Assessing Medication Exposures and Outcomes in the Frail Elderly

Assessing Research Challenges in Nursing Home Pharmacotherapy

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Background: Large administrative datasets such as Medicare and Medicaid claims have much potential utility in clinical and comparative effectiveness (CE) studies. Among their advantages are the inclusion of clinically heterogeneous populations, without exclusions typical in clinical trials; the ability to study extremely large study populations with power to examine differential outcomes across individual drugs, treatment effect modification, and the risk of uncommon outcomes. However, claims data by themselves are subject to many limitations, notably, in their lack of information on such clinical characteristics as functional status, behaviors, and symptoms, which are important both as outcomes and as covariates.

Methods: We describe data from multiple sources including standardized, electronically recorded clinical and functional data from the Nursing Home (NH) Minimum Data Set; prescription drug data from Medicaid and Medicare claims; and facility data. We present the strengths and challenges of using merged data about the NH population to study prescription drug exposures and outcomes in the frail elderly, and suggest strategies to address methodological difficulties.

Results: Merged data from NH sources can support unique study designs in CE research and provide great power. However, given the differing longitudinal structure, timing of observations, and other complex features of the underlying data sources, such studies pose many challenging design and analytic issues.

Conclusions: Integrated data on the NH population have great potential for CE research among frail elderly persons, if methodological and measurement challenges can be adequately addressed.

(*Med Care* 2010;48: S23–S31)

Although people older than 65 years comprise only about 14% of the US population, they use more than one-third of all medications.[1] Ninety percent of the elderly use 1 or more medications regularly, with >40% taking 5 or more different drugs concurrently.[2] Within the older population, gaps in outcomes evidence are particularly severe for the elderly with multiple medical conditions and functional impairments, such as those residing in nursing homes (NHs). Even more than older people in general, they are typically excluded from randomized controlled trials (RCTs), the "gold standard" for efficacy and safety of medications, due to feasibility and ethical concerns. However, it may be hazardous to assume that safety and effectiveness findings from trials in other populations generalize to the frail elderly with multimorbidity.

Despite this gap in knowledge, the complex medical problems of NH residents lead them to use medication at especially high rates; for example, 1 study found that the average resident received 9 different medications per month.[3] Because of the limitations of the available evidence base and the scarcity of outcome data in this population, the evidence base for safety and effectiveness for much pharmacotherapy among NH residents and comparably frail elders is weak and clinical decisions often rely on generalization from less-frail populations. The "generalizability gap" in the evidence base extends even to treatments that are targeted to the conditions most prevalent in the oldest old. For example, cholinesterase inhibitors and memantine are widely used among NH residents in the hopes of improving cognition and slowing progression of cognitive impairment among residents with dementia, but the preapproval clinical trials of these drugs for safety and effectiveness were mainly conducted in non-NH populations and, indeed, often used NH placement as the study end point. One review found that fewer than 10% of

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Supported by the Agency for Healthcare Research and Quality through a cooperative agreement for the Center for Research and Education on Mental Health Therapeutics at Rutgers (HS016097), as part of AHRQ's Centers for Education and Research on Therapeutics (CERTs) program; with additional support from NIMH grants MH058984, MH60831, and MH076206; AHRQ grant HS011825; and The Retirement Research Foundation grant 2007-152.

Presented an earlier version at the AHRQ-sponsored symposium on Clinical and Comparative Effectiveness Research Methods II, June 1–2, 2006, Rockville, MD.

