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Consensus List of Signals to Detect Potential Adverse Drug Reactions in Nursing Homes

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Abstract

OBJECTIVES—To develop a consensus list of agreed upon laboratory, pharmacy, and Minimum Data Set signals that can be used by a computer system in the nursing home to detect potential adverse drug reactions (ADRs).

DESIGN AND SETTING—Literature search for potential ADR signals, followed by an Internet-based, two-round, modified Delphi survey of experts in geriatrics.

PARTICIPANTS—Panel of 13 physicians, 10 pharmacists, and 13 advanced practitioners.

MEASUREMENTS—Mean score and 95% confidence interval (CI) for each of 80 signals rated on a 5-point Likert scale (5=strong agreement with likelihood of indicating potential ADRs). Consensus agreement indicated by a lower-limit 95% CI of ≥ 4.0 .

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Author Contributions: Steven Handler, led development of the study concept and design; participated in acquisition, analysis, and interpretation of the data; and led manuscript preparation. Joseph Hanlon, Stephanie Studenski, Douglas Fridsma, and Subashan Perera were involved with study design and implementation, review of data integrity, interpretation of the data, and manuscript editing. Yazan Roumani was involved with the acquisition of the data, analysis and interpretation of data, and manuscript editing. David Nace, Melissa Saul, and Nick Castle participated in discussions of the study concept and design, data interpretation, and manuscript development.

RESULTS—Panelists reached consensus agreement on 40 signals: 15 laboratory/medication combinations, 12 medication concentrations, 10 antidotes, and 3 Resident Assessment Protocols (RAPs). Highest consensus scores (4.6; 95% CI, 4.4–4.9 or 4.4–4.8) were for naloxone when taking opioid analgesics; phytonadione when taking warfarin; dextrose, glucagon, or liquid glucose when taking hypoglycemic agents; medication-induced hypoglycemia; supratherapeutic international normalized ratio when taking warfarin; and triggering the Falls RAP when taking certain medications.

CONCLUSION—A multidisciplinary expert panel was able to reach consensus agreement on a list of signals to detect potential ADRs in nursing home residents. The results of this study can be used to prioritize an initial list of signals to be included in paper or computer-based methods for potential ADR detection.

Keywords

adverse drug events; adverse drug reactions; nursing homes; Delphi technique

INTRODUCTION

Adverse drug reactions (defined as any response to a drug that is noxious or unintended, and which occurs at doses for prophylaxis, diagnosis, or therapy) are the most frequent medication-related adverse events in the nursing home setting, with an incidence ranging from 1.19 to 7.26 per 100 resident-months.¹ Other types of medication-related adverse events, include therapeutic failures and adverse drug withdrawal events. However, their precise incidence and impact have not been well characterized in the literature.² Data from the largest study on adverse drug reactions (ADRs) in nursing homes suggest that over half of the events are preventable, and that 70% are associated with monitoring errors.³ Although comprehensive chart review is the primary ADR case-finding technique for research, and is considered by some to be the “gold standard,”⁴ it is time-consuming, costly, and impractical for routine clinical use.⁵ Therefore, alternative surveillance systems are needed in nursing homes to detect and minimize the potential consequences of ADRs.

ADRs can be detected by computerized clinical event monitors via the processing of laboratory test result signals and pharmacy order signals.^{6–8} Hospital studies indicate that these automated clinical decision-support systems, which provide feedback to healthcare professionals based on information available in electronic format, are less expensive and much faster to use than manual chart reviews, and can identify events not normally detected by clinicians during the course of routine care.^{4, 9} More recently, computerized ADR detection has been examined in the ambulatory and nursing home settings using many of the same pharmacy and laboratory signals used by hospital-based systems.^{7, 10, 11}

ADR signals from pharmacy order and laboratory test results in nursing homes are likely to differ from those used in the hospital setting. This is because the number and types of medications prescribed and the laboratory tests ordered for nursing home residents vary considerably from those of hospitalized patients.¹² With the trend towards centralization of laboratory, pharmacy, and Minimum Data Set data, resident-specific information available in electronic format is becoming increasingly more available in nursing homes.¹³ The purpose of this study was to develop a consensus list of laboratory, pharmacy, and Minimum Data Set signals that can be used by a computer system in the nursing home to detect potential ADRs.

