



Supplementary Materials: Prevalence and Clinical Significance of Drug–Drug and Drug–Dietary Supplement Interactions among Patients Admitted for Cardiothoracic Surgery in Greece

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The supplementary file contains additional information regarding the clinical data that were recorded during the study, the percentages of patients exposed in DDIs during hospitalization, the full list of drug interactions that were identified with relative references that support their clinical significance and the list of drugs that were recorded in each time period of hospitalization in the CTS clinic (admission, pre-operation, post-operation, discharge).

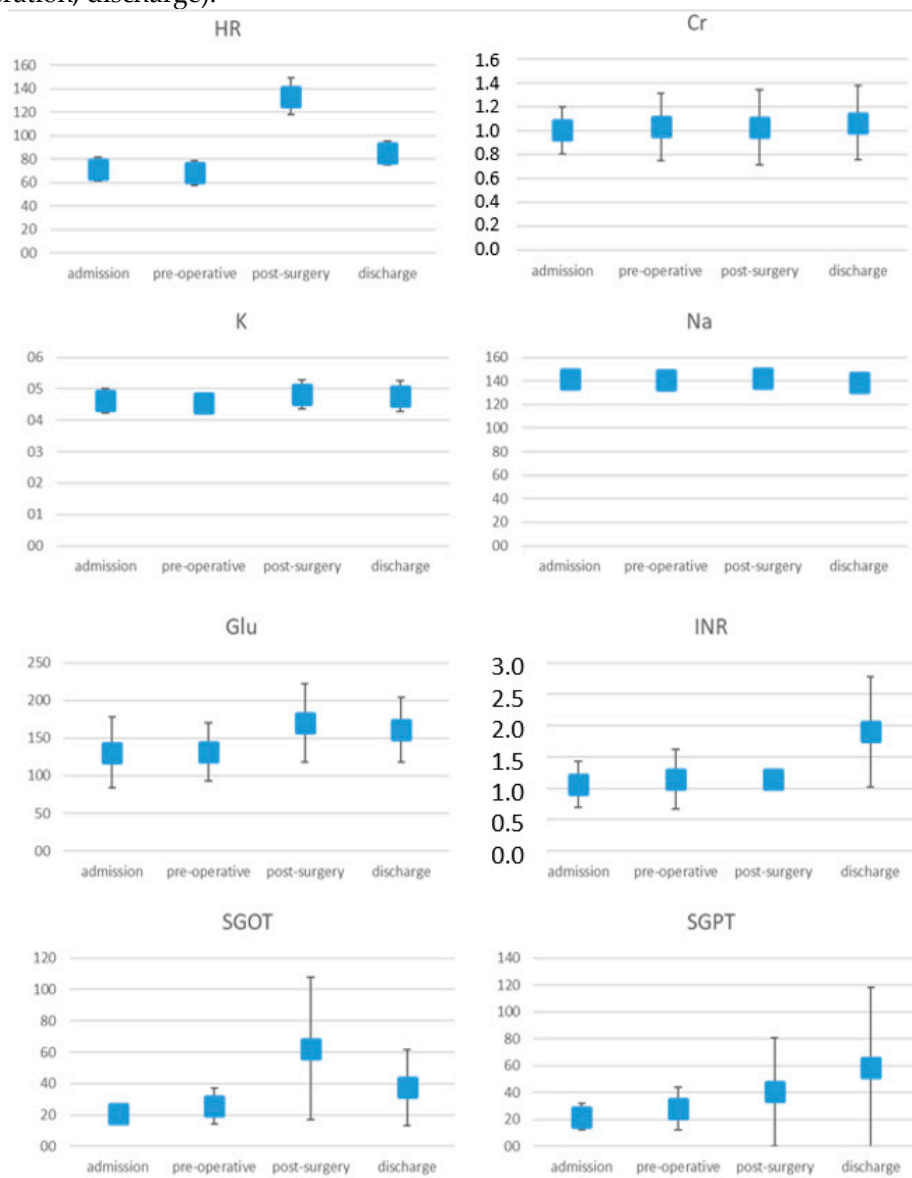
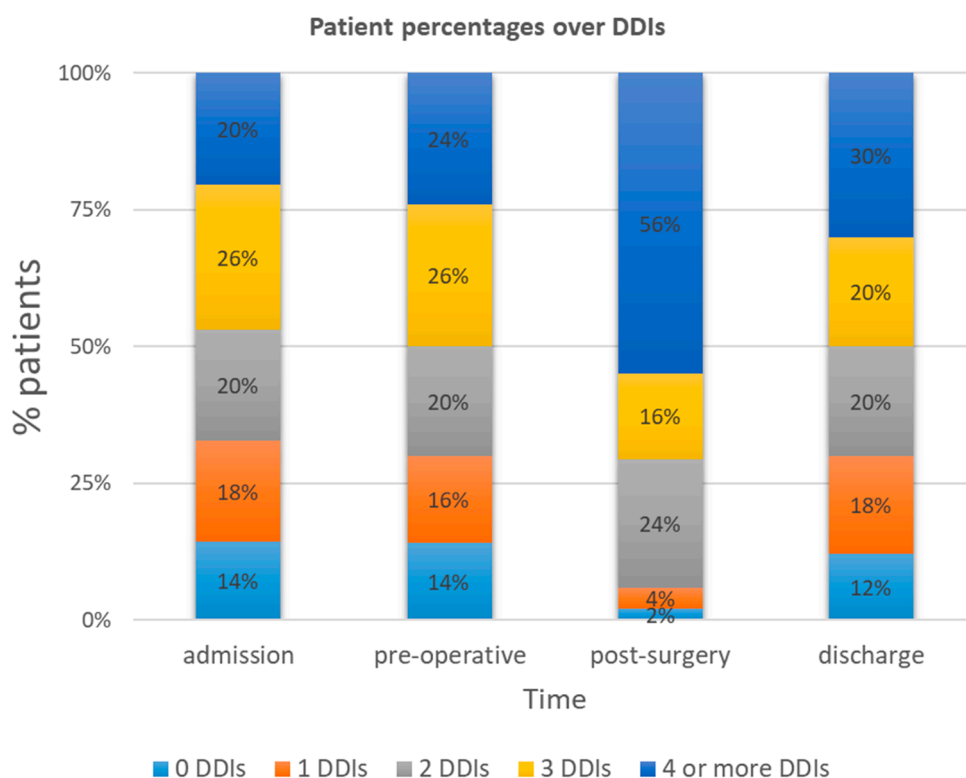