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ISSN: 0025-7079/10/4800-0023

Alzheimer patients met typical eligibility criteria for RCTs of such medications.[4] Thus, there is a pressing need for research investigating medication outcomes in the NH population. With more comorbidity and greater medication consumption, elderly patients have heightened central nervous system sensitivity and are at increased risk of exposure to potentially problematic medication, side effects, and drug interactions.[5–7]

In several cases, analyses of large claims databases have been used to examine outcomes and exposures for which RCTs are unavailable or inadequately powered. For example, analyses of administrative data from British Columbia and Pennsylvania have established that the mortality risk of first-generation APs among elderly with dementia is as great as for the second-generation drugs. This research contributed to the Food and Drug Administration 2008 extension of a black box warning to first generation drugs.[8,9] However, the absence of key clinical information, such as measures of function, activities of daily living (ADL), cognitive status, and behavioral symptoms that may confound drug group comparisons, often imposes constraints on the ability for traditional claims-based studies to advance the evidence base. Observational designs that incorporate primary data collection can address these limitations but can be extremely costly and often lack the statistical power to compare alternative treatments (particularly individual medications) and explore treatment effect heterogeneity.

However, within the NH population, a standardized electronic health record, the Minimum Data Set (MDS), provides unique opportunities for comparative effectiveness (CE) research. The MDS includes measures of physical, psychological, and psychosocial functioning and active clinical diagnoses. When these data are merged with diagnosis, treatment, and outcome information from Medicare/Medicaid claims, they create great potential for examining patterns of medication use and select outcomes. However, these studies require an appreciation of the strengths and limitations of the underlying data sources and the complexities of merging data from multiple sources. In this article, we describe these datasets, present the strengths and challenges of using merged data about the NH population to study prescription drug exposures and outcomes in the frail elderly, and suggest strategies to address methodological difficulties.

CLAIMS DATA

Medicaid and Medicare claims data provide a detailed, longitudinal record of utilization, diagnoses, procedures, and prescriptions (Table 1). Most residents participate in 1 or both of these important programs.[10] Medicare Part A/B claims reflect payments for physician, inpatient hospital, and other healthcare services used by almost all elderly NH residents (except for those who use capitated Medicare programs such as Medicare Advantage, which is an uncommon arrangement for NH residents), and Medicare functions as the first payer for residents eligible for both Medicare and Medicaid. Thus, these data are essential for providing complete diagnostic and utilization histories. Medicare Part A also pays for up to 100 days of postacute short-term NH rehabilitative and skilled nursing care.

Medicaid Analytic Extract data contain claims information standardized for all states. Calendar-year files on Medicaid eligibility, pharmacy claims, service utilization, and payment information contained in the Medicaid Analytic Extract data are extracted from the Medicaid Statistical Information System, the basic source of state-reported eligibility and claims data on the Medicaid population, their characteristics, utilization, and payments (Table 1). Through 2005, Medicaid was the primary payer for prescriptions for residents dually eligible for Medicare and Medicaid.

In 2006, Medicare beneficiaries began receiving prescription drug coverage (Part D) and, under the standard benefit for 2008, beneficiaries paid a deductible and 25% prescription drug costs up to the initial coverage limit of $2510; then, entering the coverage gap ("doughnut hole"), paid the entire cost of prescriptions up to the catastrophic threshold of $5,726. As of February 2009, 17.5 million Medicare beneficiaries were enrolled in stand-alone Part D plans; 6.3 million dually eligible for Medicaid and approximately 3.3 million receiving Low Income Subsidies received assistance during the coverage gap.[11] Within NHs, 81% of residents were enrolled in Part D in 2006, whereas 16% had other drug coverage and 3% remained without drug coverage.[12] For dual eligibles, comprising 66% of the NH population, the Medicare prescription coverage replaced their previous Medicaid drug coverage. These dual eligibles will not face a coverage gap entailing 100% cost sharing; however, they might be subject to restrictive utilization management practices such as prior authorization policies for the protected drug classes and lack of coverage for the unprotected drug classes, depending on the specific plan characteristics.

Because the initial assignment of dual eligibles to low cost benchmark plans was on a random basis, these differences in access generate variation in medication use that is exogenous to their health status, creating natural experiments that could be used for CE research. In addition, comparing health outcomes between residents in plans with and without the coverage gap, and other distinct plan characteristics, can inform the comparison of alternative coverage mechanisms. Detailed information on plan characteristics and beneficiary utilization enables careful analysis of the impact of commonly used management tools such as cost sharing, prior authorization, and step therapy on patient drug use and associated outcomes.

