Review of Federal and State Actions for the Protection of People with Severe Mental Illness and Intellectual and Developmental Disabilities: The Relevance to Nursing Facilities

Cherie Simpson, PhD, APRN CNS-BC

Review of Federal and State Actions for the Protection of People with Severe Mental Illness and Intellectual and Developmental Disabilities: The Relevance to Nursing Facilities

In 2017, there were over 92,000 residents in long-term care facilities in the state of Texas (Kaiser Family Foundation, n.d.). Demographic characteristics and statistics for these residents are provided by various sources, such as the Minimum Data Set or billing information. For example, according to the Texas Health Care Association (n.d.), 55% of nursing home residents in Texas have been medically diagnosed with dementia. One statistic that is not completely clear, however, is the number of residents with severe mental illness (SMI), which includes diagnoses of schizophrenia, bipolar disorder, depression, and anxiety. Available statistics for Texas reflect the relationship between the use of antipsychotics and a facility's rating in the Five-Star Quality Rating System, which assesses the appropriate or inappropriate use of an antipsychotic. The measure recognizes antipsychotics as an appropriate treatment for schizophrenia but not for bipolar disorder, yet antipsychotics are a standard of care for that condition (Kilgore, 2017). Both bipolar disorder and schizophrenia are therefore tracked along with antipsychotic use. In individual long-term care facilities across Texas, the most recent data for a diagnosis of schizophrenia or bipolar disorder, from 2017, range from 0% to as high as 63.3% (Brown School of Public Health, n.d.). An inclusive estimate for patients with schizophrenia, bipolar, depression, and anxiety cannot be identified, however, because the measure for antipsychotic use does not include depression and anxiety. For the entire U.S., the prevalence of SMI in nursing home residents has been estimated at 6.8%, approximately one quarter of whom are under the age of 65 (Bagchi et al. 2009). This number may not be large in comparison with those for some other subsets of nursing facility residents, but it is growing. Many people with SMI are dependent on families as primary caregivers, and as their parents age, those parents are less able

to provide care physically, emotionally, or financially for aging children with SMI. In addition, people with SMI and patients with intellectual and developmental disabilities (IDD) are now living longer and will likely require long-term assistance. For example, persons with Down's syndrome followed from 1953 to 2000 had an average life expectancy of 58.6 years, but 25% lived 62.9 years (Glasson et al., 2002). Will aging Texans with SMI or IDD be best served in nursing facilities?

Long-term care facilities or nursing facilities have been designed to meet the medical needs of residents, with less emphasis placed on meeting their psychological needs (Molinari et al., n.d.). However, it is codified that the scope of services for a skilled nursing facility should include "services to attain or maintain the highest practicable physical, mental, and psychosocial well-being of each resident," in accordance with a written plan of care (Public Health and Welfare, 2006, p. 2156). Persons with SMI or IDD may require assistance with medical needs, but if they have been living in the community previously, is a nursing facility the appropriate setting for their care? Are nursing homes prepared to meet special needs, such as those of a patient with aggressive behavior resulting from an active delusional state of schizophrenia? How are the civil rights of older adults with schizophrenia protected when these patients may not be able to speak for themselves? How does one decide whether institutional care in a nursing facility is appropriate? To begin to answer these questions, one must look at the historical experience of persons with SMI and IDD with regard to institutional care, as well as consider federal and state actions undertaken to intervene in this population's interest. This review provides a historical perspective on the development of laws, rules, and regulations at the federal and state level, and how they impact decisions about whether nursing facility care is the appropriate choice for persons with SMI or IDD.

