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Nurse-led medicines' monitoring in care homes study protocol: a process evaluation of the impact and sustainability of the adverse drug reaction (ADRe) profile for mental health medicines

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ABSTRACT

Introduction Improved medicines' management could lead to real and sustainable improvements to the care of older adults. The overuse of mental health medicines has featured in many reports, and insufficient patient monitoring has been identified as an important cause of medicine-related harms. Nurse-led monitoring using the structured adverse drug reaction (ADRe) profile identifies and addresses the adverse effects of mental health medicines. Our study investigates clinical impact and what is needed to sustain utilisation in routine practice in care homes.

Methods and analysis This process evaluation will use interviews and observations with the participants of all five homes involved in earlier research, and five newly recruited homes caring for people prescribed mental health medicines. The ADRe profile is implemented by nurses, within existing resources, to check for signs and symptoms of ADRs, initiate amelioration and share findings with pharmacists and prescribers for medication review. Outcome measures are the numbers and nature of problems addressed and understanding of changes needed to optimise clinical gain and sustain implementation. Data will be collected by 30 observations and 30 semistructured interviews. Clinical gains will be described and narrated. Interview analysis will be based on the constant comparative method.

Ethics and dissemination Ethical approval was conferred by the National Health Service Wales Research Ethics Committee. If the ADRe profile can be sustained in routine practice, it has potential to (1) improve the lives of patients, for example, by reducing pain and sedation, and (2) assist in early identification of problems caused by ADRs. Therefore, in addition to peer-reviewed publications and conferences, we shall communicate our findings to healthcare professionals, policy-makers and sector regulators.

Trial registration number NCT03110471.

Strengths and limitations of this study

- This intervention is the first simple, low-risk, low-cost, multidisciplinary strategy to check patients comprehensively for potential adverse effects of their medicines and ameliorate any harms identified.
- For the last decade, some 5%–8% of UK unplanned hospital admissions have been caused by adverse drug reactions (ADRs), most of which were preventable. Our intervention has potential to address this situation, but sustainability needs to be tested.
- The intervention was effective in a pragmatic randomised controlled trial, but a qualitative exploration of how it embeds into routine care is needed to highlight (1) how clinical gains are achieved and (2) the barriers to and facilitators of sustained implementation.
- We are working with volunteer care homes in South West Wales, and the transferability of findings will depend on readers' interpretations of their practical adequacy and professionals' assessment of the importance of using ADRe.

BACKGROUND

The success of the WHO Third Global Patient Safety Challenge on Medication Safety will depend on effective strategies to address concerns that 'medicines sometimes cause serious harm if taken incorrectly, *monitored insufficiently* or as the result of errors, accidents or communication problems'.[1] Meeting the challenge of insufficient monitoring will demand innovation and change to current practice. Most adverse drug reactions (ADRs) or side effects (glossary, online supplementary file 1) are due to poor monitoring, not poor prescribing.[2–6]

Preventable ADRs have proven an intractable problem over the last decade, causing 5%–8% of unplanned UK hospital admissions,[7 8] costing the National Health Service (NHS) £1bn–2.5bn each year.[9] The problem is at least as extensive in developing countries, at ~10% of admissions.[10] Most adverse drug events (ADEs) (glossary, online supplementary file 1), ADRs (glossary, online supplementary file 1) and medicines' mismanagement (including errors by patients and professionals) are preventable,[8 11] but there are no comprehensive systematic approaches to the problem.

Some 50% of residents in UK care homes (glossary, online supplementary file 1) are prescribed mental health medicines,[12] doses in care homes[13] and primary care[14] are often excessive, 4.8%–37% of older people with cognitive impairment have ADRs[15] and the proportion of care home residents exposed to inappropriate medications (any) ranges from 34% (definition from the Swedish National Board of Health and Welfare)[16] to >50% (definitions based on instruments selected by each study author).[17] ADRs to mental health medicines can be life-threatening (eg, cardiac arrhythmias, cardiac hypofunction) or debilitating (eg, drug-induced Parkinsonism, ataxia, postural hypotension) or subtle and mistaken for signs of ageing or underlying pathology. They can be overlooked, leading to behaviour problems, xerostomia, constipation, poor food and/or fluid intake, tremor, restlessness, sedation, pain, double incontinence or other problems, all causing potential loss of comfort and dignity.[18 19] Eighteen per cent of 13 699 UK primary care incident reports and 24% of 996 deaths or serious harms recorded from 2005 to 2013 were attributed to prescription medicines (any), mainly avoidable ADRs, largely due to inadequate monitoring, communication or decision-making.[20] We suggest that this care gap can be closed by formalised structured medicines' monitoring.[19 21–24]

A consensus is emerging around overprescribing in care homes,[13 14 16 25 26] and this work is now a priority for Welsh government. However, there is less agreement regarding the changes needed in routine care,[1 27–29] and reviewers indicate that evidence supporting single-profession interventions is equivocal.[11 29–34] The UK Department of Health's National Dementia Strategy, launched 2009,[13] and Medicines and Healthcare products Regulatory Agency recommendations[35] have not reduced antipsychotic prescribing,[36] whereas the ADRe Profile succeeded in a randomised controlled trial (RCT).[19] ADRe, formerly the West Wales ADR Profile, is available, with further information, on our website (http://www.swansea.ac.uk/adre/). It has potential to reduce costs,[19] while addressing concerns over care quality,[25 27 28 37] medicines' overuse,[14] and the responsibility of those administering medicines to report patients' changes to prescribers, despite time constraints limiting face-to-face multidisciplinary team meetings.[38]