CLINICAL AND FACILITY DATA

Clinical Data

The MDS is a national 350-item summary screening and assessment tool required of all Medicare and Medicaid-certified NHs providing data for all NH residents (Table 1). Extensive clinical and assessment data for individual residents, including physical and psychosocial functioning, active clinical diagnoses, treatments and mental health services, demographics, and payer source, are documented by nursing staff that have been trained using the standardized MDS administrative guidelines and submitted electronically.[13,14] Previous studies found that interrater reliabilities of items and internal consistency of scales are generally good to excellent for the revised MDS (v 2.0).[15] Good

TABLE 1. Nursing Home Administrative Datasets

Dataset	Description	Sources for Data and Documentation
Claims datasets		
Medicare Part A/B	Data on physician, inpatient, and other medical services for most NH residents; first payer for dual-eligible residents. History of diagnoses (ICD-9 codes) and utilization (procedure codes) with dates of service. Claims for physician services with provider identifiers can identify specialty care use and other aspects of physician care, and support analyses at physician level. Part A claims identify dates of short-term rehabilitative stays; identifying such stays is important because payment for medications is typically bundled into overall part A rate, preventing identification of use of individual medications during Part A stays.	CMS data: CMS Identifiable Data Files contain beneficiary-specific and physician-specific information and require a formal request to be submitted to CMS for approval. Information about Medicare and Medicaid Indentifiable Data Files is available at: www.cms.hhs.gov/IdentifiableDataFiles. Documents are available providing descriptions of the data, the types of data sets, and data limitations. All requests for CMS research-identifiable Medicare and Medicaid data must be developed and reviewed with the assistance of the Research Data Assistance Center (ResDAC), a CMS contractor that provides free assistance to academic, government and nonprofit researchers (www.resdac.umn.edu). At the ResDAC website, additional information is available about available data, data documentation, the process for requesting CMS data, and technical and statistical resources. It is advisable to contact ResDAC early in the process of developing a project for assistance in identifying appropriate data and developing a study protocol to delineate the objectives, background, methods, and importance of the study. Identifiable data requests are reviewed by a CMS Privacy Board, and a Data Use Agreement must be completed detailing that data will be used only for the specific purpose stated in the agreement and specifying the procedural, technical, and physical safeguards, which will prevent unauthorized use.
Medicare Part D (beginning 2006)	Provides claims information on filled prescriptions covered through private Prescription Drug Plans for all Medicare beneficiaries, including drug name and formulation (National Drug Codes). For dual eligibles, replaces previous Medicaid prescription drug coverage beginning in 2006. Beneficiaries may be subject to "doughnut hole" (see text).	
Medicaid analytic extracts (MAX)	Provides calendar-year data on Medicaid eligibility, service utilization, and payments. Includes a Personal Summary File with enrollment information and 4 claims files: Inpatient, Other Therapy, Long-Term Care (LTC), and Prescription Drug. LTC file identifies dates of Medicaid paid stays. Rx file identifies prescription drugs reimbursed by Medicaid for dual-eligible residents before 2006; Pharmacy claims provide National Drug Codes (NDCs) for drug names (brand/generic), dose, route of administration, fill dates, days' supply and quantity of medication dispensed, supporting analysis of initiation, duration, calculation of dosage, specific agents, and other characteristics of medication use. For NHs, quantity dispensed is restricted to 30 d and dose for liquids/injectables cannot be calculated from claims.	
Clinical datasets		
Minimum Data Set (MDS)	National standardized summary screening and assessment tool completed by all Medicare/Medicaid-certified NHs on admission and quarterly thereafter. Documented by NH staff trained using standardized MDS guidelines. Measures include medical and mental health conditions, cognitive, social, and physical (ADL) function, behavioral symptoms, demographics, payer source, use of psychosocial intervention programs, and use of physical restraints. Longer full assessment is used at admission, annually, and when resident shows "significant change." Subset of items used quarterly, so some data elements will be missing. Contains admission, background, and hospital transfer and discharge tracking functions.	Information about MDS data is available at: www.cms.hhs.gov/IdentifiableDataFiles. Requests for MDS data must be developed and reviewed with the assistance of ResDAC (see above).
MDS 3.0	Revised MDS 3.0, projected to be implemented October 2010, has been designed to improve the reliability, accuracy, and usefulness of the MDS. The MDS 3.0 data elements will continue to include select information by class on psychotropic medication exposures, such as antipsychotic use (item NO400) received any time during last 7 d or since admission/reentry if less than 7 d. Specific information on other drug classes, agents and dosage will still need to be supplemented with drug claims.	Information about MDS 3.0, including the revised manual, is available at: http://www.cms.hhs.gov/NursingHomeQualityInits/25_NHQIMDS30.asp#TopOfPage.