Figure S1. Clinical data for patients in the study (HR: Heart Rate (bpm), Cr: Creatinine (μmol/L), K: Potassium mEq/L, Na: Sodium Chloride mEq/L, INR: International Normalized Ratio, Glu: Blood Glucose



mg/dL).

Figure S2. Percentages of patients exposed in clinically significant DDIs.

Table S1. PK- DDIs -Serious-use alternative.

| Drug A | Drug B | Drug categories | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|--------------|---------------|-----------------|----------------------------------|---|----------|-------------------------|---------------|
| amiodarone | acenocoumarol | anti-arrhythmic | anticoagulant | PK-CYP metabolism inhibition acenocoumarol levels | 4 | Serious use alternative | Major [1] |
| amlodipine | simvastatin | Ca-blocker | antilipidemic | PK -CYP3A4 inhibition (statin-rhabdomyolysis) | 4 | Serious use alternative | Major [2] |
| aspirin | methotrexate | NSAIDs | chemo-RA | PK-Renal clearance (methotrexate toxicity) | 2 | Serious use alternative | Major [3] |
| esomeprazole | cilostazol | PPI | anti-platelet | PK-CYP2C19 inhibition of cilostazol | 2 | Serious use alternative | Major [4] |
| esomeprazole | clopidogrel | PPI | anti-platelet | reduced antiplatelet activity - CYP2C9 metabolism | 11 | Serious use alternative | Moderate [5] |
| esomeprazole | escitalopram | PPI | SSRI | PK-CYP2C19 metabolism inhibition | 1 | Monitor closely | Moderate [6] |
| haloperidol | amiodarone | antipsychotic | anti-arrhythmic | PK-CYP2D6 inhibition | 1 | Serious use alternative | Major [7] |
| ranolazine | carvedilol | angina | β-blocker | PK-CYP2D6 metabolism (carvedilol) | 3 | Monitor closely | Moderate |
| ranolazine | metformin | angina | diabetes II | PK -renal clearance (metformin) OCT2 | 2 | Serious use alternative | Moderate [8] |
| ranolazine | simvastatin | angina | antilipidemic | CYP3A4 inhibition (statin-rhabdomyolysis) | 3 | Serious use alternative | Major [19-20] |

Table S2. PK-DDIs Use with caution-Monitor.

| Drug A | Drug B | Drug categories | | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|---------------|------------------|--------------------------|------------------|---|-----------------|-------------------------|----------------|---------|
| allopurinol | acenocoumarol | uric acid | anticoagulant | PK-CYP1A2 inhibition acenocoumarol levels | 1 | Serious use alternative | Moderate | [9-11] |
| amiodarone | atorvastatin | anti-arrhythmic | antilipidemic | PK-bioavailability of atorvastatin | 2 | Monitor closely | Moderate | [12] |
| amiodarone | metoprolol | anti-arrhythmic | β -blocker | PK-CYP2D6 inhibition for metoprolol (bradycardia) | 3 | Monitor closely | Moderate | [13] |
| amiodarone | tramadol | anti-arrhythmic | analgesic | PK-CYP2D6 inhibition for tramadol | 1 | Monitor closely | Major | [14] |
| aspirin | sodium valproate | NSAIDs | antiepileptic | PK-protein binding | 2 | Monitor closely | Moderate | [15] |
| atorvastatin | valsartan | antilipidemic | ARBs | PK-OATB1 transporter | 4 | Monitor closely | Moderate | [16] |
| carvedilol | amiodarone | α,β -blockers | anti-arrhythmic | PK-CYP2D6 inhibition (carvedilol) | 1 | Monitor closely | Moderate | [13] |
| ciprofloxacin | acenocoumarol | antibiotic | anticoagulant | PK-CYP1A2 inhibition acenocoumarol levels | 2 | Serious use alternative | Major | [10,11] |
| diltiazem | budesonide | angina | corticosteroid | PK-CYP3A4 inhibition for budesonide | 1 | Serious use alternative | Moderate | [17] |
| esomeprazole | acenocoumarol | PPI | anticoagulant | PK-CYP2C9 metabolism inhibition | 1 | Minor | Moderate | [10] |
| esomeprazole | citalopram | PPI | SSNRI | PK-CYP2C19 inhibition of citalopram | 1 | Monitor closely | Major | [6] |
| haloperidol | metoprolol | antipsychotic | β -blocker | PK CYP2D6 metabolism inhibition (metoprolol) | 6 | Monitor closely | Moderate | [18] |
| omeprazole | clopidogrel | PPI | anti-platelet | PK CYP2C9 metabolism (clopidogrel) | 3 | Serious use alternative | Major | [5] |
| pantoprazole | clopidogrel | PPI | anti-platelet | PK-CYP2C19 inhibition of clopidogrel | 1 | Monitor closely | Moderate | [5] |
| ranolazine | atorvastatin | angina | antilipidemic | PK- myopathy (P-gp and OATB1 inhibition) | 2 | Monitor closely | Major | [19,20] |
| ranolazine | rosuvastatin | angina | antilipidemic | PK- myopathy (OATB1 inhibition) | 2 | Monitor closely | No interaction | [19,20] |
| ticagrelor | ivabradine | anti-platelet | angina | PK-CYP3A4 inhibition (ivabradine) | 1 | Serious use alternative | moderate | [21] |

