Prevalence of Drug-Drug Interactions and Actual Harms in Acute Care Hospitals

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Drug–Drug Interactions (DDIs)

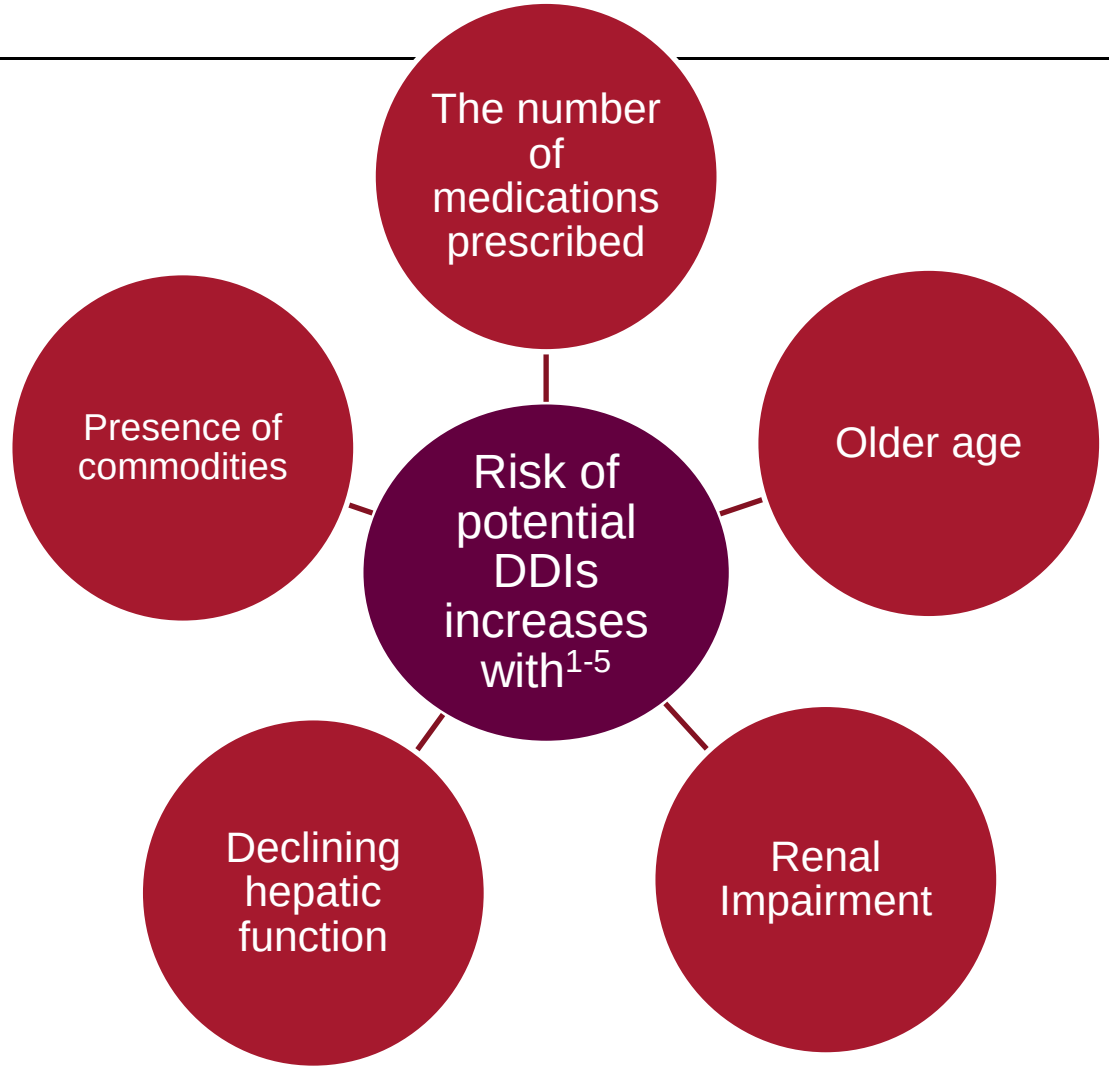
A drug-drug interaction (DDI) is a phenomenon in which the effects of a drug are altered by the presence of another drug or drugs.

Often a physician must treat a patient for several conditions simultaneously.

Many individuals use multiple drugs simultaneously.

