CLINICAL RELEVANCE OF PHARMACOLOGICAL INTERACTIONS

ENDEL G.; NEUMANN K.; BOUBELA R.; KALCHER K.; NELL G.
Hauptverband der Österreichischen Sozialversicherungsträger; VISEM; Department of Statistics and Probability Theory – Vienna University of Technology; Nell Pharma Connect Ltd
gottfried.endel@hvb.sozvers.at
www.hauptverband.at/EBM_HTA

OBJECTIVE

IN THE YEARS 2001 TO 2006 A TOTAL OF 39521 AEs WITH ICD10 CODES INDICATING DRUGS AS REASON WERE DOCUMENTED IN AUSTRIAN HOSPITALS.
ACCORDING TO EXPERT KNOWLEDGE THERE ARE PHARMACOLOGICAL INTERACTIONS WITH DIFFERENT CLINICAL RELEVANCE RANGING FROM NEGLIGIBLE TO SEVERE AND LIFE THREATENING ONES. NOW WE USE REIMBURSEMENT DATA OF THE AUSTRIAN SOCIAL INSURANCE COMPANIES COVERING THE YEARS 2006 AND 2007.
THE INFORMATION IS IMPORTANT TO ESTIMATE THE COST/EFFECTIVNESS OF A PLANNED e-MEDICATION SYSTEM.

QUESTION ONE IS THE INCIDENCE OF COMBINATIONS OF SUBSTANCES WITH A POTENTIAL OF INTERACTION OUT OF 4 ATC GROUPS

n(A)		8,300.000	%-patients	Rate/100.000
n (G1)	AMIODARONE	33925	0.41	408.7
n (G2)	BENZODIAZEPINE	234369	2.82	2823.7
n (G3)	MACROLID ANTIBIOTICS	1654460	19.93	19933.3
n (G4)	STATINS	612338	7.38	7377.6
		n obs.	obs %	
n (K1)	STATINS+ MACROLIDS	119252	1.44	1436.8
n (K2)	STATINS+ BENZODIAZPINE	45869	0.55	552.6
n (K3)	STATINS+ AMIODARONE	14759	0.18	177.8
n (K4)	BENZODIAZEPINS+ MACROLIDS	51323	0.62	618.3
n (K5)	BEZODIAZEPINS+ AMIODARONE	3287	0.04	39.6
n (KG1)	ONLY BENZODIAZEPINS	137050	1.65	1651.2
n (KG2)	ONLY STATINS	436599	5.26	5360.2

ANSWER ONE:
IN 2006 AND 2007 A TOTAL OF 234490 PERSONS (2.8% OF THE POPULATION!)WERE EXPOSED TO ONE OF THE PHARMACEUTICAL INTERACTIONS.

QUESTION TWO: TRIES TO QUANTIFY THE RISK OF HOSPITALISATION DUE TO ADVERSE EVENTS (ICD10 T36 - T46) ASSOCIATED WITH THESE INTERACTIONS.

			Cause of hospitalisation		comparison vs control group	
	Abbrev.	n-total	Drug related AEs; ICD10 T36 to T46	rates per 100000	p< vs excl. statins	p< vs excl. benzodiazepines
Statins + Macrolide antibiotics	K1	119252	36	30.2	ns	<<0.001
Statins + Benzodiazepines	K2	45869	47	102.5	<<0.001	<<0.001
Statins + Amiodarone	K3	14759	13	88.1	<0.001	<<0.001
only Statins	KG2	436590	134	30.7	na	<<0.001
Benzodiazepines + Macrolid antibiotics	K4	51323	65	126.6	<<0.001	<<0.001
Benzodiazepines + Amiodarone	K5	3287	11	334.7	<<0.001	ns
only Benzodiazepines	KG1	137050	432	315.2	<<0.001	na

ANSWER TWO:
THE RELATIV RISK INCREASE IS IN GROUP K2 230% AND IN K3 187%; SO THE NUMBER NEEDED TO HARM IS 1393 AND 1742! COMBINATIONS WITH MACROLIDS DO NOT INCREASE THE RISK FOR THESE OUTCOMES

QUESTION THREE LOOKS AT THE RISK OF HOSPITALISATION DUE TO CONSEQUNCES OF FALLS

			Cause of hospitalisation		comparison vs control group	
	Abbrev.	n-Total	Traumata	Rates per 100000	p< vs exkl. Statine	p< vs exkl. Benzo-diazepine
Statine + Makrolid-antibiotika	K1	119252	546	457,9	<<0,001	<<0,001
Statins + Benzodiazepines	K2	45869	449	978,9	ns	<<0,001
Statins + Amiodarone	K3	14759	220	1490,6	<<0,001	<0,001
only Statins	KG2	436590	4090	936,8	na	<<0,001
Benzodiazepines+Macrolid antibiotics	K4	51323	373	726,8	<<0,001	<<0,001
Benzodiazepines + Amiodarone	K5	3287	68	2068,8	<<0,001	ns
only Benzodiazepines	KG1	137050	2634	1921,9	<<0,001	na
Traumata and falls	ICD10:	M48.3, S70, S72, T79, S01, S09, S40, S41, S42, S52, S62, S70, S82, S92, T01, T02, T03, T04, T07, T96				