History

In the 1950s and 1960s, state mental hospitals were the largest care providers for people with SMI (Fisher et al., 2009). Before 1950, there was large-scale growth in asylums or hospitals, but these were overcrowded institutions where patients with SMI experienced maltreatment (OlmsteadRights, n.d.). The inadequacy of care in these facilities and their maltreatment of patients with SMI were brought to light among the general public by a series of events (Frances & Ruffalo, 2018). In 1946, Mary Jane Ward published her widely read semi-autobiographical novel *The Snake Pit*, in which she exposed the plight of the mentally ill in mental hospitals, and in 1948, her book was made into an Academy award winning film. In 1961, Thomas Szasz published *The Myth of Mental Illness*, the title of which is self-explanatory. Szasz's criticism of the treatment of patients in the U.S. as being mentally "ill" led to advocacy for patients among civil libertarians. State laws were passed that redefined who could be hospitalized; in 1972, the case of Lessard v. Schmidt changed commitment criteria for involuntary admission to psychiatric hospitals (Williams & Caplan, 2012). At the same time, political movements sought to change the treatment conditions of persons with SMI and IDD. John F. Kennedy's last presidential act was the signing of the Community Mental Health Act, which called for 1,500 outpatient mental health centers to replace state mental hospitals, providing treatment at the federal level for those with mental illness and "mental retardation"—those with IDD (Torrey, 2013). Together, these events reduced the number of hospitalized patients from 550,000 in the 1950s to 150,000 by 1970 (Williams & Caplan, 2012). It was thought that community-based care was superior to institutional care and that deinstitutionalization respected an individual's civil rights.

Treatment Advances

Another development changed the standard of care for patients with SMI and made deinstitutionalization possible: the development of antipsychotic medications. Before the 1950s, patients hospitalized for SMI received a variety of invasive, dramatic treatments to control disturbing behaviors and symptoms of diagnoses such as schizophrenia. In the 1930s, there were no successful treatments for violent or aggressive behaviors, so patients were subjected to physical restraint or heavy sedation. Experimental treatments were explored and found effective for reducing psychotic symptoms; one treatment option was offered by insulin therapy, which was used to create a hypoglycemic coma or seizures. Seizures were also evoked by administering pentylenetetrazol, but this treatment was later replaced by electroconvulsive therapy (Swayze, 1995). Such therapies had only short-term benefits, not to mention negative outcomes such as skull fractures and even death! Concurrently, neurosurgeons experimented with surgical techniques to ablate white matter tracts in the frontal lobe called leukotomies. These surgeries, begun in 1936, were revised, modified, and administered to patients with various diagnoses until the early 1950s both in the U.S. and abroad; it has been estimated that over 18,000 such procedures were done in the U.S. alone (Swayze, 1995). The initial patients for these surgeries were predominantly those with depression or bipolar disorder, but patients with schizophrenia were then added as well. Surgery outcomes were mixed; behaviors such as outbursts were reduced, but post-surgery patients were described as being changed. They were said to be dull, flat, and lacking spontaneity, with little capacity for varied emotion. Their mortality rate was high, at 18%. Many psychiatrists considered psychosurgery to be a first-line treatment, but it was not accepted by all. Some, including Szasz and others within the profession, were bold enough to speak out and protest against psychosurgery's use (Swayze, 1995).

Alternative treatments to these invasive, often ineffective, and frequently damaging treatments were not available until the development of chlorpromazine or Thorazine. As often happens, the development of chlorpromazine evolved from researchers' first looking for alternative treatments for another disease, in this case malaria. During World War II, experimentation with antihistamines to treat malaria led to the discovery that promethazine potentiated anesthetic agents; a new compound found in this research, chlorpromazine, caused patients to become sleepy without losing consciousness. In France, the first psychiatric patient treated with chlorpromazine was a person who suffered from a delusional state; the patient showed improvement within one day, with all symptoms resolved in 3 weeks of treatment (Shen, 1999). Chlorpromazine was first marketed in 1954 as Thorazine, which led not only to successful treatment of patients but to the drug's becoming widely used into the 1970s. Thorazine treatment's success created a rush to develop other agents, and by the 1990s, the FDA had approved drugs such as thioridazine, thiothixene, and haloperidol (Shen, 1999). These were first-generation antipsychotics, offering the hope that patients who had been institutionalized and subjected to almost inhumane treatments could be successfully treated and managed within the community.

Concern for Placement in Nursing Homes

In the 1970s and 1980s, new treatment options, negative perceptions of the care in state mental hospitals, political polices for driving care to become community-based, and the financial drain of state hospitals on states' economies led to a continued reduction in the numbers of patients in state hospitals. Unfortunately, however, President Kennedy's original plan for community-based care through community mental health centers (CMHCs) ultimately failed. Patients who left state hospitals received inadequate care in the community and often became

homeless or entered the penal system (Williams & Caplan, 2012). Federal funding was never sufficient, and, in 1981, President Reagan granted funds to states to provide CMHC services, which effectively killed the program on the federal level. Patients who had resources and family support did well, and those who did not did poorly (Torrey, 2013).