METHODS

Literature Review and Identification of Initial Set of Signals

We conducted a comprehensive literature search to create a preliminary list of signals that can be used to detect potential ADRs in nursing homes. With the assistance of a medical librarian, we searched OVID MEDLINE, OVID CINHAL, and EMBASE for articles published in all languages between January 1, 1985, and July 1, 2006. In OVID, we searched for the following medical subject headings (MeSH) keywords, and text words: aged, adverse drug event, adverse drug reaction, adverse drug reaction reporting systems, clinical event monitor, clinical decisions support systems, clinical laboratory information systems, clinical pharmacy information system, computer generated signals, decision support system, drug monitoring, homes for the aged, medication errors, nursing homes, and physiologic monitoring. In EMBASE, we searched for the above terms, plus the following Emtree keywords: computer assisted drug therapy and drug surveillance program. The first author (SMH) supplemented the computerized search by reviewing the reference lists from the identified articles, recent reviews, textbooks, and personal files.

A total of 29 publications were identified.^{6-8,10-35} Two authors (SMH and JTH) reviewed these publications for relevance, compiled a preliminary list of signals, and placed each potential signal into one of four categories: 1) laboratory/medication combination signals (triggered by abnormal laboratory values when certain medications are present); 2) medication concentration signals (triggered by elevated, or supratherapeutic medication concentrations); 3) antidote signals (triggered by administration of medications given to counteract the effects of a medication with toxic effects); 4) Resident Assessment Protocol (RAP)¹⁴ signals (triggered by responses to certain Minimum Data Set items, and taking of certain medications). The first author (SMH) used standard pharmacology textbooks¹⁵⁻¹⁷ to provide specific examples of medications that may be associated with the firing of each of the signals (e.g., elevated creatinine caused by diuretics or hyperglycemia caused by prednisone) with the goal of clarifying the signals. Then other members of the clinical investigative team (JTH, DAN, DBF, and SAS) reviewed and further refined the list of signals.

The final list consisted of 35 laboratory/medication combination signals, 16 medication concentration signals, 20 antidote signals, and 9 RAP signals, for a total of 80 signals (**Appendix**) to be included in the Delphi survey.

Selection of Study Methodology and Participants

Our study involved the use of an Internet-based, two-round, modified Delphi survey of experts in the field of nursing home care. The Delphi methodology is a structured group interaction process that is directed in "rounds" of opinion collection and feedback.¹⁸ We selected the modified web-based Delphi consensus method because research suggests that accurate and reliable assessments can be achieved by consulting a panel of experts and subsequently accepting the group consensus as the best estimate of the answer to a particular question.¹⁹ The modified Delphi method is especially useful in studies that deal with medication safety in older adults.²⁰⁻²³ The methodology used in this study differed from the Delphi process developed by the RAND Corporation that relies on face-to-face meetings to achieve consensus.²⁴ However, the modified method enables a group of experts to be contacted inexpensively and without geographic limitations. The rounds of the survey were completed confidentially, allowing each participant to present and react to ideas without being biased by knowing the identities of other participants.

We selected a multidisciplinary expert panel of members from three professions: physicians, pharmacists, and advanced practitioners (i.e., physician assistants or nurse practitioners). We

chose these professions because they are all involved in the monitoring phase of the medication use process (i.e., assess resident response to medication and document outcomes).²⁵ After obtaining the names of potential participants from national geriatrics or nursing home organizations, we selected individuals based on their extensive clinical practice or large number of publications in the area of nursing home care. Our goal was to have a similar number of participants from each profession. Because we had encountered a low response rate from some groups in a previous study,²⁶ we invited a total of 57 health care professionals, including 23 physicians, 13 pharmacists, and 21 advanced practitioners to participate.

