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SHORT COMMUNICATION

Errors associated with co-names of medicines: The nomenclature of combination medicinal products

Oisín N. Kavanagh[1] | Robert Lowe[2] | Jeffrey K. Aronson[3]

[1]School of Pharmacy, Newcastle University, Newcastle upon Tyne, UK

[2]Pharmacy Department, Hellesdon Hospital, Norwich, UK

[3]Centre for Evidence Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

Correspondence
Oisín N. Kavanagh, School of Pharmacy, Newcastle University, Newcastle upon Tyne, UK.
Email: oisin.kavanagh@newcastle.ac.uk

In comparison to the efforts required to bring a new drug or formulation to the clinic, bestowing a name on a medicine is relatively simple. However, if the name we choose causes confusion—by making its contents ambiguous or if it is too alike another drug—it can precipitate clinical errors. This prompted the World Health Organization to set up the International Nonproprietary Naming Committee in the 1970s to select unambiguous names for drugs. Unfortunately, multidrug products—which are becoming increasingly popular—do not fall under the remit of conventional International Nonproprietary Nomenclature. We have identified 26 combination formulations that have been historically named with the co-drug format in the United Kingdom. Most of them have also been prescribed in the United Kingdom in the past year, and although several of them are not prescribed very often, 11 were prescribed more than 2000 times. In this paper, we have explored the literature to identify prescribing errors with co-drug products and found several idiosyncrasies that have caused drug errors in the past. We advocate for a standard nomenclature (state the international nonproprietary name [INN] of each component followed by dose information in the x + y format) for these products on the box and in prescribing resources. We hope that this will enhance clarity and safety during prescribing and administration, particularly for high-volume drugs like paracetamol + codeine (co-codamol), amoxicillin + clavulanic acid (co-amoxiclav) and trimethoprim + sulfamethoxazole (co-trimoxazole).

KEYWORDS
co-amoxiclav, co-careldopa, co-codamol, co-drug, combination drugs, multidrug

1 | MAIN

The names of medicines are chosen carefully. At a glance, each can ideally tell us something about the chemical or pharmacological nature of the medicine—although not always. For example, -azole in omeprazole indicates the presence of an imidazole group, which can provide a clue about its ability to inhibit certain cytochrome P450 enzymes, and -olol in bisoprolol suggests beta-adrenoceptor blockade.[1] Conversely, -olol in stanozolol is derived from its chemical name, 17α-methyl-2'H-androst-2-eno[3,2-c]pyrazol-17β-ol. This approach to nomenclature worked well in the 1950s when the first list of international nonproprietary names (INNs) was published by the World Health Organization. At that time, the British National Formulary (BNF, 1957) had around 200 pages. Today the BNF, issue 86, has just under 2000 pages, and drug nomenclature must also consider the wider clinical context to reduce the risk of prescribing errors; this has been highlighted by literature activity on look-alike sound-alike (LASA) drugs.[2] Solutions have been proposed to these problems, such as tall man lettering (otherwise known as selective capitalisation[3] e.g., DOXOrubicin)[4] and careful label design to help busy clinicians distinguish one

product from another. While this can be readily achieved, a systematic review of tall-man letters showed that they are of limited efficacy.[5]

Increasingly, combination formulations are being used for their apparent convenience, which could translate to lower direct and indirect costs and improve adherence.[6] These formulations can contain combinations of new and old medicines (e.g., Entresto®, sacubitril + valsartan) or combinations of established generic medicines (e.g., Concor®, amlodipine + bisoprolol). They have escaped the traditional remit of the INN framework of the WHO, which states that 'INNs are selected in principle only for single, well-defined substances that can be unequivocally characterized by a chemical name (or formula). It is the policy of the INN Programme not to select names for mixtures of substances…'.[1] In the past, these drugs might have been given an entirely new name, such as dimenhydrinate (8-chlorotheophylline + diphenhydramine) or dichloralphenazone (antipyrine + chloral hydrate), which itself was a substituent of the combination formulation Midrin® (dichloralphenazone + isomethheptene + paracetamol).[7]

However, at some point, drug combinations started to be named using a co-naming scheme. For example, co-trimoxazole—a combination of trimethoprim and sulfamethoxazole—was marketed in 1969 under the proprietary names Bactrim® and Septrin® (by Roche and Burroughs Wellcome, respectively) and was referred to in the literature as sulfamethoxazole-trimethoprim as far back as 1971.[8] Since then, we have reverted to the original format (x − y, x + y or x/y), which more obviously indicates the qualitative (drug) information about a product and gives the opportunity for including quantitative (dose) information too.

However, several legacy compounds do not follow this form of nomenclature. We have identified 26 combination formulations that have been historically named with the co-drug format in the United Kingdom. Most of them have also been prescribed in

TABLE 1 Co-drugs listed in the British National Formulary† (BNF) and others identified through OpenPrescribing‡ in 2023 ($n = 26$) ranked by prescribing volume; these data reflect prescribing patterns in general practice in England and Wales. Symbol key = (a) those that are in the current version of the BNF, (b) those that have been in earlier versions but are not in the current edition; (c) those that are listed in OpenPrescribing.

