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Review Article

Clinical fatigue and weakness as Neurasthenia Spectrum Disorders in India

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Abstract. *Medically unexplained clinically significant functional fatigue and weakness are core clinical symptoms of various phenomenologically defined overlapping syndromes, which include Chronic Fatigue Syndrome, Neurasthenia, Fibromyalgia, and others. Collectively, they may be regarded as Neurasthenia Spectrum Disorders (NSDs). Clinical challenges include lack of authoritative consensus criteria, vague and inconsistent clinical formulations, lack of diagnostic tests, absence of proven interventions to prevent a chronic course, and outcomes that are frequently unsatisfactory for patients and doctors. Public health challenges include poor clinical understanding of and management guidelines for the condition, stigma, reluctance to accept mental health referrals, and imposition of a burden on health systems.*

Consideration of culture-specific syndromes has influenced development of concepts of and motivated research on somatic distress, its psychological and social determinants, and the influence of changing societal and cultural forces. Clinical diagnoses are explanatory models of professionals. Perceived causes reflect dominant cultural orientations in the community. Social analysis of NSDs suggests they reflect predicaments of society and culture that manifest as clinical psychiatric and medical problems for which patients request treatment. An interdisciplinary perspective benefits from consideration of biological, social and cultural underpinnings that include background features of nutrition, disease status, housing, sanitation, gender, livelihood opportunities, and explanatory models of patients and doctors.

Keywords: Neurasthenia, Spectrum Disorders, Chronic Fatigue Syndrome, Fatigue, Weakness, Fibromyalgia, Culture, Cultural Epidemiology, Medically Unexplained Symptoms, Functional Somatic Syndromes

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INTRODUCTION Common yet vexing symptoms and disorders of fatigue and weakness rank high among Medically Unexplained Symptoms (MUS). They are a major source of suffering for patients and a considerable burden on health systems. A study based on 314,219,000 office visits in National Ambulatory Medical Care Survey (NAMCS) in the US over a period of two years charted the reasons for visit and the diagnoses. Symptoms of tiredness and general weakness were ranked 12th and 27th among reasons for visits for primary care, apart from prenatal examination (Schroeder *et al*, 1990). The list of diagnoses, however, does not reflect the priority of these symptoms. In the absence of an identified biomedical cause, diagnoses frequently include neurotic disorders, functional digestive disorders, unspecified arthropathies, and so on. Chronic Fatigue Syndrome (CFS) has been studied with regard to its considerable economic impact on the sufferers, their families, and national productivity. Estimated annual total lost productivity was $9.1 billion for the US, amounting to $20,000 per year per patient, and about one half of household and labour productivity per average person with CFS in 2004 (Reynolds *et al*, 2004). The costs reported by the insurance industry in

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Canada were approximately $100 million annually for CFS, Fibromyalgia (FM), and repetitive strain injury (Cameron, 1995). Analyses of lost productivity in UK showed losses in the range of £75.5-£128.9 million (Collin *et al*, 2011).

HISTORICAL CONSIDERATIONS Since its revival in 1869 by George M. Beard, neurasthenia (NT) has undergone several transformations in its diagnostic formulation, names to describe it and regional priorities. However, the history dates back to centuries before Beard when the condition had previously been described. Essentially, people from various cultures have experienced different manifestations of MUS, have described them, given them various names in different cultures at different times, and have tried to make sense of their suffering in search of relief from symptoms and of restoration of full functional capacity.

Edward Shorter traced the history of various psychosomatic symptoms in the last several centuries, especially in Europe and North America (Shorter, 1994). He presents the dialectic of body, mind, society, and culture, and he distinguishes patients' perspectives that reflect the influence of social class from doctors' perspectives that influenced standards of medical practice. Diverse symptoms of psychosomatic disorders were more or less popular at different times, including fits, paralysis, fatigue, and anorexia. Social and cultural values determined the popularity of symptoms and how they are presented or downplayed. As Eisenberg (1977) explained, "Human disease inevitably and always reflects the outcome of the process of interaction between human biology and human social organization, a process in which culture occupies a central position". This is a fundamental feature of the "psychobiologic law" that he argued was a necessity.

