Perspectives

Lessons Learned From Our Elders: How to Study Polypharmacy in Populations With Intellectual and Developmental Disabilities

Jessica N. Stortz, Johanna K. Lake, Virginie Cobigo, Hélène M. J. Ouellette-Kuntz, and Yona Lunsky

Abstract

Polypharmacy is the concurrent use of multiple medications, including both psychotropic and non-psychotropic drugs. Although it may sometimes be clinically indicated, polypharmacy can have a number of negative consequences, including medication nonadherence, adverse drug reactions, and undesirable drug–drug interactions. The objective of this paper was to gain a better understanding of how to study polypharmacy among people with intellectual and developmental disabilities (IDD). To do this, we reviewed literature on polypharmacy among the elderly and people with IDD to inform future research approaches and methods on polypharmacy in people with IDD. Results identified significant variability in methods used to study polypharmacy, including definitions of polypharmacy, samples studied, analytic strategies, and variables included in the analyses. Four valuable methodological lessons to strengthen future polypharmacy research in individuals with IDD emerged. These included the use of consistent definitions of polypharmacy, the implementation of population-based sampling strategies, the development of clinical guidelines, and the importance of studying associated variables.

Key Words: polypharmacy; intellectual and developmental disabilities; autism spectrum disorders, medication

In its simplest form, polypharmacy is defined as the concurrent use of multiple psychotropic and non-psychotropic medications (Bjerrum, Rosholm, Hallas, & Kragstrup, 1997; Chutka, Takahashi, & Hoel, 2004). Polypharmacy often occurs in the context of chronic medical conditions or psychiatric and medical comorbidities when the use of multiple medications may be clinically indicated (Fulton & Riley Allen, 2005).

This paper emerges as part of ongoing health-services research on the quality of health care provided to adults with intellectual and developmental disabilities (IDD) across a series of indicators using population-based administrative health data. In the context of this research program, we selected indicators of the quality of health care based on existing clinical guidelines for adults with IDD (Sullivan et al., 2011). We identified polypharmacy as a key indicator because the use of multiple medications can be harmful and require clinical attention (Sullivan et al., 2011). In an effort to inform our study of polypharmacy at the population level, including identification of important variables to consider when studying and comparing polypharmacy rates across different population groups, we examined the literature on polypharmacy among people with IDD. In conducting this literature review, we also chose to examine literature on polypharmacy in the elderly because (a) data on medications dispensed to the elderly is available in many jurisdictions at the population level, and (b) the aging population is recognized as one at risk of polypharmacy (Chutka et al., 2004).

Adults with IDD are often diagnosed with comorbid conditions, including gastrointestinal problems, sleep disorders, epilepsy, attention deficit and hyperactivity disorder, schizophrenia, bipolar disorder, anxiety, and depression (Bauman, 2010; Levy, Mandell, & Schultz, 2009; Mahan et al., 2010; Wood, Hall, Zhang, & Hou, 2006). In addition, chronic diseases, such as diabetes, cerebrovascular disease, and cardiovascular disease, are becoming more prominent in individuals with IDD as their life expectancy has increased in recent years (Wood et al., 2006). Consequently, individuals with IDD receive more prescriptions per year and are at greater risk for polypharmacy than the...
Polypharmacy rates among individuals with IDD (Aman, Lam, & Collier-Crespin, 2003; Aman, Lam, & Van Bourgondien, 2005; Estensen, Greenberg, Seltzer, & Aman, 2009; Hurley, Folsken, & Lam, 2003; Marshall, 2004; Molyneux et al., 1999; Robertson et al., 2000; Spreat et al., 2004). In addition to high rates of medication use, individuals with IDD often have difficulty reporting and understanding side effects (Aman, Benson, Campbell, & Haas, 1999; Bradley, 2002; Gardner Wilson, Lott, & Tsai, 1998; Lunsky et al., 2008; Sametkin & Yamada, 1993), they are at heightened risk of paradoxical side effects (Gardner Wilson et al., 1998), and they may not have the capacity to consent to medication use (Aman et al., 1999; Lunsky et al., 2008).

Despite its clinical indication, polypharmacy is concerning in individuals with IDD and the more general population (Straetmans, van Schrojenstein Lantman-de Valk, Schellevis, & Dinant, 2007). In particular, the prescribing of psychotropic medication is common among individuals with IDD with rates of psychotropic medication usage estimated between 28% and 89% (Bisconer, Sine, & Zhang, 1996; Burd et al., 1997; Lott et al., 2004; Molyneux, Emerson, & Caine, 1999; National Core Indicators, 2012; Spreat, Conroy, & Fullerton, 2004). Antipsychotic drugs are the most commonly prescribed psychotropic medications among individuals with IDD (Aman et al., 2003; Aman, Lam, & Van Bourgondien, 2005; Estensen, Greenberg, Seltzer, & Aman, 2009; Hurley, Folsken, & Lam, 2003; Marshall, 2004; Molyneux et al., 1999; Robertson et al., 2000; Spreat et al., 2004). In addition to high rates of medication use, individuals with IDD often have difficulty reporting and understanding side effects (Aman, Benson, Campbell, & Haas, 1999; Bradley, 2002; Gardner Wilson, Lott, & Tsai, 1998; Lunsky et al., 2008; Sametkin & Yamada, 1993), they are at heightened risk of paradoxical side effects (Gardner Wilson et al., 1998), and they may not have the capacity to consent to medication use (Aman et al., 1999; Lunsky et al., 2008).