The Food and Drug Administration warning on antipsychotic prescribing was followed by a shift towards increased use of benzodiazepines,[39] and there is no evidence of benefit from long-term antidepressants in older adults[40]; therefore, to ensure a comprehensive approach, ADRe includes all current mental health medicines. When used by nurses, both registered nurses and nursing assistants, ADRe has improved quality of care by addressing physical health issues for all patients monitored and identifying and addressing serious adverse events in ~10% of patients. Examples of previously unsuspected problems that we identified and addressed include: cardiac arrhythmias and severe hypertension,[21] drug-induced Parkinsonism,[23] respiratory tract infections,[41] pain and nausea,[19] chest pain and valproate-induced pancreatitis.[24] No harms have been reported from use of ADRe. We now aim to explore what is needed to optimise clinical gains and sustain implementation of ADRe in routine practice (figure 1).

STUDY DESIGN AND METHODS

This evaluation will integrate data from observations and interviews to explore clinical gains and any challenges in delivering the intervention, differences between intentions and delivery, the best way to embed medicines' monitoring into practice and relationships between ADRe, clinical contexts and processes and outcomes of care.[42 43]

SETTING

We are working with 10 care homes in Abertawe Bro Morgannwg University Health Board (ABMUHB) whose management teams have volunteered to participate. This includes all five care homes involved in a previous study, who are best placed to report on sustainability,[19] and five new care homes. ABMUHB is in a region of South West Wales that receives EU convergence funding because GDP is below 75% of the community mean.[44] It serves a population of 525 000 (33 000 aged 75–84 years and 13 000 over 85 years).[45] Care homes are governed by legislation[46] and regularly inspected to ensure they meet prespecified standards.[47] Regularity of contact between care homes and pharmacists, consultants and general practitioners (GPs) varies across South West Wales.

PARTICIPANTS

Inclusion criteria for care homes are: providing residential or nursing care or both to >4 service users meeting the inclusion criteria (*vi*) and willing to use ADRe in routine practice. We excluded three homes participating in a previous feasibility study, as they are affiliated to a home that is already participating, which would have introduced ties into the data,[23] and homes with <5 residents meeting the inclusion criteria or unwilling or unable to volunteer to undertake nurse-led medicines' monitoring.

The target population for mental health medicines' monitoring is people receiving at least one of:

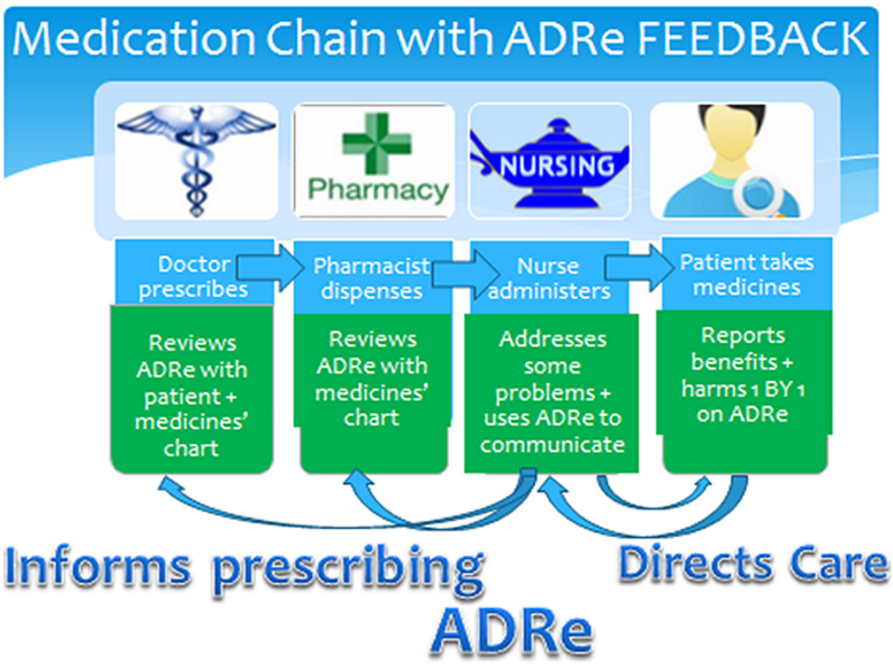

Figure 1 The medication chain.

antipsychotics, antiepileptics/mood stabilisers, antidepressants, anxiolytics or hypnotics (benzodiazepines or Z drugs). Eligibility for ADRe is based on medicines prescribed, and, previously,[19 23] we found it impractical to search service users' records to determine diagnostic categories or indications for prescribing. Therefore, we are using medication administration record (MAR) charts to identify potential participants taking at least one of the mental health medicines being monitored. (In the UK, these do not record indications for prescriptions.) Three residents per care home are being observed during one completion of ADRe. Inclusion criteria are: resident at the home and expected to continue for 1 year; currently taking any of the medicines listed above; willing and able to give informed, signed consent themselves or where capacity is lacking, having a consultee (see Consent, below) willing to give advice. We exclude those not well enough to participate, as screened by their nurses, aged <18 years or receiving active palliative care.