Taylor (2001) examined the annual reports of Queen Square Hospital, London, from 1870 to 1947 and discussed the rise and fall of neurasthenia in UK, which was supplanted by psychological diagnoses. Lee (1998) traces the history of NT in Americas and China. Various etiologies have been considered, ranging from Epstein Barr (Komaroff, 1988) to xenotropic murine leukemia virus-related virus (XMRV: Lombardi *et al*, 2009; van Kuppeveld & van der Meer, 2012) to immune dysfunction (Bansal *et al*, 2012) treatable with monoclonal antibodies (Fluge & Mella, 2009). The debate has led to a stalemate (Groves, 2011). Recent retraction of the article in *Science* attributing Chronic Fatigue Syndrome to XMRV (Lombardi *et al*, 2009) discredits viral theories of the disorder (Silverman *et al*, 2011). Psychiatric diagnostic systems have been uncertain and ambivalent (Paralikar *et al*, 2007a) but nevertheless unacceptable, even irritating to patients. Ambiguities have also influenced other medical specialties; the American College of Rheumatology has proposed changing criteria for fibromyalgia (Wolfe *et al*, 2011) so that they no longer require examination of tender points.

CONCEPT OF NEURASTHENIA SPECTRUM DISORDERS (NSDs)

Fatigue and weakness are universal experience in daily life, and the concept of neurasthenia was preferred by many to melancholia – which suggested severe depression suggesting a hereditary basis and progressive degeneration which were stigmatized. The concept took the sting out of alternative formulations of psychopathology. As such, NT was not only more acceptable to middle-class patients, but also profitable for doctors to treat. Various diagnostic formulations for a range of comparable conditions have been suggested in different parts of the world, each highlighting medically unexplained and disabling fatigue or weakness that persists, causes distress and prompts the sufferer to seek help. Such diagnostic concepts include CFS, as defined by Centres for Disease Control and Prevention (CDC) in North America (Fukuda *et al*, 1994), and Neurasthenia (NT), as described in the *ICD-10 Classification of Mental and Behavioural Disorders - Diagnostic criteria for research* (WHO, 1992). NT is also described in the *Chinese Classification of Mental Disorders* (CCMD, from Chinese Association of Neurology and Psychiatry, 1989), and NT had been proposed in the draft for Diagnostic and

Statistical Manual for mental disorders, fourth edition (DSM-IV, from American Psychiatric Association, 2000), but subsequently not included in the publication. FM or Myalgic Encephalomyelitis (ME) has been described in UK. Collectively, the various formulations of this common clinical problem may be characterized as Neurasthenia Spectrum Disorders (NSDs) (Paralikar *et al*, 2007a), based on essential core features of fatiguing disorders (Prins *et al*, 2006).
Although not included among major psychotic (schizophrenia) or mood disorders (depression and bipolar disorders), NSDs represent a substantial burden of illness that merits attention in clinical and community settings. Although recognized conditions in clinical practice in Western Europe, North America and Australia, they are a neglected component of mental health burden in low- and middle-income countries.