Table S3. PK- DDIs Moderate-Minor.

| Drug A | Drug B | Drug categories | | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|---------------|---------------|-----------------|----------------|---|-----------------|-------------------------|----------------|------------|
| acenocoumarol | simvastatin | anticoagulant | antilipidemic | PK-CYP2C9 (polymorphism dependent) | 2 | Monitor closely | Minor | [10,11] |
| amiodarone | codeine | antiarrhythmic | analgesic | PK-CYP2D6 (codeine) | 2 | Monitor closely | Moderate | [14,22,23] |
| amoxicillin | aspirin | antibiotic | NSAIDs | PK-protein binding /renal clearance | 4 | Monitor closely | No interaction | [24] |
| budesonide | acenocoumarol | corticosteroid | anticoagulant | PK-CYP3A4 induction metabolism of acenocoumarol | 13 | Monitor closely | Moderate | [10,11] |
| budesonide | alprazolam | corticosteroid | anxiolytics | PK-CYP3A4 induction metabolism | 6 | Monitor closely | No interaction | [25] |
| budesonide | amiodarone | corticosteroid | antiarrhythmic | PK-CYP3A4 induction metabolism | 6 | Monitor closely | Moderate | [17] |
| budesonide | clopidogrel | corticosteroid | anti-platelet | PK-CYP3A4 induction metabolism of clopidogrel | 5 | Monitor closely | No interaction | [17] |
| budesonide | dutasteride | corticosteroid | BPH | PK-CYP3A4 induction metabolism of dutasteride | 1 | Minor | No interaction | [17] |
| budesonide | eplerenone | corticosteroid | diuretic | PK-metabolism induction | 5 | Minor | Moderate | [17] |
| budesonide | finasteride | corticosteroid | urologicals | PK-CYP3A4 induction | 2 | Minor | No interaction | [17] |
| budesonide | quetiapine | corticosteroid | antipsychotic | PK-CYP3A4 induction | 4 | Monitor closely | No interaction | [17] |
| budesonide | ranolazine | corticosteroid | angina | PK-ranolazine | 1 | Serious use alternative | Moderate | [17] |

| | | | | | | | | |
|-----------------------------------|--------------------|-----------------------------|--------------------|---|----|--------------------|-------------------------------|------|
| carvedilol | haloperidol | β -blocker | antipsy- chotic | inhibits CYP3A4 PK- CYP2D6 in- hibition | 2 | Monitor closely | Moderate | [14] |
| ciprofloxacin | alprazolam | antibiotic | anxiolytics | PK CYP3A4 metabolism inhibition (alprazo- lam) | 3 | Minor | No inter- action | [14] |
| domperidone | alprazolam | antiemetic | anxiolytics | reduce domperi- done me- tabolism | 10 | Not listed | Not listed ^{1,2} and | [37] |
| esomeprazole | alprazolam | PPI | anxiolytics | PK CYP3A4 metabolism inhibition (alprazo- lam) | 4 | Minor | No inter- action | [26] |
| esomeprazole | cefuroxime | PPI | antibiotic | (both oral forms) modulate of pH -ab- sorption | 2 | Monitor closely | Moderate | [27] |
| esomeprazole | duloxetine | PPI | SSRI | PK -duloxe- tine GI ab- sorption | 1 | Monitor closely | Minor | [26] |
| ferrous (glu- conate, sulfate) | levothyroxine | anaemia | thyroid | PK -T4 GI absorption | 4 | Monitor closely | Moderate | [28] |
| hydrocortisone | acenocouma- rol | corticosteroid | anticoagu- lant | PK- CYP3A4 in- duction me- tabolism of acenocou- marol | 1 | Monitor closely | Moderate | [10] |
| omeprazole | carvedilol | PPI | β -blocker | PK-CYP2C9 metabolism (carvedilol) | 2 | Minor | Moderate | [26] |
| ranitidine | metformin | H2-receptor an- tagonist | diabetes II | PK- renal clearance (metform) | 2 | No interaction | Moderate | [29] |
| ranitidine | vitamin B12 | H2-receptor an- tagonist | vitamin B12 | PK-GI ab- sorption for B12 | 15 | No interaction | Minor | [30] |
| ranolazine | metoprolol | angina | β -blocker | PK- CYP2D6 metabolism (metopro- lol) | 1 | Monitor closely | Moderate | [31] |