Stakeholder interviews are being conducted with the study's care home leads (nurses, nurse managers, matrons or managers), residents, service users or their families, prescribers, pharmacists and key stakeholders, including strategic leads, and the care home inspectorate.[48]

Recruitment

All 45 eligible care homes in ABMUHB were contacted by email, and at events disseminating previous research findings,[19] to seek five volunteers for this new study. Where a home expressed interest, the manager was sent detailed information. The first to respond positively were recruited, visited and trained in using ADRe until the target number was reached. Managers are asked to identify volunteer project leads and embed ADRe into routine practice before observation is arranged. Service users to be observed are recruited by their nurses, based on inclusion criteria; this involves using their professional judgement. Professionals and service users for interview are nurses and, where possible, residents or service users from the 10 care homes and stakeholders identified by snowball sampling. Respondents receive information sheets and are followed up a week later to arrange interview locations, dates and times of mutual convenience (figure 2).

Sample size

There are no fixed rules for sample size in qualitative research.[49 50] The study addresses focused questions in a field where we have past experience.[21 51 52] We anticipate that 20–30 interviews and 20–30 observations will permit sufficiently powerful analyses[53]: 30 transcripts will allow for 4–5 themes (see Analysis) at 50% prevalence with 10 instances with 90% power.[54] We anticipate that these numbers will achieve data saturation (in the sense of no new information being forthcoming and no new themes or categories being generated), assuming that common themes are mentioned by the diverse stakeholders; we hold open the possibility of additional interviews if important issues remain unclear.

Patient and public involvement

Our intervention and research design developed as we incorporated service users' suggestions as the work evolved. Service users were actively involved in the design and redesign of the ADRe profiles by cognitively testing and reshaping the questions and scrutinising drafts,[19 23 41 55 56] together with clinicians[22] and stakeholders (patient representatives, care home staff, social workers) in interviews and focus groups.[21 41 48] Service users contributed to the development of this study and

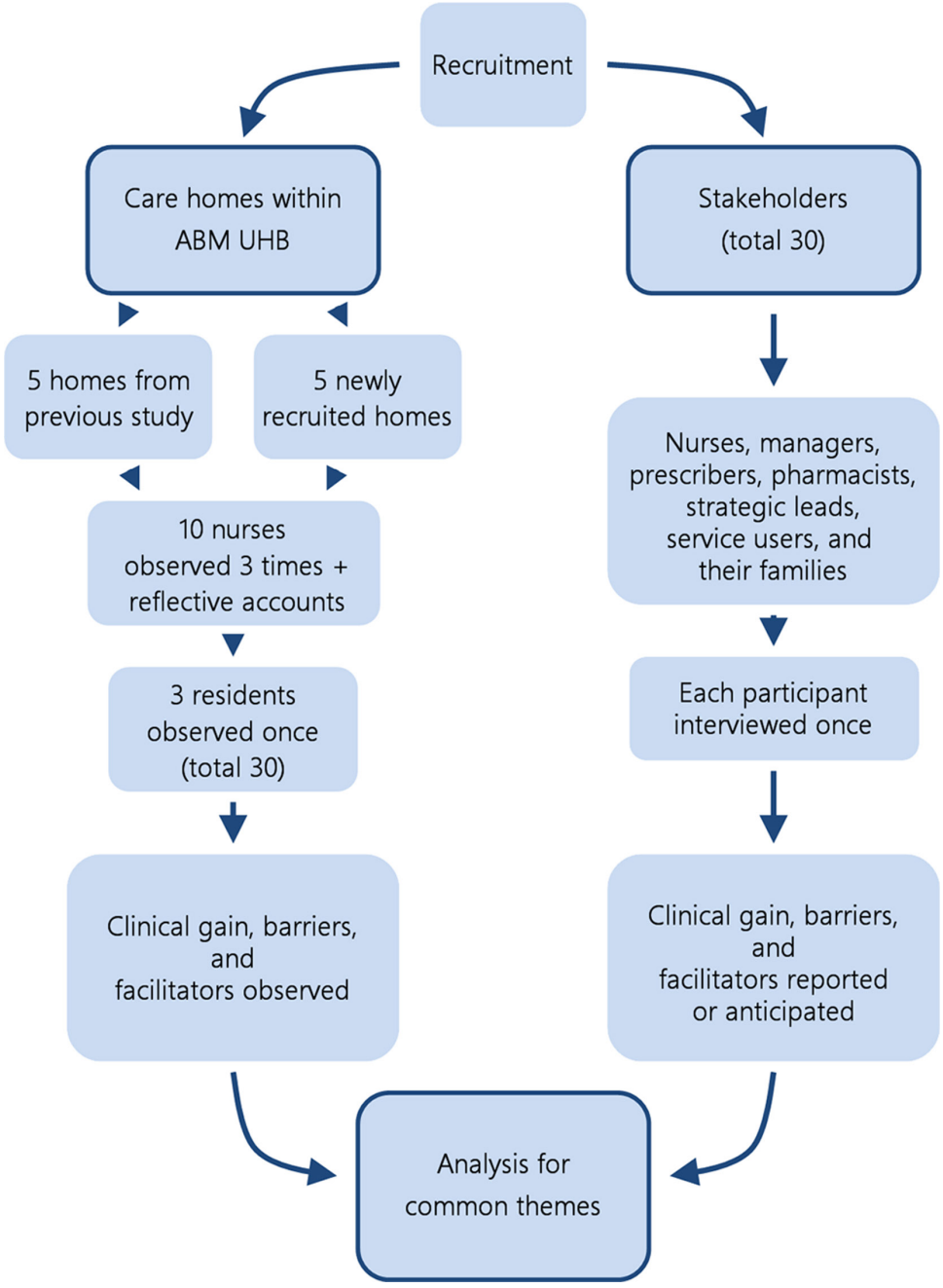

Figure 2 Participant flow diagram. ABMUHB, Abertawe Bro Morgannwg University Health Board.

will be invited to our dissemination event. Updates and research papers will be sent to participating care homes for dissemination to participating residents and their visitors.

