services. MNET: early signs of success. DHS report 051670. St. Paul, MN: State of Minnesota Department of Human Services; 2005. Available at: http://www.dhs.state.mn.us/main/groups/business_partners/documents/pub/dhs_id_051670.pdf. Accessed June 18, 2012.

[98] Pennsylvania Department of Public Welfare. Medical assistance transportation program. 2012. Available at http://matp.pa.gov/. Accessed June 18, 2012.

[99] Kentucky Division of Family Support. Medical support and benefits branch. 2012. Available at http://chfs.ky.gov/dcbs/dfs/. Accessed June 18, 2012.

[100] Torres-Harding SR, Jason LA, Taylor RR. Fatigue severity, attributions, medical utilization, and symptoms in persons with chronic fatigue. J Behav Med 2002;25:99−113.

[101] Ammassari A, Antinori A, Aloisi MS, Trotta MP, Murri R, Bartoli L, et al. Depressive symptoms, neurocognitive impairment, and adherence to highly active antiretroviral therapy among HIV-infected persons. Psychosomatics 2004;45:394−402.

[102] Decramer M, Gosselink R, Troosters T, Verschueren M, Evers G. Muscle weakness is related to utilization of health care resources in COPD patients. Eur Respir J 1997;10:417−23.

[103] Morgan AL, Masoudi FA, Havranek EP, Jones PG, Peterson PN, et al. Difficulty taking medications, depression, and health status in heart failure patients. J Card Fail 2006;12:54−60.

[104] Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, et al. Depression, self-care, and medication adherence in type 2 diabetes. Diabetes Care 2007;30:2222−7.

[105] Cukor D, Rosenthal DS, Jindal RM, Brown CD, Kimmel PL. Depression is an important contributor to low medication adherence in hemodialyzed patients and transplant recipients. Kidney Int 2009;75:1223−9.

[106] Druss BG, Rask K, Katon WJ. Major depression, depression treatment and quality of primary medical care. Gen Hosp Psychiatry 2008;30:20−5.

[107] Florez H, Luo J, Castillo-Florez S, Mitsi G, Hanna J, Tamariz L, et al. Impact of metformin-induced gastrointestinal symptoms on quality of life and adherence in patients with type 2 diabetes. Postgrad Med 2010;122:112−20.

[108] Lindau ST, Tomori C, McCarville MA, Bennett CL. Improving rates of cervical cancer screening and pap smear follow-up for low-income women with limited health literacy. Cancer Invest 2001;19:316−23.

[109] Coyle JT, Pine DS, Charney DS, Lewis L, Nemeroff CB, Carlson GA, et al. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in children and adolescents. J Am Acad Child Adolesc Psychiatry 2003;42:1494−503.

[110] Wisdom JP, Clarke GN, Green CA. What teens want: barriers to seeking care for depression. Adm Policy Ment Health 2006;33:133−45.

[111] Sharpe M, Strong V, Allen K, Rush R, Postma K, Tulloh A, et al. Major depression in outpatients attending a regional cancer centre: screening and unmet treatment needs. Br J Cancer 2004;90:314−20.

[112] Crown WH, Finkelstein S, Berndt ER, Ling D, Poret AW, Rush AJ, et al. The impact of treatment-resistant depression on health care utilization and costs. J Clin Psychiatry 2002;63:963−71.

[113] Dennis CL. Influence of depressive symptomatology on maternal health service utilization and general health. Archiv Womens Ment Health 2004;7:183−91.

[114] Luber MP, Meyers BS, Williams-Russo PG, Hollenberg JP, DiDomenico TN, Charlson ME, et al. Depression and service utilization in elderly primary care patients. Am J Geriatr Psychiatry 2001;9:169−76.

[115] Alvarenga ME, Caniato RN, Mauritz A, Braun A, Aljeesh Y, Baune BT. Health service utilization in patients with major depression and co-morbid pain. Psychiatry Clin Neurosci 2009;63:101−6.

[116] Lépine JP, Briley M. The epidemiology of pain in depression. Hum Psychopharmacol 2004;19:S3−7.

[117] Katon W, Berg AO, Robins AJ, Risse S. Depression−medical utilization and somatization. West J Med 1986;144:564−8.

[118] Thombs BD, de Jonge P, Coyne JC, Whooley MA, Frasure-Smith N, Mitchell AJ, et al. Depression screening and patient outcomes in cardiovascular care: a systematic review. JAMA 2008;300:2161−71.

