

Appendix A

Following are the guideline segments that we used in the case study, along with the comments that we added to them for clarification.

The case study contains the following five recommendations, which should be modeled as two guidelines. The examples were simplified for the case study, and therefore might contain medical errors (please comment on those).

Guideline 1 (Based on the Chronic Cough management guideline. Contains 3 recommendations)

- 1) Chronic cough is cough that lasts for at least 3 weeks. Chest radiographs should be ordered before any treatment is prescribed in nearly all patients with chronic cough (Grade II-2). Chest radiographs do not have to be routinely obtained before beginning treatment, for presumed PNDS (post nasal drip syndrome) in young nonsmokers, in pregnant women, or before observing the result of discontinuation of an ACE-I (ACE Inhibitor) for 4 weeks for patients who developed cough shortly after beginning to take an ACE-I.

(Note: In this recommendation, please pay attention to the following points:

- a) Please model chronic cough, ordering a chest radiograph, treatment (dimensions 2, 5, 7)
 - b) Please model the grade of evidence (dimension 9)
 - c) Please model the fact that Chest radiographs do not have to be routinely obtained before beginning treatment. That is, they may or may not be obtained, and both options are valid (dimension 1)
 - d) Please model the criteria: (a) presumed PNDS (post nasal drip syndrome) in young nonsmokers, (b) pregnant women, (c) before observing the result of discontinuation of an ACE-I (Angiotensin-converting Enzyme Inhibitor) for 4 weeks for patients who developed cough shortly after beginning to take an ACE-I (dimensions 5, 6, 7, 10)
- 2) Note: When the chest X-ray is normal PNDS, Asthma, and GERD (Gastroesophageal reflux disease) are the likely causes of chronic cough. In PNDS, sinusitis may be the cause up to approximately 30% of the time when cough is nonproductive, and up to approximately 60% of the time when cough is productive.

A negative recommendation: Sinus CT scans are not routinely recommended to evaluate for sinusitis as the cause of cough. Four-view sinus radiographs should be ordered instead.

Please model: evaluating sinusitis as the cause of cough, ordering Four-view sinus radiographs, not ordering sinus CT scan (dimensions 2, 5, 7,10).

- 3) While 24 hour esophageal pH monitoring is the most diagnostically useful test for assessing for GERD as the cause of cough, conventional indices used by gastroenterologists to assess for esophagitis may be misleadingly normal. Therefore, until future studies provide better guidelines, the test should be read as normal when conventional indices are within the normal range and no suspicious reflux-induced coughs appear during the monitoring session (Grade II-2).

Please model the criterion that would be used to indicate that the test results are interpreted as normal (dimension 8).

Please model the grade of evidence (dimension 9).

Guideline 2 (Based on the hypertension guideline.

Simplified (not all contraindications, relative contra-indications, and relative indications are specified).

Drug interactions simplified.

Contains 2 recommendations).

- 4) If the patient is not at the goal blood pressure, the response to the initial drug choice for hypertension is inadequate after reaching the full dose, and the patient is tolerating the first choice well, then add a second drug from another class. If a diuretic is not chosen as the first drug, it is usually indicated as a second-step agent because its addition will enhance the effects of other agents.

The possible drug classes are:

ACE I

Beta-blockers (distinguish between drugs that have intrinsic sympathomimetic activity (ISA) and those that do not)

Calcium channel blockers (distinguish between dihydropyridines and non-dihydropyridines, and between long-acting (long duration) dihydropyridines and non-long-acting dihydropyridines)

Diuretics (distinguish between thiazide-, loop- and potassium-sparing diuretics)

The following compelling indications exist (unless contra-indicated):

Indication	Drug Therapy
Diabetes mellitus (type 1) with proteinuria	ACE-I
Heart failure	ACE-I, loop-diuretics
Isolated systolic hypertension in older patients	Diuretics (preferred), dihydropyridines
Myocardial infarction	Non-ISA beta-blockers
Myocardial infarction with systolic dysfunction	ACE-I
Patient does not have co-morbidities that are compelling indications of other antihypertensives	Diuretics, beta-blockers

The following relative indication exists (unless contra-indicated)

Indication	Drug Therapy
Diabetes mellitus (type 1) with proteinuria	ACE-I (preferred), calcium channel-blockers

The following relative contraindication exist

Indication	Drug Therapy
Diabetes mellitus (type 1) with proteinuria	Beta blockers

The following contraindications exist:

Indication	Drug Therapy
Asthma or chronic airway disease	Beta-blockers
Second- or third-degree heart block	Beta-blockers, non-dihydropyridine
Pregnancy	ACE-I

The following drug interactions exist*:

Drug class	Evidence based combinations	Evidence based combinations to avoid
ACEI		Potassium-sparing diuretics
Beta-blockers	Thiazide diuretics	Non-dihydropyridines
Dihydropyridines	Beta-blockers	Non-dihydropyridines
Non-dihydropyridines		Beta-blockers, dihydropyridines

* This representation of drug interactions is based on interpretation that the physicians from the Veterans Administration Clinic in Palo Alto gave to the drug interactions that were specified in Table 11 of the original guideline. Evidence based combinations are drugs that, when taken together, have synergetic effects. Evidence based combinations to avoid are groups of drugs that should not be taken together.

We will make the following assumptions for this example:

- 1) The history of what other drugs were previously given to the patient is irrelevant.
- 2) The patient is on a single drug and another drug class will be added.
- 3) The patient is already taking the maximum dose of the drug
- 4) The response to the first drug choice for hypertension is inadequate after reaching the full dose, and the patient is tolerating the first choice well
- 5) There is no need to check if a specific patient is allergic to a specific drug.
- 6) It will be enough to suggest a drug class; it is not necessary to suggest a specific drug and dose.
- 7) Never give a contra-indicated drug to a patient.
- 8) Never choose as a second drug a drug that is in the list "Evidence-based combinations to avoid".
- 9) Compelling indications outweigh Evidence-based combinations and relative indications.

Please model the decision to add another antihypertensive drug in a modular way, which will take into account that there may be other indications, contraindications, and drug interactions that may later be added into the model. The model should be constructed in such a way that will enable adding these without changing the way the decision model is represented.

The guideline model should show not only one possible drug set that can be given, but show sets of drugs, based on contraindications, relative contraindications, Evidence-based combinations, compelling indications, and relative indications. For example:

One set can be the set of drugs that can be given (not contraindicated or a Evidence based combinations to avoid), have compelling indications and are Evidence-based combinations.

Another set can be the set of drugs that can be given (not contraindicated or a drug partner to avoid) and have compelling indications but are not Evidence-based combinations.

A third set can be the set of drugs that can be given (not contraindicated or a drug partner to avoid), do not have compelling indications and are not Evidence-based combinations.

There is no need to model the criterion the checks whether the BP goal is maintained, the patient is taking the full dose, the patient is taking only one anti-hypertensive drug, the response to the initial drug choice for hypertension is inadequate after reaching the full dose, and the patient is tolerating the first choice well (dimensions 3,5,6,7,10).

- 5) The goal of the (new) anti-hypertensive treatment discussed in recommendation (1) is to control blood pressure to < 140/90 mm Hg (systolic BP below 140 mm Hg and diastolic BP below 90 mm Hg). For patients with Diabetes Mellitus, the blood pressure should be controlled to below 130/85 mm Hg. Blood pressure should be controlled to 125/75 in patients with proteinuria in excess of 1 gram per 24 hours, and to 130/85 mm Hg in patients with proteinuria with at most 1 gram per 24 hours with whatever anti-hypertensive therapy is necessary (dimensions 5, 10).