Intervention

Structured, standardised patient questioning improves ADR reporting.[57] ADRe asks nurses to systematically check patients for the manifestation of itemised adverse side effects (glossary, online supplementary file 1) or undesirable effects of their mental health medicines, as listed in the British National Formulary (BNF) and manufacturers' Summaries of Product Characteristics (SmPCs), and seminal texts documenting known ADRs.[58 59] We are developing a formalised approach to monitoring all patients prescribed mental health medicines, regardless of diagnostic categories. The ADRe profile for mental health medicines was introduced to address nurses' and patients' concerns that patients' ADRs were neither recognised nor communicated to prescribers. It evolved from a teaching innovation[55] through before and after,[22 24] inter-rater reliability[56] and feasibility studies[23] and an RCT[19] to a clinically effective, evidence-based intervention.[22–24 52 56] ADRe opens dialogue with patients and provides the information needed to answer key questions:

- Are there previously unrecognised or unmonitored problems, such as postural hypotension, irregular

heart rate, posture/movement disorders, pain or nausea that might be better managed?
- Should care plans be modified to address these problems?
- Would any of these problems be alleviated if medication doses, formulations or administration times were changed?
- Are any prescribed medicines likely causing more problems than they are alleviating?

ADRe offers a strategy to prevent ADRs becoming serious and improve care quality by: (1) regular systematic checks and documentation of problems, however subtle, listed as 'side' or 'undesirable' effects in formularies and SmPCs; (2) transfer of information to prescribers[25 27 28 37 38]; (3) integration with NHS, for example, contacts with prescribers (GPs and specialists), dentists and opticians[60] and (4) synergy with pharmacist reviews to optimise therapeutic regimens.

During routine care, nurses work through the list with patients, address some problems themselves and feedback to pharmacists or prescribers (see figure 1). Some ADRe items identify where additional nursing care is needed to mitigate the adverse effects of medicines, for example, drug-induced xerostomia may be limiting eating and warrant additional oral care and dental examinations, or recording tremor or ataxia may trigger reassessment of risks of falls. Other problems require discussion with prescribers or referral to specialists and help from multidisciplinary teams (for example, pain, nausea, restlessness, behaviour problems)[19 22 52] (figure 3, online supplementary file 2). Therefore, we adapted ADRe to enhance team working with pharmacists.[1 25 26] Pharmacists and prescribers do not always have time to engage fully with patients to obtain their perspectives[61] or obtain details of signs and symptoms such as continence or bowel movements, particularly where patients are unable to verbalise: ADRe fills this communication gap.

Targeted questions identify 'side' or 'undesirable effects', as these signs and symptoms may indicate ADRs,[58 59 62] and merit attention regardless of aetiology. For example, tremor may indicate drug-induced Parkinsonism caused by antipsychotics or antiepileptics, but, as suggested in supporting information, alternative aetiologies warrant consideration: beta2 agonists or other stimulants, tramadol, fentanyl, hyperthyroidism, hypoglycaemia, anticholinesterases, alcohol misuse or dementia. Only careful review of medication records and patient history, usually in collaboration with pharmacist or prescriber, will identify likely causes and any candidate medicines for dechallenge. Rechallenge is not a normal practice in the UK, and specific laboratory tests are rarely available.[63] ADRe also includes health promotion/prevention advice that is particularly pertinent to users of mental health medicines. For example, xerostomia caused by antipsychotic and other antimuscarinic medicines promotes dental caries,[64] and ADRe asks nurses to check that service users have visited their dentists in the last year. Assessment of possible or likely aetiology rests with clinicians delivering care, as does the decision regarding the advisability of any dechallenge or deprescribing. Formal assessments of ADR causality[65] cannot confer certainty or prove a connection or quantify a contribution[63] and rarely achieve consensus.[65] However, prescribers and care staff need to make practical assessments as to amelioration of problems. Therefore, we are sometimes less equivocal regarding health promotion measures and the advisability of investigating the full range of possible causes of problems. For example, where a tremor is detected, it is often worthwhile to review use of alcohol and stimulants, such as cold cures or caffeine, and consider the possibility of hypoglycaemia if antidiabetic agents are administered.