¹ <https://www.mayoclinic.org/drugs-supplements/alprazolam-oral-route/precautions/drg-20061040?p=1>

² <https://www.medicines.org.uk/emc/product/556/smhc>

| | | | | | | | | |
|------------|-------------|--------|---------------|--|---|-----------------|----------|------|
| ranolazine | morphine | angina | analgesic | PK-inhibition CYP2D6 increase morphine levels | 1 | Monitor closely | Moderate | [31] |
| tamsulosin | haloperidol | BPH | antipsychotic | PK-CYP2D6 inhibition | 1 | Monitor closely | Moderate | [32] |

Table S4. PD- DDIs Serious -use alternative.

| Drug A | Drug B | Drug categories | | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|-------------|--------------------|-----------------|----------------|--|-----------------|-------------------------|-----------|------|
| alprazolam | haloperidol | anxiolytics | antipsychotic | PD-synergism sedation | 2 | Monitor closely | Moderate | [33] |
| amiloride | potassium chloride | diuretic | hypokalemia | PD-synergism hyperkalemia | 3 | Serious use alternative | Major | [34] |
| citalopram | duloxetine | SSNRI | SSRI | PD-synergism (Serotonine syndrome) | 1 | Serious use alternative | Major | [35] |
| fenofibrate | pitavastatin | antilipidemic | antilipidemic | PD-synergism | 2 | Serious use alternative | Major | [36] |
| haloperidol | amiodarone | antipsychotic | antiarrhythmic | PD-QT prolongation | 1 | Serious use alternative | Major | [37] |
| morphine | escitalopram | analgesic | SSRI | PD-serotonin syndrome | 1 | Serious use alternative | Moderate | [38] |
| quetiapine | haloperidol | antipsychotic | antipsychotic | PD-enhance antidopaminergic effect - QT prolongation | 6 | Monitor closely | Major | [33] |
| tramadol | pethidine | analgesic | analgesic | PD-synergism sedation | 2 | Serious use alternative | Major | |

Table S5. PD-DDIs Use with caution -monitor.

| Drug A | Drug B | Drug categories | | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|------------|---------------|-----------------|------------------|-----------------------------------|-----------------|-----------------|----------------|------|
| alprazolam | morphine | anxiolytics | analgesic | PD-synergism sedation | 16 | Monitor closely | Major | [39] |
| alprazolam | quetiapine | anxiolytics | antipsychotic | PD-synergism sedation | 4 | Monitor closely | Major | |
| amlodipine | metformin | Ca-blocker | diabetes II | PD-antagonism (metformin action) | 4 | Monitor closely | No interaction | [40] |
| apixaban | aspirin | anticoagulant | NSAIDs | PD-synergism | 1 | Monitor closely | Major | [41] |
| aspirin | acenocoumarol | NSAIDS | anti-platelet | PD synergism | 11 | Monitor closely | Major | [10] |
| aspirin | carvedilol | NSAIDS | β -blocker | PD antagonism and serum potassium | 11 | Monitor closely | Minor | [42] |