CULTURAL PSYCHIATRY AND NSDs Cross-cultural interests and questions about variations in psychopathology and the experience of psychiatric disorders have sparked theoretical as well as practical interest in the topic. Seminal research in China of Kleinman in the 1980s argued that neurasthenia may be regarded as a visible feature of underlying but hidden depression (Kleinman, 1982). This point has been disputed and the question of whether NT and depression are distinct remains contested (Lee & Kleinman, 2007). Kleinman's consideration of the idea of category fallacy, which has had a major influence on the development of the "new cross-cultural psychiatry" were largely rooted in analysis of neurasthenia (Kleinman, 1977). The importance of NT in Asian cultures was also discussed (Schwartz, 2002), largely restricted to East Asia. Cross-cultural comparisons among patients with NSD in China, North America, and UK are described (Lee *et al*, 2001).
Others in the field have maintained a focus on the topic of depression, neurasthenia and somatization and their complex interaction. Ontological differences or deficits in the concepts of disease and illness across various medicinal systems in different cultures, and epistemological differences in the origins and orientations of medicine in Europe, and in non-western sociocentric cultures like India or China, have been eruditely addressed (Fabrega, 1990). Fabrega asserts that the concept of somatization is a cultural and historical product of Western medicine. Inasmuch as Western medicine has become the dominant, pervasive, and contemporary medical system globally - and no less in India - contentious questions of mind-body dualism arise, even in cultures that originally were less preoccupied with the idea of body-mind dualism and more sympathetic to monistic philosophical orientations. Questions about what constitutes sufficient evidence for the biological basis of symptoms, competing with alternative psychological and social explanations, are critical for research on somatization. Also, it is important to clarify how social and cultural contexts explain medically unexplained symptoms. Elucidation of the interactions among body, mind, society and culture benefits from consideration of debates about the mind-body dualism in accounts of somatization. NSDs are not routinely used in clinical practice, and they are rarely studied in India. This limits potentially useful consideration of prominent symptoms of somatic distress and their psychological, social, and cultural underpinnings.
Various syndromes identified exclusively or predominantly in particular cultures have been elaborated as culture-bound syndromes, an approach that has been criticized as limited, prejudiced and biased. Formulations of NSDs have been included among these various syndromes identified as culture bound in different parts of the world (San Miguel *et al*, 2006; Park *et al*, 2001). CFS has also been characterized as a culture-bound syndrome of North America (Griffith *et al*, 2003). This reformulation of culture-bound syndromes from 'exotic' disorders of the 'other' culture, to culture-specific disorders has contributed to the clarity and utility of cultural psychiatry (Tseng, 2006).
Dhat syndrome, specific to South Asian cultures, attributed progressive weakness and loss of cognitive capacity to semen loss. Semen loss due to any orgasmic activity was typically regarded as dangerous according to Asian cultures, while in Judeo-Christian cultures it was more likely to be regarded as sinful (Tseng, 2003). These cultural differences in explanations of comparable conditions may help explain the association of danger with symptoms of weakness and anxiety in Asian patients and concerns from associating sinfulness and guilt with fatigue and depression among Western patients.

Health systems, and especially mental health systems, have a responsibility to provide health care for chronic conditions for which curative treatment is lacking. NSDs illustrate such needs. A scholarly discussion of the social course of chronic illness similar to its clinical course, details the dialectical social processes of marginalization and individual's resistive attempts in case of CFS (or NSDs) in the context of increasing urbanization (Ware, 1999). Novel attempts for collaboration have resulted among patients, primary care physicians, and professionals from various academic backgrounds (Chew-Graham *et al*, 2008). The use of multiple sources of knowledge and experience has facilitated a better understanding of CFS among the various participants. The success and utility of this interdisciplinary approach indicate the value of cross cultural research in NSDs to enhance mutual trust and empathy.

CONTRIBUTIONS FROM OTHER FIELDS OF MEDICINE

An extensive literature on NSDs may be found in various medical disciplines, not just psychiatry (**Table 1**). Interdisciplinary interests reflect current understanding of culture and somatic syndromes that suggest a multidimensional relationship of somatic distress with body, mind, society, and culture (Kirmayer & Sartorius, 2007). Functional somatic syndromes (FSS) and MUS are often considered as overarching categories (Barsky & Borus, 1999; Kirmayer & Robbins, 1991), although Wessely et al (1999) concluded that dimensional classification would be preferable. In DSM-IV the diagnoses typically used for NSDs are somatoform disorders, especially undifferentiated somatoform disorder.

Table 1 Functional somatic syndromes by specialty. Reproduced with permission from 'Functional somatic syndromes: one or many?' (Wessely *et al*, 1999)

Specialty	NSDs
Gastroenterology	Irritable bowel syndrome, non-ulcer dyspepsia
Gynaecology	Premenstrual syndrome, chronic pelvic pain
Rheumatology	Fibromyalgia
Cardiology	Atypical or non-cardiac chest pain
Respiratory medicine	Hyperventilation syndrome
Infectious diseases	Chronic (post-viral) fatigue syndrome
Neurology	Tension headache
Dentistry	Temporo-mandibular joint dysfunction, atypical facial pain
Ear, nose, and throat	Globus syndrome
Allergy	Multiple chemical sensitivity

Clinical and cultural conceptualizations are central for the broader social course model described above, which also discuss marginalization. The sociosomatic model of Lee (1998) recapitulated cultural history and social suffering to contextualize Shenjing Shuairuo, which earlier had been considered a synonym for NT in China. The cognitive behavioral (CBT) model of MUS deals with the interconnections and extrapolations of recent evidence in the field of psycho-neuro-immuno-endocrinology in the context of stress and the bridges between the body and the mind. In an influential theoretical and empirical review of MUS with examples of CFS and Irritable Bowel Syndrome (IBS), Deary and colleagues (2007) examine the theoretical and clinical evidence according to principles of CBT. They refer to 'autopoietic' (self-perpetuating) interactions among various factors explaining the chain of causality for maintenance of symptoms. Concepts of neuroticism (Howren & Suls, 2011; Watson & Pennebaker, 1989) and perseverative cognition (Brosschot *et al*, 2005) explain the links between stress, physiology and mood in a cognitive theory of NSDs and depression.

