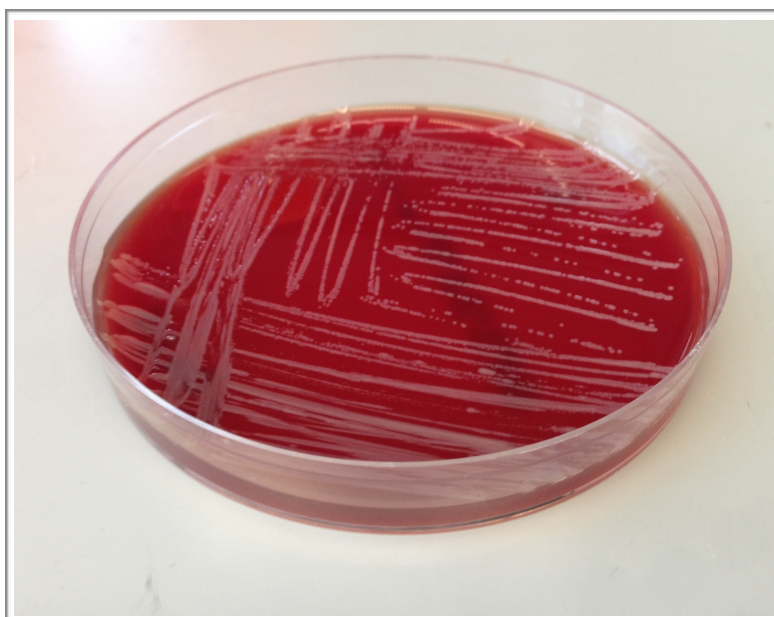


Canadian *Burkholderia cepacia* complex research and referral repository



2015 Annual Report: August 1st 2014 to July 31st 2015



a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA



Summary

2015 was a significant year for the Canadian *Burkholderia cepacia* complex research and referral repository (CBCCRRR). Thanks to an enhanced grant received from Cystic Fibrosis Canada, as of 1st April 2015 we are now funded to provide all *Burkholderia* identifications **free of charge** to all Canadian CF clinics. This covers any additional work - such as strain typing comparisons - that clinics require on those isolates either now or in the future. We are very grateful to all of those at CF Canada, the CF clinics and researchers who took part in the surveys as well as the reviewers of our application for funding for their constructive feedback.

Did you know? The 2014 revised infection control guidelines recommend submission of *Burkholderia* isolates or other Gram-negatives for which the identification is equivocal on an **at least annual** basis for each patient. The CBCCRRR is the Canadian resource for this.

Submitting isolates to us helps you because:

- i) we can alert you to species replacement
- ii) we store the isolates indefinitely so we can answer any future questions you might have
- iii) we can perform comparative strain typing to determine if any patients share strains (this service is available now and if you have a need for it please contact us).

Submitting isolates also helps people with CF by providing clinically relevant samples for understanding both epidemiology and conducting research.

To submit isolates visit: <http://cupic.cfri.ca/research/cbccrrr.html> or contact Dr. James Zlosnik: jzlosnik@cfri.ca

This year we have received 61 isolates from 46 CF patients. Several trends continue from previous years:

- *B. multivorans* continues to be the most commonly identified species.
- Identifications of new cases of *B. cenocepacia* continue, however these are usually not caused by the epidemic strain types previously present in Canada.
- Based on prevalence reported in the Canadian CF Data Registry reports, there are still many infections for which we do not routinely receive isolates. It is likely that many clinics send us the initial isolate only. However because of the risk of species replacement we strongly encourage all clinics to submit isolates on an annual basis for all patients culturing *B. cepacia* complex.