As deinstitutionalization from state hospitals took place, a concern arose that some patients would end up in nursing facilities. The National Association of State Mental Health Program Directors recognized that nursing homes would not be equipped to handle patients with SMI and led a lobbying effort that resulted in the development of the federal Preadmission Screening and Annual Resident Review program, or PASSAR (Kaldy, 2018). The Omnibus Budget Reconciliation Act of 1987 (OBRA ’87) introduced sweeping legislation for long-term care. PASSAR was included to ensure that patients with SMI or IDD were not inappropriately admitted to nursing homes; if they were inappropriately placed, specialized services were to be provided to integrate them into the community. If they were appropriately placed, their services were to be increased (Snowden & Roy-Bryne, 1998)

Federal Actions to Protect the Rights of People with SMI or IDD

OBRA ’87 was not the first legislative act designed to protect patients with SMI or IDD residing in nursing facilities. In 1980, Congress enacted the Civil Rights of Institutionalized Persons Act (CRIPA), which authorized the Department of Justice to prosecute violations of civil rights for people with SMI or IDD who were institutionalized in nursing homes, jails, and other institutions that house people with SMI or IDD. This law does not address whether a nursing facility is an appropriate placement, but it provides protection for vulnerable patients with SMI or IDD currently residing in facilities. In a review of the law’s success 25 years after its enactment, the National Council on Disability (2005) reported that the law was still needed

and made recommendations to strengthen it. At that time, 30% of the nation's nursing facilities had been cited for harming residents or putting them at risk.

The most significant legislation to advance the civil rights of persons with disabilities including those with SMI and IDD was the Americans with Disabilities Act of 1990 (ADA; ADA.gov, n.d.). This law prohibits qualified individuals from being discriminated against by exclusion from services and activities due to their disability. The law set in motion regulations that mandated integration such that public entities such as Medicaid-funded nursing facilities must provide programs, services, and activities that allow qualified individuals to become integrated into the most appropriate setting for their needs. This became the foundation for legal cases such as Helen L v. Didario, in which a woman with a disability who resided in a nursing facility and was denied attendant care services that would allow her to live in the community won the right to those services from the state of Pennsylvania (OlmsteadRights, n.d.). The ADA was also the foundation for the Olmstead lawsuit, filed in Georgia on behalf of two patients seeking help who had voluntarily been admitted to a state hospital; when it had been determined that they were ready for a community-based program, they were denied those services and were forced to remain hospitalized. The case was ultimately heard by the Supreme Court, which ruled that "unjustified segregation of persons with disabilities constitutes discrimination in violation of tittle II of the Americans with Disabilities Act" (ADA.gov, n.d.). The Court's decision outlines three criteria that, when met, ensure that public entities must provide community-based services—when the services are appropriate, when the affected person does not oppose community-based treatment, and when the community-based services can be reasonably accommodated.

Despite this major ruling, violations of civil rights persist today, as is evidenced by ongoing lawsuits in Texas. In 2010, a lawsuit was filed by Disability Rights Texas and other parties on behalf of a former patient who had spent 13 years in a facility without appropriate services to enable his integration into the community. The case was heard in 2018, and a ruling was supposed to be given in 2019; but no ruling could be found for the present review. A similar suit, Steward v. Abbott (2016), has as its main argument that the plaintiffs have been unnecessarily institutionalized and segregated and not afforded community-based support including the Medicaid home and community-based services waiver program. With these legal challenges of violations of civil rights for persons with SMI and IDD after the passage of OBRA '87 and the Olmstead decision of 1997, one must ask why, where, or how the system is broken. The answer is greater than the scope of this review, but it is relevant to examine the legislation intended to ensure that persons with SMI or IDD would not be inappropriately placed in nursing facilities.