CLINICAL INTERESTS

Diagnoses are explanatory models of the professionals (Kleinman, 1981; Lee, 1996), which are used to understand and predict the course of a condition, and to guide

appropriate interventions. Diagnoses of NSDs, however, do not adequately explain or guide treatment. For example, NICE guidelines (Baker & Shaw, 2007) advise treatment as usual in primary care with a focus on diagnosis ("After diagnosis, manage symptoms as in usual clinical practice, which may include drugs and dietary changes"). Specialist care is restricted to be conducted only by experts with experience in treating CFS/ME. Cognitive Behavior Therapy (CBT) and Graded Exercise Therapy (GET) are thus likely to be available only after a long waiting time and at high expense even in clinical practice in the developed world; it is far less available if at all, in low and middle-income countries (LMIC) with little access or expertise. Also, reliance on patients for self-monitoring of activity, rest, thoughts, feelings and behaviors, including their reaction to the diagnosis and encouraging patients to accept functional limitations is less helpful in LMIC settings. Moreover, even in the diagnostic assessment, the deficiencies in the guidelines were pointed out (Hoad *et al*, 2008), considering the numerous physiological changes associated with NSDs. Quality of life suffers. Dissatisfaction with treatment leads patients to keep seeking help from various sources contributing a burden on health care systems that have difficulty providing specific treatment for a vague problem (Paralikar *et al*, 2011). Stigma is an important component of patients' suffering, both within health systems and social networks of family, work, and community. These conditions are associated with a high degree of psychiatric morbidity (Schwartz, 2002).

Most medicine textbooks emphasize fatigue as a poorly defined complaint, rate its prevalence at 25%, and regard fatigue and weakness largely as secondary symptoms of depression, somatization, or anxiety (Schroeder *et al*, 1990). On searching for NAMCS 2005, there is no mention of tiredness or general weakness in the list of top 20 reasons for visit or diagnoses (Cherry *et al*, 2007). Similarly prioritized medical complaints e.g., 'fever of unknown origin' (although temporarily unexplained) get clarified soon, with usually favourable outcome. But NSDs linger on for years, implying prolonged pluralistic health care burden and burnt-out clinician in the end.

The very nature of NSDs, whether purely medical, purely psychiatric, or psychosomatic is unclear (Sykes, 2002) and hotly contested (Harvey & Wessely, 2009); and this has clinical consequences. Confusing and pluralistic professional nosology points to the ambivalence of professional diagnostic systems. Patients too have difficulty in grappling with their illness and explaining it (Madden & Sim, 2006). In addition to the usual pluralistic help seeking, some patients with NSDs stop consulting any doctor similar to IBS patients. Ironically, reduction in consulting behavior is considered a positive indicator of outcome (Wessely *et al*, 1998, pp. 301–302). For most other medical and psychiatric problems, in the absence of a resolution of the problem, this would be regarded as underutilization of care.

PUBLIC HEALTH INTERESTS Limited clinical understanding of a chronic condition has consequences for public health. Loss of productivity for patients and communities and repetitive demands of a chronic condition over time impose a burden not only on individuals but also on health systems. The problem is worsened by poor patient satisfaction, poor interdisciplinary collaboration in orientations to specialty treatment and reluctance to care for these patients to avoid these clinical challenges.