Overview of Identifications

Province	Clinic	# samples	# patients [# w.CF] (# new*)	<i>B. cenocepacia</i> (# new cases)	<i>B. multivorans</i> (# new cases)	<i>B. vietnamiensis</i> (# new cases)	Other (# new cases)
AB	Calgary Adult	5	5 [4] (2)	2 (1)	2 (0)	-	1 x <i>B. stabilis</i> (1)
	Calgary Children's	1	1 [1] (1)	-	-	-	1 x <i>B. cepacia</i> (1)
	Edmonton	10	5 [5] (1)	1 (0)	8 (1)	-	1 x <i>B. dolosa</i> (0)
BC	BCCH	3	3 [3] (2)	1 (0)	1 (1)	-	1 x <i>B. gladioli</i> (1)
	Royal Jubilee	3	3 [3] (0)	-	3 (0)	-	-
NL	Health Sciences Centre	3	3 [3] (2)	2 (1)	-	1 (1)	-
NS	QE2	6	5 [5] (5)	6 (5)	-	-	-
ON	Ramsey	1	1 [1] (1)	1 (1)	-	-	-
	SickKids	1	1 [0] (1)	-	1 (1)	-	-
QC	Chicoutimi	5	5 [5] (3)	-	3 (2)	2 (1)	-
	Noranda	2	1 [1] (0)	-	2 (0)	-	-
	Quebec City	1	1 [1] (1)	1 (1)	-	-	-
	Rimouski	1	1 [1] (1)	1 (1)	-	-	-
	Ste. Justine	9	2 [2] (1)	-	-	6 (0)	3 x <i>B. cepacia</i> (1)
	Hotel Dieu	6	6 [6] (5)	-	4 (4)	-	1 x <i>B. gladioli</i> (1) 1 x <i>B. anthina</i> (0)
	Hopital Laval	1	1 [1] (0)	-	1 (0)	-	-
SK	Montreal Chest	2	2 [2] (1)	-	1 (0)	-	1 x <i>B. dolosa</i> (1)
	Royal University	1	1 [1] (1)	-	1 (1)	-	-
Total		61	47 [45] (28)	15 (10)	27 (10)	9 (2)	10 (6)

Notes: Not shown are the isolates routinely collected from BC Children's and St Paul's hospital in Vancouver. * new = patient for whom we have not previously received an isolate; in the case of some clinics where we have recently started receiving isolates (e.g. NS & NL) these can represent established infections rather than new acquisitions. A new isolate may also represent a patient who has moved into a centre with an infection from another centre that had not sent us the initial isolates and therefore may also not be truly 'new'.