Name	Components	Average items dispensed per month in 2023	Source
Co-codamol†	Paracetamol and codeine	1 255 451	a, c
Co-careldopa†	Carbidopa and levodopa	114 656	a, c
Co-dydramol‡	Dihydrocodeine and paracetamol	110 506	a, c
Co-amoxiclav†	Amoxicillin and clavulanic acid	106 504	a, c
Co-beneldopa†	Benserazide and levodopa	80 419	a, c
Co-trimoxazole†	Trimethoprim and sulfamethoxazole	19 295	a, c
Co-amilofruse†	Amiloride and furosemide	15 849	a, c
Co-tenidone†	Atenolol and chlortalidone	7505	a, c
Co-amilozide†	Amiloride and hydrochlorothiazide	4441	a, c
Co-cyprindiol†	Cyproterone acetate and ethinylestradiol	4403	a, c
Co-magaldrox†	Magnesium hydroxide and aluminium hydroxide	2532	a, c
Co-proxamol‡	Dextropropoxyphene and paracetamol	423	b, c
Co-phenotrope†	Diphenoxylate and atropine	104	a, c
Co-danthramer†	Dantron and poloxamer 188	47	a, c
Co-flumactone†	Hydroflumethiazide and spironolactone	14	a, c
Co-danthrusate†	Dantron and docusate	6	a, c
Co-fluampicil†	Flucloxacillin and ampicillin	4	a, c
Co-simalcite†	Simeticone and hydrotalcite	4	a, c
Co-triamterzide‡	Triameterine and hydrochlorothiazide	<1	b, c
Co-zidocapt‡	Hydrochlorothiazide and captopril	<1	b, c
Co-codaprin‡	Codeine and aspirin	<1	b, c
Co-prenozide‡	Oxprenolol and cyclopenthiazide	0	b, c
Co-dergocrine‡	Ergoloid mesilates (dihydroergocornine, dihydroergocristine, dihydro-alpha-ergocryptine and dihydro-beta-ergocryptine)	0	b, c
Co-methiamol‡	Methionine and paracetamol	0	b, c
Co-trifamole	Trimethoprim and sulfamoxole	0	b
Co-trimazine	Trimethoprim and sulfadiazine	0	b

the United Kingdom in the past year (Table 1), and although several of them are not prescribed very often, 11 were prescribed more than 2000 times. For example, most clinicians will recognize co-codamol (paracetamol + codeine) and co-amoxiclav (amoxicillin + clavulanic acid).

The use of 'branded generics' poses problems for co-names. This term describes when a generics company markets a branded version of a generic medicine, for example, Teva's Caramet® (co-careldopa). When pharmacies purchase and dispense these medicines, they can claim for reimbursement at a price higher than the originating manufacturer's list price, which creates a profit.[9] At other times, a generics company can drop the co-name altogether. For example, Orion Pharma now markets co-careldopa, labelled only as levodopa-carbidopa, and other generics companies have developed this combination product under the brand names Apodespan® and Lecado®. Further, we have identified a recent report of a suspected adverse reaction that arose after switching between generic and branded co-careldopa.[10]

1.1 | Medication errors

Lack of standardized co-drug nomenclature could result in patient confusion and prescribing errors. To explore this, we conducted a review of medication errors for drugs that use the co-drug terminology. On 14 March 2024, using Google Scholar, Scopus and PubMed, we searched '[Drug] error*' for the drugs listed in Table 1. The abstracts of the search results were manually screened, and studies were included only if they described an error. We found instances of medication errors involving (in decreasing order of frequency) co-amoxiclav, co-amilofruse, co-beneldopa, co-careldopa, co-codamol, co-dydramol and co-trimoxazole. These are discussed separately below.

We also found hits for co-proxamol ($n = 442$), co-dergocrine ($n = 146$), co-amilozide ($n = 131$), co-danthramer ($n = 58$), co-phenotrope ($n = 56$), co-trimazine ($n = 53$), co-cyprindiol ($n = 52$), co-fluampicil ($n = 45$), co-tenidone ($n = 25$), co-codaprin ($n = 24$), co-danthrusate ($n = 23$), co-magaldrox ($n = 19$), co-trifamole ($n = 15$), co-triamterzide ($n = 9$), co-zidocapt ($n = 7$), co-flumactone ($n = 6$), co-methiamol ($n = 6$), co-simalcite ($n = 2$) and co-prenozide ($n = 1$), but they returned no relevant papers after screening.

1.1.1 | Co-amoxiclav

We identified 1900 papers, which were reduced to 17 after screening. When narrowed to prescription errors, co-amoxiclav caused just under 16% of errors ($n = 41/262$), most of which were due to inappropriate medication selection.[11] Elsewhere co-amoxiclav was found to be one of the most common drugs involved in errors involving intravenous administration.[12] Two studies showed that errors typically occur during prescribing, '…drugs most commonly reported were co-amoxiclav (16.8%, n=161), gentamicin (14.1%, n=135), and vancomycin (9.9%, n=95). Most of the reported co-amoxiclav [errors] occurred during prescribing (65.8%, n=106).'[13,14]