This article reviews and critically appraises how polypharmacy (psychotropic and non-psychotropic drugs) is studied in two highly medicated but distinct populations: the elderly and individuals with IDD. Results inform researchers on methodological considerations for future studies, including activities aimed at monitoring the quality of health care provided to people with IDD.

Methods

Comprehensive literature reviews of polypharmacy in the elderly and individuals with IDD were conducted using the following bibliographic databases: Embase and Medline. Searches were limited to English publications from January 1996 to February 2011. The following terms were used to capture medication use: polypharmacy, psychotropic drug, neuroleptic drug, antipsychotic drug, clinical indicators or health care quality. These terms were combined with additional terms and strategies aimed at identifying the populations of interest (individuals with IDD and the elderly). For the elderly, the term “elderly” was used in combination with prespecified age categories: “all aged (65 and over)” and “aged (80 and over).” For individuals with IDD, the following terms were used: developmental disability or intellectual disability or learning disability or autistic disorder or Asperger syndrome or pervasive developmental disorder—not otherwise specified. We also set age limits such that studies were included only if they focused on adults or adults as well as adolescents or children. Titles and abstracts obtained from the searches were scanned to exclude case series or reports, sources that provided no information on measurement or classification of polypharmacy or inappropriate prescribing practices in the context of multiple medications, or papers that did not examine variables associated with polypharmacy. Polypharmacy in individuals with learning disabilities, a term synonymous with intellectual disability in the British literature, were included only if it was evident that the term referred to individuals with IDD. Relevant references from papers obtained from the literature search were also used. Additional papers were obtained directly from coauthors of this review. Authors did not search for grey literature and unpublished reports.

This review presents and discusses methods used to study polypharmacy. In particular, definitions of polypharmacy used, samples studied,
analytic strategies, and associated variables are examined. To aid in the presentation of findings, variables associated with polypharmacy were categorized based on a modified framework developed by Bronskill and colleagues (2012) related to categorizing and examining population-level medication data in the elderly. Following the review, variable categorization was informed by common themes, which emerged from the literature searches and were further adapted based on team discussions. Variables associated with polypharmacy were grouped into the following categories for the current review: clinical, demographic, and organizational variables. Demographic variables were defined as the fixed characteristics of an individual (e.g., gender, age), and variables describing clinical characteristics were considered in a second category (e.g., comorbidities, cognitive functioning). Organizational variables reflected the support or care received by a specific population (e.g., residence, primary and psychiatric care).

Results

Nine articles were obtained from the elderly literature, and seven from the IDD literature. It should be noted that some polypharmacy studies examined the total number of medications, and some either separated the type of medication or only examined psychotropic medications. For studies that focused on psychotropic polypharmacy exclusively, this is indicated throughout the results. Details of each study reviewed are included in Tables 1 and 2.

Measurement and Definition of Polypharmacy

Most of the studies reviewed employed different definitions of polypharmacy. In both populations, polypharmacy was most frequently defined on the basis of a numerical cut-off value; however, this number varied, depending on the population examined. For individuals with IDD, polypharmacy often constituted the combination of two or more psychotropic drugs from the same or different medication classes, also known as intraclass and interclass polypharmacy, respectively. For the elderly, polypharmacy typically constituted the concurrent use of five or more, nine or more, or 10 or more medications (psychotropic and non-psychotropic). Some studies of the elderly examined varying levels of polypharmacy based on the number of medications prescribed, utilizing categories including polypharmacy versus excessive polypharmacy or minor versus major polypharmacy. In studies of individuals with IDD, all but one defined polypharmacy using psychotropic medications only. In contrast, all studies of polypharmacy in the elderly included psychotropic and non-psychotropic medications.

All studies of individuals with IDD based definitions of polypharmacy on what was typically reported in previous literature or commonly observed medication combinations with no reference to the appropriateness of specific medication combinations. Some studies in the elderly went beyond this to examine polypharmacy in the context of appropriateness of medication-prescribing practices. In two studies, inappropriate prescribing practices, based on medication guidelines (Medication Appropriateness Index and Beer’s Criteria) were the major outcome of interest, but both studies also examined polypharmacy (Carey et al., 2008; Hajjar et al., 2005). Another study examined medication combinations that were known to be harmful in older adults (Raymond et al., 2010).

