

# BMJ Open Barriers to HIV care among Francophone African, Caribbean and Black immigrant people living with HIV in Canada: a protocol for a scoping systematic review

Pascal Djiadeu,<sup>1,10</sup> Joseph Nguemo,<sup>2</sup> Chantal Mukandoli,<sup>3</sup> Apondi J Odhiambo,<sup>1,4</sup> David Lightfoot,<sup>5</sup> Lawrence Mbuagbaw,<sup>6,7,8</sup> LaRon E Nelson<sup>1,10,9</sup>

**To cite:** Djiadeu P, Nguemo J, Mukandoli C, *et al.* Barriers to HIV care among Francophone African, Caribbean and Black immigrant people living with HIV in Canada: a protocol for a scoping systematic review. *BMJ Open* 2019;**9**:e027440. doi:10.1136/bmjopen-2018-027440

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2018-027440>).

Received 22 October 2018  
Revised 5 December 2018  
Accepted 19 December 2018



© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

**Correspondence to**  
Dr Pascal Djiadeu;  
djiadeup@smh.ca

## ABSTRACT

**Introduction** Language is a social determinant of health. Addressing social determinants of health is paramount to successful progression along the HIV-care continuum. Canada is a bilingual country with French and English as official languages. There are few studies to date that have focused on the impact of being a French-speaking linguistic minority on the HIV-care continuum. The primary objective of this scoping, systematic review of literature is to evaluate existing gaps in access to HIV-care among French-speaking people living with HIV in Canada. Our primary outcome is healthcare services availability and access for French-speaking people living with HIV.

**Methods and analyses** Our scoping, systematic review will draw on a systematic search of published literature, both quantitative and qualitative studies published on French-speaking individuals' healthcare and HIV status in Canada, with particular emphasis on the province of Ontario. We will conduct our search in MEDLINE, the Excerpta Medica Database, the Cumulative Index to Nursing and Allied Health Literature, Web of Science, EBSCO and Google Scholar for work published between 1990 and 2018. Identified articles will be screened in duplicate and full-text articles of relevant studies will be retrieved. Data will also be extracted by two researchers working independently. Any discrepancies that arise will be resolved by consensus or by consulting a third author. Our findings will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

**Ethics and dissemination** Our proposed research will not be conducted with human participants. We will only use secondary published data and therefore ethics approval is not required. Our findings will be disseminated as peer reviewed manuscripts at conferences and student rounds, and could be of interest to government health agencies and local HIV/AIDS service organisations.

## INTRODUCTION

It is well-established that language is more than a translation of words.<sup>1</sup> In Canada, the term 'minority Francophone' refers

## Strengths and limitations of this study

- One strength is that we will conduct a comprehensive, exhaustive search strategy with an experienced research team.
- Another strength of this study is the novelty of the research question: barriers to quality HIV-care among Francophone and French-speaking African, Caribbean and Black (ACB) immigrant people living with HIV in Canada.
- One limitation is that it is unlikely that we will find experimental studies.
- Another limitation of this scoping review is that it will be focused only on Canada and therefore its global relevance is limited; however, theoretical generalisations can be postulated and tested with Francophone diaspora minorities in predominantly anglophone communities.
- Significance of the study: This scoping review will answer important questions related to access to care for Francophone HIV-infected ACB living in Canada. Furthermore, this review will evaluate the impact of intersectionality of the French language, race and HIV stigma on ACB accessibility to HIV care. The findings of this scoping systematic review will have implications for health policy and practice in the provision of care to Francophone HIV-infected and affected ACB immigrants and Canadians.

to people living outside of the province of Quebec in majority English speaking provinces and whose mother tongue or first official language spoken is French.<sup>2</sup> Francophone individuals represent approximately 5% of the Ontario population.<sup>3</sup> The Francophone population now includes immigrants from African countries with French as their official language.<sup>2-4</sup> Almost 7.5% of Francophone in Ontario speak French only, regardless of their mother tongue.<sup>3</sup> Therefore African, Caribbean and Black (ACB) people

who identify French as their primary language, represent a growing segment of the Francophone population in Ontario.

