Web-based HIV drug interaction checkers: Comprehensiveness and concordance of the Toronto and Liverpool databases

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Background:

- Drug interactions (**DI**) between antiretroviral (**ARV**) and non-ARV drugs can lead to toxicity or treatment failure.
- The Immunodeficiency Clinic at UHN Toronto General Hospital (**Toronto**) https://hivclinic.ca and University of Liverpool (**Liverpool**) www.hiv-druginteractions.org maintain web-based, HIV-focused DI checkers.
- We evaluated the comprehensiveness and concordance of these databases using a "real-world" sample of medications dispensed to HIV patients.

Methods:

- Lists of ARV and non-ARV drugs dispensed to HIV-infected, ARV-treated British Columbians age ≥19 years between 01-Jan-2010 and 31-Dec-2016 were extracted from the population-based Seek and Treat for Optimal Prevention of HIV/AIDS (STOP HIV/AIDS) cohort.*
- The STOP HIV/AIDS linked, population-based dataset includes outpatient, non-ARV dispensing records from BC PharmaNet, and ARV dispensing data from the BC Centre for Excellence in HIV/AIDS Drug Treatment Program.

*Disclaimer: All inferences, opinions, and conclusions drawn in this presentation are those of the authors, and do not reflect the opinions or policies of the data stewards.

Methods, continued:

- HIV healthcare providers (pharmacists KL, LA, JT, physician MH) checked each listed non-ARV drug for DI with all ARVs available in BC 2010-2016, using the Toronto and Liverpool databases (accessed May to Sep. 2019).
- DIs for boosted ARVs were assessed separately for cobicistat and ritonavir.
- DI database comprehensiveness and concordance were calculated overall, and by non-ARV drug class.
- **Comprehensiveness** was calculated as the percentage of non-ARV drugs included in each database.
- **Concordance** was defined as ARV+non-ARV drug pairs having the same DI severity in both databases, with severity ranked **Avoid** >**Caution** >**None**.
  - **Avoid:** Co-administration should be avoided. Toronto or Liverpool red flag.
  - **Caution:** Co-administration may require ARV or non-ARV dose adjustment, dose spacing, or enhanced monitoring. Toronto yellow flag, Liverpool orange flag.
  - **None:** No clinically important DI. Toronto green flag, Liverpool green or yellow flag.

Results:

- 659 non-ARV drugs and 27 ARVs (including distinct ARV-booster combinations) were assessed, and 15,058 ARV+non-ARV pairs evaluated.

Results continued:

Comprehensiveness: Overall, 75% of non-ARV drugs were present in at least one database; 9% were present only in Toronto and 18% only in Liverpool (Table 1).

Table 1. HIV Drug Interaction Database Comprehensiveness

Non-ARV Drugs by Drug Class	N Non-ARV Drugs	n (% of N) Non-ARV Drugs Listed in HIV-focused Drug Interaction Databases		
		Toronto	Liverpool	Both
Anti-Infective	89	45 (51)	72 (81)	40 (45)
Antineoplastic-Immune Modulating	52	37 (71)	33 (63)	29 (56)
CNS-Psychotherapeutic	47	45 (96)	37 (79)	36 (77)
CNS-Other	119	84 (71)	76 (64)	62 (52)
Cardiovascular	88	61 (69)	75 (85)	57 (65)
Gastrointestinal	51	16 (31)	26 (51)	14 (27)
Genitourinary	22	16 (73)	16 (73)	15 (68)
Hormonal-Metabolic	78	48 (62)	51 (65)	43 (55)
Respiratory	26	12 (46)	19 (73)	11 (42)
Miscellaneous	87	14 (16)	27 (31)	9 (10)
Total	**659**	**378 (57%)**	**432 (66%)**	**316 (48%)**

CNS-Psychotherapeutic: Central Nervous System drugs including antidepressants, antipsychotics.
CNS-Other: Includes anticonvulsants, opioids, sedative/hypnotics, NSAIDs and other CNS drugs.
Miscellaneous: Includes drugs for gout, osteoporosis, blood disorders, nutritional supplements and others.

Concordance: 5,254 (35%) of the ARV+non-ARV pairs were listed in both databases, 4,219 (80%) of which had concordant DI classification (Table 2). Discordant classifications were due to international differences between drug monographs and/or different interpretation of the literature.

Table 2. HIV Drug Interaction Database Concordance

Non-ARV drugs listed in both Toronto and Liverpool drug interaction databases		Concordance of ARV+non-ARV drug interaction severity n (% of N drug pairs)		
Therapeutic Class	N ARV+non-ARV drug pairs	Concordant	Discordant Higher severity Toronto	Discordant Higher severity Liverpool
Anti-Infective	714	596 (83)	94 (13)	24 (3)
Antineoplastic- Immune Modulating	495	407 (82)	62 (13)	26 (5)
CNS-Psychotherapeutic	576	372 (65)	151 (26)	53 (9)
CNS-Other	983	782 (80)	165 (17)	36 (4)
Cardiovascular	958	795 (83)	114 (12)	49 (5)
Gastrointestinal	235	204 (87)	7 (3)	24 (10)
Genitourinary	243	221 (91)	8 (3)	14 (6)
Hormonal-Metabolic	703	542 (77)	135 (19)	26 (4)
Respiratory	185	148 (80)	12 (6)	25 (14)
Miscellaneous	162	152 (94)	5 (3)	5 (3)
Total	**5,254**	**4,219 (80%)**	**753 (14%)**	**282 (5%)**

Conclusions: Combined use of Liverpool and Toronto HIV DI-checkers enhances the comprehensiveness of DI information. Discordance is infrequent, and provides insight into different interpretations of the DI literature.