In a study of 330 prescribing-related adverse incidents, co-amoxiclav and amoxicillin were both involved in 5% of reported medication errors when they were given to patients with penicillin allergy (albeit with a small sample size, $n = 15$ for each).[15] In another study, prescribing co-amoxiclav for patients with penicillin allergy was identified as a serious error in 15% ($n = 45/299$) of errors.[16] Here, co-amoxiclav was ranked 5th in a list of drugs commonly involved in prescribing errors and the rates of errors with co-amoxiclav were 17% for Foundation Year 1 and 2 doctors and 12% for all other prescribers. Two studies also identified a high rate of prescribing errors with piperacillin/tazobactam, commonly marketed as Tazocin®.[13,16] One study highlighted deaths due to missed allergy to amoxicillin in co-amoxiclav ($n = 4$).[17] In another, four cases of anaphylaxis were identified in women with known penicillin allergies: two received co-amoxiclav and two cephalosporins.[18]

Co-drugs also figured in the most common unprevented dispensing incidences in a Welsh hospital, where co-amoxiclav was ranked = 9th ($n = 9/915$).[19] Co-amoxiclav was also ranked 9th in an analysis of prescribing errors in a London hospital ($n = 30$).[20] In another study, co-amoxiclav was involved in the most errors ($n = 34$), but these errors were generally due to omission.[21]

Some studies identified errors but did not classify the error type.[22,23] In studies that provided details on the type of error, one showed that co-drugs were involved in over/under-dosing of co-codamol, co-amoxiclav, co-careldopa, co-amilofruse, co-danthramer and co-trimoxazole.[24] Other non-co-drug related errors (typically omission) have been identified.[25] Isolated examples have been identified which included the use of the wrong strength[26] and inquiries such as a caller asking, '…if co-amoxiclav is a penicillin.'[27]

1.1.2 | Co-amilofruse

Our search returned 86 articles, which were reduced to seven after screening. Some studies identified errors but did not classify the error type.[22,23] One study highlighted potential patient confusion with the co-drug name, 'Could [the General Practitioner (GP)] prescribe Frumil for this patient and not co-amilofruse, because the different generics she receives confuse her?'.[28]

Isolated examples highlight potential confusion by healthcare professionals, 'Mrs -----'s GP … was unclear about how much amiloride was contained in co-amilofruse and it is likely that he intended to give her half the dose he did.'[29] Look-alike errors were also identified with co-amilozide[30] and in one case a physician forgot to transcribe a paper prescription to the digital record.[31] The authors of one study of a small number of errors with co-drugs concluded that '… the "co-" prefix in approved names causes confusion; special vigilance is therefore required by pharmacists when presented with prescriptions for such products'.[32]

1.1.3 | Co-beneldopa

We identified 121 papers, which were reduced to five after screening. Many of the studies of this formulation focused on medication errors

with respect to the timing of the dose. We excluded these studies as they were beyond the scope of our analysis. In a retrospective analysis, co-drugs were commonly implicated in look-alike errors, grouped as drug pairs, for example, co-careldopa with co-beneldopa ($n = 7$).[33] Of 2068 error reports in a London hospital between 2001 and 2004, co-drugs were in the top 10 most implicated; co-beneldopa was ranked 4th ($n = 36$).[20] Co-drugs also figured in the most common unprevented dispensing incidences in a Welsh hospital, in which co-beneldopa was ranked 10th ($n = 8/915$).[19] We also identified reports of single cases of confusion between co-beneldopa and co-careldopa[34] and drug omission.[35]

1.1.4 | Co-careldopa

We obtained 192 hits, which were reduced to five after screening. The isolated examples identified by Anto et al.[24] and Dean et al.[34] were identified again and are not discussed here. One study highlighted an error with co-careldopa,[36] and in another case, co-careldopa was implicated in a death.[17] Another study described how 8/73 (11%) of patients receiving co-careldopa experienced a pharmacy error. Most errors (5/8; 62.5%) involved substitution of controlled release for immediate release carbidopa 25 mg + levodopa 100 mg, resulting in underdosing.[37]

1.1.5 | Co-codamol

We initially identified 478 papers, reduced to 17 after screening. Studies by Rogers et al,[32] and Anto et al.,[24] have been identified above, and as they contained no further specific details on error type rates, they were not included again in this section.

In the Welsh hospital referred to in earlier sections, co-codamol was ranked 9th ($n = 9/915$),[19] and in an analysis of prescribing errors in a London hospital ($n = 31$), co-codamol was ranked 7th.[20] In a retrospective analysis, co-codamol/co-dydramol ($n = 9$) were implicated in look-alike errors, grouped as a drug pair.[33] More generally, more than one paracetamol-containing product was prescribed for 6.5% of patients who were already taking paracetamol ($n = 392/6060$), and around 91% of those patients were at high risk of excessive dosing ($n = 323/356$).[38] In another study, duplication of therapy with paracetamol and co-codamol or co-dydramol was highlighted as a common problem.[15]

In one case a team did not identify the risk in prescribing two paracetamol products simultaneously, 'One other patient in the self-medicating group had a medication error. She had brought in her prescribed pregabalin and co-codamol 30/500 from home, and on the morning of day 1 after surgery she started self-medication and took these medications from her home pack. However the patient had been prescribed paracetamol and oxycontin post-operatively. The error was noticed by 08:30 before the patient was given her inpatient pack of medications, and oxycontin was omitted from her morning medication dosage as it was contraindicated with the co-codamol. The patient was reassessed for competency to self-medicate and was assessed as not competent, the medications from home were removed from her locker and she was placed back under the care of the ward nurses for medication delivery which adhered to the hospital prescribed regimen.'[39]

