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Effects of Medication Review on Drug-Related Problems in Patients Using Automated Drug-Dispensing Systems A Pragmatic Randomized Controlled Study

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**Effects of Medication Review on
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Supplemental Digital Content

This Supplemental Digital Content contains the table and appendices referred to in the full version of this article, which can be found at <http://adisonline.com/aging>.

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Table S1. Opinions of participating community pharmacists about the medication review process.

	Disagree	Not disagree nor agree	Agree
In general I agreed with the DRPs which were formulated by the pharmacist reviewers	0	1	5
In general I agreed with the recommendations which were formulated by the pharmacist reviewers	0	2	4
The pharmacist reviewers had a lack of relevant information to give specific recommendations	2	1	3
There was good cooperation with the GPs in medication review	2	1	3
The GP was not willing to share relevant clinical information which is important for medication review	3	2	1
The GP showed reluctance concerning the recommendations	2	1	3
Discussing DRPs and recommendations with the GP was difficult	1	1	4
It was difficult to make appointments with the GP about the pharmaceutical care plan of the patient	1	1	4
The patient was resistant to medication review and medication changes due to medication review	3	3	0
It is efficient to get a care plan from pharmacist reviewers	2	2	2
I prefer to conduct medication reviews myself instead of receiving care plans	1	1	4
I want to follow courses on medication review	2	2	2

DRPs = drug-related problems.

Appendix S1: DOCUMENT Classification System for Drug-Related Problems and Their Resolution

The following classification system has been modified from the original DOCUMENT system with permission from G. Peterson and colleagues, University of Tasmania, Australia.

Indicates a new or modified subcategory, see Appendix S2.

Blue text indicates modifications made to the original DOCUMENT system by the current study investigators.

Drug-Related Problems

Drug selection

These are problems related to the choice of drug prescribed or taken

Inappropriate drug selection can occur in a number of situations, including the prescriber's selection of the drug and the pharmacist's selection of a drug in the dispensing process. There are many factors which may have led to inappropriate selection, for example a patient with multiple prescribers or communication post-discharge or a dispensing error.

Duplication (D1)

When to Use:

Duplication refers to where a patient is prescribed and/or is using two drugs from the same therapeutic class.

When there are no obvious adverse clinical effects of the two drugs together, but it is either inappropriate or very unusual to see them prescribed or used together as they are from the same therapeutic class.

This also covers the specific compliance situation where a person may be inappropriately taking two brands of the same drug.

Examples of when to use:

- Patient prescribed ranitidine plus pantoprazole
- Patient prescribed both terbutaline and salbutamol inhalers
- Patient taking generic amiodarone and brand name *Cordarone* at the same time
- Patient taking a sample provided by a doctor as well as the same drug dispensed at the pharmacy

When Not to Use:

If the drugs involved are not of the same therapeutic class, then use "Drug selection - Drug interaction (D2)".

If there is evidence of an adverse clinical effect use "Toxicity - related to drug interaction (T2)"

Drug interaction (D2)

When to Use:

When there are no obvious adverse clinical effects of the drug interaction, but the interaction is serious enough to check if the doctor knows of it.

When there is a likely serious interaction between the patient's existing therapy and a newly prescribed or used drug, but the patient has NOT yet commenced taking the new drug.

Examples of when to use:

- Patient commenced on tramadol who is already taking fluoxetine
- Patient ceases amiodarone while continuing on warfarin
- Patient requests to purchase an over the counter antacid when taking tetracycline

When Not to Use:

If the interacting drug is of the same therapeutic class as a drug currently taken by the patient, then use "Drug selection - Duplication (D1)"

If the interaction is causing, or is suspected of causing a noticeable effect of any sort, then use "Toxicity - Caused by drug interaction (T2)".

Wrong drug (D3)

When to Use:

Where it was clear the intention of the prescriber was for a different drug from that prescribed for the patient.

When the prescription was intended to mean a different drug and there was an error or,

When the drug being taken was prescribed correctly but was dispensed as the wrong drug

Examples of when to use:

- Patient supplied with and taking Lasix (furosemide) 20 mg, while doctor prescribed Losec (omeprazole) 20 mg
- Doctor prescribes chlorpromazine 200mg bd but intended carbamazepine 200mg bd

When Not to Use:

If the drug is felt to be inappropriate because of specific patient parameters such as poor renal function, then use "Contra-indication/intolerance (D5c)".