| | | | | | | | | |
|---------------|---------------------|------------------|----------------|-----------------------------------|----|-------------------------|----------------|------|
| aspirin | citalopram | NSAIDs | SSNRI | PD-synergism (bleeding) | 1 | Monitor closely | Moderate | [43] |
| aspirin | duloxetine | NSAIDs | SSRI | PD-synergism (bleeding) | 1 | Monitor closely | Moderate | [43] |
| aspirin | escitalopram | NSAIDs | SSRI | PD-synergism (bleeding) | 1 | Monitor closely | Moderate | [43] |
| aspirin | rivaroxaban | NSAIDs | anticoagulant | PD-synergism | 1 | Monitor closely | Major | [41] |
| bisoprolol | norepinephrine | β -blocker | adrenergic | PD-antagonism | 2 | Monitor closely | Moderate | [44] |
| bromazepam | haloperidol | anxiolytics | antipsychotic | PD-synergism sedation | 2 | Monitor closely | Moderate | [33] |
| bromazepam | olanzapine | anxiolytics | antipsychotic | PD-synergism sedation | 1 | Monitor closely | Major | [45] |
| bromazepam | quetiapine | anxiolytics | antipsychotic | PD-synergism sedation | 1 | Monitor closely | Moderate | [46] |
| carvedilol | amlodipine | β -blocker | Ca-blocker | PD-synergism | 4 | Monitor closely | Moderate | [47] |
| carvedilol | furosemide | β -blocker | diuretic | PD antagonism and serum potassium | 9 | Monitor closely | Moderate | [47] |
| carvedilol | hydrochlorothiazide | β -blocker | diuretic | PD-antagonism (serum potassium) | 1 | Monitor closely | Moderate | |
| carvedilol | irbesartan | β -blocker | ARBs | PD-synergism (serum potassium) | 4 | Monitor closely | No interaction | |
| ceftriaxone | acenocoumarol | antibiotic | anticoagulant | PD -risk of bleeding | 13 | Monitor closely | Moderate | [10] |
| ceftriaxone | enoxaparin | antibiotic | anti-platelet | increases effects of enoxaparin | 21 | Serious use alternative | No interaction | [48] |
| ciprofloxacin | amiodarone | antibiotic | antiarrhythmic | PD-QT prolongation | 1 | Monitor closely | Major | [49] |
| ciprofloxacin | haloperidol | antibiotic | antipsychotic | PD -QT prolongation | 3 | Monitor closely | Major | [37] |
| clopidogrel | acenocoumarol | anti-platelet | anticoagulant | PD-synergism | 1 | Monitor closely | Major | [10] |
| clopidogrel | citalopram | anti-platelet | SSNRI | PD-synergism (bleeding) | 1 | Monitor closely | Moderate | [43] |
| clopidogrel | duloxetine | anti-platelet | SSRI | PD-synergism (bleeding) | 1 | Monitor closely | Moderate | [43] |
| codeine | tramadol | analgesic | analgesic | PD-synergism sedation | 1 | Monitor closely | Major | |
| domperidone | hydroxyzine | antiemetic | anxiolytics | PD-QT prolongation | 2 | Not listed | Not listed | [50] |
| enoxaparin | acenocoumarol | anti-platelet | anticoagulant | PD-synergism | 8 | Serious use alternative | Major | [10] |
| fenofibrate | acenocoumarol | antilipidemic | anticoagulant | PD-synergism | 1 | Serious Use alternative | Major | [10] |

| | | | | | | | | |
|--------------------|----------------|------------------|-----------------|--|----|-------------------------|-----------------|------|
| furosemide | empagliflozin | diuretic | diabetes II | PD-synergism | 2 | Monitor closely | Moderate | [51] |
| haloperidol | ipratropium | antipsychotic | anticholinergic | PD -synergism additive anticholinergic effects, hypoglycemia | 7 | Monitor closely | Moderate | [33] |
| haloperidol | lorazepam | antipsychotic | anxiolytics | PD-synergism sedation | 1 | Monitor closely | Moderate | [33] |
| haloperidol | melatonin | antipsychotic | sedative | PD-synergism sedation | 2 | Monitor closely | No interactions | [33] |
| haloperidol | morphine | antipsychotic | analgesic | PD-synergism sedation | 1 | Monitor closely | Major | [33] |
| haloperidol | tiotropium | antipsychotic | anticholinergic | PD -synergism additive anticholinergic effects, hypoglycemia | 1 | Monitor closely | Moderate | [33] |
| hydrocortisone | enoxaparin | corticosteroid | anti-platelet | reduced anti-platelet activity | 1 | Monitor closely | No interactions | [52] |
| hydroxyzine | morphine | anxiolytics | analgesic | PD synergism | 3 | Monitor closely | Major | [39] |
| lisinopril | aspirin | ACE | NSAIDs | PD -antagonism (decrease renal function) | 2 | Serious use alternative | Moderate | [47] |
| methylprednisolone | enoxaparin | corticosteroid | anti-platelet | reduced anti-platelet activity | 1 | Monitor closely | No interactions | [52] |
| metoprolol | furosemide | β -blocker | diuretic | PD -antagonism (serum potassium) | 25 | Monitor closely | Moderate | [47] |
| metoprolol | norepinephrine | β -blocker | adrenergic | PD-antagonism -potential diminished cardiac response | 4 | Monitor closely | Moderate | [53] |
| olanzapine | ipratropium | antipsychotic | anticholinergic | PD -synergism additive anticholinergic effects, hypoglycemia | 2 | Monitor closely | Moderate | [54] |
| olanzapine | metformin | antipsychotic | diabetes II | PD-synergism hypoglycemia | 2 | Monitor closely | Moderate | [54] |
| olanzapine | morphine | antipsychotic | analgesic | PD-synergism sedation | 1 | Monitor closely | Major | [54] |
| olanzapine | pethidine | antipsychotic | analgesic | PD-serotonin syndrome | 1 | Monitor closely | Major | [54] |
| olanzapine | sitagliptin | antipsychotic | diabetes II | PD-synergism hypoglycemia | 2 | Monitor closely | Moderate | [54] |
| olmesartan | metformin | ARBs | diabetes II | PD-synergism (lactic acidosis) | 1 | No interaction | No interaction | [55] |

| | | | | | | | | |
|--------------|---------------|---------------|-----------------|---|---|-------------------------|----------|---------|
| perindopril | metformin | ACE | diabetes II | PD-synergism (hypoglycemia) | 6 | Monitor closely | Moderate | [55] |
| piperacillin | acenocoumarol | antibiotic | anticoagulant | PD-synergism anticoagulation | 2 | Serious use alternative | Moderate | [10,11] |
| quetiapine | ipratropium | antipsychotic | anticholinergic | PD-synergism anticholinergic effects, hypoglycemia, QT-prol | 8 | Monitor closely | Moderate | [56] |
| quetiapine | morphine | antipsychotic | analgesic | PD-synergism sedation | 2 | Monitor closely | Major | [39] |
| quetiapine | tiotropium | antipsychotic | anticholinergic | PD-synergism anticholinergic effects, hypoglycemia, QT-prol | 1 | Monitor closely | Moderate | [56] |
| zopiclone | bromazepam | hypnotic | anxiolytics | PD-synergism | 1 | Monitor closely | Moderate | [57] |
| zopiclone | morphine | hypnotic | analgesic | PD-synergism | 1 | No interaction | Major | [57] |