'Unique selling points' and distinguishing features of ADRe

Searches[56 66–68] and reviews[69 70] have not identified other comprehensive nurse-led instruments for checking patients' reactions to mental health medicines.[2 56 66 71] Searching English language work for 'adverse drug reactions' (as a MeSH entry term), nursing (as nurs*) and 'monitoring' in PubMed and the Cochrane library identified only two groups with empirical work in the area (Swansea and Antwerp)[66] (search repeated 6.3.18). Cochrane reviews[67 68] on optimising prescribing in care homes identified medication reviews, case-conferencing, education initiatives, decision-support technology and information transfer trials, but no structured medicines' monitoring. Other side-effect checklists include only antipsychotics or posture and movement problems, despite the prevalence of mental health polypharmacy,[72 73] are designed for patient self-administration (our participants are not well enough) or the measurement of subjective beliefs, are very brief and lack guidelines for action.[66 69 70] Uniquely, ADRe includes estimates of change to prompt referral or actions and starts with vital signs, including postural hypotension and oxygen saturation: these have been pivotal in obtaining prescriber reviews.[19] We recognise that physical health medicines, particularly cardiovascular medicines and analgesics, are important causes of ADRs,[16] and ADRe's guidelines indicate this and seek to support clinical judgement in addressing the causes of problems identified. Work on decision support[74] and multidisciplinary team communication[75] is underway, but ADRe remains unique.

Data collection

We are undertaking interviews and non-participant observations with the participants of our five previous homes[19] and five newly recruited care homes. We are observing nurses administering the ADRe Profiles, noting any discrepancies between 'as intended' and 'as operationalised', for example, items omitted or re-ordered and difficulties with equipment. Consistency between fieldworkers is ensured by preparation at team meetings and structured interview and observation schedules derived from earlier work. We aim for contextual and detailed descriptions of participants' experiences of the ADRe profile

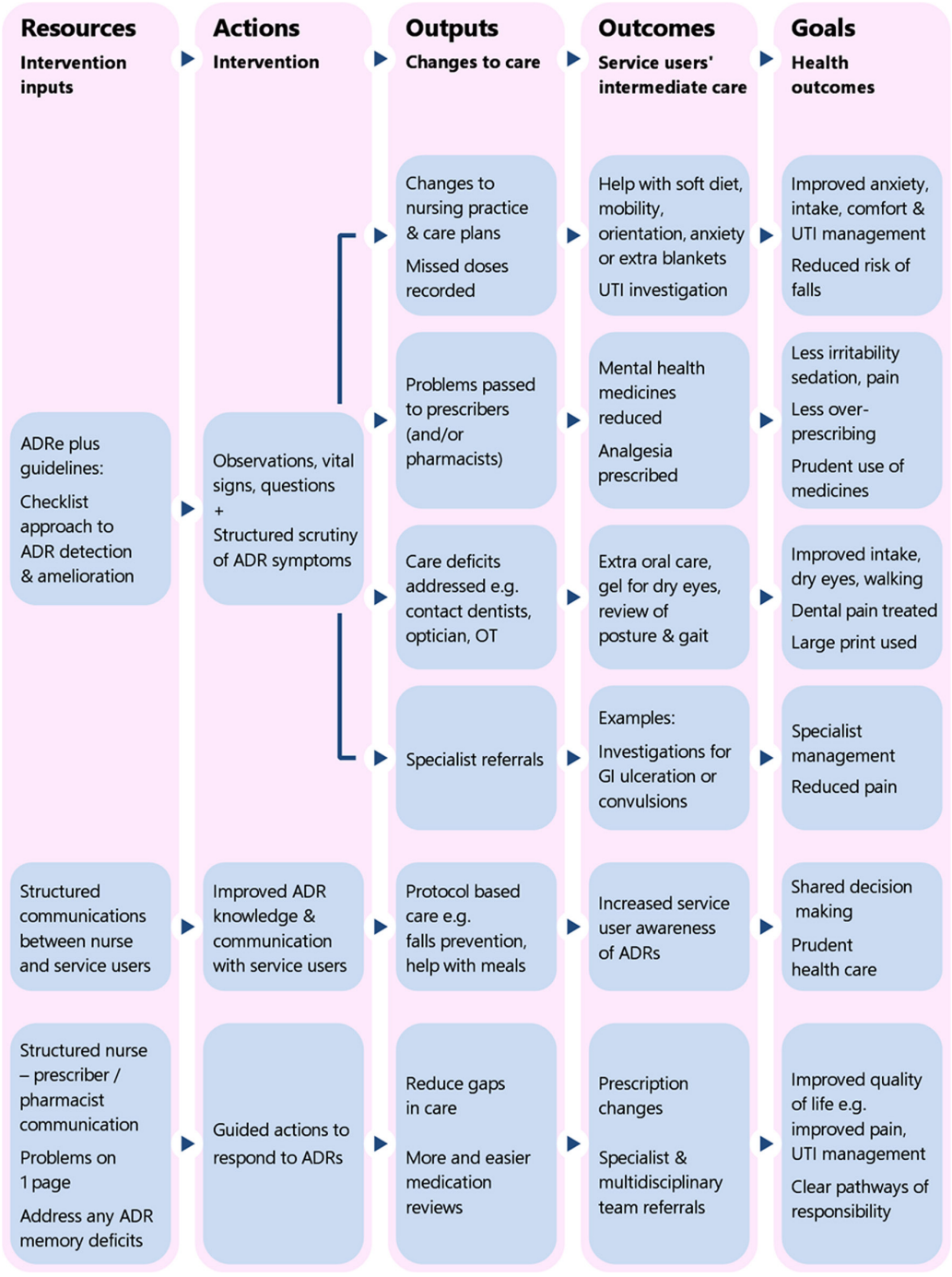

Figure 3 Logic model for ADRe: resources–actions–outputs–outcomes–goals. ADR, adverse drug reaction. GI, gastrointestinal; OT, occupational therapist; UTI, urinary tract infenction.

and nurse-led medicines' monitoring as an innovative and incompletely understood social situation.[76 77] We shall explore interest in combining ADRe with digital technologies and non-invasive patient monitoring[78] and expanding to other medication groups (figure 2).