As noted earlier, polypharmacy concerns the concurrent use of medications. In the studies reviewed for both populations, definitions of “concurrent” medication use were inconsistent. The majority of studies counted all medications dispensed on an arbitrary census date. No studies included in this review allowed for a prescription-overlap period, and any overlap in drug therapy was considered concurrent use.

Samples Studied

Studies of polypharmacy among individuals with IDD tended to employ clinic (Hurley et al., 2003; Stolker et al., 2001) or convenience samples (Esbensen et al., 2009; McGillivray & McCabe, 2006). As a result, samples of individuals with IDD were relatively small with cohorts composed of 109 (Stolker et al., 2001) to 2,052 (Stolker, Koedoot, Heerdink, Leufkens, & Nolen, 2002) individuals. In contrast, many studies of polypharmacy in the elderly included large, population-based cohorts composed of more than 100,000 subjects (Bjerrum, Sogaard, Hallas, & Kragstrup, 1998; Carey et al., 2008; Haider, Johnell, Weitsof, Thorslund, & Fastbom, 2009; Raymond et al., 2010).
<table>
<thead>
<tr>
<th>Study reference</th>
<th>Location</th>
<th>Sample</th>
<th>Polypharmacy definition</th>
<th>Variables associated with polypharmacy (Y/N)</th>
<th>Major statistical analyses conducted to determine association with polypharmacy</th>
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<tbody>
<tr>
<td>Burd et al., 1997</td>
<td>United States</td>
<td>Survey of residents in every group home for people with intellectual disability in North Dakota</td>
<td>More than one psychotropic medication prescribed at time of survey</td>
<td>Clinical: Psychiatric and medical comorbidities (Y)</td>
<td>Bivariate analysis</td>
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<tr>
<td>Esbensen et al., 2009</td>
<td>United States</td>
<td>Adolescents and adults over a 4.5-year time period recruited from service agencies, schools, diagnostic clinics, and the media in Massachusetts and Wisconsin</td>
<td>Examined drug class and the use of two and three or more psychotropic medications over time. Non-psychotropic medications also examined.</td>
<td>Demographic: Age (Y)</td>
<td>Bivariate analysis</td>
</tr>
<tr>
<td>Hurley et al., 2003</td>
<td>United States</td>
<td>Medical chart review of patients at psychiatric clinic in a hospital in Boston</td>
<td>Total number of psychotropic drug classes (prescribed therapy by drug class) prescribed at the end of the psychiatric evaluation</td>
<td>Clinical: Intellectual and adaptive functioning (N)</td>
<td>Bivariate analysis</td>
</tr>
<tr>
<td>Study reference</td>
<td>Location</td>
<td>Sample Size and sampling strategy</td>
<td>Age range</td>
<td>Diagnoses</td>
<td>Polypharmacy definition</td>
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<tr>
<td>McGillivray &amp; McCabe, 2006</td>
<td>Australia</td>
<td>$n = 873$ Chemical restraint reports to Intellectual Disabilities Review Panel</td>
<td>Mean age: 38 years Age range: 6.8–88 years</td>
<td>All subjects had intellectual disability</td>
<td>One or more antipsychotics; measured number of prescriptions for psychotropic drugs and interclass and intraclass polypharmacy also, but did not look at variables associated; counted number of prescriptions at time report was completed</td>
</tr>
<tr>
<td>Robertson et al., 2000</td>
<td>United Kingdom</td>
<td>$n = 500$ Questionnaires and interviews with members of support teams for individuals living in 18 residences across the United Kingdom</td>
<td>Mean age: 40–48 years Age range: Unknown</td>
<td>All subjects had intellectual disability</td>
<td>Prescription for more than one psychotropic medication at time of questionnaires/interviews; interested in specific psychotropic medication combinations only</td>
</tr>
<tr>
<td>Study reference</td>
<td>Location</td>
<td>Size and sampling strategy</td>
<td>Sample</td>
<td>Diagnoses</td>
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<tr>
<td>Stolker et al., 2001</td>
<td>Netherlands</td>
<td>Medical records for individuals admitted to a psychiatric hospital ward</td>
<td>$n = 105$</td>
<td>Mean age: 27 years, Age range: 16–57 years</td>
<td>All subjects had borderline intellectual functioning or an intellectual disability; some participants had a psychiatric diagnosis, some had a behavioral diagnosis</td>
</tr>
<tr>
<td>Stolker et al., 2002</td>
<td>Netherlands</td>
<td>Staff questionnaires and medical records to obtain information about residents from 573 group homes in the Netherlands (random and nonrandom selection of subjects)</td>
<td>$n = 2052$</td>
<td>Mean age: 39–42 years, Age range: 18+ years</td>
<td>All subjects had intellectual disability; some had psychiatric/behavioral symptoms</td>
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</table>
Table 2
Studies Examining Variables Associated With Polypharmacy in the Elderly

