Do they all agree? – comparing expert signal assessment outcomes

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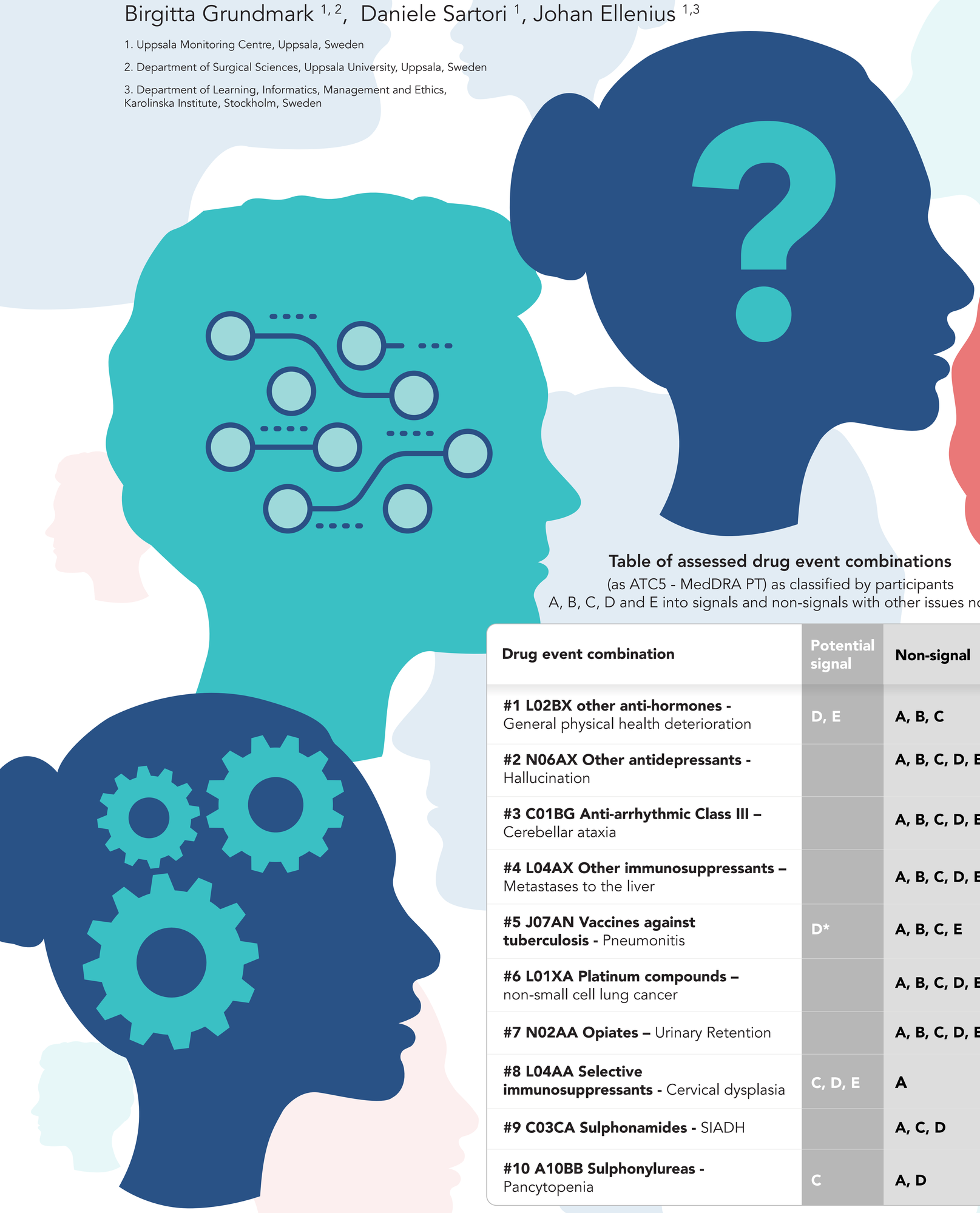

Table of assessed drug event combinations
(as ATC5 - MedDRA PT) as classified by participants A, B, C, D and E into signals and non-signals with other issues noted.

Drug event combination	Potential signal	Non-signal	Other issue
#1 L02BX other anti-hormones - General physical health deterioration	D, E	A, B, C	
#2 N06AX Other antidepressants - Hallucination		A, B, C, D, E	
#3 C01BG Anti-arrhythmic Class III – Cerebellar ataxia		A, B, C, D, E	
#4 L04AX Other immunosuppressants – Metastases to the liver		A, B, C, D, E	D
#5 J07AN Vaccines against tuberculosis - Pneumonitis	D*	A, B, C, E	B*
#6 L01XA Platinum compounds – non-small cell lung cancer		A, B, C, D, E	
#7 N02AA Opiates – Urinary Retention		A, B, C, D, E	B
#8 L04AA Selective immunosuppressants - Cervical dysplasia	C, D, E	A	
#9 C03CA Sulphonamides - SIADH		A, C, D	A
#10 A10BB Sulphonylureas - Pancytopenia	C	A, D	

SIADH = syndrome of inappropriate ADH secretion
***** participant did not check or identify in labelling

Background: Despite available methods and guidance for causality assessment and signal management[1,2], in-depth analyses on manual signal assessment and prioritisation[3] are sparse.

Objective/Aim: The aim was to compare the primary signal assessment outcome by experienced MD assessors as part of a study aiming to describe in detail their individual methodological approach.

Methods: A list of 20 previously unassessed drug event combinations (DEC) were extracted from VigiBase, the WHO global database of individual case safety reports, using the statistical signal detection method vigiRank[4]. Substances and events could further appear only once in the list, and some well acknowledged DECs were excluded manually. Five experienced Uppsala Monitoring Centre MDs were provided with the DEC list with basic data on cases: de/re-challenges, number of reporting countries, outcome, disproportionality measure and the full case-series, including narratives. Over the course of 3 hours, using any information sources available to them, they were asked to classify as many DECs as possible into signals for subsequent in-depth assessment or non-signals. Within 24 hours, participants were interviewed regarding assessment outcomes and their detailed methodological approach. Interviews were recorded, transcribed verbatim and analysed using inductive thematic analysis (ongoing).

Results: The participants completed 46 DEC assessments (7-11 each) where 4 DECs were classified by 1-3 participants as signals for in-depth assessment, see table. In 5 DECs, participants noted "other issues" worth pursuing. Four participants put most of their effort into DEC #1, despite early comments from all that it was not worth pursuing due to the unspecific event-term and the nature of the indication. DECs were generally not dismissed as non-signals without screening narratives for possible new signal-worthy aspects. The DEC that the assessors spent the least time on differed: two assessors named the same DEC (#6) where the ADR term was ultimately identified by all as disease spill-over[5], i.e. the indication incorrectly coded as an event. Examples of "other issues" which may require further action include: investigating related/wider ADR terms and/or drug class for signal value, personal interest, and proposing to inform about important pharmacokinetic issues.

Conclusion: Concordance regarding signal/non-signal classification of DECs was relatively high. Non-concordant classifications were partly due to differences in depth of assessment between assessors. The in-depth analysis of cognitive strategies is ongoing with plans to broaden the study sample.

References:
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Disclosure:
The authors are indebted to the national centres that contribute data to the WHO Programme for International Drug Monitoring. However, the opinions and conclusions in this study are not necessarily those of the various centres, nor of WHO.

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