The French Language Service Act, 1986<sup>5</sup> guarantees the right of individuals to receive French-language services from the Ontario government ministries and agencies, including access to French healthcare services. However, providing high quality French healthcare services remains a challenge across the province of Ontario and other English speaking provinces in Canada.<sup>4 6-9</sup> A study done in New Brunswick, the only official bilingual province in Canada, has shown that francophone individuals are less likely to report their health as being 'good' compared with their Anglophone-majority counterparts.<sup>10</sup> Other studies have reported that the quality of French healthcare services in Canadian Anglophone provinces is suboptimal.<sup>4 7 9 11 12</sup>

In the USA, language barriers and immigration status have been identified as barriers to HIV testing for new immigrants from sub-Saharan Africa and the Caribbean.<sup>13</sup> Immigrants, once healthy when compared with their Canadian-born counterparts, have self-reported poor health associated with language barriers, discrimination and immigration status.<sup>14 15</sup> In some places, the quality of French healthcare services has resulted in avoidance of care by the francophone living in anglophone-majority provinces.<sup>16</sup> In 2016, the Public Health Agency of Canada reported that an estimated 36319 people were living with HIV (PLWH) in Ontario, with about one third of them from the ACB communities.<sup>17</sup> Social determinants of health such as language barriers, stigma and discrimination have negative consequences on linkage and engagement to care for HIV positive immigrants and ACB in Ontario,<sup>4 12</sup> and may be worse in ACB Francophone minorities. The core of any community services providing support to PLWH is health promotion, quality of care, counselling and preventive care as well as case management and patient satisfaction.<sup>18 19</sup>

The purpose of this systematic scoping review is to inform policy makers, community health centres and HIV organisations on the outcomes associated with being a Francophone minority living with HIV in Canada. The primary objective of this scoping systematic review is to document access to health services by French-speaking people living with HIV in Canada. The secondary objective is to assess the state of the HIV-care continuum for Francophone ACB people living with HIV in Canada. HIV-care continuum or cascade includes the following: HIV diagnosis, linkage and retention to care, receipt of antiretroviral therapy (ART) and achievement of viral suppression.<sup>20</sup> We will also summarise data on participation in health promotion, finding a regular provider, receiving preventive care, satisfaction with care, the effects of race, stigma and discrimination, including immigration status.

## METHODS AND ANALYSES

We will adopt the scoping review approach proposed by Peterson *et al* that ensures that the review is executed such that it can inform practice, policy, education and research.<sup>21</sup> The scoping review approach is different from the standard systematic review in that we will not attempt to answer a specific research question, but rather appraise a broad body of evidence in order to describe HIV care for French-speaking people living with HIV in Canada. HIV-care continuum or cascade includes the following: HIV diagnosis, linkage and retention to care, receipt of ART and achievement of viral suppression.

### Patient and public involvement

Patients and public will not be involved in the study.

### Inclusion criteria for studies

#### Types of studies

We will consider experimental (randomised or non-randomised) and observational studies (longitudinal, cross-sectional), evidence syntheses (systematic reviews) and qualitative or mixed-method studies.

For a study to be eligible, it must include data on French-speaking people with HIV in an anglophone-majority Canadian province and address at least one of the outcomes of interest. Studies from Quebec will be excluded.

### Outcomes

Our primary outcome is the quality of and access to health services for francophones living with HIV in anglophone-majority provinces in Canada. We will look at the HIV-care cascade which includes HIV diagnosis, linkage and retention to care, receipt of ART and achievement of viral suppression.

#### Our secondary outcomes

The secondary outcomes will focus on the participation of Canadian Francophone ACB PLWH in health promotion, their proximity to healthcare centres and quality of life. We will extract data on the quality of care provided to this population as well as the effect of race, stigma and discrimination on care provided. Furthermore, we will also collect data on access of Francophone ACB PLWH to bilingual healthcare providers and preventive care and patient satisfaction.