PASRR

The original PASARR was implemented to ensure that patients with SMI or IDD were not inappropriately or unnecessarily placed in nursing facilities and, if nursing home placement was appropriate, to ensure that individuals received appropriate care. When initially implemented, this prescreening and review applied to all patients currently residing in Medicaid-funded facilities as well as to new admissions, and reviews had to be done annually. In 1996, the law was changed to omit the annual requirement (Snowden & Roy-Byrne, 1998). Currently, the Centers for Medicare & Medicaid Services (CMS) have proposed new rules that would modernize PASARR; public comments were accepted until April 20, 2020. Some of the proposed rule changes would simply clarify terminology and make documents consistent. For

example, the word *pre-admission* wil be replaced by *preadmission* and PASARR (the original acronym) by PASRR (the term used since annual review was deleted; Proposed Rules, 2020, p. 9991). More substantial changes include proposals to change the term *mental disorder* to *mental illness* (p. 9992) and to update the definition of mental illness (MI) from the current diagnostic criteria (diagnosis as in the DSM-III-R: must have experienced a functional impairment in the previous months, received intensive psychiatric treatment or social supports in the previous 2 years) to one more in line with current diagnostic criteria and treatment settings. For instance, the new definition says that a person would be considered to have MI if the person has met the criteria for a DSM-5 diagnosis in the past year: determined by a qualified clinician to be in acute or partial remission, with a disorder that has resulted in functional impairment of a major life activity and that is not secondary to a primary diagnosis of dementia (Proposed Rules, 2020, p. 9995). The proposed changes eliminate the criterion of having to have had a specific type of treatment. This allows people with SMI who have been treated successfully with other therapies (e.g., an intensive outpatient programs) or who are currently stable and in remission to meet the PASRR criteria.

The new rules also propose an updated definition of dementia. Although the diagnosis of dementia has not been a qualifying diagnosis for PASRR MI eligibility in the past, the proposed rule change aligns dementia with the DSM-5 terminology for major and minor neurocognitive disorder, with Alzheimers and other disease processes describing different forms. The new criteria would also require that a qualified clinician must confirm that dementia is primary when the individual experiences both dementia and a co-occurring diagnosis of MI (Proposed Rules, 2020, p. 9996). An individual with minor neurocognitive disorder—what was formerly termed mild cognitive impairment—is not considered as having dementia for PASRR consideration.

Regarding the definition of intellectual disability, previous versions used the terminology of mental retardation, and there was no specific definition of "intellectual disability." The proposed rule changes will align the definition of intellectual disability with that of the American Association on Intellectual and Developmental Disabilities to describe persons that have experienced the onset of an intellectual disability before the age of 18 and have significant limitation in both intellectual functioning and adaptive behavior (Proposed Rules, 2020, p. 9996). The new rules proposes retaining the previous definition of "persons with related conditions" found in the Title 42, CFR §435.1010 (Public Health, 2007, p. 176), which includes severe and chronic disabilities such as cerebral palsy and epilepsy and related conditions that result in functional limitations in at least three life activities.

Another important area of recommended rule change includes redefining "specialized services." These services are above and beyond the scope of services that a nursing facility provides and that are included in the per diem reimbursement rate. In the current regulations, specialized services are divided between people with MI and those with ID, and in the past they were often limited to institutional services. The Proposed Rules (2020, p. 10003) redefine specialize services to be state-defined services for nursing facilities that must be:

- developed by an interdisciplinary team, that would include, at minimum, a physician and a mental health professional (for people with MI) or intellectual disability or developmental disability professional (for people with ID or related conditions);
- designed to address needs related to MD or ID;
- of greater intensity, frequency or customization than the NF services for MI or ID required in part 483, subpart B;
- designed in a person-centered manner that promotes self-determination and independence;
- designed to prevent or delay loss of, or support increase in, functional abilities; and
- if the individual is admitted to or remains in an institutional setting, designed to support any goals the individual may have of transition to the most integrated setting appropriate.

The significance of this change for the CMS is to emphasize that the goal is not only to have specialized services for the sole purpose of transitioning an individual from the nursing facility to the community, but to maintain individuals in the most integrated setting appropriate, which may actually be the nursing facility.

Implementation and the Role of the State

Much like the shift of the responsibility for the CMHCs from the federal government to the states, the implementation and execution of PASRR fall to the states. The proposed rules require that each state must have a plan that meets the federal requirements. The rules provide clear definitions of the roles of each state's Medicaid Agency, Mental Health Agency, and Intellectual Disability Authority. It will be each state's responsibility to meet the basic purpose of PASSR, which is to have processes in place that "result in determinations for NF applicants and residents with MI and ID, based on a physical and mental evaluation of the individual" (Proposed Rules, 2020, p. 9997). This requirement includes identification of all applicants who have a possible MI or IDD; and preadmission screening and resident reviews must be performed when there is a change in status (this replaces annual reviews). The role of the State Medicaid Agencies (SMAs) is clarified to ensure and enforce PASSR program compliance and interagency agreements by designating entities to perform evaluations of individuals with MI and do so with timely, acute reporting of data. The intent of the proposed rule changes is to clarify the SMA's role but also increase and improve PASRR data collection.