(*Continued*)

TABLE 1. (*Continued*)

Dataset	Description	Sources for Data and Documentation
	Additional diagnostic codes such as the new code for psychotic disorders other than schizophrenia (I.15950) should increase specificity of recorded psychiatric conditions. In addition to existing resident clinical characteristics such as Activities of Daily Living (ADL) score (G01101.a-j), MDS 3.0 will now include several new validated scales. Level of cognitive impairment will now be measured using the validated Brief Interview for Mental Status (BIMS) (C0100-C0500) or the staff assessment for mental status (C0700-C1000); depressive symptoms will be measured using the PHQ-9 mood interview scale (D0100-D0300) or staff assessment of resident mood PHQ-9-OV scale (D0500-D0600); behavioral symptoms presence, frequency and severity (E0200-E1100) will be indicated; and delirium will be measured using the Confusion Assessment Method (CAM) (C1300).	
Facility data		
Online Survey Certification and Reporting System (OSCAR)	A uniform computerized data system maintained by CMS, which contains facility and aggregated resident data from all Medicare/Medicaid certified NHs. Includes bed size, ownership, chain affiliation, staffing, casemix and deficiencies recorded by state surveyors. Data are reported by facilities and validated by state agencies as part of the yearly recertification process. Data undergo extensive edit checks by CMS. It is possible to merge OSCAR facility level observations to each resident level observation using the closest survey date to the resident assessment date.	Data is available from Cowles Research Group, www.longtermcareinfo.com. Survey forms, data file layouts and costs available at website. Data needs cleaning of improbable values (see Harrington C, Carrillo H, Wellin V, Burdin A. *Nursing Facilities, Staffing, Residents, and Facility Deficiencies, 2002 through 2006.* San Francisco: Department of Social and Behavioral Sciences, University of California, 2007.) CMS guidelines for surveyors: State Operations Manual for Surveyors, 2006. Available at: http://www.cms.hhs.gov/SurveyCertificationGenInfo/.

correspondence to research quality instruments has been found for cognition, ADL, and diagnoses, with reliability of .73 for the 62 items in the Disease Diagnosis section and .74 for the 8 items in the Medication Use section.[16–18]

All Centers for Medicare & Medicaid Services (CMS)-certified NHs are required to complete comprehensive MDS assessments on admission of each resident, annually, and when a resident shows "significant change in status." A subset of the full MDS is conducted quarterly. The MDS contains select information on medication exposures, including the use of antipsychotics, antidepressants, antianxiety, and sedatives/hypnotics by class for the 7 days before assessment. Specific information about other classes, specific agents, dosage, or prescriber characteristics are not available from the MDS, but data can be supplemented with Medicaid and/or Medicare Part D prescriptions drug claims to provide more detailed information needed on exposure over time for CE and outcomes research. Using rigorous study designs that take into consideration the time-varying nature of antipsychotic use, confounding effects, and the hierarchical data structures inherent in NH research, studies have successfully examined excess risks of several outcomes (eg, hip fracture, venous thromboembolism, cerebrovascular events, ventricular arrhythmias, and diabetes onset) associated with antipsychotic agents and classes using these integrated datasets.[19–21]

A revised MDS 3.0, projected to be implemented October 2010, has been designed to improve the reliability, accuracy, and usefulness of the MDS.[22] The MDS 3.0 data elements will continue to include select information by class on psychotropic medication exposures, such as antipsychotic use received any time during last 7 days or since admission/reentry if less than 7 days. Additional diagnostic codes such as the new code for psychotic disorders other than schizophrenia should increase specificity of recorded psychiatric conditions. In addition to existing resident clinical characteristics such as ADL score, MDS 3.0 will now include several new validated scales (Table 1).