### Search strategy for identification of studies

We will conduct an exhaustive search for published studies in English and French reporting on health and healthcare in francophone populations in Canada. The search will include the search terms listed in [box 1](#) and will be adapted for each database ([box 1](#)).

### Electronic searches

We will conduct our searches in MEDLINE, Excerpta Medica Database, Cumulative Index to Nursing and Allied Health Literature, Web of Science, EBSCO and Google Scholar from 1990 (date that the French Language

**Box 1 Proposed search strategy for MEDLINE**
**Database: MEDLINE**

## Search strategy:

1. exp 'Emigrants and Immigrants'/'
2. immigrant\*.mp.
3. Emigrant\*.mp.
4. migrant\*.mp.
5. (landed adj5 status).tw.
6. (landed adj5 person\*).tw.
7. (landed adj5 resident\*).tw.
8. exp Refugees/
9. asylum.tw.
10. new Canadian.tw.
11. resident.tw.
12. refugee.tw.
13. \*POPULATION/
14. communit\*.tw.
15. exp MINORITY GROUPS/
16. MINORITY HEALTH/
17. minorit\*.tw.
18. exp patient/or patient.tw.
19. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
20. french.tw.
21. francophone\*.tw.
22. Francophonie.mp.
23. exp Language/
24. (french or francais or franco\* or quebec\*).tw.
25. 23 and 24
26. ((french or francais or franco\*) adj5 language).tw.
27. 20 or 21 or 22 or 25 or 26
28. exp African Continental Ancestry Group/
29. (Africa\* or African or Afrique or Africain\*).tw.
30. Benin.tw.
31. Burkina Fas\*.tw.
32. Burundi.tw.
33. Cameroon.tw.
34. 'Central African Republic'.tw.
35. Centrafrique.tw.
36. centrafricain\*.tw.
37. Caribbean.mp. or exp Caribbean Region/
38. exp CHAD/
39. (Congo or congol\*).tw.
40. Brazzaville.tw.
41. Kinshasa.tw.
42. Djibouti.tw.
43. Guinea.tw.
44. French africa.tw.
45. Gabon\*.tw.
46. Haiti\*.tw.
47. (Ivory Coast or Ivoire or Ivorian).tw.
48. Madagascar.tw.
49. Mali.tw.
50. Morroc\*.tw.
51. Niger.tw.
52. Rwanda\*.tw.
53. (St? Martin or saint Martin).tw.
54. Senegal\*.tw.
55. Togo.tw.
56. Black-White.tw.

Continued

**Box 1 Continued**

57. Black.ti,ab.
58. 'black canadian'.tw.
59. mixed race.tw.
60. 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 58 or 59
61. 19 and 60
62. canada/
63. (Canada or Canad\*).tw.
64. (canada or or or or or or or canadian\$ or alberta or british columbia or columbie britannique).tw.
65. (saskatchewan or manitoba or ontario or quebec or new brunswick or nouveau brunswick).tw.
66. (nova scotia or nouvelle ecosse or prince edward island or ile du prince edward or newfoundland or terre neuve or labrador or nun?v?t or nun?v?t or nwt or territoires du nord ouest or north-west territories or yukon).tw.
67. OHIP.tw.
68. 'health canada'.tw.
69. 'sante canada'.tw.
70. medicare.tw.
71. CIHR.tw.
72. ('Alberta Health Care Insurance Plan' or AHCIIP).tw.
73. ('Medical Services Plan' or MSP).tw.
74. Manitoba health.tw.
75. ('Vitalite Health Network' or 'Horizon Health Network').tw.
76. 'Department of Health and Community Services'.tw.
77. 'Health Care Card'.tw.
78. ('Nova scotia health card' or MSI).tw.
79. Nunavut Health Insurance Card.tw.
80. ('Carte d'assurance maladie' or 'Health Insurance Card' or 'RAMQ').tw.
81. (health card adj25 canada).tw.
82. 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81
83. 61 and 82
84. exp 'Delivery of Health Care'/'
85. proximity.ti,ab.
86. 'healthcare or health care'.tw.
87. exp Health Care Quality, Access/and Evaluation/
88. Quality of care/
89. Health Promotion/
90. Primary Health Care/
91. Patient Acceptance of Health Care/
92. Healthcare Disparities/
93. exp racism/
94. multilingualism/
95. Needs Assessment/
96. exp Culturally Competent Care/
97. Health Services Accessibility/
98. exp Physicians, Family/
99. quality indicators/
100. Patient Medication Knowledge/
101. Patient Navigation/
102. Patient Compliance/
103. exp patient satisfaction/
104. exp HIV/
105. Preventive Medicine/
106. HIV.mp.