Observations

In each home, we shall observe three episodes of care involving ADRe administration and record events using templates and freehand notes, as previously described.[22] We shall note how medicines' monitoring is operationalised, practical barriers and facilitators and any clinical gains and harms.[21] Observations will be followed by debriefing to discuss any findings from the profile in relation to the guidelines and any suggestions for modifying practice.

Completed profiles plus the MAR charts will be passed to the study pharmacist for review. The pharmacist will make written recommendations as to how problems identified on ADRe might be addressed by changes in prescribing and raise awareness of any modifications of

nursing care or additional monitoring needed. These are one-off reviews by a consultant pharmacist with care home expertise for the purpose of this study. Care home managers will be asked to facilitate any changes needed. For urgent matters, prescribers will be contacted directly.

Interviews

Interviewing end users as key stakeholders[48] will explore experiences of ADRs, drivers of change, barriers and facilitators of medicines' monitoring to identify differing concerns and facilitate mutual understanding and joint working.[79] This will determine the best way to integrate and embed medicines' monitoring in routine care, relate the profile to processes and outcomes of care and develop implementation strategies.

Data analysis

Observational data will be used to compile a record of clinical benefits and disbenefits and pharmacist recommendations.

Analysis of interviews will be based on the constant comparative method[80] to identify predictors of successful adoption and any changes to profiles, working arrangements and oversight needed to embed use. This systematic, reiterative method of comparing and contrasting emerging codes, categories and concepts ensures that theoretical perspectives are embedded in the data. Interviews and observation fieldwork will be coded, categorised, analysed and closely interpreted by at least two researchers and discussed at team meetings, with consistency checks.[81] The first 10 and 20 interview transcriptions will be reviewed for coding, categorisation, saturation, cases in contrast and the development of the sample.

Data from interviews, observations and pharmacist feedback will be integrated to enhance understanding, depth, rigour and validity.[82] Previous themes of clinical gains, barriers, facilitators and proposals for change offer a provisional template.[21 22 51] Final codes and themes and data saturation will reflect collective decisions.

Outcomes

Outcome measures are clinical impact and barriers to and facilitators of sustainability.

Impact

The primary outcome of the observations is evidence of clinical impact (anticipated and actual), which will be described as: number of participants benefiting from ADRe, additional care or nursing actions and number and nature of problems addressed (including prescription changes), as noted on ADRe or reported by nurses. The outcome of pharmacist's reviews will be the number and nature of recommendations to (1) prescribers and (2) nurses made using ADRe.

Sustainability

Barriers (eg, time, interruptions, distractions) and facilitators of ADRe administration and adoption, the changes needed to embed ADRe into routine care (figure 3, online supplementary file 2) and factors that would promote or block adoption of ADRe and new technologies will be identified in thematic analyses of interviews, supported by observation data.

Ethics

Approval was obtained on 17 February 2017 from Wales Research Ethics Committee 6 who will review any protocol modifications (reference no 16/WA/0358, IRAS ID 213050). The study is sponsored by Swansea University. Written and verbal information is offered, and potential participants are given as much time as they need to decide whether to participate. Written informed consent is sought for all interviews, observations, debriefing and review of documentation or accounts. As an addition to routine nursing documentation, embedding ADRe into routine documentation falls outside the NHS Health Research Authority definition of research,[83] and cluster studies do not follow the same principles as individually randomised trials in requiring individual participants' consent for non-intrusive research.[84–87] Non-intrusive clinical research, including retrospective review of patient notes, where there is neither inconvenience nor hazard to patients, does not usually require expressed consent.[88] The only questions ADRe asks are those that should be asked as part of routine care[89–92] and confer no greater risk of harm.[88] All questions relate to potential ADRs and physical health problems and are designed to ensure patient safety.

The study is not unduly invasive, in that it does not go beyond the experiences of daily life or routine medical examination,[93] and all previous participants benefited.[19 22–24] In all 10 care homes, three residents meeting the inclusion criteria are approached by their nurses and asked to consent to researchers observing administration of ADRe and reviewing their clinical records, including completed profiles and medicines charts. Signed consent is taken by registered nurses fully aware of the Mental Capacity Act 2005.[94] For those without capacity to consent, consultees are approached. For many participants, the consultee is a relative in regular contact; however, for residents who have no regular visitors and rely on professional support, the consultee may be a care home clinician who knows the resident and is not involved in the research.[93] In the unlikely event that we observe breaches of the NMC code of conduct,[95] these will be pursued in accordance with the code.

Data handing

All data are anonymised on collection and kept strictly confidential. Participants and care homes are assigned study numbers, and personal names only appear on consent forms. Service users' ages, sex, medicines and medical conditions are recorded. Professionals' roles, but not personal information, are recorded. Data are managed in accordance with the Data Protection Act 1998[96] and the Research Governance Framework for Health & Care Wales (2010).[97]

Status of the study

Care homes have been recruited, and data collection has started.