If the drug prescribed is unavailable for dispensing (either because your pharmacy has no stock or the manufacturer/distributor has no stock) then use "Non-clinical (N0)".

If the patient is experiencing symptoms of toxicity use "Toxicity evident (T3)"

Wrong dosage form (D4)

When to Use:

When the formulation of the product is inappropriate or incorrect when considering its intended use.

Also covers the specific situation where an error by the prescriber results in an absurd set of instructions (eg, salbutamol inhaler, apply three times a day).

Examples of when to use:

- Vancomycin oral capsules prescribed to treat systemic infection
- Ear drop product ordered or supplied for an eye problem

When Not to Use:

If the patient has a physical problem with the administration of the dosage form as it is intended to be used (eg. swallowing a particular form of the medication whole, cannot appropriately insert suppositories, arthritis limiting the use of an inhaler) then use "Compliance - Difficulty using dosage form (C4)".

If the difficulty is related to a technical problem with the use of an administration device such as an aerohaler, then use "Education - Demonstration of device (E3)".

If the difficulty is not a technical one, and related to lack of understanding of the use of the dose form, then use "Education - Confusion about therapy (E2)".

Lack of indication or unclear indication (D5a)[#]

When to Use:

When a drug is felt to be unnecessary based on the conditions the patient has.

Examples of when to use:

- Patient commenced omeprazole when they were taking celecoxib for a sore knee. Celecoxib has been ceased, but they are still taking omeprazole.

Lack of effectiveness (D5b)[#]

When to Use:

When you believe a more effective drug is available and you suggest it instead of the current therapy.

When current guidelines recommend another therapy

Examples of when to use:

- Use of drugs such as promethazine, betahistine, mebeverine etc
- Doxazosin as monotherapy for hypertension in patients with diabetes

When Not to Use:

Dosage is too low for drug to be effective, choose O2: Dosage too low

Contraindication/intolerance (D5c)[#]

When to Use:

When there is a contraindication to the use of a drug because of an underlying condition in the patient.

When a drug or drug group is prescribed for the patient to which there has previously been a major adverse reaction.

Examples of when to use:

- Propranolol in patients with diabetes

- Patient has an history of allergic reactions for a certain antibiotic and receives a repeat prescription for this antibiotic

When Not to Use:

If the patient is currently experiencing symptoms of toxicity, then use "Toxicity/Adverse reaction - Toxicity evident (T3)"

Other drug selection problem (D0) #

When to Use:

When a less expensive or alternative brand is substituted purely for cost reasons.

When the drug being used is out of date or deteriorated in some other way.

Examples of when to use:

- Patient has nitroglycerine tablets for use that are over 2 years old and have been stored incorrectly.

When Not to Use:

If a less expensive brand is substituted because the ordered brand is unavailable, then use "Non-clinical (N0)".

Over or underdose prescribed

Problems related to the prescribed dose or schedule of the drug

These problems relates to an inappropriate dose, either the individual dose or the cumulative dose of the drug. These are situations where the dose prescribed is not appropriate either based on previous dosage or reference dose ranges.

Dose too high (O1)

When to Use:

When the total daily dose of a medication prescribed is too high for the patient, either based on previous dosage or reference dose ranges. Includes situations where the dose is too high for the patient in relation to their renal function or weight, age etc.

This also includes situations where the dose that is prescribed is too high by unintentional error.

Examples of when to use:

- Patient is prescribed gliclazide MR 180mg in the morning
- Patient is prescribed dexamethasone 50mg daily (doctor was thinking of prednisolone dose)
- Patient prescribed spironolactone 100mg bd for heart failure

When Not to Use:

If the patient is taking too high a dose as a result of not following the appropriate directions, then the situation relates to compliance use "Compliance - Taking too much (C2)".

Dose too low (O2)

When to Use:

When the dose prescribed is either too low based on reference dose ranges or too low based on previous therapy.

This includes situations where the dose that is prescribed is too low by unintentional error

Examples of when to use:

- Locum doctor prescribes irbesartan 150mg daily, when previous therapy was 300mg daily
- Prescription for prazosin 0.5mg bd for hypertension

When Not to Use:

If the actual dose per day is suitable, but the duration is too short, then use "Over/under dose - Other (O0)"

If the patient is taking too low a dose of a drug as a result of not following the appropriate directions, then the situation relates to compliance use "Compliance - Taking too little (C1)".

Other Dose Problem (O3)

When to Use:

When the duration of use of the product is inappropriate - either it is too short or too long.