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Location</th>
<th>Sample</th>
<th>Polypharmacy definition</th>
<th>Variables associated with polypharmacy (Y/N)</th>
<th>Major statistical analysis method for determining associations with polypharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bjerrum et al., 1998</td>
<td>Denmark</td>
<td>$n_{total} = 466,567$</td>
<td>Concurrent use of more than one prescription medication on any day of the study period; two different definitions: two to four drugs (minor polypharmacy) and five or more drugs (major polypharmacy); prescription medications only (psychotropic and non-psychotropic); oral contraceptives, sedatives, and hypnotics were excluded from medication count</td>
<td>Demographic: Gender (Y), age (Y)</td>
<td>Bivariate analysis</td>
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<td></td>
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<td>$n_{elderly} &gt; 3,684$</td>
<td>16+ years</td>
<td>Elderly: 65+ years</td>
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<tr>
<td></td>
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<td>Prescription records from 1993–1994 of all individuals living in Funen, Denmark</td>
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<td></td>
<td></td>
<td>Mean age: Unknown</td>
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<td>Age range: 16+ years</td>
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<p>| Carey et al., 2008 | United Kingdom | $n = 218,567$ | Main outcome of interest was potentially inappropriate prescriptions, but adjusted for number of medications; counted “repeat” prescriptions only if patient had received at least three prescriptions for a particular medication in a year, medication was counted; prescription medications only (psychotropic and non-psychotropic) | Demographic: Age (N), socioeconomic status (Y), geographic region (N) | Multivariate analysis |
|                   |              | Records from 201 general physician practices |                                      |                                             |                                                                             |
|                   |              | Mean age: Unknown |                                      |                                             |                                                                             |
|                   |              | Age range: 65+ years |                                      |                                             |                                                                             |</p>
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<tr>
<th>Study reference</th>
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<tbody>
<tr>
<td>Haider et al., 2009</td>
<td>Sweden</td>
<td>$n = 626,258$ General population records from a drug register</td>
<td>Two different definitions: Concurrent use of five or more medications (polypharmacy), concurrent use of nine or more medications (excessive polypharmacy); counted number of prescriptions over a 3-month period; prescription medications only (psychotropic and non-psychotropic); medications used in hospitals/nursing homes were not captured in the registry and excluded from medication count</td>
<td>Demographic: Gender (Y), age (Y), socioeconomic status (Y), geographic region (Y) Clinical: Psychiatric and medical comorbidities (Y)</td>
<td>Multivariate analysis</td>
</tr>
<tr>
<td>Hajjar et al., 2005</td>
<td>United States</td>
<td>$n = 384$ Medical records of a random sample of patients at hospital discharge</td>
<td>Main outcome of interest was unnecessary drug use, but adjusted for number of medications; counted medications at hospital discharge; prescription medications only (psychotropic and non-psychotropic)</td>
<td>Clinical: Psychiatric and medical comorbidities (Y) Organizational: Primary and psychiatric care (Y)</td>
<td>Multivariate analysis</td>
</tr>
<tr>
<td>Jorgensen et al., 2001</td>
<td>Sweden</td>
<td>$n = 4642$ Prescription records from community pharmacies in Tierp, Sweden Elderly living in long-term care facilities were not included</td>
<td>Prescription for five or more medications during 1 year; prescription medications only (psychotropic and non-psychotropic)</td>
<td>Demographic: Gender (N), age (Y) Clinical: Psychiatric and medical comorbidities (Y) Organizational: Primary and psychiatric care (Y)</td>
<td>Multivariate analysis</td>
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<tr>
<td>Study reference</td>
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<td>Jyrkka et al., 2009a</td>
<td>Finland</td>
<td>$n = 523$ Interviews with random sample of home-dwelling elderly individuals living in Kuopio, Finland</td>
<td>Two different definitions: Use of six to nine medications concomitantly, and use of 10 or more drugs concomitantly, counted at the time of interview; prescription and nonprescription medications (psychotropic and non-psychotropic) and vitamins included in medication count; herbal products excluded</td>
<td>Demographic: Gender (Y), age (Y) Clinical: Psychiatric and medical comorbidities (Y), intellectual and adaptive functioning (N) Organizational: Residence (N)</td>
<td>Multivariate analysis</td>
</tr>
<tr>
<td>Jyrkka et al., 2009b</td>
<td>Finland</td>
<td>$n = 601$ Interviews with random sample of home-dwelling and institutionalized elderly individuals living in Kuopio, Finland</td>
<td>Two different definitions: Use of six to nine drugs concomitantly, and use of 10 or more drugs concomitantly, counted at the time of interview; prescription and nonprescription medications (psychotropic and non-psychotropic) and vitamins included in medication count; herbal products excluded</td>
<td>Demographic: Gender (Y), age (Y) Clinical: Psychiatric and medical comorbidities (Y), intellectual and adaptive functioning (N) Organizational: Residence (Y)</td>
<td>Bivariate analysis</td>
</tr>
<tr>
<td>Linjakumpu et al., 2002</td>
<td>Finland</td>
<td>$n = 1197$ Survey of all community-dwelling elderly individuals living in Lieto, Finland</td>
<td>Use of more than five medications concomitantly in the 7 days preceding the survey; prescription drugs only (psychotropic and non-psychotropic)</td>
<td>Demographic: Gender (Y), age (Y), marital status (Y) Clinical: Psychiatric and medical comorbidities (Y) Organizational: Primary and psychiatric care (Y), residence (Y)</td>
<td>Bivariate analysis</td>
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<tr>
<td>Study reference</td>
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<tr>
<td>Raymond et al., 2010</td>
<td>n = 314,014 Community pharmacy prescription records for community-dwelling and personal care home-dwelling individuals in Manitoba, Canada</td>
<td>Age range: Mean age: Unknown Age range: &gt;65 years</td>
<td>Prescription for a combination of second-generation antipsychotics with benzodiazepines or related medications, filled at least once in a particular quarter of a fiscal year; examined prevalent and incident usage; prevalent defined as individuals who filled a prescription during the study period and did fill a prescription for the same medication (or combination of medications) in the fiscal year prior to analysis; incident defined as individuals who filled a prescription during the study period and did not fill a prescription for the same medication (or combination of medications) in the fiscal year prior to analysis</td>
<td>Demographic: Gender (Y), age (Y), socioeconomic status (N), geographic region (Y) Organizational: Residence (Y)</td>
<td>Multivariate analysis</td>
</tr>
</tbody>
</table>
Analytic Strategies
Most studies conducted in individuals with IDD employed bivariate analyses, comparing individual variables (e.g., age, gender, marital status, residence, intellectual and adaptive functioning, behavioral problems, and psychiatric or medical comorbidities) between groups prescribed multiple medications to those not prescribed multiple medications. Multivariate analysis, which allows for examination of how two or more variables are associated with polypharmacy, was used in only one study of individuals with IDD (Stolker et al., 2001). Using multivariate logistic regression, Stolker and colleagues examined multiple patient parameters including age, gender, comorbidities, intellectual functioning, and behavioral problems with a small sample of 105 patients. In contrast to research conducted in groups with IDD, the majority of polypharmacy studies conducted in the elderly assessed the impact of multiple variables and, as described previously, utilized large population-based cohorts.