To improve the response rate and reduce the possibility of nonrespondent bias, we employed multiple methods, including university sponsorship, nominal monetary incentives (\$75 upon completion of both rounds), and having respondents complete the rounds on the Internet.²⁷

Administration and Analysis of the Survey

We contacted the experts through an e-mail invitation included with round 1. We asked them to complete each survey round within 2 weeks, and sent them a reminder e-mail if they did not do so. During each round, we provided participants with a list of signals, a list of medications that might be associated with the firing of each signal, and supporting references concerning the signals. We asked them to use a 5-point Likert scale to evaluate their agreement or disagreement with statements concerning the likelihood that each signal would be associated with a potential ADR in the nursing home setting. The scale ranged from 1, (indicating strong disagreement), to 5, (indicating strong agreement). For the purposes of the study, we operationally defined a nursing home as having custodial, skilled, and subacute levels of care. At the completion of round 1, we gave the participants the opportunity to modify existing signals or provide suggestions for additional signals to include in round 2. We determined in advance that we would include any new or modified signals that were suggested by 2 or more participants.

After round 1, we compiled the scores and computed a weighted mean score and 95% confidence interval (CI) for each signal. The weighting of individual ratings was designed to ensure that all three professions had equal influence, regardless of the number of participants in each profession. Based on work previously published by our group,^{28–30} we examined the lower and upper limits of the 95% CIs, and then classified each signal into one of three categories: accepted signals, defined as those having a score with a lower-limit 95% CI of ≥ 4.0 (indicating consensus agreement); rejected signals, defined as those having a score with an upper-limit 95% CI of < 3.0 (consensus disagreement); or equivocal, defined as those having a score with a lower-limit 95% CI between 3.0 and 3.9 (indicating the need for reevaluation).

In round 2, we did not include the signals that were already accepted or already rejected. We included only the equivocal signals from round 1. For each equivocal signal, we provided each participant with his or her round 1 individual score and with the round 1 weighted mean group score to aid in the consensus-building process.

After round 2, we repeated the processes of compiling scores and computing weighted scores and 95% CIs. Again, the weighting of individual ratings ensured that all three professions had equal influence. We again classified signals as accepted if they had a lower-limit 95% CI of ≥ 4.0 (indicating consensus agreement). We classified all other signals as rejected.

For all statistical analyses, we used SAS version 9 for Windows (SAS Institute, Inc., Cary, NC). The University of Pittsburgh Institutional Review Board approved the study as exempt;

hence, informed consent was not needed for study participation. The external funding sources had no involvement in study design or collection, analysis, or interpretation of data, nor did they review or approve this manuscript.

RESULTS

Round 1

For round 1, the study included 13 physicians, 10 pharmacists, and 13 advanced practitioners, for an overall response rate of 63.2% (36/57). The response rate was 56.5% (13/23) for the invited physicians, 61.9% (13/21) for the invited advanced practitioners, and 76.9% (10/13) for the invited pharmacists. The majority of participants were female (66.7%), were affiliated with an academic medical center (63.9%), and worked in the nursing home setting for a median of 5 years (100%).

At the end of round 1, of the 80 signals that were considered, 32 were accepted, 0 were rejected, and 48 were equivocal. The accepted signals were 13 laboratory/medication combination signals (Table 1), 6 medication concentration signals (Table 2), 10 antidote signals (Table 3), and 3 RAP signals (Table 4). There were no signals suggested by two or more panelists.

Round 2

For round 2, the study included 11 of the 13 physicians, all 10 of the pharmacists, and all 13 of the advanced practitioners. The overall response rate for round 2 was 94.4% (34/36). At the end of round 2, of the 48 signals that were reconsidered because of their earlier equivocal classification, 8 were accepted. The accepted signals were 2 laboratory/medication combination signals (Table 1) and 6 medication concentration signals (Table 2).

Overall, 15 of 35 (42.9%) of the laboratory/medication combination signals, 12 of 16 (75%) of the medication concentration signals, 10 of 20 (50%) of the antidote signals, and 3 of 9 (33.3%) of the RAP signals reached consensus and were accepted.

The highest consensus scores (4.6; 95% CI, 4.4–4.9 or 4.4–4.8) were for naloxone when taking opioid analgesics; phytonadione (Vitamin K) when taking warfarin; dextrose, glucagon, or liquid glucose when taking hypoglycemic agents; medication-induced hypoglycemia; supratherapeutic international normalized ratio when taking warfarin; and triggering the Falls RAP when taking certain medications.