DISCUSSION

Prescribed medicines (any) benefit between 4% and 25% of patients,[98] whereas ADRs affect 7.8% (95% CI 7.2% to 8.4%) of patients in primary care,[11] 11.0% (95% CI 5.1% to 16.8%) of hospitalised patients,[99] killing 0.25%,[100] and 4.8%–37% of people with cognitive impairment.[16] However, systematic review indicates that healthcare professionals consistently underestimate harms and overestimate benefits of prescribed medicines.[101] Consultations are often brief, informal and led by professionals with, at most, a general inquiry as to 'any side effects'.[102 103] By avoiding detailed directed questions, professionals risk failing to capture patients' experiences of ADRs[104] and allow ADRs to worsen, unmonitored, to the point of requiring secondary care, for example, due to falls[105 106] or pneumonia.[107 108] Structured monitoring facilitates social coproduction and recognition of problems that may be ADRs, as listed in the BNF and SmPCs, circumventing non-disclosure or denial by patients and professionals.[66 109 110] Insidious onset of problems, familiarity with the patient and overlap between some ADRs (such as falling, incontinence, sedation, confusion) and the signs and symptoms of ageing or disease militate against ADR recognition by fostering entrapment by prior expectation.[111] Failure to recognise ADRs is attributable, in part, to their complexity and diversity, difficulties in remembering full lists of possible ADRs (10–20 per medicine) for multiple medicines (up to 20 per patient) and any associated deficits in education,[112] knowledge[113–116] or patients' and nurses' confidence in their knowledge.[55] ADRs to prescribed medicines are not coincident with prescribing (they develop after the doctor has left); therefore, a mechanism is needed to transfer information[117] from patient to prescriber, across geographical and social distance. Comprehensive, formalised structured monitoring by administration of the ADRe Profile before scheduled appointments or reviews has potential to bridge this hiatus in communications and care, introduce a nursing voice into the refinement of therapeutic regimens and involve nurses in ADR management.[118]

Systematised, protective reporting: before not after a serious ADR

The published literature on ADRs is limited by non-disclosure of data,[119] whereas ADR recognition has become reliant on expert decisions, detached from social contexts.[110] Most evidence of harm comes from retrospective analyses of large databases, and each analytical method has its proponents and detractors.[120] Some 5% of serious ADRs are reported via spontaneous reporting systems, such as the iconic 'yellow card' scheme.[121] Reliance on volunteer reporting renders spontaneous reporting systems vulnerable to respondent and notoriety biases.[122 123]

Pharmacovigilance focuses on regulators' assessments of any need to discontinue or restrict medicines and usually focuses on serious, rare and unpredictable ADRs, such as *torsade*, anaphylaxis or acute liver failure, rather than mundane but socially disabling ADRs, such as tremors, xerostomia, incontinence and sedation.[124 125] Similarly, prescribing indicators track potentially problematic medicines, rather than patient outcomes.[126] ADRe has a different focus: it is a protective strategy, aiming to prevent ADRs by regular comprehensive monitoring, embedding problem recognition in local contexts, as illustrated from earlier work (online supplementary file 2).

Potential cost savings

Decision aids in several contexts enhance professionals' perceptions of knowledge and judgement, but at the cost of extended consultation time.[127] Our intervention involves nurses or care assistants, who know their patients, with support from registered nurses. We estimated ~£20 for an initial profile completion.[19] Monthly administration would therefore be offset by the estimated additional medication costs incurred by patients with ADRs (US$31.7 or £23 per month, exchange rate: 1USD$=0.79 GBP as of 22 March 2018).[128]

ADEs (underprescribing or overprescribing of medicines) (glossary, online supplementary file 1) are responsible for 8% of healthcare spend in the USA.[129] In Sweden, 9.5% of direct healthcare costs are attributed to ADEs: each ADE incurs direct treatment costs of US$444.9, 264–625 (£320, 10–449) for the initial episode.[130] However, the average societal cost of an ADE illness is higher—US$6235.0 (5442.8 to 7027.2) (£4481, 3911–5050), comprising direct costs for the illness of US$2830.1 (2260.7 to 3399.4) (£2034, 1625–2443) (45%) plus indirect costs for lost earnings or other commitments of US$3404.9 (2899.3 to 3910.4) (£2447 (£2083–2809.8)).[130] In the Netherlands, each preventable medication-related admission costs €5461 (£4866),[131] and each admission due to a fall costs ~£20 k,[132] suggesting that improved falls risk assessments, vision checks, reduction of sedatives and antipsychotics following use of ADRe could generate significant savings. Additional costs relating to pain, sedation, poor oral hygiene and poor eyesight, and their amelioration, are hard to quantify, but affect the quality of life,[19] which is generally lower in those with ADRs or undertreated conditions.[128] Ten completions of ADRe cost ~£200 in nursing time, and some 10% of participants have a serious ADR, that would have led to admission costing ~£4 k,[9 131] prevented by ADRe.[19 22 24]

Policy fit

Information alone rarely changes clinical practice.[133] More surprisingly, consultant-led medication review,[134] decision support,[135] academic detailing,[136] deprescribing[137] and pharmacist-led interventions did not enhance clinical

outcomes[30] or quality of life, and Cochrane reviewers found evidence for implementation to be equivocal and low quality.[67 68] Some psychosocial person-centred care initiatives reduce the prescribing of antipsychotics, but are time intensive, often with ill-defined clinical outcomes and unsupported by research evidence.[31] However, time, not weak evidence, is the major barrier to therapeutic drug monitoring[138] and shared decision-making.[61]

Faced with resource constraints, increasing demand from an ageing population, concerns that social class gradients in antipsychotic prescribing[139] may be compounding health inequalities, and stretched services, Welsh government's attention has focused on avoidable harm, *primum non nocere*, and minimising any adverse effects of care.[66 117] Any harm from medicines is obfuscated by professional boundaries: prescribers (GPs and specialists) typically see residents for 7–15 min at review, whereas those working in care homes see the subtle, insidious adverse effects of medicines every day, but may not recognise their provenance without ADRe support. Deprescribing is often a complex decision based on detailed conversations, making repeat prescribing a quicker and easier option[140]: ADRe facilitates deprescribing by gathering the information needed.