In Texas, PASRR is overseen by Texas Health and Human Services (THHS). This agency provides education and is responsible for the state's plan to ensure compliance with federal regulations and oversight of that compliance. The THHS rules and regulations underwent major revision in 2013, when Texas was found to be non-compliant. New procedures were put in

place to remove nursing facilities from the PASSR evaluation process. The process now requires that specialized service needs be identified prior to nursing facility admission. The system to notify that a PASSR evaluation is needed has been automated (Krueger, 2014). The first of two levels of assessment of any applicant are now performed prior to admission to a nursing home, rather than after admission. It is now the responsibility of the referring entity, whether a hospital or community-based physician, to complete PASSR Level 1 (PL1) screening to identify an individual who might have MI or IDD. If, on the basis of PL1 screening, the applicant is suspected of having MI or IDD, a PASSR evaluation (PE) is performed to confirm the MI or ID and to assess the applicant's need for nursing facility services as well as specialized services or specialized rehabilitative services. This evaluation is done by a specialist in mental health or intellectual disabilities. It is not the purpose of the present review to fully describe the PASRR process, but rather to emphasize that all potential residents of nursing homes should be evaluated and assessed prior to admission by specialists who are not related to the respective facilities themselves and who have expertise in mental health and intellectual disabilities. This ensures that people with SMI or IDD are provided an appropriate choice of living arrangements and services. Readers who seek a better understanding of the PASRR program should review the information provided at the THHS (n.d.) website on preadmission screening and resident review.

In America, persons with SMI and IDD have a history of segregation in institutional care, resulting in reduction of personal freedom and often in reduction of the individual's potential. For centuries, science and treatment have been inadequate, but even with the development of modern care, integration into society through community-based care has not occurred successfully for all patients with SMI and IDD. Federal legislation has provided guidance, but states have been left to interpret, implement, and finance mental health care and specialized

services. The results vary from state to state. In 2013, Street et al. showed that only six states had specific nursing facility regulations regarding the care of SMI, which varied from the provision of secure units to the presentation of details about staff training for mental illness. Nine states briefly referenced mental illness in their policies with respect to regulations for admission and transferring residents rather than the care that patients should receive once admitted. Texas, along with 16 other states, has specific regulations regarding residents with dementia but nothing about SMI. In 2013, 18 states did not mention SMI or dementia at all. Texas, with no specific regulations about the care of SMI or IDD beyond the rules and regulations of the PASRR program, suggests the following question: How are nursing facilities prepared to deal with a possible growing number of aging Texans with SMI and IDD, both now and in the future?

References

ADA.gov. (n.d.) *Information and technical assistance on the Americans with disabilities act*. www.ada.gov/olmstead/olmstead_about.htm

Bagchi, A. D., Verdier J. M., & Simon, S. E. (2009). How many nursing home residents live with a mental illness? *Psychiatric Services, 60*(7), 958–964. https://doi.org/10.1176/ps.2009.60.7.958

Brown School of Public Health. (2020). *Long-term care: Facts on care in the US*. LTCFocus.org. http://www.ltcfocus.org/map/50/percent-schizophrenic-or-bi-polar-prevalence#2010/TX/col=0&dir=asc&pg=60&lat=31.690781806136822&lng=-98.7890625&zoom=5

Fisher, W. H., Geller, J. L., & Pandiani, J. A. (2009). The changing role of the state psychiatric hospital. *Health Affairs*, *28*(3), 676–684. https://doi.org/10.1377/hlthaff.28.3.676

Frances, A., & Ruffalo, M. L. (2018, July 3). Mental illness, civil liberty and common sense. *Psychiatric Times*, *35*(7). https://www.psychiatrictimes.com/couch-crisis/mental-illness-civil-liberty-and-common-sense