Variables That May Explain Variations in Rates of Polypharmacy
Clinical variables. The relationship between psychiatric comorbidities and polypharmacy was investigated in individuals with IDD. Individuals with IDD who had an additional psychiatric or seizure diagnosis (Burd et al., 1997) and those specifically diagnosed with a psychotic disorder (Stolker et al., 2001) were more likely to be prescribed psychotropic polypharmacy compared to individuals without these diagnoses (Burd et al., 1997; Stolker et al., 2001). Similarly, individuals prescribed psychotropic polypharmacy were significantly more likely to display bizarre and aggressive behavior compared to individuals who were not prescribed psychotropic polypharmacy (Stolker et al., 2001). In another study, a group with problem behaviors, defined by mental health issues including psychosis, aggression, autism, paranoia, depression, and avoidant personality disorder, was prescribed multiple psychotropic drugs more often than a group with less severe behavioral problems (Stolker et al., 2002). No studies in the IDD literature examined the relationship between other medical comorbidities and polypharmacy—likely because the vast majority of studies defined polypharmacy as the concurrent use of psychotropic medications and did not consider non-psychotropic medications.

Results from studies investigating polypharmacy and cognitive functioning in people with IDD found no differences across individuals with mild, moderate, or severe developmental disabilities recruited from an outpatient clinic or psychiatric hospital ward (Hurley et al., 2003; Stolker et al., 2001). No studies examined the specific relationship between adaptive functioning and polypharmacy; however, level of intellectual disability does account for adaptive functioning in addition to cognitive functioning.

In contrast to the literature on polypharmacy among people with IDD, which focused almost exclusively on psychiatric comorbidities, both psychiatric and medical comorbidities were associated with polypharmacy in the elderly, and rates increased with the number of comorbidities (Haider et al., 2009; Hajjar et al., 2005; Jorgensen, Johansson, Kennerfalk, Wallander, & Swedberg, 2001; Jyrkka et al., 2009a, 2009b; Linjakumpu et al., 2002). The association between polypharmacy and cognitive and adaptive functioning is less well understood in the elderly, with whom findings have been inconsistent (Jyrkka et al., 2009a, 2009b). Further, it is unclear whether the relationship between polypharmacy and cognitive functioning is caused by or predicted by medication use.