A study of >2 billion US patient visits revealed that 65% of patients were being treated with multiple medications.[1] 23% were using high-risk medications

Risk of potential DDIs



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2. Moura CS et al. *J Pharm Pharm Sci.* 2009;12(3):266–72.
3. Doan J et al. *Ann Pharmacother*. 2013;47(3):324–32.
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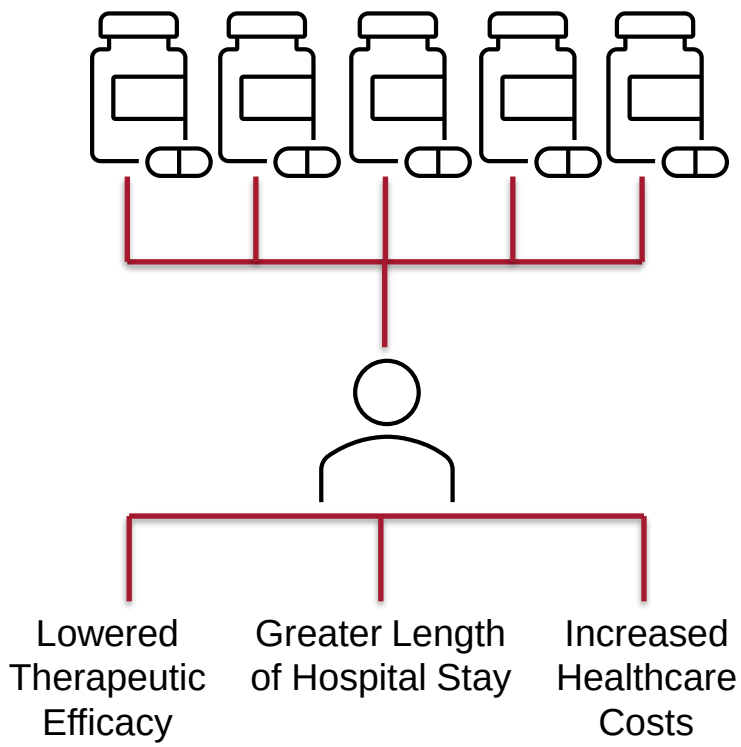
DDIs Have the Potential to Cause Patient Harm



- **The likelihood of harm associated with DDIs** depends on factors relating to the drug, patient, and clinical setting
- It is valuable to identify
  - **clinically relevant DDIs (cDDIs),** *i.e. DDIs that could lead to patient harm, taking into account a patient's individual clinical profile, drug effects and severity of potential harmful outcome*; and
  - **subsequent actual harm** among hospitalised patients

Study Aims

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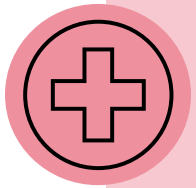


Primary

To determine the prevalence of **potential DDIs** (pDDIs), **clinically relevant DDIs** (cDDIs) and **subsequent actual harm** during admission among hospitalised patients

Secondary

To examine the **impact of transitioning from paper-based medication charts to electronic medication management** (eMM) on DDIs and patient harm.

- data collection occurred at pre- and post-eMM periods
- eMM without DDI alerts

Study Design

- **Multisite retrospective audit/review**
- 3 public hospitals in Sydney, Australia
  - A: Regional acute with 250 beds
  - B: Regional acute with 300 beds
  - C: Metropolitan principal with 820 beds
- Study patients were randomly selected from all admitted patients during two time periods

