



Polypharmacy of concomitant medications in HIV-infected Australian adults is common, and associated with adverse events

ASHM – Canberra 2017

Siefried KJ¹; Mao L²; Cysique LA^{1,3}; Rule J^{4,5}; Giles ML^{6,7}; Smith DE^{5,8}; McMahon J^{6,7,9}; Read TR^{10,11}; Ooi C^{12,13}; Tee BK¹⁴; Bloch M^{15,16}; de Wit J^{2,17}; Carr A¹;
On behalf of the PAART study investigators

¹ St Vincent's Centre for Applied Medical Research, St Vincent's Hospital, Sydney; ² Centre for Social Research in Health, UNSW, Sydney; ³ Neuroscience Research Australia, UNSW, Sydney; ⁴ National Association of People with HIV Australia; ⁵ School of Public Health and Community Medicine, UNSW, Sydney; ⁶ Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne; ⁷ Monash Infectious Diseases, Monash Health, Melbourne; ⁸ Albion Centre, South Eastern Sydney Local Hospital Network, Sydney; ⁹ Centre for Population Health, Burnet Institute, Melbourne; ¹⁰ Melbourne Sexual Health Centre, Alfred Health, Melbourne; ¹¹ Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne; ¹² Western Sydney Sexual Health Centre, University of Sydney, Parramatta; ¹³ Westmead Clinical School, Sydney Medical School, University of Sydney, Westmead; ¹⁴ Centre Clinic, St Kilda (Melbourne); ¹⁵ Holdsworth House Medical Practice, Sydney; ¹⁶ The Kirby Institute, UNSW, Sydney; ¹⁷ Department of Interdisciplinary Social Science, Utrecht University, The Netherlands

Funding

- Gilead Sciences (unrestricted educational grant)
- The Balnaves Foundation
- Western Australia Health
- Victorian Department of Health and Human Services
- ACT Ministry of Health

Disclosures

- KJS: conference and travel sponsorships (Gilead, ViiV), Gilead Fellowship
- LM: no interests to declare
- LAC: NHMRC career development fellowship, research support (Gilead)
- JR: no interests to declare
- MLG: research support (Gilead)
- DES: advisory boards (Gilead, MSD), consultant and lecturer (Gilead)
- JM: research support (Gilead)
- TRR: NHMRC fellowship
- CO: no interests to declare
- BKT: no interests to declare
- MB: lecture and travel sponsorships (Gilead, ViiV, MSD)
- JdW: lecture sponsorship (BMS Australia)
- AC: research funding (BMS, Gilead, ViiV), lecture and travel sponsorships (BMS, Gilead, ViiV), advisory boards (Gilead, ViiV)

Background

- In addition to ART, concomitant medications are often prescribed to:
 - mitigate ART side effects
 - treat comorbid conditions associated with HIV / ART / normal aging processes
- Polypharmacy is commonly defined as ≥ 5 medications
 - more common in HIV-infected adults than the general population
 - in the general population increases the risk of:
 - morbidity
 - non-adherence
 - drug interactions
 - side effects
- No complete polypharmacy data in HIV-infected Australian adults:
 - multiple-prescribers, patient self-report vs physician documentation
 - over the counter and alternative preparations
 - no data on concomitant medication non-adherence or adverse effects

Edelman 2013, Gnjidic 2012, Marcum 2012, Marzolini 2010

Methods

PAART study

- 522 participants at 17 Australian GP, sexual health and hospital sites

Eligibility

- HIV+ adult ≥ 18 years of age
- on stable ART for previous 3 months (minimum)
- plasma HIV-RNA < 50 cp/mL

Assessments

- 90-item participant survey
- neurocognitive function: Cogstate
- pharmacy ART dispensing data
- clinical and virological data
 - concomitant medications by prescribed and participant self-report

AIDS in press, 2017

Methods

Polypharmacy

- Polypharmacy defined as ≥ 5 concomitant medications
 - including over-the-counter and alternative medications (excluding ART)
- Factors associated with polypharmacy were identified by multivariable binary logistic regression
- Pearson's chi-squared test was used to evaluate the relationship between polypharmacy and the following specifically assessed adverse events:
 - nausea
 - diarrhoea
 - fatigue
 - sleep disturbance
 - myalgia
 - rash
 - peripheral neuropathy
- Associations between polypharmacy and adverse effects were adjusted for comorbid disease burden using the Charlson index

AIDS in press, 2017

Results

- 94.5% male
- Age - 51 years
- HIV duration - 12 years
- 75% (n=392) took ≥ 1 concomitant medication
 - 5.0 (SD 4.4) concomitant medication pills / day vs 3.0 (SD 2.2) ART pills / day
- Most common concomitant medications: lipid-lowering, antidepressant, anti-viral, PPIs, anti-coagulants, PDE5 inhibitors, oral anti-diabetics, anticonvulsants
- 23% (122) had polypharmacy:
 - higher age (57 years vs 51 years)
 - higher rate previous AIDS (36% vs 23%)
 - current comorbidity (84% vs 57%)