Roberts et al.[40] found that 'The 10 drugs most commonly involved in dispensing errors accounted for 19 per cent of the errors and 27 per cent of the seriously detrimental/fatal outcomes. These drugs were… co-codamol [ranked 9th] …'. Co-codamol was also one of the medications that was most commonly involved in errors in a study by Lynskey et al.[41] Co-codamol ($n = 3$) and co-beneldopa ($n = 3$) were included in a group of medicines implicated in more than one dispensing error/near-miss in a 4-week study.[42] Isolated cases of prescribing errors can also be found,[43] and in another case, a junior doctor did not realize that codeine (to which the patient was allergic) was present in co-codamol.[44] The same case was later reported again by Lewis et al.[45] Another report described a nurse who '…described how she administered co-codamol instead of codeine whilst busy and could only recall that the patient was prescribed co-codamol previously'.[46]

The authors of a study of methodological variability in drug error studies noted that errors with co-codamol may not be recorded, as 'Many errors were comparatively minor, such as not specifying the strength of co-codamol (available in two strengths). A ward pharmacist is likely to amend these without consulting the prescriber and may not consider them to be [an error] worth recording. We estimate that one in four [prescribing errors] fell into this category.'[47] Failure to report drug errors may also be related to their frequency, since a common error may be amended by a pharmacist without consultation or recording. There is some evidence to suggest that prevented events (i.e., errors that do not reach the patient) are more frequent than those that are not prevented.[48]

1.1.6 | Co-dydramol

We identified 260 papers, which were reduced to seven after screening. A small number of reports identified by Schneider and Barber[28] and by Rogers et al.[32] and reports from Avery et al.,[22] and Lysheim[43] emerged again and are not discussed here.

Some reports have highlighted the potential for errors when new strengths of co-dydramol were marketed.[49] In one case, co-dydramol was given five times a day rather than four,[50] and in another, the drug pair co-proxamol/co-dydramol ($n = 7$) was implicated in look-alike errors.[33]

1.1.7 | Co-trimoxazole

Our search returned 6930 records, which were reduced to 1310 with the addition of 'prescribing' in the search term. After screening, this was further reduced to 11 reports. Although specific details were absent, co-amoxiclav and co-trimoxazole have been identified as common drugs implicated in 'unintended medication discrepancies'.[51] We

also identified a few reports of co-prescription of co-trimoxazole with phenytoin, affecting folate metabolism[52] and a look-alike error with the drug pair co-trimoxazole and clotrimazole.[53] Work from Anto et al.,[24] re-emerged here, as discussed in an earlier section (co-amoxiclav).

This search identified a new kind of error: '[trimethoprim-sulfamethoxazole] is one of the few combined therapy [sic] where its dosing is usually referred to a single component of the whole product (i.e. trimethoprim) … Most of those errors [n = 12] were due to mistakenly verifying and/or calculating the prescribed dose as a total combined quantity rather than based on [the trimethoprim] component only and that led to a lower than intended dose being administered to the patient.'[54] Often the doses of these products are combined in prescriptions, for example, 'co-amoxiclav 625 mg'. One report reported a textbook description of a dose of co-trimoxazole as, 'IV 8-10 mg/kg TMP div. q6h', that is, 8–10 mg/kg of the trimethoprim component, divided across four doses, spaced 6 h apart, but this was interpreted to mean 8–10 mg/kg every 6 h.[55]

'In South Africa, the only case of mismanagement of severe allergy that ended in a guilty verdict … was that of a general practitioner who chose to ignore the warnings of a history of an allergic reaction to sulpha drugs, and administered co-trimoxazole.'[56] The link to the original reference source is unavailable and the citing study does not provide further detail. In a separate study, allergy prompted 10/87 interventions for co-amoxiclav and 40/774 interventions for amoxicillin.[57] In another study, of nine indication errors, four involved a co-drug prescribed for a patient known to be allergic to one of the components—co-amoxiclav ($n = 3$) and co-trimoxazole ($n = 1$).[58]

Another study highlighted that a third of serious co-trimoxazole-induced adverse drug reactions (ADRs) could have been avoided if the use of co-trimoxazole had been appropriate or if it had complied with the Summary of Product Characteristics (SmPC).[59] This was confirmed in a later study, in which the rate of preventable ADRs was 58%.[60] This could have been related to adverse effects of sulfamethoxazole, and not necessarily co-drug nomenclature.