Summary

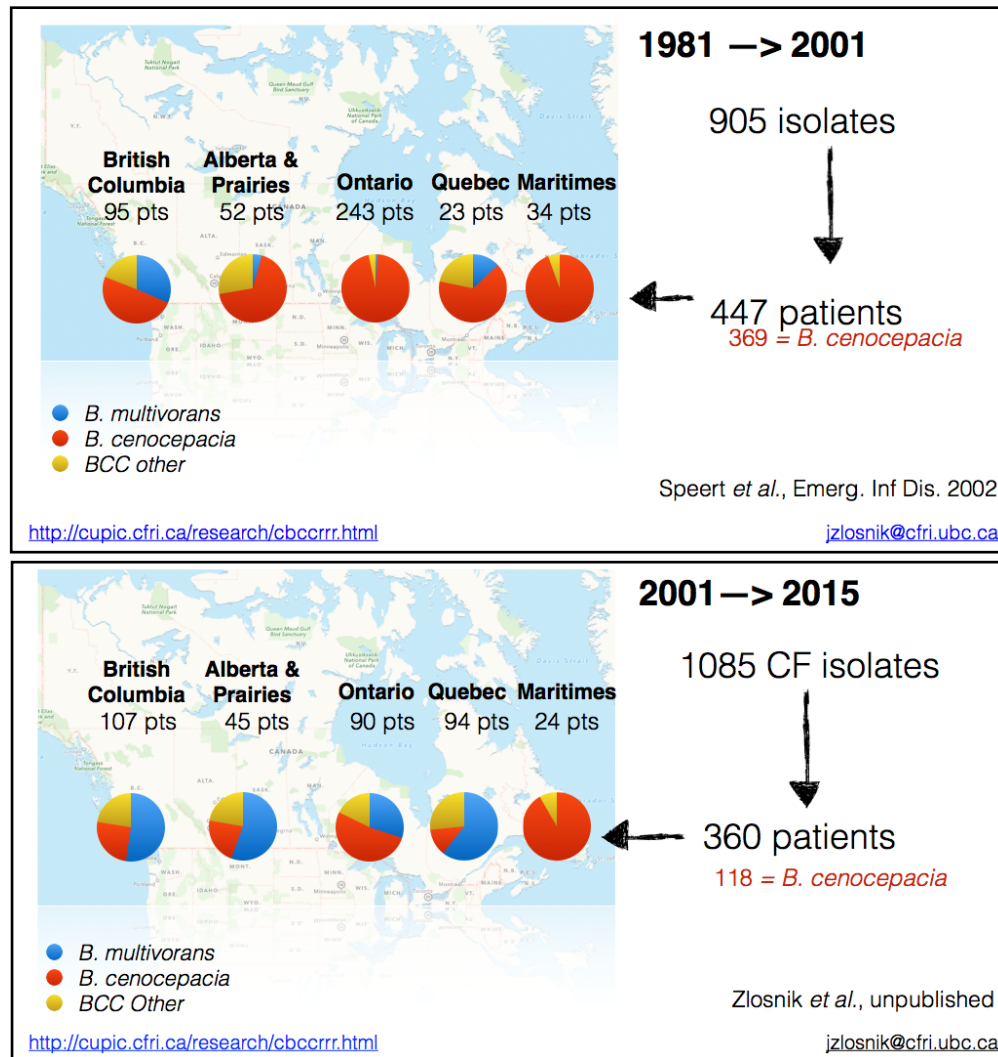
- This year continues the trend of *Burkholderia multivorans* being the most commonly identified species in samples sent to us, accounting for just under 50% of samples sent to us.
- *B. cenocepacia* was the second most identified species. However, for at least some of the centres, we know from conversations with the clinic staff that many of these are not new infections.
- New acquisitions of *B. cepacia* complex in people with CF are continuing, despite infection control. The source of these infections is unclear, but in most cases does not seem to be from other people with CF.
- There are still a number of clinics from whom we do not routinely receive isolates. We currently receive all the isolates for our local Vancouver clinics (we saved 38 isolates from 24 patients and as of August 2015 we will save all isolates sent to us). Additionally, we have seen in recent years excellent submission from clinics in Alberta, Quebec and Nova Scotia. We also welcome that we have started to receive isolates from centres (including Nova Scotia) from whom, until recently, we had not received any in a number of years.
- We expect in the next 6 months to be contacting all clinics who have submitted isolates to us in the last 5 years to provide them with a list of the isolates we have ID'd for them as well as comparative strain typing data.
- The CBCCRRR is currently exploring options for an approach to strain typing that will provide a robust output which permits cross-Canada comparisons. In the meantime, we are able to provide clinics with a report of whether any of their patients share strains at any time upon receipt of a request.

Did you know: the CBCCRRR is available to help CF clinics and their microbiology labs at any time with regards to *Burkholderia* spp. bacteria.

To discuss your needs contact Dr. James Zlosnik: jzlosnik@cfri.ca

Overview of the CBCRRR and *Burkholderia* in Canada

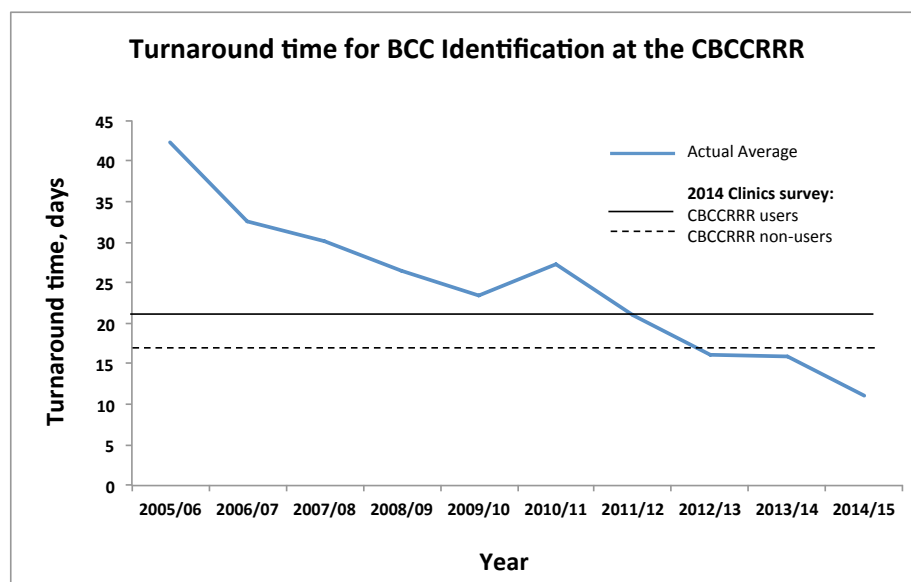
At the 2015 International *Burkholderia cepacia* Working Group meeting, we presented an overview of BCC infections in Canada. This analysis was based on isolates submitted to us for identification as well as our comprehensive collection of isolates from the Vancouver clinics from 1981. The trend was clear - as can be seen in the Figures below - in Canada the prevalence of *B. cenocepacia* has dropped and in many provinces has been replaced by *B. multivorans* as the dominant species.