Demographic variables. Only one study of persons with IDD examined gender and polypharmacy, and no gender differences in rates of psychotropic polypharmacy were observed (Stolker et al., 2001). With respect to the age of the groups studied, polypharmacy studies in individuals with IDD varied. Some samples included only adolescents and adults, and others included adults, adolescents, and children. One study reported no age differences among individuals prescribed psychotropic polypharmacy (Stolker et al., 2001), and another study reported that individuals between 30 and 55 years of age were significantly more likely to be prescribed one or more antipsychotics compared to older and younger age groups (McGillivray & McCabe, 2006). No studies investigated the relationship between socioeconomic measures, marital status, or geographic region and polypharmacy in individuals with IDD.

In contrast, a number of demographic variables beyond just age and gender have been studied in the elderly. Gender (Bjerrum et al., 1998; Carey et al., 2008; Haider et al., 2009; Jyrkka et al., 2009a, 2009b; Linjakumpu et al., 2002), age (Bjerrum et al., 1998; Haider et al., 2009; Jorgensen et al., 2001;
Few organizational polypharmacy is defined. Consistent definitions are necessary when assessing the probability of potentially harmful drug–drug interactions. It is particularly important to consider a medication-overlap period when studying psychoactive medications because the dosage of some concurrent medications used to define polypharmacy varied greatly across studies, making comparisons between studies of the same population challenging. Studies of individuals with IDD typically considered two or more psychotropic drugs as polypharmacy, but other studies defined polypharmacy as combinations of specific psychotropic drug classes. In the elderly, polypharmacy definitions ranged from two to 10 or more medications. In studies of persons with IDD, polypharmacy research was strictly focused on psychotropic medications although studies of the elderly typically measured the total number of medications an individual was prescribed. Given the medical complexities experienced by people with IDD, researchers must be cognizant of all medication classes prescribed for concurrent use, particularly when assessing the probability of potentially harmful drug–drug interactions.

Most polypharmacy studies employed an arbitrary census date to count the number of medications and did not consider a medication-overlap period. It is particularly important to consider a medication-overlap period when studying psychotropic medications because the dosage of some

Jyrkka et al., 2009a, 2009b; Linjakumpu et al., 2002; Raymond et al., 2010, measures of socioeconomic status (Carey et al., 2008; Haider et al., 2009), and geographic region (Haider et al., 2009) have all been associated with polypharmacy. Overall, findings from this research indicate that females, older individuals, and those of lower socioeconomic status were most likely to be prescribed polypharmacy. Findings, however, were not consistent across all polypharmacy research in the elderly, as other studies reported no association between polypharmacy and these variables (Carey et al., 2008; Jorgensen et al., 2001; Raymond et al., 2010).

Organizational variables. Few organizational variables were studied among people with IDD. No studies examining the association between access to primary or psychiatric care, continuity of care, or frequency of care and polypharmacy in people with IDD were identified for inclusion in this review. The only organizational variable examined in this population was residential setting. Individuals with IDD living in large residential facilities were more likely to be prescribed multiple antipsychotics or a combination of antipsychotics and antidepressants compared to those in smaller residential settings although demographic and clinical variables were not controlled for in the analysis (Robertson et al., 2000).

In contrast, organizational variables, such as measures of health care receipt and residence, have been more extensively studied in polypharmacy literature among the elderly. After adjusting for demographic and clinical variables, studies found lower continuity of care (Hajjar et al., 2005) and higher frequency of primary care visits (Jorgensen et al., 2001) were associated with polypharmacy in the elderly. In terms of residence, while controlling for demographic and clinical variables, two studies observed no significant difference in the likelihood of being prescribed potentially inappropriate medications or polypharmacy between elderly individuals living in residential or nursing homes and in the community (Carey et al., 2008; Jyrkka et al., 2009b).

Discussion

This review provides a critical appraisal of research methods used to study polypharmacy, including measurement and definition of polypharmacy, study samples, analytic strategies, and variables that may explain variations in rates of polypharmacy. As polypharmacy research methods varied greatly between populations and even within the IDD literature, it is difficult to determine exactly how to use polypharmacy rates as an indicator of quality health care among persons with IDD. The review does, however, highlight a number of important lessons to inform future research in the area of polypharmacy and IDD.

Lesson 1: It is essential to be consistent in how polypharmacy is defined. To use polypharmacy rates as an indication of quality of health care, including comparisons of rates across health care jurisdictions or time points, it is crucial that standardized definitions of polypharmacy be employed for individuals with IDD. For example, one definition of polypharmacy could include both psychotropic and non-psychotropic medications, and another definition could examine only psychotropic polypharmacy. Consistent definitions are necessary to better understand and draw conclusions about polypharmacy in a given population. It is important to consider the number of drugs prescribed, the type of drugs prescribed, and when drugs are prescribed.