Barriers to care may be attributed to patients, health systems, and the nature of NSDs (Lin *et al*, 2009). Patients often doubt that their health care professional cannot understand their suffering. Health systems are reluctant to deal with these patients and are preoccupied with meeting targets to reduce their burden and expense, rather than investing time to understand and explain patients' distress, for which biomedical investigations add little beyond ruling out other conditions. Patients simply avoid care if the fatigue level is high. Burden of disease computations are incomplete and extremely difficult due to the undefined and hidden burden of NSDs. It is also believed that the burden is more when the sufferer has to face the disability each moment, rather than from a catastrophic non-progressive event (de Savigny, 2011, *personal communication*). Health care delivery is also challenged due to poor patient-acceptance of mental health referral or intervention that is necessary considering high psychiatric

comorbidity of NSDs. Pluralistic non-medical and medical help seeking are matters of concern that need to be studied. Jones and colleagues (2007) reported from US experience that 77% of NSD patients used complementary and alternative medicine (CAM) independent of rural-urban, age, or income characteristics; and women used significantly more CAM. Interestingly, higher education was associated with more frequent CAM use. Patients could share and discuss their experience of CAM with their physician if the perceived severity of NSD was high indicating the importance of illness characteristics of perceived seriousness.

Burden of care is borne by health systems, including public and private sectors, and by patients, who are willing to spend disproportionate amounts of time in search for care that seems elusive. Patients' preferences are based on cost, convenience, and prospects for desired outcome (Paralikar *et al*, 2011).

SITUATION IN INDIA It is often criticized that NSDs are not real disorders, but just a source of malingering for patients and profit-making for doctors. Labelling theorists would argue that NSDs will be extra burden on public health due to labelling. If it were true, then the disorder should have vanished on its own. In India patients do not even have a name for their NSD, and doctors hardly attend to them. Similar situations did not cause schizophrenia or depression to vanish from other communities just because they were not recognized (Eisenberg, 1977).

Research has been lacking in India on the clinical and public health issues, such as burden of disease and control strategies, pluralistic help seeking, high and chronic disability and stigma of the condition. Non-acute presentations of these patients may explain this inattention. Consensus guidelines are also lacking. Considering the significance of the topic for clinical and cultural psychiatry, research is warranted to understand and improve the management of NSDs in clinics and communities.

Although research on NSDs in India is limited, a population-based prevalence study of chronic fatigue has been reported (Patel *et al*, 2005). A clinic-based study has also been published (Paralikar *et al*, 2007b). Other relevant literature includes case reports and historical accounts of the Dhat syndrome (Raguram *et al*, 1994), characterized by a culture-specific explanation of symptoms as a result of semen loss in South Asia (Perme *et al*, 2005). Although Malhotra and Wig suggested in 1975 that the Dhat syndrome would likely fade among clinical presentations with increasing awareness and literacy (Malhotra & Wig, 1975), it appears to have persisted in India (Perme *et al*, 2005) and Pakistan (Khan, 2005). Moreover, its current relabeling into non-specific categories, or as FSS or MUS offers no help in understanding or management.

With the advent of Western biomedicine, combined specialty of dermatology and venereology caters to skin-problems as well as sex-related concerns or maladies. Because of highly conservative and traditional values in recent past, having to see a dermatologist for sexual concern was a stigma. Consultants trained in Western biomedicine, usually alienated from or ashamed of various beliefs in their own culture, are at a loss to interpret them. Due to limited or no privacy in Dermatology clinic, patients are reluctant to share their intimate concerns, feeling compelled to seek help from the often exploitative and so-called 'sex-VD specialists' without authentic credentials or identity. Also the perception of 'extra heat in the body' based on passing warmer or dark urine, or white discharge from urine are culturally derived concerns with sexual meanings indicating the cultural models of patients in Dermatology and Ayurved.

Dhat (a Hindi word for semen) syndrome was classically described as a culture-bound symptom complex (Malhotra & Wig, 1975), which can be regarded as a local or regional cultural formulation of NSDs. It is characterized not only by the *clinical* picture of severe anxiety and preoccupation over semen loss believed to be leading to progressive physical and sexual weakness or eventual impotence, intellectual, and emotional deterioration, but by *patient's* attribution of these symptoms to semen loss. Seminal fluid was considered an elixir of life both in the physical and in the mystical sense. Its preservation was believed to be virtuous and promoting health, longevity, and even mystical powers. It is not surprising to see that this syndrome being rooted in cultural physiological concepts, would

logically lead patients to seek more herbal treatment, traditional help, or even magical cures, or the so-called 'sex and venereal disease clinics'– selling herbal medicines under new or no names.