When the total dose of a medication is suitable, but the frequency or the dosage schedule is inappropriate.

Examples of when to use:

- Patient prescribed cephalexin 500mg tds for 3 days for cystitis.
- Simvastatin ordered as 40mg in the morning
- Gliclazide MR prescribed as three times daily

When Not to Use:

If the patient is not taking the appropriate dose of a product as a result of a lack of understanding of the dosage regimen, then a compliance related code would be more appropriate.

Compliance

Problems related to the way the patient takes the medication

These are situations where a problem arises because of the way in which the patient takes the medication. The influences behind compliance issues are numerous. If the patient decides to take the medication in a way other than prescribed by the doctor then the issue is one of compliance.

Taking too little (C1)**When to Use:**

When the patient uses too little of a medication as a result of forgetfulness or lack of understanding of the dosage regimen prescribed. (refill rate <0.8)

Examples of when to use:

- Patient taking *metformin* only when required rather than regularly
- Patient using *Transiderm-Nitro* patches only every few days, not regularly
- Patient not taking medication because they believe it will "stop working later on"

When Not to Use:

If the underuse is appropriate because of the resolution of symptoms or a condition, then use "Other drug selection problem (D0)" and specify that the drug may no longer be required.

If the patient has a physical problem with the administration of the dosage form as it is intended to be used (eg. swallowing a particular form of the medication whole, cannot appropriately insert suppositories, arthritis limiting the use of an inhaler) then use "Compliance - Difficulty using dosage form (C4)"

Taking too much (C2)**When to Use:**

When the patient uses too much of a medication as a result of forgetfulness or lack of understanding of the dosage regimen prescribed. (refill rate > 1.2)

Examples of when to use:

- Patient presents requesting a second *salbutamol* inhaler 11 days after the previous one was provided.
- Patient continuing to take 50mg daily of *prednisolone*, had forgotten to commence a dose reduction schedule as instructed by the doctor.
- Patient believes they have forgotten a medication and takes a second dose on the same day.

When Not to Use:

If the overuse is due to an appropriate increase in use because of increased symptoms, then use "Untreated indication - Condition not adequately treated (U1)"

If the overuse consists of inappropriately taking two different brands or forms of the same ingredient unknowingly, then use "Drug selection - Duplication (D1)".

Intentional drug misuse (C3)**When to Use:**

When there is an intentional overuse of a particular, potentially abusable, product. Includes the situation where the prescription appears to be a forgery. Situations where misuse is suspected can also be recorded.

Examples of when to use:

- Patient presents a third prescription for paracetamol/codeine within 2 weeks, each of the prescriptions was written by a different doctor.
- Patient presents a hand written prescription for morphine slow release and the quantity of tablets appears to have been altered.

When Not to Use:

If the overuse is due to an appropriate increase in use because of increased symptoms, then use "Untreated indication - Condition not adequately treated (U1)"

Difficulty using dosage form (C4)**When to Use:**

When the patient has a physical problem with the administration of the dosage form or device as it is intended to be used

Examples of when to use:

- Patient cannot swallow her slow release *diltiazem* capsules
- Patient with scoliosis cannot insert suppositories
- Controlled release tablet ordered for a patient who must crush all oral medications
- Arthritis is limiting the patient's use of their *salbutamol* inhaler.

If the difficulty is related to a technical problem with the use of an administration or monitoring device such as an aerohaler, then use "Education - Demonstration of device (E3)".

If the difficulty is not a technical one, and related to lack of understanding of the use of the dose form, then use "Education - Confusion about therapy (E2)".

Other Compliance Problem (C5)**When to Use:**

When the patient is aware of the way to take the drug, is physically able to take the drug, and understands its purpose, but does not wish to take it.

Examples of when to use:

- Patient unwilling to use *mirtazapine* after reading the package insert.

When Not to Use:

If the compliance issue results in two drugs of the same therapeutic class being taken inadvertently, then use "Drug selection - Duplication (D1)".

If the patient does not wish to take the medication because it is causing an adverse event of some sort, then a "Toxicity or adverse event" category would be appropriate.

Untreated indications

Problems relating to actual or potential conditions that require management

This category encompasses the situations where the current disease management is suboptimal. It is also relevant where there are potential conditions which could be avoided through preventative therapy.