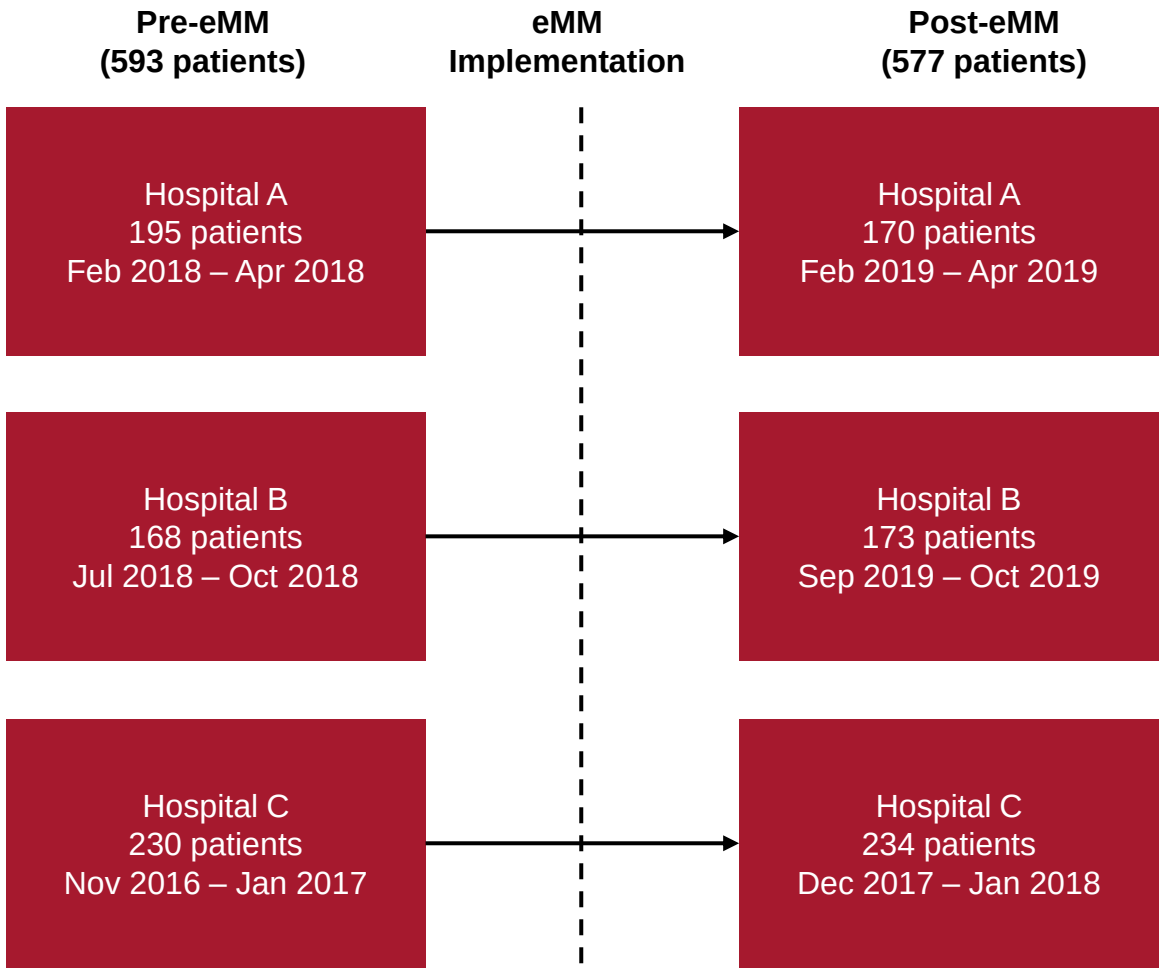


Chart review and harm assessment

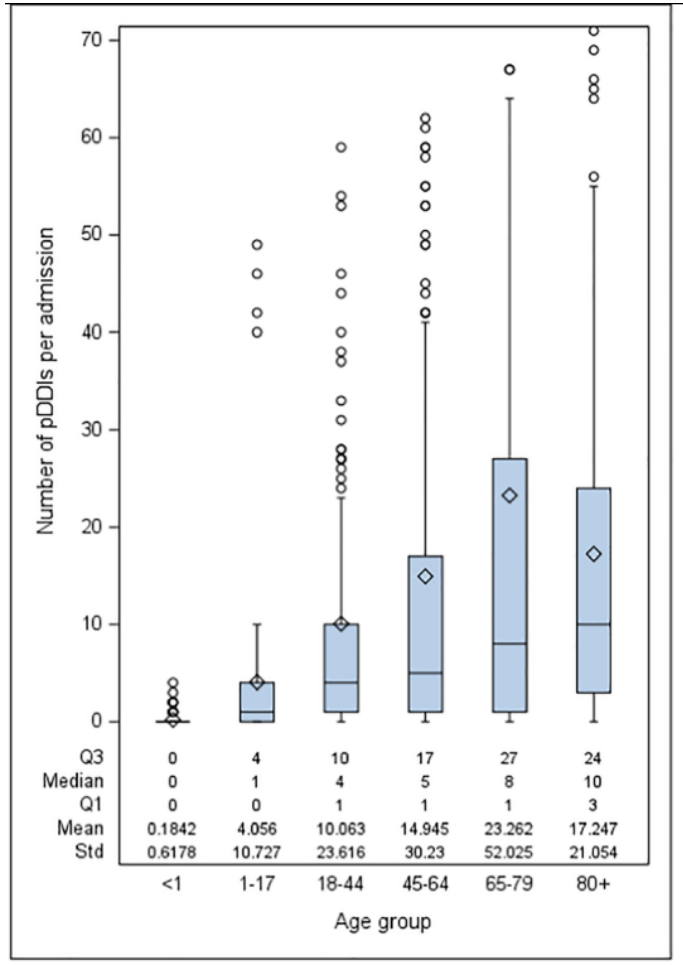
- Chart review was conducted by independent clinical research pharmacists.
  - All moderate or severe DDIs specified by **Stockley's Drug Interactions Checker** (a standard international reference used in Australian hospital practice) were classified as **pDDIs.**
  - **26 clinical contextual factors** were used to determine whether a pDDI was clinically relevant, i.e. cDDIs.
    - 11 drug factors
    - 11 patient factors
    - 4 setting and other factors
- **Actual harm** was assessed by an expert panel (2 clinical pharmacologists)
  - **Severity** levels (from no harm to severe)
  - **Plausibility (**WHO-UMC Causality Categories -Unlikely, possible, probable, certain)