Facility Data

Information about facility characteristics that can influence prescribing patterns is available from the Online Survey Certification and Reporting (OSCAR) system, a uniform computerized data system maintained by CMS.[10] OSCAR contains facility and aggregated resident data from all Medicare/Medicaid certified NHs (Table 1). OSCAR data are reported by facilities before, and validated by state agencies as part of, the yearly recertification process. Data are entered into a uniform, computerized database and undergo extensive edit checks by CMS.[23] Data on most facility characteristics are considered adequately reliable for research,[24] and consequently OSCAR is widely used as the primary source of data on facility characteristics and deficiency citations.[10] Facility characteristics such as acuity level and casemix adjust for the differences in clinical characteristics between NH residents, which can lead to selection effects. A variety of NH characteristics have been studied, including facility size, payer mix, staffing, and citations for deficiencies.[25,26] Information on

quality indicators such as deficiency citations, staffing levels, and physical restraints is extremely useful to test effects or control for variation in quality of care between facilities while assessing the impact of medications and other interventions on health outcomes.[27,28] Previous studies have used combined MDS-OSCAR data to examine the impact of NH characteristics on resident outcomes.[25,26,29–31]

STRENGTHS AND COMPARATIVE ADVANTAGES

Analyses of claims data have several key strengths for studying prescription drug use, including very large numbers of covered lives with relatively comprehensive benefit information of the full continuum of care in most settings, strong representation of vulnerable populations, and diagnostic and treatment information from providers rather than consumers (Table 2).[32] The lack of clinical and contextual information in claims data can be partially ameliorated by supplementing these datasets with data from other routinely collected data sources such as the MDS and OSCAR. For example, MDS data have been linked to Medicare claims and other detailed medication records to study medication use and hospitalizations in NHs.[33–36] Within the NH setting, medications are administered by staff, so that nonadherence is less an issue than with community-dwelling elderly. Combining prescription drug claims with MDS assessments substantially increases the potential to examine important details of medication use including dosage, duration, and use of specific drugs within medication classes, as in current work on guideline consistent use of antipsychotic medications in the NH.[37]

Because of the very large populations available to study, merged NH data offer unique opportunities to examine outcomes in particular subgroups of concern, to compare outcomes across individual drugs within and between classes, to assess risks of rare but serious adverse outcomes not detectable in typical clinical trials, and to examine outcomes over longer follow-up times. These data include large numbers of individuals in vulnerable subgroups such as minority, low-income, and/or individuals with disabilities, providing a vital resource for research on disparities. For example, pre-

