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Incidence of adverse drug events and medication errors in Japan Japan Adverse Drug Events (JADE) Study

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Background

- Increased concerns about patient safety in Japan
- Measurement of impact of injuries due to medical care is the first step
- Scanty data on adverse drug events (ADEs) in Japan
 - Epidemiology
 - Association with medication errors
 - Risk factors

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Adverse Drug Events

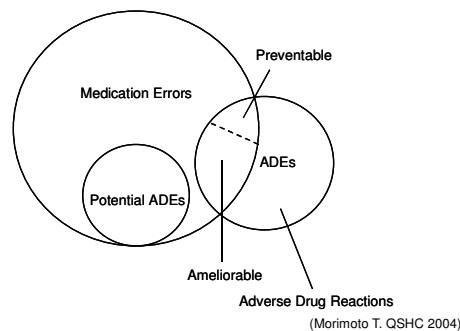
- #1 cause of injuries from medical care
 - 19% / US (Leape LL. NEJM 1991)
- 6.5 per 100 admissions / US
 - 28% preventable (Bates DW. JAMA 1995)
- Can be intervened
 - Ex. computerized physician order entry
 - 55% reduction of nonintercepted serious medication errors (Bates DW. JAMA 1998)

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Definitions



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Methods

- Prospective cohort study at 3 teaching hospitals in Japan
- All patients who admitted the select wards and aged 15 years old or greater
 - Randomly selected 7 medical wards, 8 surgical wards, and 3 ICUs with stratification
- Trained research nurses followed the patients
 - Charts; prescriptions; labs; incident reports; reconciliation from pharmacy

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Methods

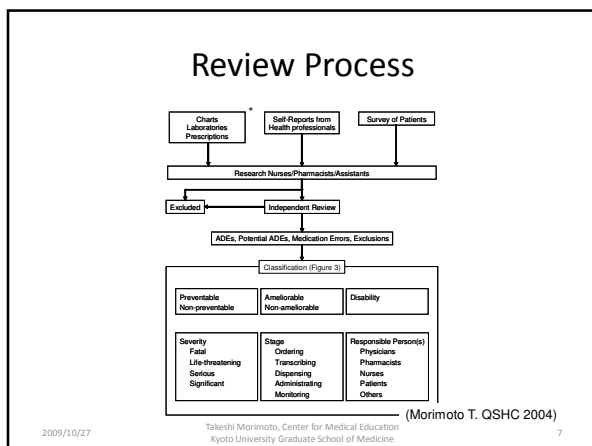
Indicators	JAPAN	USA *
Study year	2004	1993
Study period	6 months	6 months
Setting	3 teaching hospitals	2 teaching hospitals
Reviewers	Trained nurses	Trained nurses
Wards	7 Medical 8 Surgical 3 Intensive care unit	4 Medical 2 Surgical 5 Intensive care unit
Patients	3445	4031
Patient-days	58870	21412

*Bates DW. JAMA 1995

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- ### Data
- Patients' characteristics
 - Background; ward; diagnosis for admission; physical examinations; laboratories; comorbidities
 - Medication use
 - On admission
 - Before events
 - All potential events which seemed associated with medication use or its follow-up=>review
 - Description; outcomes; process; literature support
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Results

- 3445 patients were enrolled
- 58870 patient-days

Characteristics (n=3445)	n (%) or mean (SD) or median (IQR)
Age, year	66 (17)
Men	1953 (57)
Medical ward	1522 (44)
Surgical ward	1466 (43)
ICU	457 (13)
Emergency admission	1803 (52)
History of previous allergy	259 (9)

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- ### Events
- Adverse drug events
 - 994 events / 718 patients
 - 126 preventable (12.7%)
 - 11 ameliorable
 - 857 not associated with medication error
 - Potential adverse drug events
 - 332 events / 289 patients
 - 164 intercepted
 - 168 nonintercepted
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Incidences

Events	JAPAN	USA*	Unit
ADEs	16.9	11.5	/1000 PD
Preventable	2.1	3.2	/1000 PD
Nonpreventable	14.7	8.3	/1000 PD
ADEs	28.9	6.1	/ 100 AD
Preventable	3.7	1.7	/ 100 AD
Nonpreventable	25.2	4.4	/ 100 AD