[119] Haynes BR, McKibbon AK, Ronak K. Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications. Lancet 1996;348:383−6.

[120] Artazcoz L, Artieda L, Borrell C, Cortès I, Benach J, García V. Combining job and family demands and being healthy. Eur J Public Health 2004;14:43−8.

[121] Malmo RB, Shagass C. Physiologic study of symptom mechanisms in psychiatric patients under stress. Psychosom Med 1949;11:25−9.

[122] Jiang W, Alexander J, Christopher E, Kuchibhatla M, Gaulden LH, Cuffe MS, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. Arch Intern Med 2001;161:1849−56.

[123] Peyrot M, McMurry JF Jr, Kruger DF. A biopsychosocial model of glycemic control in diabetes: stress, coping and regimen adherence. J Health Soc Behav 1999;40:141−58.

[124] Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab 2002;87:978−82.

[125] DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40:794−811.

[126] Pladevall M, Williams LK, Potts LA, Divine G, Xi H, Elston Lafata J. Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. Diabetes Care 2004;27:2800−5.

[127] McDermott MM, Schmitt B, Wallner E. Impact of medication nonadherence on coronary heart disease outcomes: a critical review. Arch Intern Med 1997;157:1921−9.

[128] Mannheimer S, Friedland G, Matts J, Child C, Chesney M. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. Clin Infect Dis 2002;34:1115−21.

[129] Haubrich RH, Little SJ, Currier JS, Forthal DN, Kemper CA, Beall GN, et al, Group tCCT. The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. AIDS 1999;13:1099−107.

[130] McNabb J, Ross JW, Abriola K, Turley C, Nightingale CH, Nicolau DP. Adherence to highly active antiretroviral therapy predicts virologic outcome at an inner-city human immunodeficiency virus clinic. Clin Infect Dis 2001;33:700−5.

[131] Gill CJ, Griffith JL, Jacobson D, Skinner S, Gorbach SL, Wilson IB. Relationship of HIV viral loads, CD4 counts, and HAART use to health-related quality of life. J Acquir Immune Defic Syndr 2002;30:485−92.

[132] Ammassari A, Antinori A, Cozzi-Lepri A, Trotta MP, Nasti G, Ridolfo AL, et al, AdICoNA, Groups tLS. Relationship between HAART adherence and adipose tissue alterations. J Acquir Immune Defic Syndr 2002;31:S140−4.

[133] Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. JAMA 2007;297:177−86.

[134] Gallagher EJ, Viscoli CM, Horwitz RI. The relationship of treatment adherence to the risk of death after myocardial infarction in women. JAMA 1993;270:742−4.

[135] Mitchell M, Klein R. The sequelae of untreated maternal hypothyroidism. Eur J Endocrinol 2004;151:U45−8.

[136] Fenley J, Powers PS, Miller J, Rowland M. Untreated anorexia nervosa: a case study of the medical consequences. Gen Hosp Psychiatry 1990;12:264−70.

[137] Flack JM, Novikov SV, Ferrario CM. Benefits of adherence to antihypertensive drug therapy. Eur Heart J 1996;17:16−20.

[138] Morris AD, Boyle DIR, McMahon AD, Greene SA, MacDonald TM, Newton RW. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. Lancet 1997;350:1505−10.

[139] Balkrishnan R, Rajagopalan R, Camacho FT, Huston SA, Murray FT, Anderson RT. Predictors of medication adherence and associated health care costs in an older population with type 2 diabetes mellitus: a longitudinal cohort study. Clin Ther 2003;25:2958−71.

[140] Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43:521−30.

[141] Pehrsson K, Larsson S, Oden A, Nachemson A. Long-term follow-up of patients with untreated scoliosis. A study of mortality, causes of death, and symptoms. Spine 1992;17:1091−6.

[142] Wang H, Parker JD, Newton GE, Floras JS, Mak S, Chiu KL, et al. Influence of obstructive sleep apnea on mortality in patients with heart failure. J Am Coll Cardiol 2007;49:1625−31.

[143] Bindman AB, Grumbach K, Osmond D, Komaromy M, Vranizan K, Lurie N, et al. Preventable hospitalizations and access to health care. JAMA 1995;274:305−11.