Across all populations reviewed, polypharmacy was most commonly defined as the concurrent use of multiple medications; however, the number of concurrent medications used to define polypharmacy was inconsistent across studies, making comparisons between studies of the same population challenging. Studies of individuals with IDD typically considered two or more psychotropic drugs as polypharmacy, but other studies defined polypharmacy as combinations of specific psychotropic drug classes. In the elderly, polypharmacy definitions ranged from two to 10 or more medications. In studies of persons with IDD, polypharmacy research was strictly focused on psychotropic medications although studies of the elderly typically measured the total number of medications an individual was prescribed. Given the medical complexities experienced by people with IDD, researchers must be cognizant of all medication classes prescribed for concurrent use, particularly when assessing the probability of potentially harmful drug–drug interactions.
The use of polypharmacy as an indicator of quality of health care, including the use of polypharmacy as an indicator of quality of health care, enhances the quality of polypharmacy research, allowing researchers to study individuals who are not receiving services or who are unable or unwilling to participate in research. It is possible that specific groups of individuals with IDD, for example, those with more severe disabilities who are unable to consent to participate in research, may be excluded using clinic or convenience-sampling strategies, limiting generalizability of findings to the general IDD population.

More recent studies and unpublished reports suggest an emerging shift toward population-based research of polypharmacy in persons with IDD (Cobigo, Stortz, Lake, Ouellette-Kuntz, & Lunskey, 2012; National Core Indicators, 2012; Wood et al., 2006). The use of administrative databases, which included medication use in those with IDD, will aid in obtaining large, population-based samples and enhance the quality of polypharmacy research, including the use of polypharmacy as an indicator of quality of health care.

Lesson 3: The study of polypharmacy must be linked to the development of specific clinical guidelines. It is important to recognize that the receipt of multiple medications may be clinically indicated in certain individuals and therefore appropriate. Examining inappropriate prescribing practices, specifically unnecessary medications and dangerous combinations, may provide researchers with a more meaningful way to assess quality of care with respect to medication receipt rather than simply counting people prescribed multiple medications. Guidelines detailing potentially dangerous or inappropriate medication combinations specific to the elderly exist and have been applied to some studies of polypharmacy in the elderly, including Beer’s Criteria (Fick et al., 2003) and START/STOPP Criteria (Gallagher, O’Connor, & O’Mahoney, 2011; O’Mahoney et al., 2010), but similar lists of medication combinations have not been developed specific to individuals with IDD. Existing medication guidelines for persons with IDD, for example, the consensus guidelines for primary health care of adults with developmental disabilities (Sullivan et al., 2011), The International Consensus Handbook: Psychotropic Medications and Developmental Disabilities (Reiss & Aman, 1998), the Frith Prescribing Guidelines in Adults with Learning Disability (Bhaumik & Branford, 2005), the Practice Parameters of the Assessment and Treatment of Children, Adolescents and Adults with Mental Retardation and Comorbid Mental Disorders (Szymanski & King, 1999), and the American Academy of Pediatrics Guidelines on the Management of Autism Spectrum Disorders (Myers & Plauche Johnson, 2007), all highlight the risks of polypharmacy or warn against polypharmacy. However, only one guideline advises against specific medication combinations, and none provide information on dosing or consideration of medication appropriateness for individuals with specific medical or psychiatric comorbidities. Further, when guidelines do discuss polypharmacy, they focus only on psychotropic medications and not specific risks associated with combinations of psychotropic and non-psychotropic medications.

Medication guidelines specific to the elderly discourage the prescription of certain psychotropic medications, including long-term use of antipsychotics and the prescription of antidepressants for persons with cognitive impairment (O’Mahoney et al., 2010). Antipsychotic and antidepressant medications are among the most frequently prescribed psychotropic medication classes in populations with IDD (Aman et al., 2003; Burd et al., 1997;
Esbensen et al., 2009; Hurley et al., 2003; Lake et al., 2012; Lott et al., 2004; Lunsky & Elserafi, 2012; Martin, Sechill, Klin, & Volkmar, 1999; Marshall, 2004; Molyneux et al., 1999; Robertson et al., 2000; Spreat et al., 2004), yet guidelines specific to the care of these individuals do not advise beyond general psychotropic medication considerations. It is clear that population-specific, explicit guidelines for prescribing medications are necessary to aid in assessing and improving the quality of care received by this population. These guidelines could also guide future research examining medication prescribing in persons with IDD by allowing researchers to monitor adherence to guidelines and appropriateness of medications prescribed, and to use this criteria as an indication of the quality of care with respect to medication received by those with IDD.

**Lesson 4:** It is important to study the association between polypharmacy and clinical, demographic, and organizational variables. It is not enough to simply describe polypharmacy rates; we need to also examine what variables are associated with polypharmacy to understand why polypharmacy rates differ within populations. In addition to clinical variables directly related to medication needs, there is evidence to suggest that other parameters may influence prescribing practices and the likelihood of an individual being dispensed polypharmacy. It is important to examine multiple clinical, demographic, and organizational variables in order to understand why individuals are prescribed polypharmacy in a particular population.