DDI prevalence

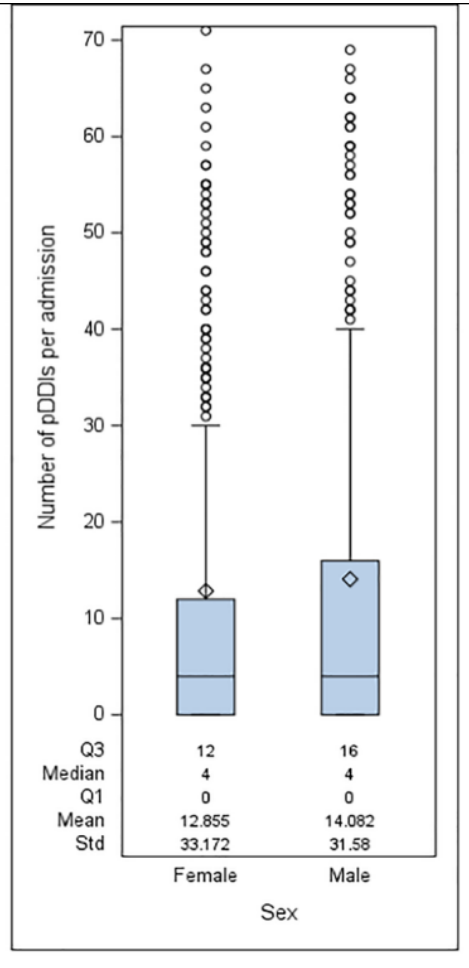
	Pre-eMM N (%)	Post-eMM N (%)	All N (%)
Patients, total number (row %)	**593 (50.7)**	**577 (49.3)**	**1170 (100)**
Total number of admissions (row %)	**597 (50.3)**	**589 (49.7)**	**1186 (100)**
Median number of drugs (IQR)	7 (3–13)	7 (2–14)	7 (3–13)
Admissions with a pDDI	**420 (70.4)**	**411 (69.8)**	**831 (70.1)**
Median number of pDDIs (IQR)	4 (0–14)	4 (0–13)	4 (0–13)
Median Number of pDDIs/10 drugs (IQR)	6 (1–13)	6 (2–12)	6 (2–13)
Admissions with a CDDI	**255 (42.7)**	**250 (42.4)**	**505 (42.6)**
Median number of CDDIs (IQR)	0 (0–2)	0 (0–2)	0 (0–2)
Median Number of cDDIs/10 drugs (IQR)	0 (0–3)	0 (0–3)	0 (0–3)