1.1.8 | Miscellaneous

The compounds discussed in the previous sections account for ~99% ($n = 1\,702\,680/1\,722\,166$) of general practice prescriptions for co-drugs in England and Wales. Isolated incidences were also identified with co-danthramer ($n = 58$).[24,61] Co-proxamol ($n = 443$) hits were reduced to two: Cox et al., picked up previously with co-dydramol,[33] and Schnider et al.[28] Co-amilozide produced 113 hits, which was reduced to two reports after screening, one was due to a simple oversight[62] and one was identified above under co-amilofruse.[24]

1.1.9 | Implications of the findings

Although there are many examples of errors involving co-drugs, it is difficult to tease out precisely why these errors occurred in every case, as much of the literature focuses on enumerating drug errors and classifying the errors in discrete bins. Studies that give specific

FIGURE 1 A selection of paracetamol-codeine (co-codamol) products available on the UK market; this highlights inconsistencies in the labelling of these products—some do not prominently display the individual contents and in others the strength is unclear. Medical pack information obtained from public sources on 2 July 2024, copyright is retained by the licence holder.

details often ascribe an error to confusion with the drug name. However, the paucity of evidence may reflect the fact that these 'naming errors' are probably corrected by pharmacists before they become errors. This was picked up by one of the studies in this analysis.[47]

The strengths of some formulations, particularly antibiotics, are often referred to as the total amounts of the components present in the formulations. This unusual nomenclature invites errors that are exclusive to combination products. As a co-drug name does not explicitly identify its components, this approach creates broader problems. For example, although adverse reactions have been observed in patients taking co-trimoxazole plus an angiotensin-converting enzyme (ACE) inhibitor[63] and glyburide plus co-trimoxazole,[64] we do not know which component was responsible. This eliminates the possibility of using this evidence to write a prescription that excludes the causative agent, potentially resulting in sub-optimal care. Furthermore, while the contents of co-codamol are arguably known by experienced clinicians, it is reasonable to suspect that patients may not be aware. We found evidence of risky prescribing behaviour where more than one paracetamol product was prescribed at the same time[38]; given that paracetamol is one of the drugs most commonly associated with accidental poisoning,[65] and since co-codamol products are among the most common products sold over the counter, these products are of particular concern, this error type has been classified previously.[66] In addition, the labelling of these products is very inconsistent, and this may contribute to errors (Figure 1).

For the same reasons that we advocate standardized nomenclature via WHO's INN committee, we should aim to standardize the nomenclature of these products. Indeed, it is difficult to see why these co-names stuck, particularly as these problems were identified as far back as the early 1970s when the first co-drugs were entering the market.[67] At that time, it was felt that more education was needed—but perhaps we should just name them properly.

We suggest that a standard nomenclature for these products should use the + symbol. It is easily keyed, its natural interpretation suggests a combination product and it is not used as a symbol in any other drug names, allowing compound products to be readily identified. Other options include a hyphen (-), the en rule (–) or a slash (/). A slash may generate confusion as it is currently used to identify both the British Approved Names and INNs rather than to indicate compound products, for example, 'adrenaline/epinephrine' and 'noradrenaline/norepinephrine'. Some might argue an en rule or dash is best, given its use to join words of equal importance that do not modify one another, but it could also be interpreted as a prefix or modifier, which would be misleading. The slash or hyphen has historically been the approach used for these products, but we argue that this can become linguistically complex, which might lead to errors. We reflect on trimethoprim/sulfamethoxazole 800/160 mg, trimethoprim-sulfamethoxazole 800/160 mg or trimethoprim 800 mg + sulfamethoxazole 160 mg, and suggest that the latter option is more explicit. The advantages of our proposal become more apparent with the anti-retroviral Symtuza®, darunavir/cobicistat/emtricitabine/tenofovir alafenamide 800/150/200/10 mg, which could be written as, darunavir 800 mg + cobicistat 150 mg + emtricitabine 200 mg + tenofovir alafenamide 10 mg.

While we focus on oral drug products with the co-drug nomenclature, these principles should be applied to multidrug products more generally—whether they be proprietary, generic or unlicensed products. In particular, we would like to draw our reader's attention to oral contraceptives such as Mercilon (ethinylestradiol 20 μg + desogestrel 150 μg) and Marvelon (ethinylestradiol 30 μg + desogestrel 150 μg) and inhaled products like Spiolto® (tiorpopium 2.5 mg + olodaterol 2.5 mg).

In summary, we suggest that it is better to explicitly state the INN of each component in the medicine in the x dose + y dose format. Our findings suggest that this might reduce errors, particularly for high-volume drugs containing paracetamol, amoxicillin + clavulanic acid (co-amoxiclav) and trimethoprim + sulfamethoxazole (co-trimoxazole). We also suggest that the co-name should still be included for these medicines to avoid confusion for patients who might be familiar with the co-drug (e.g., co-codamol: paracetamol 500 mg + codeine 30 mg). This standard nomenclature should extend beyond the product literature and find utility in prescribing resources to minimize confusion and prevent medication errors.

AUTHOR CONTRIBUTIONS

Oisin N. Kavanagh: conceptualization, writing—first draft. **Jeffrey K. Aronson** and **Robert Lowe:** writing—reviewing and editing. All authors agreed on the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to declare.

DATA AVAILABILITY STATEMENT

Data is available as a Supplementary file.