Table S6. PD-DDIs moderate-minor.

| Drug A | Drug B | Drug categories | | Pharmacological-Clinical outcome | Number of cases | Medscape | Drugs.com | Refs |
|-----------|-------------|-----------------|---------------|--|-----------------|-------------------------|------------|------|
| aspirin | furosemide | NSAIDs | diuretic | PD antagonism and serum potassium | 44 | Monitor closely-Minor | Minor | [47] |
| aspirin | gliclazide | NSAIDs | diabetes II | PD -hypoglycemia | 3 | Not listed | Not listed | [58] |
| aspirin | glimepiride | NSAIDs | diabetes II | PD -hypoglycemia | 2 | Monitor closely-Minor | Moderate | [58] |
| aspirin | insulin | NSAIDs | diabetes I | PD synergism | 22 | Monitor closely | Moderate | [58] |
| aspirin | irbesartan | NSAIDs | ARBs | PD-antagonism (kidney function) | 6 | Monitor closely-Minor | Moderate | [59] |
| aspirin | perindopril | NSAIDs | ACE | PD -antagonism kidney (decrease in renal function) | 11 | Serious use alternative | Moderate | [47] |
| aspirin | ramipril | NSAIDs | ACE | PD -antagonism kidney (decrease in renal function) | 6 | Serious use alternative | Moderate | [47] |
| aspirin | valsartan | NSAIDs | ARBs | PD-antagonism (kidney function) | 3 | Monitor closely | Moderate | [59] |
| biperiden | alprazolam | parkinson | anxiolytics | PD-synergism CNS and Respiration depression | 4 | Not listed | Moderate | [60] |
| biperiden | haloperidol | parkinson | antipsychotic | PD-synergism anticholinergic effect | 2 | Not listed | Moderate | [60] |

| | | | | | | | | |
|---------------|---------------|--------------------|--------------------------|--|----|-----------------|------------|---------|
| biperiden | ipratropium | parkinson | anticholinergic | PD-synergism anticholinergic effect | 2 | Not listed | Moderate | [60] |
| biperiden | quetiapine | parkinson | antipsychotic | PD-synergism anticholinergic effect | 4 | Not listed | Moderate | [60] |
| biperiden | tiotropium | parkinson | anticholinergic | PD-synergism anticholinergic effect | 1 | Not listed | Moderate | [60] |
| biperiden | valproic acid | parkinson | anticonvulsant | PD-synergism CNS and Respiration depression | 1 | Not listed | Moderate | [60] |
| bisoprolol | dobutamine | β -blocker | β -1-agonist | PD -antagonism (serum pottasium) | 1 | Monitor closely | Moderate | [61] |
| bisoprolol | formoterol | β -blocker | β -2-agonist | PD-antagonism (b2-receptors) | 2 | Monitor closely | Moderate | [62] |
| bisoprolol | furosemide | β -blocker | diuretic | PD-antagonism (serum potassium) (pt2) | 17 | Monitor closely | Moderate | [47] |
| bromazepam | morphine | anxiolytics | analgesic | PD-synergism sedation | 25 | Monitor closely | Major | [39] |
| ceftriaxone | furosemide | antibiotic | diuretic | nehprotoxicity | 35 | Minor | Moderate | [63] |
| ciprofloxacin | insulin | antibiotic | diabetes I | PD synergism hypoglycaemia | 2 | Monitor closely | Major | [63] |
| codeine | morphine | analgesic | analgesic | PD -synergism | 3 | Monitor closely | Major | [22,39] |
| codeine | pethidine | analgesic | analgesic | PD-synergism sedation | 17 | Monitor closely | Major | [22,39] |
| dobutamine | agomelatine | β -1-agonist | antidepressant | PD-antagonism | 1 | Not listed | Not listed | |
| dobutamine | carvedilol | β -1-agonist | α,β -blockers | PD-antagonism (serum pottasium) | 1 | Monitor closely | moderate | |
| domperidone | alfuzosin | antiemetic | BPH | PD synergism - QTc prolongation | 3 | Not listed | Not listed | [37] |
| domperidone | amlodipine | antiemetic | Ca-blocker | PD synergism - QTc prolongation | 5 | Not listed | Not listed | [37] |
| domperidone | haloperidol | antiemetic | antipsychotic | PD-QT prolanga-tion | 1 | Not listed | Not listed | [33] |
| empagliflozin | amiloride | diabetes II | diuretic | PD-synergism (increased urine volume) | 1 | Monitor closely | Moderate | |
| empagliflozin | furosemide | diabetes II | diuretic | PD-synergism (increased urine volume) | 2 | Monitor closely | Moderate | |
| enoxaparin | irbesartan | anti-platelet | ARBs | PD- hyperkalemia | 1 | Monitor closely | Moderate | [64] |
| enoxaparin | ramipril | anti-platelet | ACE | PD-suppress aldosterone secretion-hyperkalemia | 7 | Monitor closely | Moderate | [64] |
| enoxaparin | valsartan | anti-platelet | ARBs | PD- hyperkalemia | 1 | Monitor closely | Moderate | [64] |