Potential DDIs per Admission

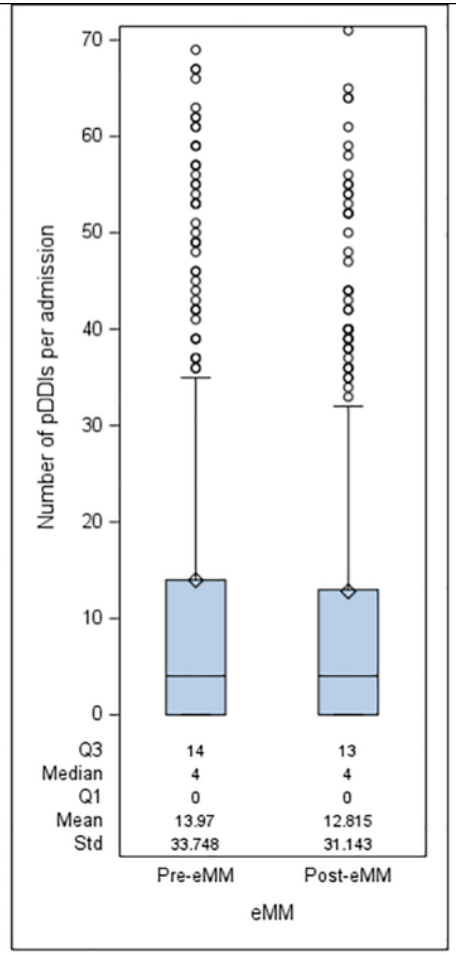
Age



Sex

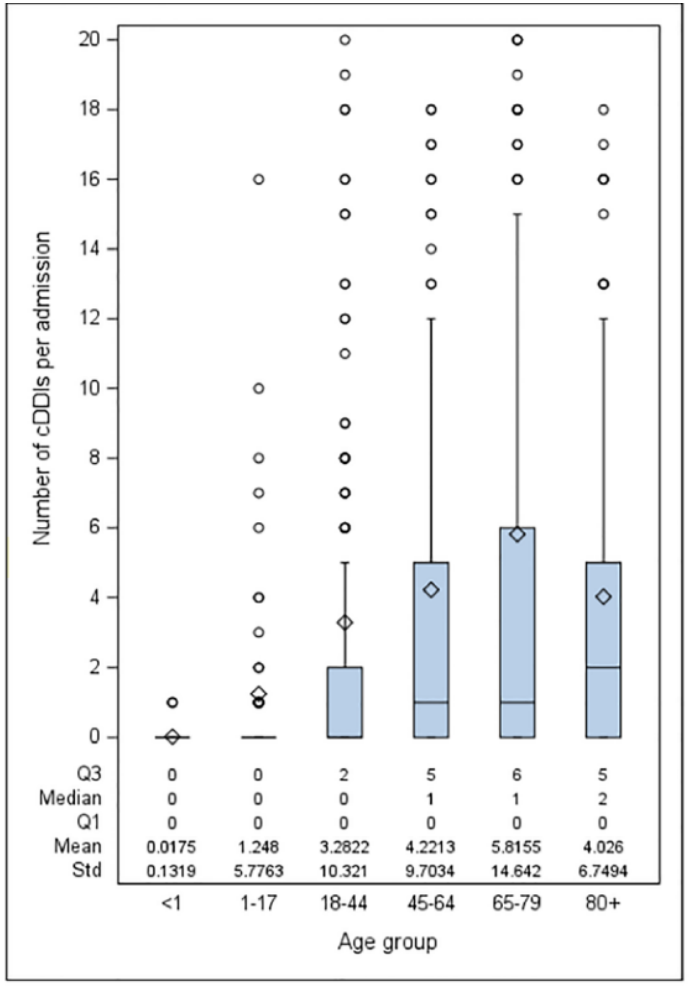


eMM

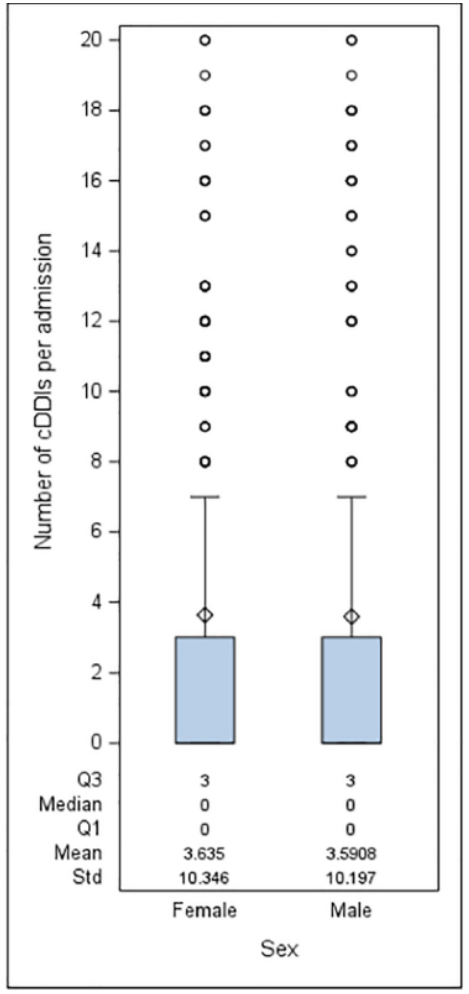


cDDIs per Admission

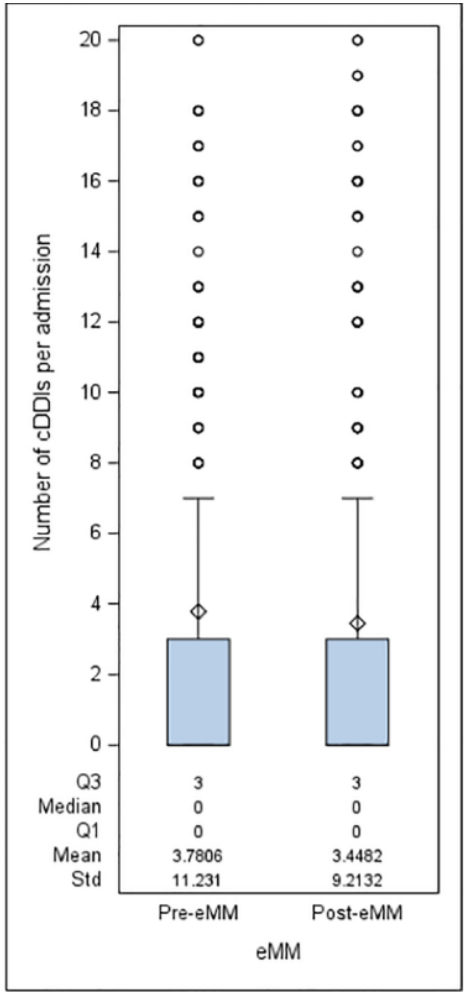