TABLE 2. Strengths and Comparative Advantages of Merged Nursing Home Data

Dataset Characteristic	Advantages and Implications for CER in Nursing Homes
Very large numbers of covered lives, with comprehensive information about clinical and functional status from MDS.	Strong statistical power supports detailed analyses of subgroups of elderly individuals, rare conditions, and comorbidities, including individuals with complex combinations of diagnoses.
	Supports study of low-incidence severe adverse outcomes not detectable in clinical trials.
	Sufficient power to compare outcomes across individual drugs within and between classes; however, comparisons across individual drugs may require data from multiple states.
	Ability to identify treatment effect heterogeneity.
Rich array of clinical, functional, diagnostic, treatment, and outcome information.	Provides a depth and range of covariate information to reduce confounding.
	Allows study of a variety of outcomes, eg, metabolic outcomes, falls, fractures, cerebrovascular events, diabetes onset, guideline consistent use of antipsychotics.
	Reliability and internal consistency of clinical data adequate for many constructs although variation exists across items and scales.
Strong representation of vulnerable populations, including racial/ethnic minorities.	Supports analysis of outcomes for a diverse population and for racial/ethnic and other subgroups; supports analyses on disparities; allows analysis of effect modifiers for treatments (eg, differential effects across subpopulations).
Detailed longitudinal claims information from both Medicare and Medicaid.	Facilitates building complete longitudinal histories from all relevant payers to provide information needed for exposure over time needed for CE research.
	Long-term follow-up is possible for beneficiaries who are consistently enrolled.
	Because medication fills and administration are facility supervised, Rx-related analyses less confounded by nonadherence than is the case in community populations.
	Important source for comparing prescription drug experience before and after Medicare Part D for dual eligibles; eg, Part D plan characteristics such as exposure to coverage gap, cost sharing, prior authorization.
	Enables event history analyses of temporal relationships among health care events, such as incidence and timing of hospitalizations. Dates of healthcare events can be used to construct episodes of care of consistent duration.
National data with information on care of patients for all participating providers; provides geographic detail and data about provider characteristics.	Individual-level data can be aggregated to create provider-level and area-level estimates of treatment patterns; supports multilevel analyses of treatment and outcome patterns.
	Supports study designs that incorporate linkage to other sources of contextual data, such as vital records, Medicare cost reports, community characteristics and resources, and policy variables.
	Supports characterization of usual care for the full covered population, including facility characteristics such as casemix and acuity level, which are important to control for selection into facilities.
Unobtrusive data collection; diagnostic and treatment information from providers rather than consumers.	Avoids biases related to self-report and differential study participation.
	Supports studies that include beneficiaries with limited ability to self-report such as those with cognitive impairment/dementia.

liminary analyses of 2005 MDS data by the authors indicate that among 690,000 residents aged 65 years and older with stays of at least 1 year, 12% were African American and 3% Hispanic, 61% had recorded diagnoses of dementia, and 50% were diagnosed with depression.

Very large numbers also increase the ability to examine treatment effect heterogeneity, construct narrowly tailored new-treatment cohorts for pharmacoepidemiologic studies, and facilitate advanced statistical methods such as high dimensionality propensity scoring and instrumental variables. These designs are remarkably demanding of power and may require multiyear national data to generate statistical variation, which facilitates identification and provide sufficient numbers for controlled study of rare conditions or comparisons between specific medications. These data allow extended longitudinal follow-up utilization, diagnoses, procedures, and prescriptions for clinically heterogeneous populations, including those with multiple morbidities. Longitudinal modeling allows within-person analysis of medication utilization and outcomes over time, which can shed light on processes and potential modifiable factors leading to adverse health outcomes.

LIMITATIONS, CHALLENGES, AND STRATEGIES

The Medicare, Medicaid, and MDS data mentioned earlier contain individual beneficiary and provider identifiers, which allow the data to be linked and are subject to the Privacy Act and other Federal government rules and regulations. CMS uses strict security measures to safeguard individual privacy and requires review of data requests by a CMS Privacy Board. All requests for identifiable data must be developed and reviewed with the assistance of the Research Data Assistance Center, and include a Data Use Agreement, detailing specific procedures to assure protection of the data (Table 1). Obtaining CMS data, particularly for multiple years, represents a substantial financial investment and may take several months. Use of these identifiable data likely will also require approval by the Institutional Review Board of the researcher's organization.

In addition to privacy and financial concerns, the datasets require a substantial investment of time in becoming familiar with the associated documentation. A researcher must become familiar with comprehensive data dictionaries detailing diagnosis codes, procedure codes, and National Drug Codes. In planning studies, researchers need to become familiar with published treatment recommendations[38,39] and/or team with clinical partners familiar with treatment practices in NH. In addition, projects using these complex data require analysts with advanced programming skills to process the data accurately and efficiently.