Ayurved is a medical system originating in India nearly two thousand years ago representing a continuous cultural tradition that remains influential. It has a theoretical basis and approach to assessing and managing various health problems, including fatigue and weakness (Fabrega, 1990). Visiting Ayurved clinic for weakness is not an obvious stigma – though similar concerns could be discussed with relative impunity. Patients with weakness as a symptom rather than as a cause would see Medicine clinic doctors in the hope of replenishing the presumed deficiency in the body. Help seeking in psychiatry generally results from referral, rather than own choice. Prominent presence of psychotic patients and practice of electroconvulsive treatment (popularly feared as 'shock treatment') have stigmatized this clinic. Thus patients could see Medicine or Ayurved clinics without fear of blame, but the other two only reluctantly.

The clinical relevance and validity of NSDs in India has been discussed with reference to research in four specialty outpatient clinics (Paralikar *et al*, 2007b) and community (Patel *et al*, 2005). Poor agreement among overlapping case definitions suggested a spectrum of disorders (Paralikar *et al*, 2007b) rather than adequate coverage by formulations in current use. NSDs cannot be diagnosed by a laboratory test, and the question of an underlying medical basis is an especially important consideration for clinical practice in India because of the likelihood of undiagnosed infectious diseases and malnutrition. This issue was addressed in the context of routine practices along with high psychiatric comorbidity (Paralikar *et al*, 2008). Depression with fatigue has been emphasized in North American, European, and Australian settings. A distinctive Indian profile highlights the importance of weakness and anxiety. Cultural epidemiological findings also highlight pluralistic help seeking, and they suggest the role of social changes influenced by urbanization, changing roles of women, and the epidemiological health transition that enhances the priority of chronic diseases (Paralikar *et al*, 2011).

RESEARCH NEEDS

Better understanding of social and cultural contexts that generate these disorders would help serve the clinical and public health needs. Research related to NSDs in ethnic minorities in UK (Bhui *et al*, 2011) that is locally valid and globally useful, should be pertinent for Indian situation that is also multicultural and beset with inequalities.

Mental health challenges are enhanced due to urbanization (Srivastava, 2009). Rapid urbanization poses special challenges in physical, social and interpersonal spheres, especially depression and anxiety among low-income women (Harpham, 1994; Caracci & Mezzich, 2001). The challenging rate of development of urbanization fuelled by industrialization, privatization, liberalization, and globalization are affecting social and cultural milieu in India, including health sector (Brijnath & Manderson, 2011). Ambition is fuelled in promising times, but lack of matching social abilities has been argued to explain cultural genesis of NSDs (Abbey & Garfinkel, 1991). Fast life style, uncertainty, instability, isolation, alienation, objectification and commodification create contexts for enhanced vulnerability. The changing ethos of Indian family structure and role-functioning has reduced traditional support systems, which used to be a crucial resource for psychiatric and psychosomatic conditions.

Future research should bear in mind the relative position of NSDs as culture-specific variants of sociocultural predicaments that can often be explained physiologically and psychologically, though not medically and psychiatrically. Also it is necessary to note that NSDs are a dynamic manifestation of complex interaction among body, mind, society and culture, in which all members of society, including doctors, play an important role.

Genetic studies may focus on vulnerable groups, biomedical on elucidating and documenting the role of physiology in the origin and maintenance of symptoms, and psychological on setting-specific comprehensive assessments of dimensional distress. Study of personality, stressors, supports and attachment patterns in relational functioning will be useful for holistic assessment, prognostication and management. Sociocultural settings must be studied critically, as they are not just passively shaping the

illness manifestations, but generating and ameliorating them actively in a dynamic interaction with patient's body and mind. Cultural attitudes to women, stigma and livelihoods appear to be crucial risk factors or protective factors. Study of depression and stigma are therefore important.

CONCLUSION Assessment of NSDs in clinical settings should be based on criteria of clinical significance, leaving the cultural assessments for interdisciplinary teams. Interdisciplinary management can generate datasets for population health objectives of measurement of burden – including the opportunity costs and stigma, preventive strategies, and disability limitation. It should also be recognized that NSDs are matters of broad social significance with implications beyond clinical treatment and the responsibilities of health systems. Adverse effects of rapid urbanization in developing countries require consideration, so that culturally appropriate measures to mitigate problems and promote resilience may play a role in intersectoral strategies for limiting vulnerabilities and promoting resilience.

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