Some medicines' management strategies focus on record keeping and storage, rather than patient monitoring.[60] However, other policy documents note that those administering medicines are responsible for regularly monitoring patients and reporting to prescribers any changes that may emanate from medication or if assessment of the patient indicates that the medicine is no longer suitable.[38 141] Mental health medicines have many adverse effects, cautions and contraindications—and few can remember them all. Therefore, ADRe obviates reliance on memory by packaging this knowledge into a format that is convenient for passing to prescribers and amenable for incorporation into electronic records. However, to work in care homes, interventions improving quality of life must be congruent with staff attitudes, priorities, time allocation,[142] experience, values[143] and shared understandings.[144]

Study limitations

Generalisation

Our study involves non-random selection of a sample of care homes in one University Health Board area in South West Wales, and further studies will be needed to confirm the transferability of findings to other local areas. We acknowledge the potential for volunteer bias in all research designs[145] and the difficulties (ethical and practical) of obtaining information on the reasons for non-response to research invitations. Similarly, the pharmacist reviews are compiled by one expert pharmacist, to test the feasibility of this approach, and we do not know if less experienced pharmacists would react differently. Only policy initiatives can determine whether our findings will transfer to struggling organisations,[37] as they are less likely to volunteer for research projects, and may be less likely to have sufficient staff to offer support to those withdrawing from antipsychotics.[146] Participant recruitment to observations and interviews is at the discretion of nurses, and we cannot discount the possibility of selection bias. Generalisation of findings will depend on logical inferences.[147] However, medicines management is a widespread problem, in urgent need of effective interventions.[1]

Study size

We recognise that 30 interviews encompassing the full range of stakeholders may not offer data saturation in some categories, particularly the 'hard to reach' category of national strategic leads. We estimated sample size[53 54] to plan ahead before applying for funding and acknowledge the limitations of this pragmatic approach, which will not affect data analysis. Our analysis will be based on common themes from multiple perspectives. When assessing practical adequacy, readers will be asked to juxtapose the clinical impact of ADRe observed here with findings of previous studies.[19 22–24 52 56] Resource constraints restrict each resident to a single observation, and it may not be possible to follow progress to ascertain whether recommendations have been enacted.

Nurses' reporting

ADRe relies on nurses' reports of ADRs, and many residents are non-verbal. It is, therefore, vulnerable to nurses' interpretation, and we acknowledge that nurses may under-report residents' ADRs.[148] However, we are exploring how ADRe enhances delivery of care and communications and cannot discount the possibility that some problems may be misreported. Time pressures in the NHS usually limit doctor–patient contact to 7–15 min, insufficient to review all aspects of care, although some 50% of the items on ADRe can be identified in care homes' notes, the information takes ~1 hour to retrieve.[19] We therefore suggest that ADRe, despite limitations, might improve care.

Prescription-based inclusion criteria

Everyone prescribed mental health medicines is vulnerable to their adverse effects: pharmacodynamics does not respect diagnostic categories and service boundaries. Dementia diagnoses are often not recorded in the UK.[149] Accordingly, our inclusion criteria centre on prescriptions and associated vulnerability to ADRs and are not restricted by diagnostic groups. Residents' medical records containing diagnoses are held by GPs and are not available in care homes.

CONCLUSION

The WHO's Third Patient Safety Challenge 'Medication Without Harm' calls for action to strengthen monitoring systems and facilitate improvements in monitoring practices.[1 150] The previous WHO Global Patient Safety Challenge was effectively met by a checklist approach.[151] We hope to build a consensus around a

similar communication approach to enhance the systems and practices of medication management. ADRe could contribute to the WHO 'Medication Without Harm' challenge, complementing and reinforcing error-reduction strategies[71] and addressing problems identified by WHO,[150] NICE,[8] DoH,[13] Public Health Wales,[14] the Older People's Commissioner,[25] the Andrews' Report[28] and others.[1 152] However, political will, consensus, organisational commitment,[14] morale,[143] activation of a shared sense of urgency and flexible levels of engagement[43] will determine whether ADRe can be sustained and ADRs addressed.

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Contributors SJ was the principal investigator and drafted the manuscript. TB contributed to the design and conduct of the study, assisting with analysis and review. MG-W contributed to the study design and implementation of the study. JMM contributed to the implementation and review of the study. JR contributed to the economic evaluation of the study. SS contributed to the design, analysis and implementation of the study. MS was the study coordinator and assisted with the management of the study and its implementation. DW contributed to the study design and analysis. DH contributed to the study design, conduct and analysis. All authors have been involved in the revision of the manuscript, read and approved the final manuscript to be published, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved and monitored the data. TB will provide an expert review of the findings of the observations.

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