Continued

**Box 1 Continued**

- 107. exp HIV infections/
- 108. seropositivity/
- 109. seroconversion/
- 110. Quality of Life/
- 111. (HRQOL or karnofsky).tw.
- 112. 84 or 86 or 87 or 90 or 91 or 92 or 95 or 96 or 97 or 98 or 100 or 101 or 102 or 104 or 106
- 113. 19 and 27 and 60 and 83 and 112

Service Act was enacted in Ontario) to 2018.<sup>5</sup> We will use specific search terms in various combinations. The search will be conducted by a health sciences librarian at the Scotia Bank Health Sciences library at St. Michael's Hospital.

**Reference lists**

The reference lists of all relevant citations will be searched for available related articles.

**Grey literature**

We will search for available theses and reports. Furthermore, experts, authors and relevant organisations such as African and Caribbean Council on HIV/AIDS in Ontario, Association Francophone pour le Savoir, The Ontario HIV Treatment Network and CATIE (Canada's source for HIV and hepatitis C information) will be contacted.

**Data collection and analyses**

Data will be collected from each study independently and in duplicate by PD and JN. We will extract data from eligible studies such as publication details, study design, sample populations, outcomes measured and specific barriers.

**Screening**

We will import all citations obtained using the search strategy into DistillerSR to facilitate study screening and selection and de-duplication of citations prior to undertaking the abstract review. DistillerSR will also allow screeners to check each other's work.

A customised form reflecting the previously described inclusion criteria will be pilot-tested by two reviewers. Specifically, the data collection form will be developed and applied by two reviewers independently to a sample of 50 abstracts to ensure consistency of use and clarity of the instrument. Cohen's kappa statistic<sup>22</sup> will be estimated to measure inter-rater reliability and screening will begin when >60% agreement is achieved.

Study selection will proceed according to the following: first, we will conduct a title and abstract screening. The full text of potentially relevant articles will be retrieved and screened in detail for relevance prior to data extraction. All screening, data extraction and quality assessment will be conducted in duplicate by (PD and JN). Disagreements will be resolved by consensus. When consensus cannot be reached, a third author will arbitrate (LM or LN).

**Data extraction**

We will extract bibliometric information such as author names, journal and year of publication, in addition to the location of the study, study design, number of participants, outcomes reported, outcome measures overall and outcome measures in French-speaking participants. For each outcome, measures of mean, SD or percent (95% CIs<sup>23</sup>) and where possible, measures of effect of the outcome in French-speaking people versus non-French speaking people (odds or risk ratios, mean differences, accompanied with 95% CIs) will also be extracted.

**Assessment of methodological quality of the included studies**

Two authors will independently appraise the methodological quality of the studies using the Cochrane Risk of Bias Tool or the Newcastle-Ottawa Scale for randomised and non-randomised studies respectively.<sup>24</sup> Systematic reviews will be assessed using the Risk Of Bias in Systematic Review Tool<sup>25</sup> and the Assessing Quality of Systematic Reviews criteria.<sup>26</sup>

**Analyses and reporting**

Our findings will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>27 28</sup> Our findings will be summarised narratively and using tables. Data will be grouped by outcomes, with the number of studies, their design and their methodological quality. Key findings of each study will also be summarised using tables. We will conduct a narrative synthesis of the data to identify common themes and knowledge gaps.