Condition not adequately treated (U1)**When to Use:**

When the patient has a symptom or disease condition that is either not being treated, or is not being treated adequately

Examples of when to use:

- Patient taking *triamterene/hydrochlorothiazide* and *perindopril* for high blood pressure, but blood pressure continues to be high
- Patient develops nausea as part of a viral illness and requires addition of anti-nauseant medication.

When Not to Use:

*If the patient requires additional therapy as a preventative strategy (e.g. *potassium* when on a loop diuretic), then use "Untreated indication - Preventive therapy required (U2)".*

Preventive therapy required (U2)**When to Use:**

When the patient requires additional therapy to prevent a likely adverse event as a result of the patient's therapy, coexisting diseases or risk factors

Examples of when to use:

- Patient commences on *morphine* slow release and you suggest the addition of a stool softener
- You suggest addition of *omeprazole* to antiplatelet therapy in a person older than 80.

When Not to Use:

If the patient already has treatment for a particular problem, but it is not effective enough, then use "Untreated indication - Condition not adequately treated (U1)".

Other Untreated indication Problem (U3)**When to Use:**

When you think the patient has any other problem relating to actual or potential conditions that requires management.

Monitoring

Problems related to monitoring the efficacy or adverse effects of a drug

Where the situation primarily involves monitoring the effect of the drug, this can include laboratory monitoring (INR, drug level) or non-laboratory monitoring (blood pressure)

Laboratory Monitoring (M1)

When to Use:

When, in the absence of any adverse effects, you believe that a laboratory test is required (e.g. potassium, creatinine, white cell count, INR)

Also covers the situation where you undertake the monitoring in question and provide a recommendation following the result. (eg INR monitoring and suggesting a change of warfarin dose)

When, in the absence of any adverse effects, you believe that drug level monitoring is required.

Examples of when to use:

- Patient recently increased *furosemide* dose from 40mg daily to 120mg daily without a change in potassium replacement.
- Patient commenced on *amiodarone* and you recommend a thyroid function test
- Elderly woman on *digoxin*, who has not had a blood test for two years

When Not to Use:

If there are adverse effects associated with the parameter, then use “Other Toxicity problem (T0)”, and specify the parameter to be tested and the symptom or sign. (Eg, patient with leg cramps, suggest magnesium level)

If the need for laboratory level monitoring comes about as a result of a newly commenced drug, then use “Drug selection - Drug interaction (D2)”. The monitoring then becomes a recommendation, not the primary problem

If the patient is experiencing an adverse effect of some sort, which you believe is due to elevated drug levels, then use “Toxicity - Caused by dose (T1)”.

Non-Laboratory Monitoring (M2)

When to Use:

When, in the absence of any adverse effects, you believe that non-laboratory monitoring is required. (e.g. BP, BSL, temperature, weight)

Also covers the situation where the test is undertaken as a screening process.

Examples of when to use:

- A patient with heart failure has an appropriate increase in his dose of *furosemide* and you advise him to weigh himself each day for the next week.
- A patient has recently changed blood pressure medication and you encourage her to keep a record of blood pressure.

When Not to Use:

If you recommend monitoring of a parameter (e.g. weight, BSL) as a result of another drug problem, then that recommendation should be recorded in the Recommendation code section. The type of problem that leads to this recommendation may vary.

Other Monitoring Problem (M3)

When to Use:

When the patient has another problem related to the monitoring of his drugs for either efficacy or adverse effects.

When the patient should be having monitoring done, but has problems with attending the laboratory, or paying for the test or equipment needed.

Education or information

Problems related to knowledge of the disease or its management

This category includes situations where the patient is seeking information from the pharmacist. This information relates to their current therapy either in relation to the management or the disease process. When pharmacists are approached for information from other health professionals these should be recorded under this category.

Patient drug information request (E1)

When to Use:

When the patient has a reasonable understanding of their condition, but requests further information about their medication.

Examples of when to use:

- Patient requests information about *alendronate* and you provide a CMI
- Patient is travelling OS and asks you what immunisations he would require.

When Not to Use:

If the patient requests information primarily about the disease state, rather than a drug, then use “Education – Disease management or advice (E4)”

If the patient does not request the information, but you discover that they need the information in the course of your routine dispensing, then use “Education - Confusion about therapy (E2)”.

If the request is not about a specific drug, but a therapeutic device, then use “Education - Demonstration of device (E3)”

Confusion about therapy (E2)**When to Use:**

When the patient does not understand the reasons for the use of a medication, but they still take the medication as directed (i.e. correct dose and time).