Age



Sex



eMM



Potential DDIs per 10 Drugs

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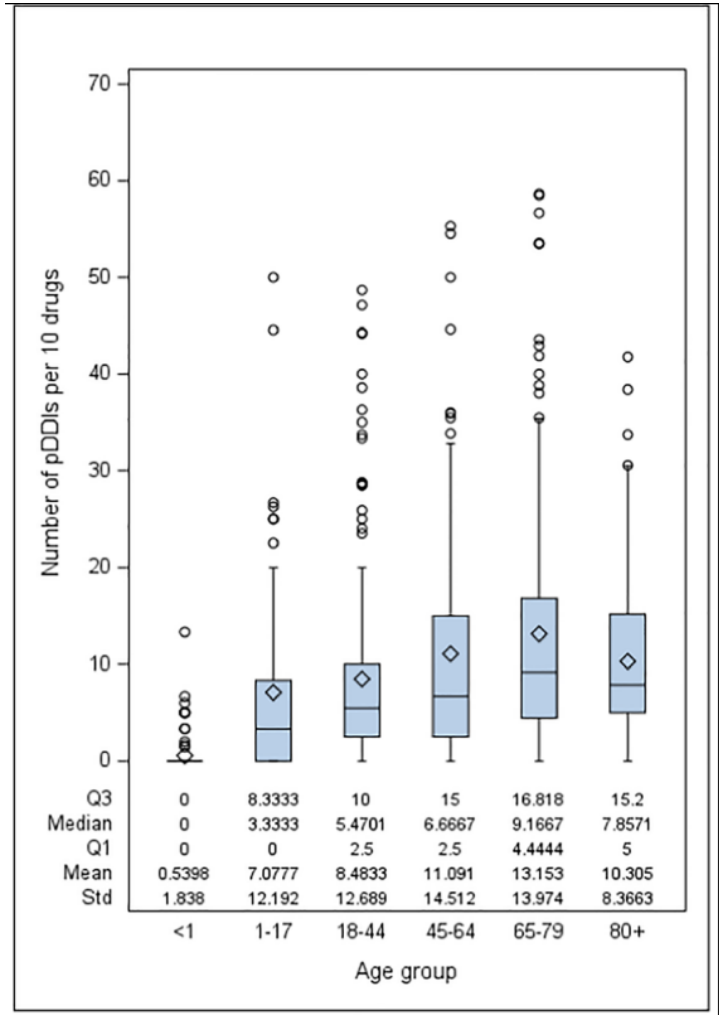
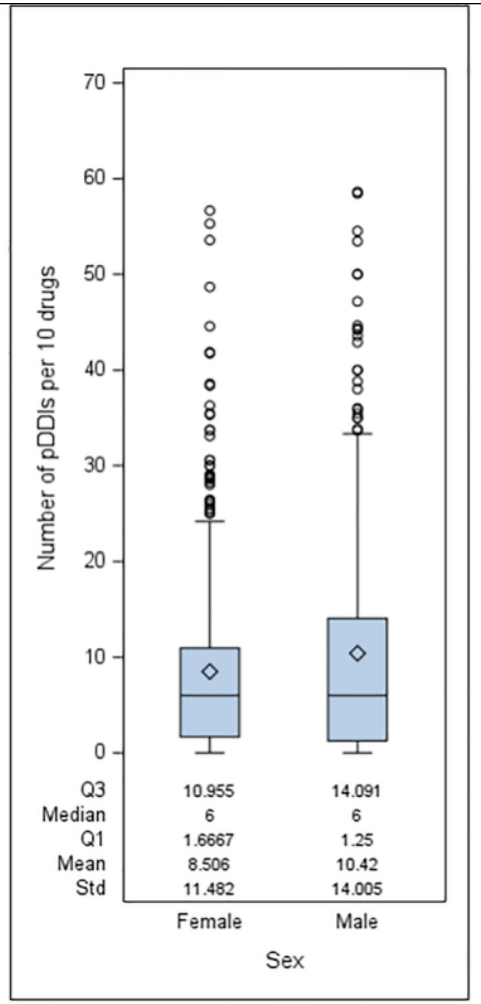
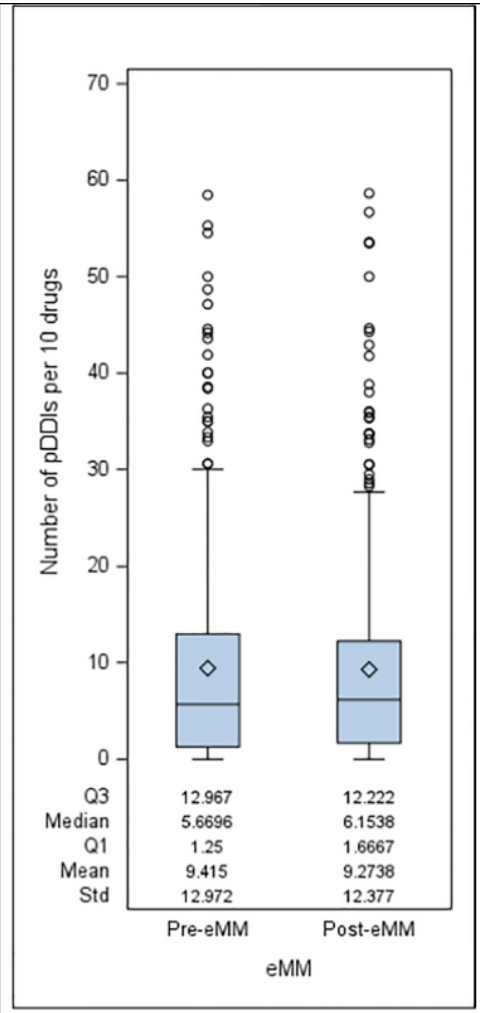
Age