**DISCUSSION**

The evidence of lack of French Language Healthcare Services in Ontario has been highlighted in previous research.<sup>8</sup> Stigma, discrimination and race are associated with poor HIV- care retention and access to care.<sup>29-31</sup> In this review we will answer important questions related to access to care for francophone ACB living in Canada. Furthermore, we will evaluate the impact of intersectionality of French language, race and HIV stigma on ACB accessibility to HIV care. The findings of this scoping systematic review will have implications for health policy making and how community organisations and HIV/AIDS centres provide care to Francophone ACB immigrants and Canadians.

One limitation of this scoping review is that it is focused only on Canada and, therefore, its global relevance is limited; however, theoretical generalisations can be postulated and tested with francophone diaspora minorities in predominantly Anglophone communities. Nonetheless, we will conduct a comprehensive exhaustive search, on a novel topic with an experienced research team.

**Author affiliations**

<sup>1</sup>Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St Michael Hospital, Toronto, Ontario, Canada

<sup>2</sup>Daphne Cockwell School of Nursing, Ryerson University, Toronto, Ontario, Canada

<sup>3</sup>Toronto People With AIDS Foundation, Toronto, Ontario, Canada  
<sup>4</sup>Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada  
<sup>5</sup>Health Sciences Library, St. Michael's Hospital, Toronto, Ontario, Canada  
<sup>6</sup>Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada  
<sup>7</sup>Biostatistics Unit, Father Sean O'Sullivan Research Centre, St Joseph's Healthcare, Hamilton, Ontario, Canada  
<sup>8</sup>Centre for Development of Best Practices in Health (CDBPH), Yaoundé Central Hospital, Yaoundé, Cameroon  
<sup>9</sup>Yale School of Nursing, Yale University, New Haven, Connecticut, USA  
<sup>10</sup>School of Nursing, University of Rochester, Rochester, New York, USA

**Contributors** The study was conceived by PD, LM, JN and LEN. All authors revised the research question and provided content to the design. Manuscript was written and edited by PD, LM, JN, LEN, CM, AJO and DL. Principal investigator of the study is LEN. All authors read and approved the final version of the manuscript.

**Funding** This paper was made possible through the Ontario HIV Treatment Network Applied HIV Research Chair in HIV Program Science with African, Caribbean and Black Communities #AHRC-1066. This publication was also made possible through core services and support from the University of Rochester Center for AIDS Research (CFAR), an NIH-funded program (P30 AI078498).