Using administrative data requires understanding and accounting for certain well-known limitations of the underlying data sources.[29] In the NH context, it is particularly important to use information from multiple sources to account for transitions in settings and payer sources (Table 3). For example, use of medications cannot be observed in claims data for periods of inpatient hospitalization or short-term rehabilitative NH stays funded by Medicare Part A. Such stays often follow a hospitalization, creating a time period during which observation of medication use should be treated as censored. Careful attention is also needed to state variations in policies, particularly before 2006. For example, before Medicare Part D, the New York Medicaid program bundled reimbursement for some drugs (maintenance medications) into Medicaid per diem rates for NH care, and certain states did not report days supplied on Medicaid prescription drug claims in all years.

State variations also exist in MDS data. Most notably, state requirements for quarterly assessments vary, so that less information may be available on quarterly assessments in states not participating in the Prospective Payment System, limiting longitudinal tracking of some measures (eg, comorbidities and psychotic symptoms) to comprehensive assessments only. An important issue that needs further exploration is the extent of facility or state variation in the recording of MDS information, because some states currently base reimbursement for Medicaid and Medicare patients on functional status of residents. Such use of MDS clinical assessment information for payment and for quality measurement has the potential to influence recording.[15] In addition, NHs and states have provided varying resources and training for completing the MDS, which may affect reporting of information.[40] Differences have been found between facilities in interrater reliability levels of MDS assessment items, but it is unclear which facility characteristics are related to these differences.[17]

As discussed earlier, many studies have supported the reliability and validity of many of the MDS 2.0 data elements and summary scales. However, other studies have questioned the validity of some elements such as pain frequency and intensity, measures of mood, visual acuity, and incontinence.[41–45]

Longitudinal tracking of clinical information about NH residents can be complex. Although assessments are completed at approximately 90-day intervals, assessments are also completed when a resident experiences a "significant change" in function, which may change the timing of subsequent assessments. Hospitalizations of residents also interrupt the timing and detail of assessments. Although MDS assessments occur at roughly 90-day intervals, they must be matched to daily drug claims to construct meaningful medication histories. Meaningful assembly of covariates over time is challenging, as health status changes between assessment points, potentially resulting in misclassification of MDS-based measures. To address this issue, we have, for example, limited analyses to MDS assessments within 2 weeks before claims-based exposure/outcome assessment to avoid misclassification of clinical measures from the MDS; however, this may diminish study samples.

In addition, combining MDS data with claims requires careful specification of measures of outcomes, clinical covariates, and treatments. MDS assessments generally reflect status within the 7 days before the assessment. However, some sections specify other time frames. For example, continence items refer to status in the past 14 days, and some items in the mood and behavior patterns section refer to the past 30 days. Therefore, specifying models requires careful

TABLE 3. Challenges and Strategies in Working With Merged Nursing Home Data

Challenges	Strategies
Claims are generated for administrative and reimbursement rather than clinical or research purposes.	Include clinical and functional information from MDS to provide context and address confounding.
	Understanding nonclinical influences in coding processes, such as reimbursement consideration, is important to interpreting data in claims.
	Familiarity with NH treatment guidelines and quality measures is important (see text).
Raw data must be organized into meaningful diagnosis and treatment variables.	Variable construction should be informed by clinical understanding of relevant conditions, treatment, and outcomes, as well as organizational context of nursing home.
	Drug treatment episodes must be carefully constructed to provide timely clinical information and specific information about drug names, fill dates, and dosages.
Combining MDS assessments (generally collected at 90 d intervals) with daily drug claims requires careful specifications of drug use and clinical covariates.	Construction of medication "calendars" based on fill dates and days-supply is important in combining data with different temporal structure and identifying treated and non periods. A look-back period may be necessary to identify new users of medications and/or determine clinical history.
	To avoid misclassification of MDS clinical data, analyses can be limited to only those subjects with assessments within a short period before drug initiation.
Prescription drug claims histories reflect complex patterns of use over time.	Insight into medication outcomes must incorporate analysis of duration of treatment spells and consistency of use over time.
	Choice of measures should be consistent with recognized clinical guidelines for NHs and recommendations regarding appropriate medication use patterns.
	For NH claims, amount dispensed is restricted to 30 d and dose for liquids/injectables cannot be calculated from claims.
Some sections of MDS have variable results for reliability and validity.	Careful consideration is needed of available information on reliability and validity of measures. Further studies of validity are needed. In some cases, sensitivity can be increased by combining data from MDS with information recorded in Medicare/Medicaid claims. More validation studies needed.
State variations exist in data recording; eg, in type of quarterly MDS assessment used and in drug claims data available.	Be alert for missing variables in quarterly MDS assessments and missing data in pharmacy claims; consultation with state experts may be necessary to understand state variations in data recording.
Part A nursing homes stays, such as hospitalizations, have medication costs bundled into payment rates.	Treat hospitalizations and Part A nursing home stays as censored periods during which medication use is not observed.
Observations may be clustered in complex ways, violating assumptions of independence and complicating inferences.	Consider use of statistical tools such as generalized estimating equations that are robust in the face of clustered data.
	Variation at multiple levels of clustering (eg, repeated observations within individuals, residents within facilities) can be modeled explicitly with multilevel methods.
Implementation of MDS 3.0 will complicate assessment of MDS data serviceability. Variables will change in some domains.	Updated reliability/validity studies will be needed to provide data on quality of MDS 3.0 recording.