Some studies of the elderly investigated demographic, clinical, and organizational variables and utilized multivariate analyses, which allowed researchers to control for potential confounding variables and more clearly assess the relationships between polypharmacy and variables of interest. In all but one study of people with IDD, researchers failed to employ this type of analysis, making it harder to draw definite conclusions from the results presented. In the only published IDD paper in our review that employed multivariate analysis, over 10 variables were tested in the regression model with a sample of only 105 individuals. A general rule of thumb when conducting regression analyses is that a minimum of 10 to 20 outcome events are required per predictor (Nunnally, 1978); thus, results from the previous analysis may not be valid. In addition, because the sample was obtained from a psychiatric hospital ward, the generalizability of these findings to the greater IDD population is questionable. No studies of individuals with IDD examined clinical, demographic, and organizational variables, and therefore, they were not able to control for clinical variables, which may have confounded relationships between polypharmacy and demographies or organizational variables. As a result, it is unclear whether differences in rates of polypharmacy are attributable to the medication needs of specific populations or to external factors, such as prescribing physician or residence. Without this information, it is difficult to assess the extent to which nonclinical variables may influence prescribing practices.

Additionally, other variables, including psychotherapeutic and psychosocial therapies have not been investigated and may influence the likelihood of receiving polypharmacy in individuals with IDD. In terms of organizational variables, it may also be important to consider whether specific medications are paid out of pocket or funded by government and/or insurance programs. Consideration of clinical, demographic, and organizational variables in the study of polypharmacy will aid researchers in understanding external factors that drive prescribing practices for populations with IDD and provide additional information that will assist in interpretation of polypharmacy rates as they relate to quality of care.

**Conclusions and Future Directions**

Research on polypharmacy among individuals with IDD is still in its infancy. We know that polypharmacy occurs at high rates in this population, but the long-term consequences and why it occurs remain unclear. We also know that some clinical, demographic, and organizational variables appear to be associated with polypharmacy, but it continues to be challenging to synthesize findings given the methodological limitations of many studies. To begin to address these research gaps and to use polypharmacy as an indicator of quality of care received by individuals with IDD, we must heed the four lessons identified through this review.

Consistency in the number of medications studied is necessary across polypharmacy studies. In the absence of detailed guidelines related to medication appropriateness for people with IDD, categorization of polypharmacy should, at minimum, examine the use of two or more medications. It may also be informative to further categorize...
those prescribed multiple medications, similar to research conducted in the elderly, which has considered varying levels of polypharmacy (Bjerrum et al., 1998; Haider et al., 2009; Jyrkka et al. 2009a, 2009b). Veehof, Steward, Meyboom-de Jong, and Haaijer-Ruskamp (1999) utilized the following medication categories to define minor, moderate, and major polypharmacy in the elderly: 2–3, 4–5, and >5. A similar categorization scheme may be useful in the study of polypharmacy in individuals with IDD. When feasible, we must also consider all medication types and build in an acceptable medication-overlap period or, if not possible, interpret polypharmacy rates with caution. Based on recommendations for monitoring prescription medications in the consensus guidelines for the primary health care of adults with developmental disabilities (Sullivan et al., 2011), medications should be examined at three months and six months of concurrent use.

Conducting population-level, prospective cohort studies in individuals with IDD represent an ideal starting point for this research; however, issues of feasibility may make this work challenging to carry out. Large administrative databases containing medication information are an ideal data source for polypharmacy studies; however, identifying groups with IDD within these databases can be difficult (Cobigo et al., 2012). It is evident from the polypharmacy literature that population-based research in persons with IDD is imperative to increase generalizability and to gain a greater understanding of polypharmacy in this population. For some individuals, polypharmacy is warranted, and the number of medications in itself is not an indication of inappropriate care. In order to assess the appropriateness of specific medications and medication combinations, medication guidelines that address these issues for persons with IDD must be developed. Current guidelines address the use of two antipsychotic medications concurrently (Reiss & Aman, 1998; Taylor, Paton, & Kapur, 2012), but more detailed guidelines addressing appropriateness of other medications and combinations for individuals with IDD are required. Collaboration among scientists, policymakers, pharmacists, and medication prescribers is needed to help facilitate the further development of medication guidelines for people with IDD. Collaborating with experts across these different fields will inform the types of questions we ask, and will help determine how best to translate findings into meaningful change for the care of individuals with IDD. These collaborations also play a key role in the development of research to enhance our knowledge and understanding of polypharmacy in this population. Finally, to use rates of polypharmacy as an indicator of quality of health care over time or across systems may require adjusting for covariates. Going forward, research on polypharmacy in persons with IDD should involve multivariate analyses to better understand what factors impact the likelihood of receiving polypharmacy.

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