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## REFERENCES

- Bowen S. The Impact of Language Barriers on Patient Safety and Quality of care: société Santé en français. 2015.
- ÉL F, R.; Boudreau J. Identifying Francophones: an analysis of definitions based on census variables. 2009.
- Canada Census 2016.
- Samson AA, Spector NM. Francophones living with HIV/AIDS in Ontario: the unknown reality of an invisible cultural minority. *AIDS Care* 2012;24:658–64.
- Go O. MoHaL-T C, ed. *The French Language Services Act, 1986 (FLSA)*, 1986.
- Deroche FC. French-language health care services in Ontario. *Healthc Manage Forum* 1994;7:5–11.
- Bouchard LGI, Chomienne AH, et al. La santé en situation linguistique minoritaire. *Healthcare Policy* 2009;4:36–42.
- Farmanova E, Bonneville L, Bouchard L. Active offer of health services in French in Ontario: analysis of reorganization and management strategies of health care organizations. *Int J Health Plann Manage* 2018;33:e194–e209.
- Ngwakongnwi E, Hemmelgarn BR, Musto R, et al. Experiences of french speaking immigrants and non-immigrants accessing health care services in a large Canadian city. *Int J Environ Res Public Health* 2012;9:3755–68.
- Bélanger M, Bouchard L, Gaboury I, et al. Perceived health status of francophones and anglophones in an officially bilingual Canadian province. *Can J Public Health* 2011;102:122–6.
- Bouchard L, Desmeules M. [Linguistic minorities in Canada and health]. *Health Policy* 2013;9:38–47.
- Simbiri KO, Hausman A, Wadenya RO, et al. Access impediments to health care and social services between Anglophone and Francophone African immigrants living in Philadelphia with respect to HIV/AIDS. *J Immigr Minor Health* 2010;12:569–79.
- Ojikutu B, Nnaji C, Sithole-Berk J, et al. Barriers to HIV testing in black immigrants to the U.S. *J Health Care Poor Underserved* 2014;25:1052–66.
- Ng E, Pottie K, Spitzer D. Official language proficiency and self-reported health among immigrants to Canada. *Health Rep* 2011;22:15–23.
- Pottie K, Ng E, Spitzer D, et al. Language proficiency, gender and self-reported health: an analysis of the first two waves of the longitudinal survey of immigrants to Canada. *Can J Public Health* 2008;99:505–10.
- de Moissac D, Bowen S. Impact of language barriers on access to healthcare for official language minority Francophones in Canada. *Healthc Manage Forum* 2017;30:207–12.
- Bourgeois AC, Edmunds M, Awan A, et al. HIV in Canada-surveillance report, 2016. *Can Commun Dis Rep* 2017;43:248–56.
- Wilson MG, Husbands W, Makoroka L, et al. Counselling, case management and health promotion for people living with HIV/AIDS: an overview of systematic reviews. *AIDS Behav* 2013;17:1612–25.
- Ngangue P, Gagnon MP, Bedard E. Challenges in the delivery of public HIV testing and counselling (HTC) in Douala, Cameroon: providers perspectives and implications on quality of HTC services. *BMC Int Health Hum Rights* 2017;17:9.
- Yehia BR, Stephens-Shields AJ, Fleishman JA, et al. The HIV Care Continuum: changes over time in retention in care and viral suppression. *PLoS One* 2015;10:e0129376.
- Peterson J, Pearce PF, Ferguson LA, et al. Understanding scoping reviews: definition, purpose, and process. *J Am Assoc Nurse Pract* 2017;29:12–16.
- Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Fam Med* 2005;37:360–3.
- Ahlm C, Wallin K, Lundkvist A, et al. Serologic evidence of puumala virus infection in wild moose in northern sweden. *Am J Trop Med Hyg* 2000;62:106–11.
- Hopp L. Risk of bias reporting in Cochrane systematic reviews. *Int J Nurs Pract* 2015;21:683–6.
- Banzi R, Cinquini M, Gonzalez-Lorenzo M, et al. Quality assessment versus risk of bias in systematic reviews: AMSTAR and ROBIS had similar reliability but differed in their construct and applicability. *J Clin Epidemiol* 2018;99:24–32.
- Shea BJ, Hamel C, Wells GA, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. *J Clin Epidemiol* 2009;62:1013–20.
- Bernardo WM. PRISMA statement and PROSPERO. *Int Braz J Urol* 2017;43:383–4.
- Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
- Logie C, James L, Tharao W, et al. Associations between HIV-related stigma, racial discrimination, gender discrimination, and depression among HIV-positive African, Caribbean, and black women in Ontario, Canada. *AIDS Patient Care STDS* 2013;27:114–22.
- Loutfy M, Tharao W, Logie C, et al. Systematic review of stigma reducing interventions for African/Black diasporic women. *J Int AIDS Soc* 2015;18:19835.
- Earnshaw VA, Bogart LM, Dovidio JF, et al. Stigma and racial/ethnic HIV disparities: moving toward resilience. *Am Psychol* 2013;68:225–36.