*Bates DW. JAMA 1995; PD: patient-days; AD: admissions

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Incidences

Events	JAPAN	USA*	Unit
Potential ADEs	5.6	9.1	/1000 PD
Intercepted	2.9	5.2	/1000 PD
Nonintercepted	2.8	3.9	/1000 PD
Potential ADEs	9.6	4.8	/ 100 AD
Intercepted	4.8	2.7	/ 100 AD
Nonintercepted	4.9	2.1	/ 100 AD

*Bates DW. JAMA 1995; PD: patient-days; AD: admissions

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Severity

Severity*	JAPAN, %	USA†, %
Fatal	1.3	1
Life-threatening	4.3	12
Serious	27.6	30
Significant	66.8	57

Fatal: Patient died due to the incident
Life-threatening: Patient transferred to ICU, Patient falls and gets intracranial hemorrhage
Serious: Gastrointestinal bleed, Excessive sedation, Increase creatinine due to medication, Decrease in blood pressure
Significant: Rash, Diarrhea due to antibiotics

*Morimoto T. QSHC 2004; † Bates DW. JAMA 1995

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Outcomes due to ADEs

	Number (n=994)	%
Symptoms within 1 day	314	31.6
Abnormal labs necessitate treatment change	6	0.6
Symptoms for days or prolonged hospital stay	619	62.3
Injuries at discharge	40	40.2
Permanent injuries	0	0
Dead	13	1.3

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Drugs associated with ADEs

Drug	JAPAN, %	USA*, %
Analgesics	13	30
Antibiotics	36	24
Sedatives	8	8
Antineoplastic	3	7
Cardiovascular	9	4
Anticoagulants	3	3
Antipsychotics	2	2
Diabetes	1	2

*Bates DW. JAMA 1995

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Symptoms of ADEs

Symptom	Number (n=994)	%
Gastrointestinal	400	40
Metabolism, hepatic (Lab)	199	20
Central nerve (including fall)	137	14
Allergic reaction, skin	133	13
Hematopoietic	44	4.4
Cardiovascular, vital sign	21	2.1
Hemorrhage	19	1.9
Renal dysfunction	17	1.7
Respiratory	8	0.8

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Medication errors

- Total 503 errors / 424 patients
 - 137 ADEs (126 preventable + 11 ameliorable)
 - 332 Potential ADEs
 - 34 Errors without risk for injury
- Incidences
 - 8.5 / 1000 patient-days
 - 9.6 / 100 admission

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Severity

Severity*	ADE (n=137), %	Potential ADE (n=332), %
Fatal	4.4	0
Life-threatening	8.0	0.9
Serious	32.1	81.6
Significant	55.5	17.4

Fatal: Patient died due to the incident
Life-threatening: Patient transferred to ICU, Patient falls and gets intracranial hemorrhage
Serious: Gastrointestinal bleed, Excessive sedation, Increase creatinine due to medication, Decrease in blood pressure
Significant: Rash, Diarrhea due to antibiotics

*Morimoto T. QSHC 2004

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Preventability

	Number (n=503)	%
Actually intercepted	189	38
Preventable	261	52
Nonpreventable but ameliorable	53	11
(severity)	(50)	
(duration)	(53)	

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Stage and health professionals

Stage	Number (n=503)	%
Order	334	66
Prescription	11	2.2
Administration	158	31

Health professionals	Number (n=503) Multiple personnel	%
Doctors	355	71
Nurses	158	34
Pharmacists	6	1.2

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Univariate risk factors for ADEs

Risk Factor (n)	Factor +, n (%)	Factor -, n (%)	p-value
Aged 65+ (2144)	517 (24)	201 (15)	<.0001
ICU (457)	69 (15)	649 (22)	.0008
Resident physician (929)	221 (24)	497 (20)	.006
Transferred from other wards (39)	15 (38)	703 (21)	.01

Not for Gender, Ethnicity, History of allergy, Number of drugs

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Summary of findings

- Adverse drug events are common in Japan
 - Incidences are similar to those in the US
 - PADEs: Japan<US <=> ADEs: Japan>US
 - Higher cases/pt because of longer hospital stay
 - Drug profiles, severity and preventability are also consistent with the US studies
- Medication errors are also common in Japan
 - Physicians / ordering stage are most causative
- Some risk factors for ADEs

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Clinical implications

- Recognize and share the fact that ADEs are very common “disease”.
 - Nature is the same worldwide.
 - Difference in healthcare system may be associated with manifestation.
- Intervention focuses on ordering by physicians would be the first step.
 - Others: elderly, junior physicians, hand-off
- Patients should also be aware of the fact.

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