AIDS in press, 2017

Polypharmacy multivariable logistic regression

Covariates Independently Associated with Polypharmacy

Covariate	AOR	95% CI	p-value
HIV managed in a general practice (vs sexual health clinic)	1.9	1.0-3.7	0.038
HIV managed in a hospital-based clinic (vs sexual health clinic)	2.0	1.0-3.6	0.030
Monthly or more benzodiazepine ("benzos") use	2.8	1.1-7.7	0.035
Clinical trial participation	3.5	1.3-9.0	0.011
Renal impairment (eGFR <60mL/min/1.73m ²)	3.8	1.5-10.1	0.006
Diagnosed comorbidity	4.2	2.0-8.6	<0.001

AIDS in press, 2017

Adverse effects

Adverse effects

Concomitant medication use			
Adverse effect	Odds Ratio	95% CI	p-value
Sleep disturbance	2.6	1.5-4.2	<0.001
Myalgia	2.1	1.1-3.9	0.019
Lipodystrophy	6.0	2.2-17.0	<0.001

Adverse effects

Concomitant medication use			
Adverse effect	Odds Ratio	95% CI	p-value
Sleep disturbance	2.6	1.5-4.2	<0.001
Myalgia	2.1	1.1-3.9	0.019
Lipodystrophy	6.0	2.2-17.0	<0.001
Polypharmacy of concomitant medications			
Adverse effect	Odds Ratio	95% CI	p-value
Diarrhoea	1.6	1.0-2.4	0.046
Fatigue	1.7	1.1-2.6	0.015
Myalgia	1.7	1.0-2.9	0.033
Peripheral neuropathy	3.9	2.4-6.4	<0.001
Lipodystrophy	2.4	1.4-4.1	0.001

Adverse effects – adjusted for comorbidity

Polypharmacy of concomitant medications			
Adverse effect	Adjusted Odds Ratio	95% CI	p-value
Diarrhoea	1.9	1.1-3.0	0.013
Fatigue	1.7	1.0-2.6	0.032
Myalgia			
Peripheral neuropathy	3.1	1.8-5.2	<0.001
Lipodystrophy			

Summary & Conclusions

- Concomitant medication polypharmacy present in 23%
- Polypharmacy associated with several adverse effects
- Management of concomitant medications to prescribe fewer concomitant medications with fewer effects is warranted

AIDS in press, 2017

Acknowledgements

Albion Centre (Sydney)

- Ms Gesalit Cabrera, Ms Denise Smith, Mr Michael Stewart

The Alfred Hospital (Melbourne)

- Ms Mellissa Bryant, Ms Jess Costa, Ms Cath Downs

Brookong Centre (Wagga Wagga)

- Ms Sally-Anne Brennan, Dr Kym Collins, Ms Alison Kincaid, Ms Jennifer Macleod

Cairns Sexual Health

- Ms Faith Bassett, Ms Colette Cashman, A/Prof Darren Russell

Canberra Sexual Health Centre

- Ms Lauren Baden, Ms Anne Baynes, Mr Rendry Del Rosario, Ms Ruth Evans, Ms Angela Knight, Dr Sarah Martin

Centre Clinic (Melbourne)

- Ms Helen Lau

East Sydney Doctors

- Dr David Baker, Ms Melissa Benson, Ms Vicki Ieroklis, Ms Elizabeth Odgers, Ms Katherine Ognenovska, Ms Philippa Pattinson, Ms Elena Shirley, Ms Lesley Williams

Fremantle Hospital / Fiona Stanley Hospital (Perth)

- Ms Amanda Bearcroft, Dr John Dyer, Ms Jacqueline Kerth, Ms Wendy Lam, Ms Annamaria Palermo

Statistical & presentation support: Mr Tom Gates, Dr Steve Kerr

Administrative support: Ms Stephanie Riches

Holdsworth House Medical Practice (Sydney)

- Ms Lily Alldridge, Ms Toni Gauson, Dr Avindra Jayewardene, Ms Kate Morris, Ms Jessie Payne, Ms Trina Vincent

Melbourne Sexual Health Centre

- Ms Helen Kent, Ms Julie Silvers

Monash Health (Melbourne)

- Ms Mellissa Bryant, Ms Jess Costa

Royal North Shore Hospital Clinic 16 (Sydney)

- Ms Anisa Cheshire, Prof Suran Fernando

SHAIDS Sexual Health Service (Lismore)

- Ms Kate Allardice, Ms Nikki Keefe, Ms Ariane Minc, Dr David Smith, Ms Amber Tarver, Ms Debbie Wilson

St Vincent's Hospital (Sydney)

- Ms Nicola MacKenzie, Ms Dianne Morris, Ms Stephanie Riches, Mr Chris Rofe, Ms Kate Sinn

Sydney Sexual Health Centre

- Dr Damian Conway, Dr Rosalind Foster, Ms Ruthy Mclver, A/Prof Anna McNulty, Ms Elizabeth Scally, Dr Caroline Thng

Taylor Square Private Clinic (Sydney)

- Ms Sophie Dinning, Dr Robert Finlayson, Ms Shruti Gupta, Mr Phuoc Loc Le, Mr David Ninham, Ms Ching Tan

Western Sydney Sexual Health

- Ms Karen Biggs, Ms Melissa Power