Examples of when to use:

- When providing a new prescription for metoprolol for a patient with newly diagnosed hypertension, you find that she believes that the drug may cure the condition and she can stop the drug in a few months.
- Patient has been prescribed two antibiotics and they ask you why they need to take both.

When Not to Use:

If the patient requests further information, then use either “Education - Drug information request (E1)” or “Education - Disease management or advice (E4)” as appropriate.

If the confusion would have (or did) resulted in a change in compliance (either taking too much or too little of the medication), then an appropriate compliance code should be selected.

If the request is not about a specific drug, but a therapeutic device, then use “Education - Demonstration of device (E3)”

Demonstration of device (E3)**When to Use:**

When the patient has a technical problem with the use of an administration or monitoring device.(eg inhaler, BSL Monitor, Turbuhaler)

Examples of when to use:

- A patient is changed from a metered dose inhaler to an aerohaler and requests a demonstration of how to use the device.
- Patient has decided to start using a dosage administration aid and they ask the pharmacist how to use it correctly.

When Not to Use:

If the patient understands how to use the device, but has a physical reason for not being able to use it, then use “Compliance - Difficulty using dosage form (C4)”.

Disease management or advice (E4)**When to Use:**

When the primary purpose of the interaction with the patient was to inform them of critical aspects of the management or prevention of a disease or condition.

Also covers the situation where the patient requests the information or where there is confusion about a fundamental aspect of a condition they have

Examples of when to use:

- You counsel a patient with heart failure about fluid restriction
- You provide information about weight loss or smoking cessation for a person who has cardiovascular disease.

When Not to Use:

If the patient request information primarily regarding a drug, then use “Education - Drug information request (E1)”

Other Education or Information Problem (E0)**When to Use:**

When another health care worker (e.g. a doctor or another pharmacist) requests information. Also covers any other education or information related problem.

Non-clinical

Problems related to administrative aspects of the prescription

These problems are essentially administrative, in particular where details of the prescription need some clarification.

Not sub-classified (N0)

When to Use:

When an illegible prescription requires clarification.

When the prescription does not meet PBS requirements.

When the drug is unavailable from the manufacturer or is out of stock temporarily.

When the dose of the medication is not specified on the prescription.

When the prescriber is not authorised to prescribe that particular medication.

When the patient has problems getting to the pharmacy or collecting prescriptions.

Examples of when to use:

- Physeptone 5mg tablets not available, substitute 10mg tablets with dose adjustment

When Not to Use:

If a less expensive or alternative brand is substituted purely for cost reasons, then use “Other drug selection problem (D0)” and specify brand substitution for cost reasons.

Toxicity or adverse reaction

Problems related to the presence of signs or symptoms which are suspected to be related to an adverse effect of the drug. In the presence of a sign or symptom of toxicity the situation must be recorded under this category. It also includes situations where it is suspected that the issue is an adverse drug reaction.

Dose related (T1)

When to Use:

When the patient has signs or symptoms that suggest an adverse reaction that is likely to be dose related. Also where compliance issues have lead to symptoms of toxicity.

Examples of when to use:

- Patient has increased their dose of *tramadol* and develops headache, sweating and agitation
- *Promethazine* and *amitriptyline* together causing worsening of dry mouth
- Patient prescribed *Diamicron MR* three times daily and has significant hypoglycaemic symptoms
- Patient intentionally misusing medication presents with signs or symptoms of toxicity

When Not to Use:

If the patient does not have any signs or symptoms of adverse effects and you believe the dose is too high, then use “Over or underdose - Dose too high (O1)”

Caused by drug interaction (T2)

When to Use:

When the patient has signs or symptoms that suggest an adverse reaction that relates to the presence of an interacting drug

Examples of when to use:

- Patient taking *warfarin* develops an elevated INR after commencing *metronidazole*
- Patient taking *perindopril* and *furosemide*, who commences *diclofenac* and develops renal dysfunction

When Not to Use:

If the patient has an interacting drug present, but there are NO signs or symptoms of the interaction causing an adverse effect, then use “Drug selection - Drug interaction (D2)”. Also where the patient has been prescribed interacting drugs but has not taken the medications

Toxicity/Adverse reaction evident (T3)

When to Use

When there are symptoms of toxicity but the cause is not due to interaction or dose but there is a suspected medication cause.