DISCUSSION

A multidisciplinary expert panel of nursing home physicians, pharmacists, and advanced practitioners were able to reach consensus agreement on a list of 40 signals that can be used by a computer system to detect potential ADRs in the nursing home setting. Laboratory/medication combinations accounted for over one-third of all signals that reached consensus. Of the 15 laboratory/medication combination signals that the panelists agreed were appropriate for the nursing home setting, 8 were not reported in the 2005 study of Gurwitz et al.,¹¹ which to our knowledge is the only published study concerning a clinical event monitor to detect potential ADRs in nursing homes. These 8 additional signals were drug-induced episodes of the following: hypoglycemia, hyponatremia, leukopenia, agranulocytosis/neutropenia, a supratherapeutic activated partial thromboplastin time, a supratherapeutic thyroid stimulating hormone concentration, an elevated creatinine or blood urea nitrogen concentration, and an elevated creatine phosphokinase concentration.

The next most common signal category reaching consensus was medication concentrations. The goal of therapeutic medication monitoring is to guide dosing by means of drug concentration measurements. This is particularly useful in cases in which the range between the dose necessary to achieve beneficial effects and the dose causing ADRs is narrow, and when the medication concentration is not readily predictable from the dose prescribed. Moreover, serum medication concentrations are likely to be most useful when used to help confirm or refute a resident's signs or symptoms suggestive of toxicity or lack of efficacy. When the panelists were asked to consider 16 medication concentration signals, they achieved consensus on 12 (75%), and it is not surprising that these were for drugs with narrow therapeutic ranges.

A recent study by Raebel et al.,³¹ suggests that monitoring narrow therapeutic range drugs is not being done routinely, with as many as 50% of older adults not receiving drug concentration monitoring during 1 year of use. To reduce the potential for ADRs in the nursing home setting, the Center for Medicare and Medicaid Services (CMS) recommends routine periodic medication monitoring for most narrow therapeutic range drugs listed in their F329 guidelines (the deficiency citation for unnecessary drugs).³² This CMS recommendation extends to all residents, regardless of whether they are exhibiting signs or symptoms suggestive of toxicity or lack of efficacy. It is important to note however that if a medication concentration comes back elevated when ordered for diagnostic purposes, the likelihood of a potential ADR is significantly higher than if it was being ordered on a routine basis. The rationale for this is that the prior odds of a potential ADR are significantly increased because the underlying assumption is that the resident is already receiving the medication of interest, and the prescribing clinician is aware of the possibility of an ADR.³³ Of note, our panelists reached consensus on 3 narrow therapeutic range drugs not mentioned in the F329 guidelines—namely, concentrations of Class Ia antiarrhythmics including: procainamide, disopyramide, and quinidine.

Antidote signals accounted for one-quarter of the final 40 signals. Four of the 10 antidote signals had not been reported in the study of Gurwitz et al.,¹¹ and these were the administration of epinephrine, digoxin immune Fab, lepirudin, or a medication with anticholinergic properties to treat extrapyramidal symptoms. Four of the 10 antidote signals that had been reported by Gurwitz et al.¹¹ did not reach consensus in our study, and these were the administration of an antihistamine, an oral or topical steroid, or topical nystatin and the administration of a hypoglycemic agent to an individual taking glucocorticoids. It is important to note, that in a recent systematic review of the signals used by hospital-based clinical event monitors to detect potential ADRs, the antidote signal category had the lowest overall positive predictive values.³⁴ The authors of this review concluded that the performance characteristics of this signal category was lowest because antidotes can be used to treat multiple medical conditions, only a fraction of which are related to the presence of an ADR.

Unique to this study was that consensus was reached on 3 RAP signals. Studies in the nursing home setting are currently evaluating the effectiveness of computerized decision support systems on 2 of the RAP signals on which our panelists reached consensus—namely, the Falls RAP and the Delirium RAP.³⁵ This reflects that the evidence for certain medications being associated with these specific geriatric syndromes is generally well accepted.^{36, 37} Participants also reached consensus that the Dehydration/Fluid Maintenance RAP be used as a signal to detect potential ADRs for individuals taking certain medications.