attention to temporal relationships and clinical understanding of relevant conditions.

For CE research, the addition of clinical information from MDS assessments performs 2 primary functions: it provides (1) clinical detail that improves ability to control for confounding between comparison groups and (2) outcome measures not available in claims data. MDS-based clinical variables can be integrated as covariates into CE analyses in the same way as variables based on diagnostic codes or drug utilization from claims. Assuming a new-user design, both types of variables would be assessed for a defined preinitiation period (commonly the same period that established new exposure treatment episodes) and used for baseline adjustments between the comparison groups, either using traditional multivariate methods or summary variable approaches such as propensity scores. When particular concern exists about misclassification of MDS-based variables from more distant assessments (eg, when clinical practice suggests that treatment initiation is commonly preceded by sudden changes in important patient characteristics observed in the MDS), analyses can be limited to only those subjects with MDS assessments within a shorter time period (eg, 7 or 14 days) before initiation. Of course, addition of MDS to claims data will only improve confounder adjustment in areas where MDS collects data, ie, largely functional and behavioral measures and does not, for example, provide laboratory or imaging results. Thus, the greatest benefit of merged NH data lies in analyses where behavioral and functional measures constitute important confounders, such as mental health interventions; however, they may also be useful in other clinical areas as more general proxies for frailty. Similarly, MDS-based variables may be used as outcome measures for either binary outcomes (eg, falls, infections, dysphagia, or feeding tube use), or—with adjustment for their baseline values—for continuous variables such as body mass index, cognition, social engagement, physical function, and ADL performance.

CONCLUSIONS

In conclusion, RCT data are often inapplicable to populations of frail elderly with complex comorbidities, such as

the typical resident population in NHs. A better understanding of prescription drug use and outcomes in the NH population is not only important in its own right but can also serve as an important test bed for outcomes in similarly frail but less well-observed elderly in other settings. The combination of administrative data available for NH residents presents unique opportunities to combine clinical and functional assessments with diagnosis and medication exposure information. The high level of detail on clinical characteristics, functioning, and interventions has the potential for overcoming some of the traditional limitations of administrative data by providing richer clinical information and can support a variety of statistical methods to reduce confounding. New-user designs, advanced statistical methods, such as use of instrumental variables, examination of effect modifiers in heterogeneous populations, and comparisons across individual drugs are all extremely demanding of power. Cell sizes dwindle rapidly, and national multiyear data may be necessary to address rare outcomes.

Merging multiple data sources has great potential but can be challenging to implement for an individual study given the complexity and labor intensiveness of this work. Because highly detailed information about individuals is necessary, data are potentially identifiable, requiring rigorous procedures to assure protection of confidentiality. More effective and systematic linkage of these rich data resources has considerable potential to advance the state of the art in CE, medication safety, and other health services research on the frail elderly.

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