| | | | | | | | | |
|-------------|------------|------------------|--------------------|----------------------------------|---|-------------------------|----------------|------|
| hydroxyzine | alprazolam | anxiolytics | anxiolytics | PD -synergism increase sedation | 1 | Monitor closely | No interaction | [65] |
| hydroxyzine | bromazepam | anxiolytics | anxiolytics | PD -synergism increase sedation | 1 | Monitor closely | No interaction | [65] |
| irbesartan | insulin | ARBs | diabetes I | PD-ARBs enhance hypoglycemia | 1 | Monitor closely | Moderate | [66] |
| lisinopril | enoxaparin | ACE | anti-platelet | PD-hyperkalemia | 2 | Monitor closely | Moderate | [64] |
| lisinopril | insulin | ACE | diabetes I | PD-synergism | 5 | Monitor closely | Moderate | [67] |
| metoprolol | dobutamine | β -blocker | β -1-agonist | PD -antagonism (serum potassium) | 2 | Monitor closely | Moderate | |
| metoprolol | formoterol | β -blocker | β -2-agonist | PD-antagonism (b2-receptors) | 1 | Monitor closely | Moderate | |
| morphine | melatonin | analgesic | sedative | PD-synergism sedation | 1 | Monitor closely | No interaction | [68] |
| morphine | pregabalin | analgesic | antiepileptic | PD-synergism sedation | 1 | Monitor closely | Major | |
| olmesartan | enoxaparin | ARBs | anti-platelet | PD-hyperkalemia | 2 | Monitor closely | Moderate | |
| olmesartan | insulin | ARBs | diabetes I | PD -hypoglycemic effect | 5 | Monitor closely | Moderate | [66] |
| perindopril | enoxaparin | ACE | anti-platelet | PD-hyperkalemia | 7 | Monitor closely | Moderate | [64] |
| perindopril | furosemide | ACE | diuretic | PD-synergism | 2 | Monitor closely | Moderate | [47] |
| perindopril | insulin | ACE | diabetes I | PD-synergism | 5 | Monitor closely | Moderate | [67] |
| perindopril | pregabalin | ACE | antiepileptic | angioedema | 3 | Serious use alternative | Moderate | [67] |
| quetiapine | insulin | antipsychotic | diabetes I | PD-hyperglycemia | 3 | Monitor closely | Moderate | [69] |
| quetiapine | metformin | antipsychotic | diabetes II | PD-antagonism glucose levels | 6 | Monitor closely | Moderate | [69] |
| ramipril | furosemide | ACE | diuretic | PD-synergism | 9 | Monitor closely | Moderate | [47] |
| valsartan | insulin | ARBs | diabetes I | PD-ARBs hypoglycemic effect | 2 | Monitor closely | Moderate | [66] |

Table S7. List of administered drugs and frequency of administration for each time point.

| | Admission | Pre-operation | Post-operation | Discharge |
|-----------------|-----------|---------------|----------------|------------|
| acenocoumarol | | | 38% | 38% |
| acetylcysteine | 2% | 58% | 86% | 6% |
| agomelatine | 2% | 2% | 2% | 2% |
| alendronic acid | 2% | | | 2% |
| alfacalcidol | 2% | | | 2% |
| alfuzosin | 6% | 6% | 6% | 6% |
| allopurinol | 10% | 10% | 10% | 10% |

| | | | | |
|------------------------------------|------------|------------|-------------|------------|
| alogliptin(+metformin) | 6% | | | 6% |
| alprazolam | 12% | 28% | 4% | 4% |
| amiloride | | | 6% | 4% |
| amiodarone | | | 18% | 8% |
| amlodipine | 14% | 18% | | 12% |
| amoxicillin (+/- clavulanic acid) | 2% | | | 2% |
| apixaban | 2% | | | 2% |
| aspirin | 68% | 2% | 60% | 68% |
| atorvastatin (+/- ezetimide) | 60% | 34% | 4% | 16% |
| biperiden HCl | 2% | 2% | | 2% |
| bisacodyl | 6% | | | |
| bisoprolol | 32% | 30% | 20% | 20% |
| bromazepam | 2% | 56% | 6% | 2% |
| budesonide (+/- formoterol) | 6% | 86% | 94% | 2% |
| calcium/cholecalciferol | 2% | | | 2% |
| carvedilol | 18% | 16% | 8% | 12% |
| ceftriaxone | | 14% | 82% | |
| cefuroxime | | 2% | | 2% |
| cilostazol | 2% | 2% | | 2% |
| ciprofloxacin | | 8% | 6% | 2% |
| citalopram | 2% | | | |
| clopidogrel | 36% | | 8% | 12% |
| codeine | | | 2% | |
| dapagliflozin | 2% | | 2% | |
| diltiazem | 2% | 2% | | |
| dobutamine | | | 30% | |
| domperidone | 2% | 86% | | 2% |
| duloxetine | 2% | | | |
| empagliflozin | 4% | | | 6% |
| enoxaparin | | 50% | 50% | |
| epiorenone | 6% | 6% | 4% | 4% |
| escitalopram | 2% | 2% | | |
| esomeprazole | 30% | 12% | 16% | 8% |
| ezetimibe | 8% | 8% | | 8% |
| fenofibrate | 6% | 2% | 2% | 6% |
| ferrous (all salts +/- folic acid) | 6% | | | 4% |
| finasteride | 2% | 2% | 2% | 2% |
| fluticasone/salmeterol | 2% | | | |
| folic acid | 4% | 2% | | 4% |
| fondaparinux | | 2% | | |
| furosemide | 16% | 12% | 100% | 64% |
| furosemide (+amiloride) | 2% | | 82% | 10% |
| gabapentin | 2% | | | |
| gliclazide | 4% | | | 4% |
| glimepiride | 2% | | | 2% |