The most likely reason for the decline in *B. cenocepacia* % prevalence is the implementation of infection control measures. We recently published a comprehensive analysis of the Vancouver BCC population and found that infection control was associated in an almost immediate cessation in acquisition of epidemic strains of *B. cenocepacia*. This mirrors data from the US and other countries. While the prevalence in the Maritimes has not changed, we understand that the isolates submitted after 2001 were from patients infected many years earlier.

CBCCRRR Update

The CBCCRRR continues to be operated and managed on a day to day basis by Dr. James Zlosnik, with Dr. Speert as the laboratory director. Since the last report our head technologist, Mr Trevor Hird, has left to take a position elsewhere. Trevor has been replaced in the lab by Ms. Rebecca Hickman, who has been fully trained in the identification of BCC. Overall, our operations are running effectively and efficiently, with a continued improvement in our turnaround time, which averaged 11 days despite our staff turnover. Indeed in the last 4 years we have more than halved the time it takes to report out identifications (see graph below).



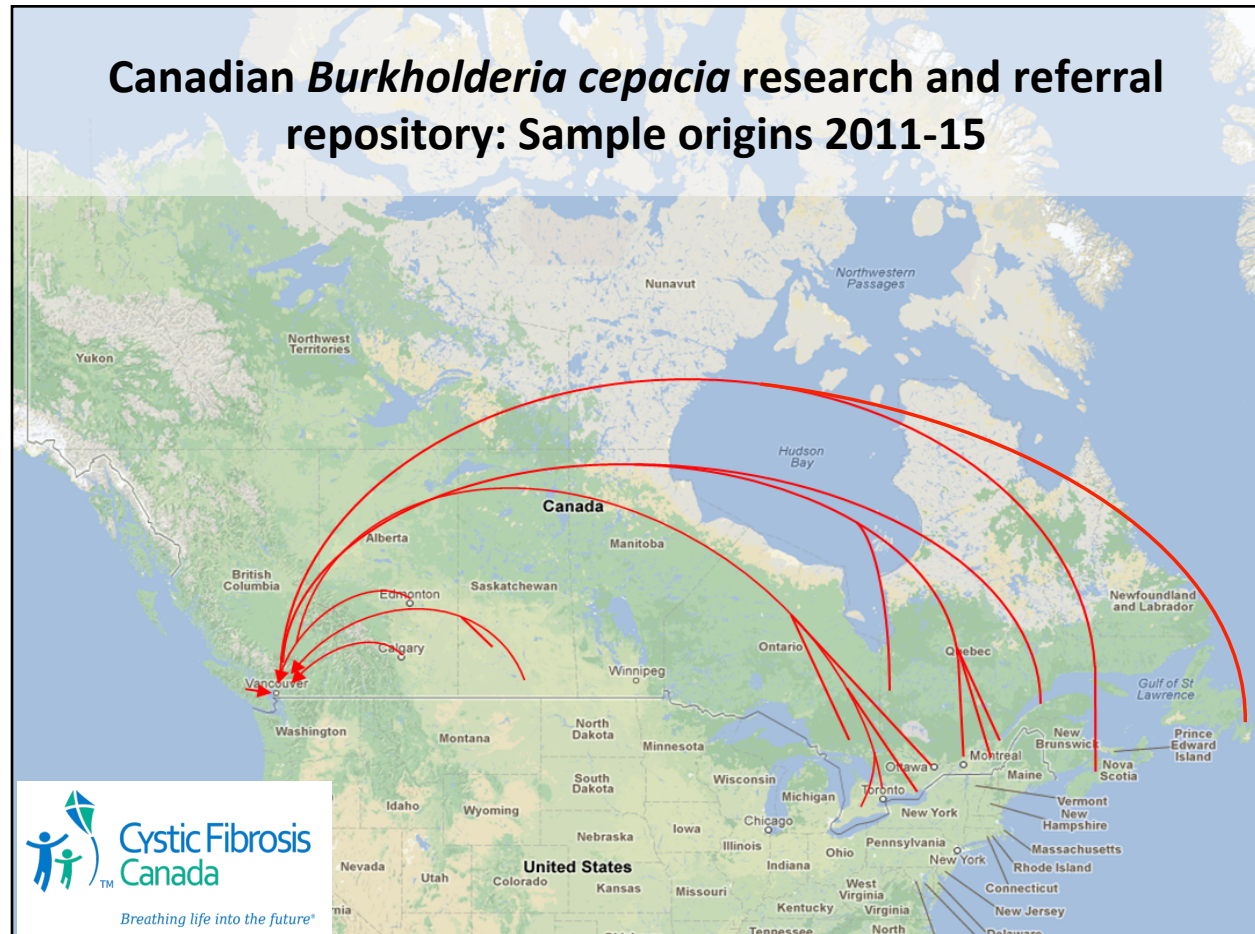
Over the course of the next year we expect to continue to enhance our service to clinics and the CF community. This should include:

- **Providing each clinic individually with a list of their reported isolates for the past 5 years.**
- **Revising the report form to make it easier to interpret the individual results and add in the results of the bacterial genetic tests.**
- **We will begin working with the Canadian CF Patient Data Registry and Healthcare Advisory council to determine ways that we could routinely provide our data to the registry.**
- **We are also in the process of determining if it is possible to routinely and cost effectively apply a cutting edge strain typing technique called MLST, to bacterial isolates. This has many advantages, not least of which is it will give clinics an easy to interpret number that will allow them to compare strains between their patients and across Canada.**

2014 Clinics Survey

In the past 5 years, we have served many clinics across Canada (see below). As part of our application for increased funding, Cystic Fibrosis Canada solicited feedback from both the clinical and research communities about our service. Of those clinics that responded to the survey, approximately 75% use our service and 95% of those report that the information they receive from us directly influences patient care. Of the 25% that do not currently use our service, 86% reported that they would do so if the service we provided free of charge.

In response to feedback from the clinics, we will be proactively contacting all CF clinics over the course of the next year to discuss their needs and how we might go about receiving samples from those that do not currently submit to us.



CBCRRR Publications in 2014/15

We have published or contributed to a number of peer-reviewed publications in the past year, including:

- A comprehensive overview of the epidemiology of *Burkholderia* spp. in Vancouver over the last 30 years:

Zlosnik JEA, Zhou G, Brant R, Henry DA, Hird TJ, Mahenthiralingam E, Chilvers MA, Wilcox P, Speert DP. *Burkholderia cepacia* complex infection in cystic fibrosis patients in British Columbia, Canada: 30 years' experience. *Annals ATS*. 12(1):70-8.

- The description of the 19th and 20th species of the *Burkholderia cepacia* complex:

De Smet B, Mayo M, Peeters C, Hird TJ, Spilker T, Zlosnik JEA, Lipuma JJ, Kidd T, Jacobs J Currie B and Vandamme P. *Burkholderia stagnalis* sp. nov. and *Burkholderia territorii* sp. nov., two novel *Burkholderia cepacia* complex species from environmental and human sources. *International Journal of Systematic and Evolutionary Microbiology*. Jul;65(7): 2265-71

- A collaboration examining the efficacy of high dose tobramycin against BCC bacteria:

Ratjen A, Yau Y, Wettlaufer J, Matukas, L, Zlosnik JEA, Speert DP, Lipuma JJ, Tullis E, Waters V. In vitro efficacy of high dose tobramycin against *Burkholderia cepacia* complex and *Stenotrophomonas maltophilia* isolates from cystic fibrosis patients. *Antimicrob. Agents Chemother.* 59(1): 711-13.