[144] Bolen SD, Bricker E, Samuels TA, Yeh HC, Marinopoulos SS, McGuire M, et al. Factors associated with intensification of oral diabetes medications in primary care provider-patient dyads: a cohort study. Diabetes Care 2009;32:25−31.

[145] Maddox TM, Ross C, Tavel HM, Lyons EE, Tillquist M, Ho PM, et al. Blood pressure trajectories and associations with treatment intensification, medication adherence, and outcomes among newly diagnosed coronary artery disease patients. Circ Cardiovasc Qual Outcomes 2010;3:347−57.

[146] May C, Finch T, Mair F, Ballini L, Dowrick C, Eccles M, et al. Understanding the implementation of complex interventions in health care: the normalization process model. BMC Health Serv Res 2007;7:142.

[147] May C, Mair F, Finch T, MacFarlane A, Dowrick C, Treweek S, et al. Development of a theory of implementation and integration: Normalization Process Theory. Implement Sci 2009;4:29.

[148] Martin DP, Diehr P, Cheadle A, Madden CW, Patrick DL, Skillman SM. Health care utilization for the ''newly insured'': results from the Washington Basic Health Plan. Inquiry 1997;34:129−42.

[149] Kogut SJ, Andrade SE, Willey C, Larrat EP. Nonadherence as a predictor of antidiabetic drug therapy intensification (augmentation). Pharmacoepidemiol Drug Saf 2004;13:591−8.

[150] Grant R, Adams AS, Trinacty CM, Zhang F, Kleinman K, Soumerai SB, et al. Relationship between patient medication adherence and subsequent clinical inertia in type 2 diabetes glycemic management. Diabetes Care 2007;30:807−12.

[151] Ho PM, Magid DJ, Shetterly SM, Olson KL, Peterson PN, Masoudi FA, et al. Importance of therapy intensification and medication nonadherence for blood pressure control in patients with coronary disease. Arch Intern Med 2008;168:271−6.

[152] Stephenson BJ, Rowe BH, Haynes RB, Macharia WM, Leon G. Is this patient taking the treatment as prescribed? JAMA 1993;269:2779−81.

[153] May C, Montori VM, Mair FS. We need minimally disruptive medicine. Br Med J 2009;339:485−7.

[154] Cole AJ, Scott J, Ferrier IN, Eccleston D. Patterns of treatment resistance in bipolar affective disorder. Acta Psychiatr Scand 1993;88:121−3.

[155] Sturmey P. Secretin is an ineffective treatment for pervasive developmental disabilities: a review of 15 double-blind randomized controlled trials. Res Dev Disabil 26:87−97.

[156] Vollmer-Conna P, Hickie M, Hadzi-Pavlovic B, Tymms M, Wakefield M, Dwyer P, et al. Intravenous immunoglobulin is ineffective in the treatment of patients with chronic fatigue syndrome. Am J Med 1997;103:38−43.

[157] Ross CE, Mirowsky J, Pribesh S. Powerlessness and the amplification of threat: neighborhood disadvantage, disorder, and mistrust. Am Sociol Rev 2001;66:568−91.

[158] Weinrath M, Gartrell J. Victimization and fear of crime. Violence Vict 1996;11:187−97.

[159] May C. Mundane medicine, therapeutic relationships, and the clinical encounter. In: Pescosolido B, Martin JA, Rogers AE, editors. Handbook of the sociology of health, illness, and healing: blueprint for the 21st century. New York, NY: Springer; 2011.

[160] Nutting PA, Miller WL, Crabtree BF, Jaen CR, Stewart EE, Stange KC. Initial lessons from the first national demonstration project on practice transformation to a patient-centered medical home. Ann Fam Med 2009;7:254−60.

[161] Brod M, Skovlund S, Wittrup-Jensen K. Measuring the impact of diabetes through patient report of treatment satisfaction, productivity and symptom experience. Qual Life Res 2006;15:481−91.

[162] Preston SH, Hill ME, Drevenstedt GL. Childhood conditions that predict survival to advanced ages among African-Americans. Soc Sci Med 1998;47:1231−46.

[163] Corser W, Holmes-Rovner M, Lein C, Gossain V. A shared decision-making primary care intervention for type 2 diabetes. Diabetes Educ 2007;33:700−8.

[164] Mullan RJ, Montori VM, Shah ND, Christianson TJH, Bryant SC, Guyatt GH, et al. The diabetes mellitus medication choice decision aid: a randomized trial. Arch Intern Med 2009;169:1560−8.