Strengths and Limitations

Our study had several strengths. First, we chose to include a multidisciplinary panel of physician, pharmacist, and advanced practitioner experts to determine which signals can be

used to detect potential ADRs. Our methodology ensured that all clinicians involved in the monitoring phase of the medication use process in the nursing home setting were included, and that their responses were weighted to ensure that each profession had an equal influence on the results. Second, to improve the survey response rate and reduce the possibility of nonrespondent bias, we employed multiple methods, including university sponsorship, monetary incentives, providing the survey on the Internet, and the distributing reminders to participants.²⁷ The overall initial and second round response rates in our study exceeded the minimally acceptable mean response rate of 60% for mail surveys reported in the medical literature.³⁸

Our study had several potential limitations. First, we used a convenience sample of physician, pharmacist, and advanced practitioner experts to participate in the Delphi survey. As a result, the majority of respondents were affiliated with an academic institution. Using a random sampling technique may have strengthened the study by increasing the generalizability to the universe of clinical practitioners. Second, we did not hold face-to-face meetings of the panelists, a practice that is sometimes done with Delphi surveys.^{19, 24, 39} Bringing the panelists together allows individual respondents to incorporate the perspectives of others, and may have resulted in further refinement of the signals while facilitating the consensus process. However, in person meetings might have limited the broad geographic representation we were able to achieve with the use of the Internet. In addition, by offering two rounds in the survey, respondents did benefit from seeing the opinions of others. Third, we did not provide 95% confidence intervals for equivocal signals to panelists during the second round. Information on the distribution of responses may have been useful to the panelists in order to achieve consensus. Fourth, the panelists reached consensus on 40 signals at this time. As new research contributes more information about medication safety, the list of signals will need to be modified and may expand.

Implications and Further Research

The Institute of Medicine recommends that all health care facilities continuously assess medication safety through the development and evaluation of various types of data-driven triggers for detecting ADRs. This assessment should occur during routine monitoring, and for diagnostic confirmation of signs or symptoms suggestive of toxicity or lack of efficacy.^{40, 41} Clinical event monitors can address this recommendation by integrating various sources of information for the purpose of ADR detection. All nursing homes are currently capable of transmitting Minimum Data Set information electronically, and the use of computerized laboratory and medication records is likely to increase significantly over the coming years.⁴² These monitors are feasible given knowledge of the data structure of the information resources and certain programming capacity. In nursing homes with appropriate health information technology infrastructure, the results of our study can be used to create or modify clinical event monitor systems to automate the detection of potential ADRs.

In nursing homes without appropriate infrastructure, the results can be used to prioritize the signals to be included in a paper-based trigger tool. The trigger tool methodology, developed in part by the Institute of Healthcare Improvement, greatly simplifies the chart review process by allowing rapid and systematic examination of charts to extract relevant data. Trigger tools have been successfully used to demonstrate the benefits of low-cost error detection strategies focused on high-risk medications in a variety of clinical settings.^{43, 44} Regardless of whether computer or paper-based methods for detecting potential ADRs are used, a more detailed assessment of the resident would be required to determine if an actual ADR is present.

Further research is needed in several areas. Formal research is needed to determine the incidence and the positive predictive values of individual signals in nursing homes with

different levels of care (e.g., custodial, skilled, and subacute care). Future studies are also needed to improve the performance characteristics of antidote signals, which can possibly be enhanced by linking the use of these medications to changes in drug therapy or interventions that occurred prior to their use. These data will help nursing homes further prioritize the signals to be included in their computerized or paper-based trigger tools, and will thereby help them maximize the detection of potential ADRs, and minimize the number of false-positive alerts. Studies should also be conducted to determine if certain errors of omission, including the failure to monitor narrow therapeutic index medications or conduct laboratory studies while prescribing certain medications, may lead to an increase in potential ADRs in the nursing home setting. Research is also needed to determine if ADR detection rates can be improved by combining multiple data sources (e.g., laboratory, pharmacy, and health care records) to gain a better understanding of the context of the data as they relate to residents' underlying medical conditions.^{45–47}