Sex

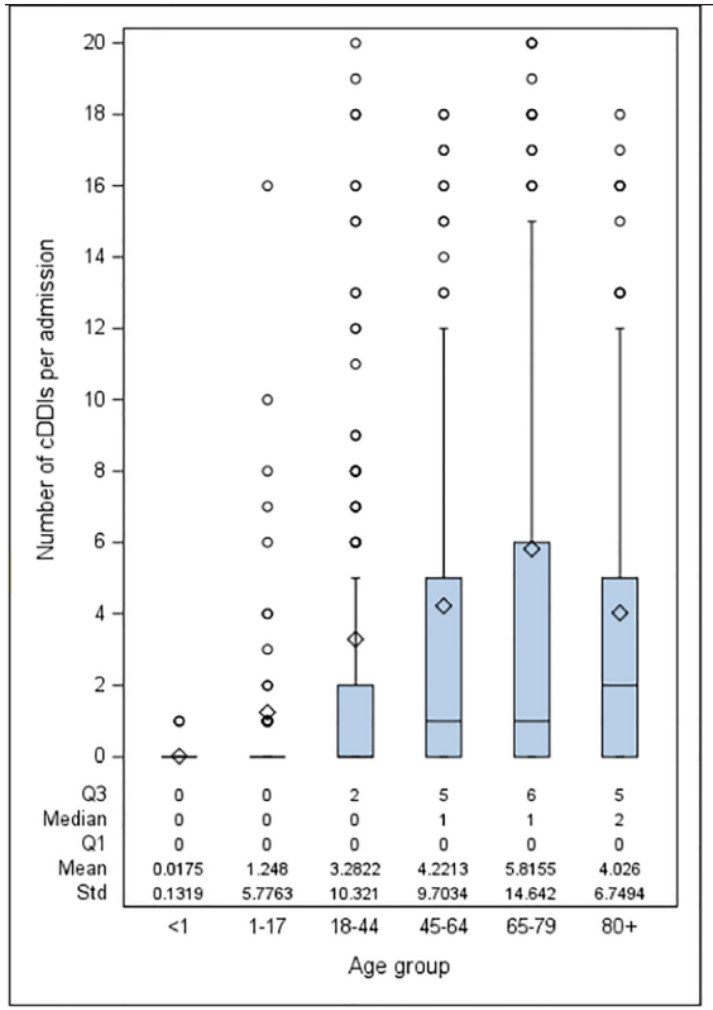


eMM

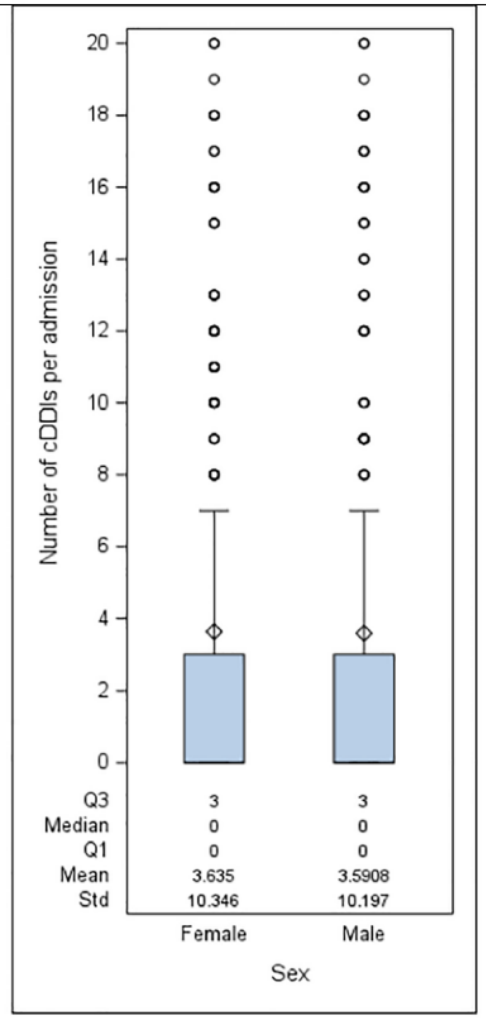


cDDIs per 10 Drugs

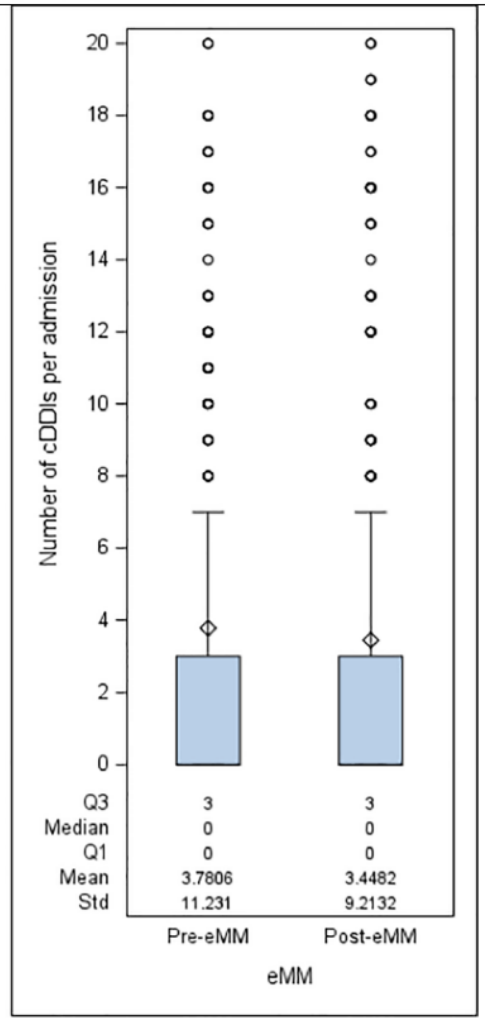
Age



Sex



eMM



Contextual Factors affecting clinical relevance of pDDIs

	cDDIs N (%)	Non cDDIs N (%)	All pDDIs N (%)
Total Number (row %)	**4285 (27.0)**	11,575 (73.0)	**15860 (100)**
Drug Factors			
Dose	61 (1.4)	**3439 (29.7)**	3500 (22.1)
Route	8 (0.2)	1174 (10.1)	1182 (7.5)
Formulation	4 (0.1)	19 (0.2)	23 (0.1)
Duration/frequency	23 (0.5)	1077 (9.3)	1100 (6.9)
Timing of doses	43 (1.0)	60 (0.5)	103 (0.6)
Patient Factors			
Age	**601 (14.0)**	494 (4.3)	1095 (6.9)
Sex	157 (3.7)	0 (0)	157 (1.0)
Patient has renal/hepatic impairment	**838 (19.6)**	0 (0)	838 (5.3)
Patient has a medical condition that may increase significance of DDI	**582 (13.6)**	0 (0)	582 (3.7)

Actual Harm^ Experienced by Patients Due to DDIs

76 cDDIs (**1.8%** of 4285 cDDIs) in 11 patients (**0.9%** of 1170 patients)

	Pre-eMM (N=2256 cDDIs, 593 patients)		Post-eMM (N=2029 cDDIs, 577 patients		**All (N=4285 cDDIs, 1170 patients)**	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Total cDDIs that led to actual harm	57	2.5 (2.0 - 3.3)	19	0.9 (0.6 - 1.5)	**76**	**1.8 (1.4 - 2.2)**
Patients who experienced actual harm	8	1.3 (0.7 - 2.6)	3	0.5 (0.2 - 1.5)	**11**	**0.9 (0.5 - 1.7)**

^A cDDI was classified as leading to actual harm when its plausibility was rated as probable or certain, and severity as minor or above