Glasson, E. J., Sullivan, S. G., Hussain, R., Petterson, B. A., Montgomery, P. D., & Bittles, A. H. (2002). The changing survival profile of people with Down's syndrome: Implications for genetic counseling. *Clinical Genetics, 62*(5), 390–393. https://doi.org/10.1034/j.1399-0004.2002.620506.x

Kaiser Family Foundation. (n.d.). *Total number of residents in certified nursing facilities*. State Health Facts. https://www.kff.org/other/state-indicator/number-of-nursing-facility-residents/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D

Kaldy, J. (2018). When mental illness and aging make nursing homes necessary: What next? *Caring for the Ages*, *19*(5), 1, 10, 11. https://doi.org/10.1016/j.carage.2018.04.001

Kilgore, C. (2017). New guidelines help with schizophrenia diagnosis. *Caring for the Ages*, *18*(6), 3. https://doi.org/10.1016/j.carage.2017.05.004

Krueger, V. (2014). *Pre-admission screening and resident review (PASRR)*. Texas Department of State Health Services, North Central Texas Aging and Disability Resource Center. http://www.nctadrc.org/presentations/PASRR_101714.pdf

Molinari, V., Carney, K.O., & Duffy, M. (n.d.). *Psychological services in long-term care resource guide*. American Psychological Association. https://www.apa.org/pi/aging/resources/guides/long-term-care.pdf

National Council on Disability. (2005). *The civil rights of institutionalized persons act: Has it fulfilled its promise?* https://ncd.gov/rawmedia_repository/c769a668_74d4_4aa7_91d5_bee4338f9b5f.pdf

OlmsteadRights (n.d.). *Olmstead v. LC: History and current status*. https://www.olmsteadrights.org/about-olmstead/

Proposed Rules. (2020). *Federal Register*, *85*(34), 9990–10028. https://www.govinfo.gov/content/pkg/FR-2020-02-20/pdf/2020-03081.pdf

Public Health, 42 C.F.R. § 435.1010. (2007, October 1). Definitions relating to institutional status. Centers for Medicare & Medicaid Services. https://www.govinfo.gov/content/pkg/CFR-2007-title42-vol4/pdf/CFR-2007-title42-vol4-sec435-1010.pdf

Public Health and Welfare, 42 U.S. Code § 1395i–3 (2006). Requirements for, and assuring quality of care in, skilled nursing facilities. https://www.govinfo.gov/content/pkg/USCODE-2008-title42/pdf/USCODE-2008-title42-chap7-subchapXVIII-partA-sec1395i-3.pdf

Shen, W. W. (1999). A history of antipsychotic drug development. *Comprehensive Psychiatry*, *40*(6), 407–414. https://doi.org/10.1016/s0010-440x(99)90082-2

Snowden, M. & Roy-Byrne, P. (1998). Mental illness and nursing home reform: OBRA-87 ten years later. *Psychiatric Services*, *49*(2), 229–233. https://doi.org/10.1176/ps.49.2.229

Steward v. Abbott, Civil No. 5:10–cv–1025–OLG (2016). Leagle. https://www.leagle.com/decision/inadvfdco170411000263#

Street, D., Molinari, V., & Cohen, D. (2013). State regulations for nursing home residents with serious mental illness. *Community Mental Health Journal*, *49*, 389–395. https://doi.org/10.1007/s10597-012-9527-9

Swayze, V. W. (1995). Frontal leukotomy and related psychosurgical procedures in the era before antipsychotics (1935–1954): A historical overview. *The American Journal of Psychiatry*, *152*(4), 505–515. https://doi.org/10.1176/ajp.152.4.505

Texas Health and Human Services. (n.d.). *Preadmission screening and resident review (PASRR)*. https://hhs.texas.gov/doing-business-hhs/provider-portals/long-term-care-providers/resources/preadmission-screening-resident-review-pasrr

Texas Health Care Association. (n.d.). *Quick Facts*. https://txhca.org/quick-facts/

Torrey, E. F. (2013, February 4). Fifty years of failing America's mentally ill. *Wall Street Journal*. https://www.wsj.com/articles/SB10001424127887323539804578260023200841756

Williams, A. R., & Caplan, A. L. (2012). Thomas Szasz: Rebel with a questionable cause. *The Lancet*, *380*(9851), 1378–1379. https://doi.org/10.1016/S0140-6736(12)61789-9