CONCLUSION

A multidisciplinary expert panel was able to reach consensus agreement on a defined list of signals of potential ADRs in nursing home residents. This is a necessary initial step toward detecting and reducing the future occurrence and impact of ADRs in the nursing home setting. The results of this study can be used to prioritize an initial list of signals to be included in paper or computer-based method for potential ADR detection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Final Consensus List of Laboratory/Medication Combination Signals for Detecting Adverse Drug Reactions in the Nursing Home Setting*

Laboratory/Medication Combination Signals	Mean Score	95% CI
Hypoglycemia (as indicated by a low or decreasing glucose concentration) is found in an individual taking a drug that may cause or worsen hypoglycemia	4.6	4.4–4.8
Supratherapeutic (above upper limit of normal range) international normalized ratio (INR) is found in an individual taking warfarin	4.6	4.4–4.8
<i>Clostridium difficile</i> toxin is found in an individual taking a drug that may cause pseudomembranous colitis	4.5	4.3–4.7
Hyperkalemia (as indicated by a high or increasing potassium concentration) is found in an individual taking a drug that may cause or worsen hyperkalemia	4.5	4.3–4.7
Hypokalemia (as indicated by a low or decreasing potassium concentration) is found in an individual taking a drug that may cause or worsen hypokalemia	4.5	4.3–4.7
Thrombocytopenia (as indicated by a low or decreasing platelet count) is found in an individual taking a drug that may cause or worsen thrombocytopenia	4.5	4.3–4.7
Supratherapeutic activated partial thromboplastin time (PTT) is found in an individual taking heparin	4.4	4.2–4.7
Subtherapeutic concentration (below lower limit of normal range) of thyroid-stimulating hormone (TSH) or elevated concentration of thyroxine (T4) is found in an individual taking a drug that may cause hyperthyroidism	4.4	4.2–4.6
Hyponatremia (as indicated by a low or decreasing sodium concentration) is found in an individual taking a drug that may cause or worsen hyponatremia	4.4	4.2–4.5
Leukopenia (as indicated by a low or decreasing white blood cell count) is found in an individual taking a drug that may cause or worsen leukopenia	4.3	4.1–4.6
Elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) concentration is found in an individual taking a drug that may cause hepatocellular toxicity	4.3	4.1–4.5
Elevated creatinine or blood urea nitrogen (BUN) concentration is found in an individual taking a drug that may increase creatinine or BUN	4.3	4.1–4.5
Supratherapeutic concentration of TSH or decreased concentration of T4 is found in an individual taking a drug that may cause hypothyroidism [†]	4.3	4.1–4.4
Agranulocytosis or neutropenia (as indicated by a low or decreasing neutrophil count) is found in an individual taking a drug that may cause or worsen agranulocytosis or neutropenia [†]	4.2	4.1–4.3
Elevated creatine phosphokinase (CPK) concentration is found in an individual taking a drug that may increase CPK	4.2	4.0–4.4

* Panel members rated each item on a 5-point Likert scale, with 5 indicating strong agreement with the likelihood that the item signaled an adverse drug reaction. The mean likelihood score and 95% confidence interval (CI) were calculated for each item. Panel consensus was indicated by a lower-limit 95% CI of ≥ 4.0 .

[†] Panel consensus was not reached until round 2 of the Delphi survey.

Table 2

Final Consensus List of Medication Concentration Signals for Detecting Adverse Drug Reactions in the Nursing Home Setting*