Examples of when to use

- Patient on *captopril* develops a dry cough.
- Patient develops hypotension after commencing *prazosin*, even though the dose is controlling the prostatic hypertrophy

When not to Use

If there are no signs or symptoms of toxicity or adverse reaction

Risk of adverse effects (T4) #

When to Use:

When you believe (prolonged) use of a drug gives a high risk of adverse effects (or has a low risk of severe adverse effects.)

Examples of when to use:

- Patient is taking *diazepam* for years and has a increased risk of falling.
- *Rosiglitazone* has been associated with an increased risk of heart attacks.

Possible drug treatment in response to adverse effect (T5) #

When to Use:

When the patient is using a drug which seems indicated for an adverse effect of another drug.

Examples of when to use

- Patient on *captopril* is also using *codeine*.
- Patient on *diltiazem* has recently started a laxative.

Other Toxicity/Adverse Effect problem (T0)

When to Use:

When the patient has signs or symptoms but the situation doesn't fit under the other toxicity subcategories. Expand on the situation in the notes section.

Appendix S2: Modifications to the Original DOCUMENT Classification System

Drug selection

1. We have divided the original subcategory “Other drug selection problem (D0)” into four new subcategories.

The original subcategory was:

Other drug selection problem (D0)

When to Use:

When there is a contraindication to the use of a drug because of an underlying condition in the patient.

When a less expensive or alternative brand is substituted purely for cost reasons.

When a drug is felt to be unnecessary based on the conditions the patient has.

When a drug or drug group is prescribed for the patient to which there has previously been a major adverse reaction.

When the drug being used is out of date or deteriorated in some other way.

When you believe a more effective drug is available and you suggest it instead of the current therapy.

Examples of when to use:

- *Maxolon* prescribed and doctor contacted to change to *Pramin*
- Patient has *Anginine* tablets for use that are over 2 years old and have been stored incorrectly.
- Patient commenced *omeprazole* when they were taking *Celebrex* for a sore knee. *Celebrex* has been ceased, but they are still taking *omeprazole*.

When Not to Use:

If a less expensive brand is substituted because the ordered brand is unavailable, then use “Non-clinical (N0)”.

If the patient is currently experiencing symptoms of toxicity, then use “Toxicity/Adverse reaction - toxicity evident (T3)”

This subcategory was replaced by:

Lack of indication or unclear indication (D5a)

When to Use:

When a drug is felt to be unnecessary based on the conditions the patient has.

Examples of when to use:

- Patient commenced *omeprazole* when they were taking *Celebrex* for a sore knee. *Celebrex* has been ceased, but they are still taking *omeprazole*.

Lack of effectiveness (D5b)

When to Use:

When you believe a more effective drug is available and you suggest it instead of the current therapy.

When current guidelines recommend another therapy

Examples of when to use:

- Use of drugs such as promethazine, betahistine, mebeverine etc
- Doxazosin as monotherapy for hypertension in patients with diabetes

When Not to Use:

Dosage is too low for drug to be effective, choose O2: Dosage too low

Contra-indication/intolerance (D5c)

When to Use:

When there is a contraindication to the use of a drug because of an underlying condition in the patient.

When a drug or drug group is prescribed for the patient to which there has previously been a major adverse reaction.

Examples of when to use:

- Propranolol in patients with diabetes
- Patient has a history of allergic reactions for a certain antibiotic and receives a repeat prescription for this antibiotic

When Not to Use:

If the patient is currently experiencing symptoms of toxicity, then use "Toxicity/Adverse reaction - toxicity evident (T3)"

Other drug selection problem (D0)

When to Use:

When a less expensive or alternative brand is substituted purely for cost reasons.

When the drug being used is out of date or deteriorated in some other way.

Examples of when to use:

- Patient has Anginine tablets for use that are over 2 years old and have been stored incorrectly.
- If a less expensive brand is substituted because the ordered brand is unavailable, then use "Non-clinical (N0)".

Toxicity or Adverse reaction

2. We have added two new subcategories.

The new subcategories are:

Risk of adverse effects (T4)

When to Use:

When you believe (prolonged) use of a drug gives a high risk of adverse effects (or has a low risk of severe adverse effects.)

Examples of when to use:

- Patient is taking *diazepam* for years and has a increased risk of falling.
- *Rosiglitazone* has been associated with an increased risk of heart attacks.

Possible drug treatment in response to adverse effect (T5)

When to Use:

When the patient is using a drug which seems indicated for an adverse effect of another drug.

Examples of when to use

- Patient on *captopril* is also using *codeine*.
- Patient on *diltiazem* has recently started a laxative.