| | | | | |
|---|------------|------------|-------------|------------|
| glycopyrronium bromide | 2% | | | |
| haloperidol | 4% | 2% | 12% | 10% |
| human serum albumin | | | 2% | |
| hydrocortisone | | 2% | 2% | |
| hydroxychloroquine | 4% | 2% | 2% | 4% |
| hydroxyzine | | 6% | | |
| indapamide | 2% | | | 2% |
| Insulin (all sub-types) | 22% | 10% | 38% | 22% |
| ipratropium bromide | | 88% | 100% | |
| irbesartan (+/- hydrochlorothiazide) | 4% | 10% | 2% | 4% |
| isosorbide mononitrate | 16% | 10% | | |
| ivabradine | 4% | 6% | 4% | 10% |
| lactulose | | 2% | | |
| lansoprazole | 16% | 2% | | |
| lercanidipine | 10% | 2% | | |
| letrozole | 4% | | | |
| levothyroxine | 18% | 14% | 18% | 18% |
| linezolid | | | | 2% |
| lisinopril | 2% | 4% | 2% | 2% |
| lorazepam | | | 2% | |
| magnesium aspartate HCl | 10% | 20% | | |
| melatonin | 4% | 2% | | 2% |
| metformin (+/- empagliflozin/stiaglitpin/vildagliptin) | 26% | | | 26% |
| methotrexate | 2% | | | 2% |
| methylprednisolone | | 4% | | |
| metoprolol | 20% | 16% | 28% | 46% |
| morphine | | 82% | | |
| moxonidine | 4% | 2% | | |
| nebivolol | 2% | 2% | | |
| nifedipine | | 2% | | |
| nitroglycerin | 4% | 4% | 10% | |
| norepinephrine | | | 18% | |
| olanzapine | 2% | 2% | 2% | 2% |
| olmesartan (+/- medoxomil/amlodipine/hydrochlorothiazide) | 8% | 8% | 2% | 6% |
| omeprazole | 8% | 4% | | |
| ondansetron | | | 2% | |
| paracetamol (+/- codeine) | 8% | | 84% | |
| perindopril (+/- amlodipine or indamamide/amlodipine). | 20% | 18% | 6% | 4% |
| pethidine | | | 40% | |

| | | | | |
|---|-----|-----|-----|-----|
| piperacillin (+/- tazobactam) | | 2% | | 2% |
| piperacillin | | 4% | | 12% |
| pitavastatin | | | | |
| pitavastatin | 2% | 2% | | 2% |
| potassium chloride | | | | 8% |
| prasugrel | 2% | | | |
| pregabalin | 4% | 4% | 2% | 4% |
| propafenone | | | | 2% |
| quetiapine | 6% | 4% | 4% | 6% |
| ramipril (+/- hydrochlorothiazide) | 24% | 16% | 4% | 6% |
| ranitidine | 18% | 80% | 84% | 84% |
| ranolazine | 8% | 2% | | |
| rivaroxaban | 2% | | | 2% |
| rosuvastatin | 10% | 10% | | 10% |
| simvastatin (+/- ezetimibe) | 12% | 6% | 2% | 8% |
| sitagliptin (+/- metformin) | 4% | | | 4% |
| Sodium valproate | 2% | | 2% | 2% |
| spironolactone | 2% | 2% | | |
| tamsulosin (HCL +/- dusteride) | 6% | 6% | 6% | 6% |
| telmisartan/amlodipine | 2% | 2% | | |
| ticagrelor | 8% | | | |
| tiotropium bromide | 6% | | | |
| tramadol | | | 8% | |
| trimetazidine | 2% | 2% | | 2% |
| valsartan (+/- amlodipine or hydrochlorothiazide or amlodipine/hydrochlorothiazide) | 18% | 10% | | |
| vancomycin | | 2% | 72% | |
| vildagliptin (+/- metformin) | 6% | | | 8% |
| Vitamin B1,6,12 | | | | 2% |
| zofenopril | 2% | 2% | | |
| zopiclone | 2% | 2% | 2% | 2% |

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