Medication Concentration Signals	Mean Score	95% CI
Aminoglycoside peak or trough concentration is supratherapeutic in an individual taking an aminoglycoside antibiotic (e.g., amikacin, gentamicin, or tobramycin)	4.4	4.2–4.7
Phenytoin concentration is supratherapeutic in an individual taking phenytoin	4.4	4.1–4.7
Lithium concentration is supratherapeutic in an individual taking lithium [†]	4.3	4.1–4.5
Theophylline trough concentration is supratherapeutic in an individual Taking theophylline	4.3	4.0–4.7
Digoxin concentration is supratherapeutic in an individual taking digoxin	4.3	4.0–4.6
Procainamide concentration or N-acetylprocainamide (NAPA) concentration is supratherapeutic in an individual taking procainamide	4.3	4.0–4.6
Primidone (Mysoline) concentration or phenobarbital concentration is Supratherapeutic in an individual taking primidone	4.3	4.0–4.5
Quinidine concentration is supratherapeutic in an individual taking quinidine [†]	4.2	4.1–4.4
Valproic acid concentration is supratherapeutic in an individual taking Valproic acid [†]	4.2	4.1–4.4
Phenobarbital concentration is supratherapeutic in an individual taking phenobarbital [†]	4.2	4.0–4.5
Carbamazepine concentration is supratherapeutic in an individual taking carbamazepine [†]	4.2	4.0–4.4
Disopyramide (Norpace) concentration is supratherapeutic in an individual taking disopyramide [†]	4.2	4.0–4.4

* Panel members rated each item on a 5-point Likert scale, with 5 indicating strong agreement with the likelihood that the item signaled an adverse drug reaction. The mean likelihood score and 95% confidence interval (CI) were calculated for each item. Panel consensus was indicated by a lower-limit 95% CI of ≥ 4.0 .

[†] Panel consensus was not reached until round 2 of the Delphi survey.

Table 3

Final Consensus List of Antidote Signals for Detecting Adverse Drug Reactions in the Nursing Home Setting*

Antidote Signals	Mean Score	95% CI
Naloxone (Narcan) is given to an individual taking an opioid analgesic	4.6	4.4–4.9
Phytonadione (vitamin K) in oral, subcutaneous, or intravenous form is given to an individual taking warfarin	4.6	4.4–4.9
Dextrose 50%, glucagon, or liquid glucose is given to an individual taking a drug that may cause hypoglycemia	4.6	4.4–4.8
Protamine sulfate is given to an individual taking heparin	4.5	4.3–4.8
Digoxin immune Fab (Digibind) is given to an individual with a supratherapeutic digoxin concentration	4.5	4.2–4.8
Epinephrine is given to an individual taking a drug that may cause an anaphylactic reaction	4.4	4.1–4.8
Metronidazole (oral) or vancomycin (oral) is given to an individual who has recently taken a drug that may cause pseudomembranous colitis	4.4	4.1–4.7
Benzotropine (Cogentin), diphenhydramine, or trihexyphenidyl (Artane) is given to an individual taking a drug that may cause extrapyramidal symptoms	4.4	4.1–4.6
Lepirudin (Refludan) is given to an individual taking a drug that may cause heparin-induced thrombocytopenia	4.4	4.1–4.6
Sodium polystyrene (Kayexalate) is given to an individual taking a drug that may cause hyperkalemia	4.3	4.0–4.6

* Panel members rated each item on a 5-point Likert scale, with 5 indicating strong agreement with the likelihood that the item signaled an adverse drug reaction. The mean likelihood score and 95% confidence interval (CI) were calculated for each item. Panel consensus was indicated by a lower-limit 95% CI of ≥ 4.0 . For all items shown, panel consensus was reached during round 1 of the Delphi survey.

Table 4

Final Consensus List of Resident Assessment Protocol (RAP) Signals for Detecting Adverse Drug Reactions in the Nursing Home Setting*

RAP Signals	Mean Score	95% CI
Falls RAP is triggered in an individual taking a drug that may cause or worsen falls (falls with or without injury)	4.6	4.4–4.8
Delirium RAP is triggered in an individual taking a drug that may cause or worsen delirium (periodic disordered thinking or awareness)	4.5	4.3–4.7
Dehydration/Fluid Maintenance RAP is triggered in an individual taking a drug that may cause or worsen dehydration (fluid loss exceeding the amount of fluid intake)	4.4	4.2–4.6

* Panel members rated each item on a 5-point Likert scale, with 5 indicating strong agreement with the likelihood that the item signaled an adverse drug reaction. The mean likelihood score and 95% confidence interval (CI) were calculated for each item. Panel consensus was indicated by a lower-limit 95% CI of ≥ 4.0 . For all items shown, panel consensus was reached during round 1 of the Delphi survey.