ORCID

Oisín N. Kavanagh https://orcid.org/0000-0001-7369-4611
Jeffrey K. Aronson https://orcid.org/0000-0003-1139-655X

REFERENCES

1. World Health Organization. *Guidelines on the Use of International Nonproprietary Names (INNs) for Pharmaceutical Substances*. World Health Organization; 1997.
2. Lambert BL, Lin SJ, Chang KY, Gandhi SK. Similarity as a risk factor in drug-name confusion errors: the look-alike (orthographic) and sound-alike (phonetic) model. *Med Care*. 1999;37(12):1214-1225. doi:10.1097/00005650-199912000-00005
3. Heck J. Challenging patriarchic nomenclature: is the term "tall man" lettering still appropriate? *Am J Health-Syst Pharm*. 2022;79(12):933-934. doi:10.1093/ajhp/zxac052
4. Filik R, Purdy K, Gale A, Gerrett D. Labeling of medicines and patient safety: evaluating methods of reducing drug name confusion. *Hum Factors*. 2006;48(1):39-47. doi:10.1518/001872006776412199

5. Bryan R, Aronson JK, Williams AJ, Jordan S. A systematic literature review of LASA error interventions. *Br J Clin Pharmacol*. 2021;87(2):336-351. doi:10.1111/bcp.14644
6. Kavanagh ON, Albadarin AB, Croker DM, Healy AM, Walker GM. Maximising success in multidrug formulation development: a review. *J Control Release*. 2018;283:1-19. doi:10.1016/j.jconrel.2018.05.024
7. Kavanagh ON. An analysis of multidrug multicomponent crystals as tools for drug development. *J Control Release*. 2024;369:1-11. doi:10.1016/j.jconrel.2024.03.034
8. Reeves DS. Sulphamethoxazole-trimethoprim: the first two years. *J Clin Pathol*. 1971;24(5):430-437. doi:10.1136/jcp.24.5.430
9. Anonymous. Branded generics [internet]. Community Pharmacy England. [cited 2024 Apr 8]. Available from: https://cpe.org.uk/funding-and-reimbursement/pharmacy-funding/funding-distribution/branded-generics/
10. Robinson J. 'Devastating effects' caused by switching between branded and generic Parkinson's disease medication [internet]. *Pharm J*. 2023. [cited 2024 Apr 8]. Available from: https://pharmaceutical-journal.com/article/news/devastating-effects-caused-by-switching-between-branded-and-generic-parkinsons-disease-medication
11. Patel N, Desai M, Shah S, Patel P, Gandhi A. A study of medication errors in a tertiary care hospital. *Perspect Clin Res*. 2016;7(4):168-173. doi:10.4103/2229-3485.192039
12. Wirtz V, Barber ND, Taxis K. An observational study of intravenous medication errors in the United Kingdom and in Germany. *Pharm World Sci*. 2003;25(3):104-111. doi:10.1023/A:1024009000113
13. Hamad A, Cavell G, Wade P, Hinton J, Whittlesea C. Risk of medication safety incidents with antibiotic use measured by defined daily doses. *Int J Clin Pharmacol*. 2013;35(5):772-779. doi:10.1007/s11096-013-9805-9
14. Hamad AA. *Evaluating, Understanding and Managing Medication Incidents with High-Risk Antibiotics [Internet]*. [Thesis], London: King's College London; 2015. Available from: https://kclpure.kcl.ac.uk/portal/files/45225832/2015_Hamad_Anas_1045375_ethesis.pdf
15. Lane N, Hunter I. Lessons learned: using adverse incident reports to investigate the characteristics and causes of prescribing errors. *BMJ Open Qual*. 2020;9(2):e000949. doi:10.1136/bmjoq-2020-000949
16. Patel R, Green W, Martinez MM, Shahzad MW, Larkin C. A study of Foundation Year doctors' prescribing in patients with kidney disease at a UK renal unit: a comparison with other prescribers regarding the frequency and type of errors. *Eur J Hosp Pharm*. 2015;22(5):291-297. doi:10.1136/ejhpharm-2014-000620
17. Härkänen M, Vehviläinen-Julkunen K, Murrells T, Rafferty AM, Franklin BD. Medication administration errors and mortality: incidents reported in England and Wales between 2007 2016. *Res Social Adm Pharm*. 2019;15(7):858-863. doi:10.1016/j.sapharm.2018.11.010
18. McCall S, Bunch K, Brocklehurst P, et al. The incidence, characteristics, management and outcomes of anaphylaxis in pregnancy: a population-based descriptive study. *BJOG*. 2018;125(8):965-971. doi:10.1111/1471-0528.15041
19. James KL, Barlow D, Burfield R, Hiom S, Roberts D, Whittlesea C. A study of unprevented dispensing incidents in Welsh NHS hospitals. *Int J Pharm Pract*. 2010;16(3):175-188. doi:10.1211/ijpp.16.3.0008