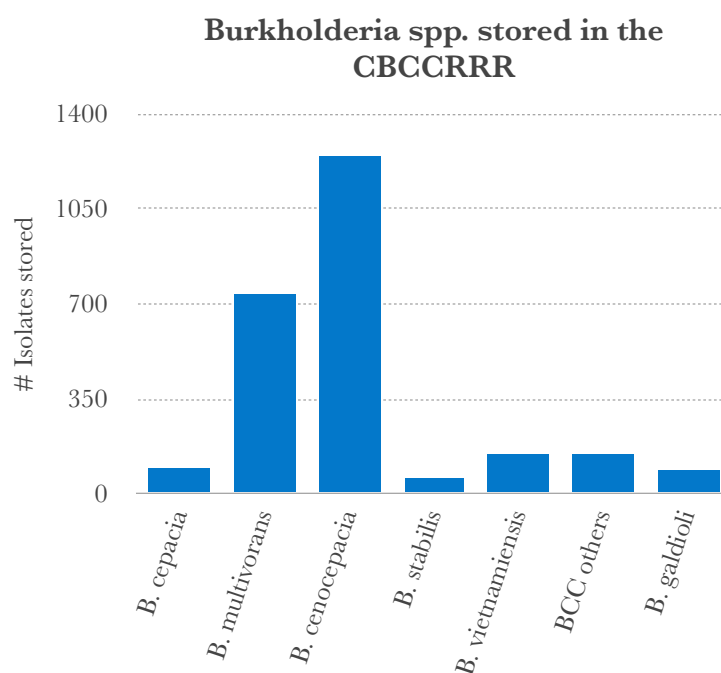
We also have 2 further manuscripts in preparation and have collaboration with the St Paul's CF clinic examining eradication therapy for BCC, which has been invited for oral presentation at this years North American CF Conference in Phoenix:

Ho A, Su VC, Espinosa B, Lilquist A, Chilvers MA, Quon BS, Wilcox PG, Zlosnik JEA. Evaluation of *Burkholderia cepacia* complex eradication in cystic fibrosis (CF) patients. North American Cystic Fibrosis Conference, Phoenix, October 2015.

In addition to academic publications, the CBCRRR co-organised, with Dr. Silvia Cardona (University of Manitoba), the 19th meeting of the International *Burkholderia cepacia* Working Group (IBCWG) which was held in April 2015 in Vancouver. At this meeting Dr. Speert was invited to present the keynote talk and Dr. Zlosnik presented an overview of BCC in Canada over the past 30 years.

The CBCCR RR for Researchers

The CBCCR RR is a resource for researchers as well as clinics and we welcome contact from researchers who wish to discuss their needs. All the isolates sent to us for identification are frozen and stored indefinitely and most are available to researchers de-linked from their clinical identifiers. Isolates are available either as part of a collaboration (to academic researchers - requiring minimal shipping charges) or on a cost recovery basis to both academic researchers and industry.



In addition to *Burkholderia*, researchers might like to note that we house a large collection of CF clinical isolates of other bacteria. This includes:

- More than 13,000 isolates of *Pseudomonas aeruginosa* from CF infections (including many sequential clonal isolates)
- Many other species of Gram-negative bacteria isolated from CF: *Achromobacter spp.*, *Acinetobacter spp.*, *Pandoraea spp.*, *Ralstonia spp.*, *Stenotrophomonas maltophilia* among others.

Did you know: the CBCCR RR contains thousands of clinical samples of *Burkholderia* species bacteria as well as other CF pathogens.

To request isolates and discuss your needs contact Dr. James Zlosnik: jzlosnik@cfri.ca