ANSWER THREE:
THE RELATIV RISK INCREASE IS IN GROUP K3 60% AND IN K5 8%; SO THE NUMBER NEEDED TO HARM IS 180 AND 681! COMBINATIONS WITH MACROLIDS DO NOT INCREASE THE RISK FOR THESE OUTCOMES

DISCUSSION

PATIENT SAFETY
PATIENT SAFETY IS OF HIGH PRIORITY IN EVERY HEALTH CARE SYSTEM.
THE NUMBER OF ADVERS EVENTS USUALLY IS UNKNOWN AND NOT EVERY „ERROR" HAS CLINICAL CONSEQUENCES. THE GOAL IS TO QUANTIFY THE FREQUENCY OF POTENTIALLY HARMFULL COMBINATIONS OF PHARMACEUTICALS USING ANONYMISED REIMBURSEMENT DATA.

OUTCOME MEASUREMENT
HOSPITALISATIONS ARE SERIOUS EVENTS FOR PATIENTS. SO WE DECIDED TO QUALIFY HOSPITALISATIONS WITH CERTAIN MAIN DIAGNOSES FOLLOWING AN EXPOSURE TO A PRESCRIPTION ERROR AS OUTCOME.

E-HEALTH
ELECTRONIC DATA ENTRY SYSTEMS FOR PHARMACEUTICAL PRESCRIPTIONS ALLOW A TECHNICAL CONTROL OF THE WHOLE MEDICATION OF A PATIENT USING INTERACTION DATABASES. SUCH e-MEDICATION SYSTEMS ARE A MANDATORY PART OF EVERY ELECTRONIC HEALTH RECORD SYSTEM. AS TO BUILD AND MAINTAIN AN EHR IS EXPENSIVE IT IS NECESSARY TO QUANTIFY POTENTIAL BENEFITS.

BASE RATE
THE BASE RATE OF ADVERSE EVENTS IN THE CONTROL GROUPS KG1 AND KG2 ARE - ESPECIALLY FOR THE OUTCOMES ASSOCIATED WITH FALLS - HIGH AND NEED FURTHER RESEARCH.

CLINICAL IMPLICATIONS
FOR THIS FIRST EVALUATION WE FOCUSED ON THE PERSPECTIVE OF THE HEALTH CARE SYSTEM AND DID NOT EXAMINE THE CLINICAL IMPLICATIONS.

ECONOMIC PERSPECTIVE
A NEXT STEP WILL BE THE ECONOMIC PERSPECTIVE AS FROM 2001 – 2006 1,2 BILLION € OF PAYMENTS WERE CONNECTED WITH CODED AEs. NOW WITH THE ANONYMISED DATA OF 2006 AND 2007 IT IS POSSIBLE TO CALCULATE POTENTIAL SAVINGS ACCOUNTABLE TO THE USE OF THE PLANNED e-MEDICATION SYSTEM WHICH WILL PROVIDE A TECHNICAL CONTROL OF PHARMACEUTICAL COMBINATIONS WITH KNOWN INTERACTIONS.

FOUR GROUPS OF PHARMACEUTICALS WERE CHOSEN: ATC (ANATOMICAL THERAPHEUTICAL CODE)

DRUG GROUP	ATC	ABREVIATION
AMIODARONE	C01BD	A
BENZODIAZEPINES	N05BA B	B
MAKROLID ANTIBIOTICS	J01FA	C
"STATINS"	C10AA S	D

K1 Statins and macrolid antibiotics D+C
K2 Statins and benzodiazepines D+B
K3 Statins and amiodarone D+A
K4 Benzodiazepines and macrolide antibiotics B+C
K5 Benzodiazepines and amiodarone B+A
KG1 benzodiazepins alone B
KG2 statins alone D

OTHER MEDICATION WAS NOT EXAMINED!

LOOKING FOR RHABDOMYOLYSIS BROUGHT NO SIGNIFICANT RESULTS.
OUTCOMES OF CLINICAL RELEVANCE CAN BE FOUND FOR PHARMACEUTICALS WHICH ARE USED FOR CHRONIC CONDITIONS LIKE STATINS AND FOR THE BENZODIAZEPINES WHICH CAN LEED TO ADICTION.
AMIODARONE AS A DRUG FOR „SPECIALISTS" MAY NOT BE WELL KNOWN FOR IST POTENTIAL OF INTERACTIONS.
REIMBURSEMENT DATA CAN BE USED TO DETECT ADVERSE EVENTS!

LIMITATION

CODING OF THE MAIN DIAGNOSES IN A DRG SYSTEM MAY NOT ALLWAYS REPRESENT THE BEST FIT DIAGNOSE. SO WE ALSO WILL EXAMINE THE CORRELATION TO SECONDARY DIAGNOSES.
ONLY THREE AREAS OF ICD10 WERE INCLUDED. THERE MAY BE OTHER (MAIN OR SECONDARY) DIAGNOSES CORRELATED TO INTERACTIONS.
FOR CLINICAL QUESTIONS AGE AND GENDER OF PATIENTS AND ALL OTHER PHARMACEUTICALS REIMBURSED IN THE TIME OF INTEREST HAVE TO BE LOOKED AT.

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