20. Roberts DE, Burfield R, Waller J, Whittlesea C. Dispensing errors in NHS hospitals 2001-2004. *Int J Pharm Pract*. 2004;12:R45-R45.
21. Acheampong F, Tetteh AR, Anto BP. Medication administration errors in an adult emergency department of a tertiary health care facility in Ghana. *J Patient Saf*. 2016;12(4):223-228. doi:10.1097/PTS.0000000000000105
22. Avery AA, Barber N, Ghaleb M, et al. *Investigating the prevalence and causes of prescribing errors in general practice: the PRACtICe study*; 2012.
23. Ho CYW, Dean BS, Barber ND. When do medication administration errors happen to hospital inpatients? *Int J Pharm Pract*. 2011;5(2):91-96. doi:10.1111/j.2042-7174.1997.tb00891.x
24. Anto B, Barlow D, Oborne CA, Whittlesea C. Incorrect drug selection at the point of dispensing: a study of potential predisposing factors. *Int J Pharm Pract*. 2011;19(1):51-60. doi:10.1111/j.2042-7174.2010.00072.x
25. Sin CMH, Young MW, Lo CCH, Ma PK, Chiu WK. The impact of computerised physician order entry on prescribing in general paediatric units in Hong Kong. *Int J Pharm Pract*. 2021;29(2):164-169. doi:10.1093/ijpp/riaa018
26. Chen YF, Neil KE, Avery AJ, Dewey ME, Johnson C. Prescribing errors and other problems reported by community pharmacists. *Ther Clin Risk Manag*. 2005;1(4):333-342.
27. Marvin V, Park C, Vaughan L, Valentine J. Phone calls to a hospital medicines information helpline: analysis of queries from members of the public and assessment of potential for harm from their medicines. *Int J Pharm Pract*. 2011;19(2):115-122. doi:10.1111/j.2042-7174.2010.00081.x
28. Schneider J, Barber N. Provision of a domiciliary service by community pharmacists. *Int J Pharm Pract*. 2011;4(1):19-24. doi:10.1111/j.2042-7174.1996.tb00834.x
29. Howard R. A qualitative exploration of the underlying causes of preventable drug-related morbidity in primary care, resulting in hospitalisation. *Pharmacy Practice Research Trust*; 2008:49.
30. Sagripanti M, Dean B, Barber N. An evaluation of the process-related medication risks for elective surgery patients from pre-operative assessment to discharge. *Int J Pharm Pract*. 2011;10(3):161-170. doi:10.1111/j.2042-7174.2002.tb00604.x
31. Spencer R, Avery A, Serumaga B, Crowe S. Prescribing errors in general practice and how to avoid them. *Clin Risk*. 2011;17(2):39-42. doi:10.1258/cr.2010.010072
32. Rogers PJ, Fletcher G, Rees JE. Clinical interventions by community pharmacists using patient medication records. *Int J Pharm Pract*. 2011;3(1):6-13. doi:10.1111/j.2042-7174.1994.tb00779.x
33. Cox AR, Phull S, Price V, et al. Retrospective analysis of pharmacy dispensing errors: twelve years experience in a UK Hospital. *Drug-Safety*. 2008;31(10):885-885, 960. doi:10.2165/00002018-200831100-00174
34. Dean BS, Barber ND. A validated, reliable method of scoring the severity of medication errors. *Am J Health-Syst Pharm*. 1999;56(1):57-62. doi:10.1093/ajhp/56.1.57
35. Brady D, Franklin BD. An evaluation of the contribution of the medical admissions pharmacist at a London teaching hospital. *Int J Pharm Pract*. 2010;12(1):1-6. doi:10.1211/0022357023213
36. Baptista R, Williams M, Price J. Using xPIRT to record pharmacy interventions: an observational, cross-sectional and retrospective study. *Dent Health*. 2022;10(12):2450. doi:10.3390/healthcare10122450
37. Khadem NR, Nirenberg MJ. Carbidopa/levodopa pharmacy errors in Parkinson's disease. *Mov Disord*. 2010;25(16):2867-2871. doi:10.1002/mds.23311
38. Manyemba J, Batty GM, Grant RR, et al. Prescription of paracetamol-containing medications as indicator of quality of prescribing. *Age Ageing*. 2007;36(5):582-584. doi:10.1093/ageing/afm090
39. Deane KHO, Gray R, Balls P, et al. Patient-directed self-management of pain (PaDSMaP) compared to treatment as usual following total knee replacement; a randomised controlled trial. *BMC Health Serv Res*. 2018;18(1):346. doi:10.1186/s12913-018-3146-2
40. Roberts DE, Spencer MG, Burfield R, Bowden S. An analysis of dispensing errors in NHS hospitals. *Int J Pharm Pract*. 2002;10(S1):R6-R6.
41. Lynskey D, Haigh SJ, Patel N, Macadam AB. Medication errors in community pharmacy: an investigation into the types and potential causes. *Int J Pharm Pract*. 2007;15(2):105-112. doi:10.1211/ijpp.15.2.0005