Introduction of electronic Medication Management (eMM)

- eMM implementation without DDI alerts did not significantly reduce harm

Outcome	Pre-eMM n/N (%)	Post -eMM n/N (%)	**Adjusted Odds Ratio (95% CI; p)**
cDDI (n) among pDDIs (N)	2256/8316 (27.1%)	2029/7544 (26.9%)	1.14 (0.73-1.77; 0.6)
Both drugs in cDDI (N) administered (n)	1645/2256 (72.9%)	1255/2029 (61.9%)	0.56 (0.43-0.73; <0.0001)
cDDI (N) that led to actual harm (n)	57/2256 (2.5%)	19/2029 (0.9%)	0.62 (0.26-1.48; 0.3)

Adjusted odds ratios (AORs) and confidence intervals (CIs) were estimated from multilevel logistic models accounting for patient-level cluster and adjusted for hospital, patient age, number of drugs and relevant contextual factors

Large Proportions of Inpatients Experienced pDDIs ~75% Were not Clinically Relevant to Patients

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Prevalence in Hospital

70% of patients experienced a potential DDI, **40%** a clinically relevant DDI, and **<1%** experienced an actual harm

Clinical Relevance

<30% of pDDIs were clinically relevant

Future Improvements

Contextual factors associated with clinically relevant DDIs identified in this study could be used to design more targeted interventions to improve medication safety in hospitals

Acknowledgement

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