42. Chua SS, Wong ICK, Edmondson H, et al. A feasibility study for recording of dispensing errors and 'near misses' in four UK primary care pharmacies. *Drug-Safety*. 2003;26(11):803-813. doi:10.2165/00002018-200326110-00005
43. Lysheim AR. Continuity of care during hospital stay: a review and evaluation of medicines reconciliation on admission. Vol. 69; 2009.
44. Dornan T, Ashcroft D, Heathfield H, et al. *An in depth investigation into causes of prescribing errors by foundation trainees in relation to their medical education. EQUIP study*. [Internet], University of Manchester Medical School Teaching Hospital: General Medical Council; 2009. p. 83. Available from: https://www.gmc-uk.org/-/media/documents/final-report-prevalence-and-causes-of-prescribing-errors_pdf-28935150.pdf
45. Lewis PJ, Seston E, Tully MP. Foundation year one and year two doctors' prescribing errors: a comparison of their causes. *Postgrad Med J*. 2018;94(1117):634-640. doi:10.1136/postgradmedj-2018-135816
46. Keers RN, Plácido M, Bennett K, Clayton K, Brown P, Ashcroft DM. What causes medication administration errors in a mental health hospital? A qualitative study with nursing staff. *PLoS ONE*. 2018;13(10):e0206233. doi:10.1371/journal.pone.0206233
47. Franklin BD, Birch S, Savage I, et al. Methodological variability in detecting prescribing errors and consequences for the evaluation of interventions. *Pharmacoepidemiol Drug Saf*. 2009;18(11):992-999. doi:10.1002/pds.1811
48. James KL, Barlow D, Burfield R, Hiom S, Roberts D, Whittlesea C. Unprevented or prevented dispensing incidents: which outcome to use in dispensing error research? *Int J Pharm Pract*. 2011;19(1):36-50. doi:10.1111/j.2042-7174.2010.00071.x
49. Anonymous. Co-dydramol—specify the strength. *DTB*. 2018;56(4):38-39. doi:10.1136/dtb.2018.4.0605
50. Hogan H, Olsen S, Scobie S, et al. What can we learn about patient safety from information sources within an acute hospital: a step on the ladder of integrated risk management? *BMJ Qual Saf*. 2008;17(3):209-215. doi:10.1136/qshc.2006.020008
51. Moges TA, Akalu TY, Sema FD. Unintended medication discrepancies and associated factors upon patient admission to the internal medicine wards: identified through medication reconciliation. *BMC Health Serv Res*. 2022;22(1):1251. doi:10.1186/s12913-022-08628-5
52. Tesh D, Beeley L. Errors of drug prescribing. *Br J Clin Pharmacol*. 1975;2(5):403-409. doi:10.1111/j.1365-2125.1975.tb00548.x
53. Irwin A, Mearns K, Watson M, Urquhart J. The effect of proximity, tall man lettering, and time pressure on accurate visual perception of drug names. *Hum Factors*. 2013;55(2):253-266. doi:10.1177/0018720812457565
54. Bakdach D, Elajez R. Trimethoprim–sulfamethoxazole: new lessons on an old antimicrobial; a retrospective analysis. *J Pharm Health Services Res*. 2020;11(3):269-274. doi:10.1111/jphs.12358
55. Lewis JD, Aleman JD. Ambiguous dosing information in *Guide to Antimicrobial Therapy*. *Am J Hosp Pharm*. 1989;46(11):2251. doi:10.1093/ajhp/46.11.2251
56. Marian A. Severe allergies and the law—the case of anaphylaxis: ethics. *Curr Allergy Clin Immunol*. 2012;25(3):156-160.
57. Hayes CV, Parekh S, Lecky DM, Loader J, Triggs-Hodge C, Ashiru-Oredope D. The National Implementation of a Community Pharmacy Antimicrobial Stewardship Intervention (PAMSI) through the English Pharmacy Quality Scheme 2020 to 2022. *Antibiotics*. 2023;12(4):793. doi:10.3390/antibiotics12040793
58. Hardmeier B, Braunschweig S, Cavallaro M, Giger M, Meier PJ, Fattinger K. Adverse drug events caused by medication errors in medical inpatients. *Swiss Med Wkly*. 2004;134(4546):664-664. doi:10.4414/smw.2004.10801
59. Chaby G, Valeyrie-Allanore L, Duong TA, et al. Severe cutaneous adverse reactions due to inappropriate medication use. *Br J Dermatol*. 2018;179(2):329-336. doi:10.1111/bjd.16365
60. Coppry M, Duret S, Berdaï D, et al. Adverse drug reactions induced by cotrimoxazole: still a lot of preventable harm. *Fundam Clin Pharmacol*. 2022;36(2):421-426. doi:10.1111/fcp.12735
61. Hawkey CJ, Hodgson S, Norman A, Daneshmend TK, Garner ST. Effect of reactive pharmacy intervention on quality of hospital prescribing. *BMJ*. 1990;300(6730):986-990. doi:10.1136/bmj.300.6730.986
62. Dobrzanski S, Hammond I, Khan G, Holdsworth H. The nature of hospital prescribing errors. *Br J Clin Governance*. 2002;7(3):187-193. doi:10.1108/14664100210438271
63. Fralick M, Macdonald EM, Gomes T, et al. Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: population based study. *BMJ*. 2014;30(349):g6196. doi:10.1136/bmj.g6196
64. Juurlink DN. *The clinical epidemiology of poisoning in Ontario* [Internet]; University of Toronto; 2003 [cited 2024 Mar 20]. Available from: https://library-archives.canada.ca/eng/services/services-libraries/theses/Pages/item.aspx?idNumber=56683597
65. Larson AM, Polson J, Fontana RJ, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. *Hepatology*. 2005;42(6):1364-1372. doi:10.1002/hep.20948
66. Heck J, Krichevsky B, Stichtenoth DO, Siederdissen CH, zu, Krause O. Duplicate prescriptions—proposal of a clinically oriented categorisation. *Eur J Clin Pharmacol*. 2021;77(10):1589-1591. doi:10.1007/s00228-021-03143-8
67. Cromie BW. Combination products. *Postgrad Med J*. 1974;50(580):103-106. doi:10.1136/pgmj.50.580.103

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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