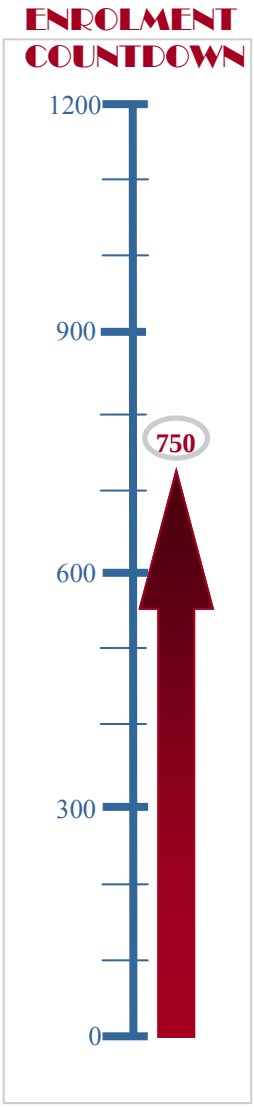
THE REDOXS© CIRCULAR

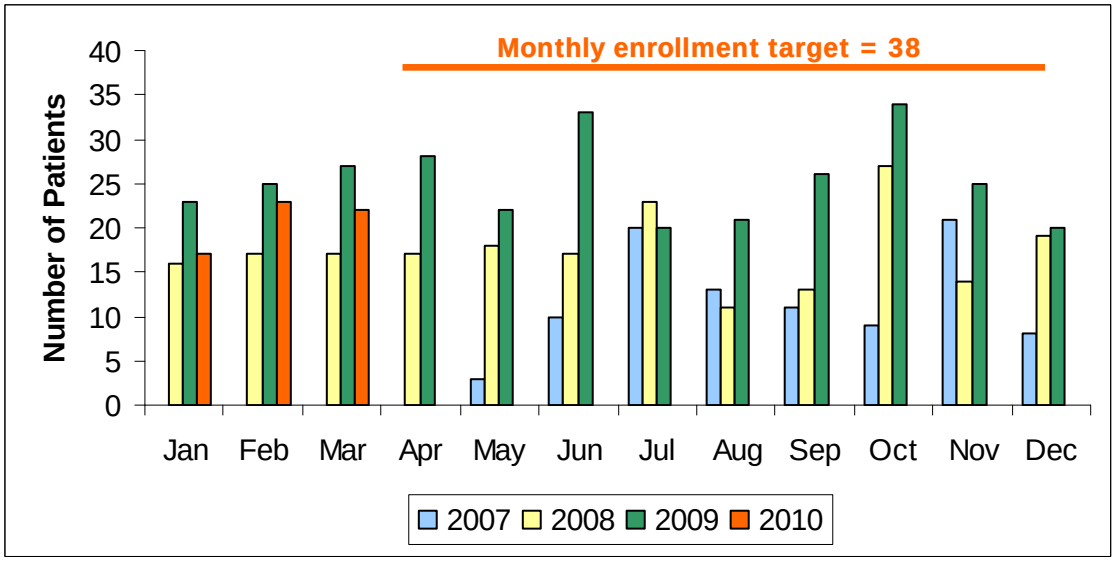
Data current to 31-Mar-2010

Site #	Institution	Mar	Cumulative
1	Kingston General	2	74
2	St. Joseph Healthcare	4	52
3	Ottawa General	3	126
4	Ottawa Civic	1	49
5	Vancouver General		19
6	Sacre-Coeur		62
7	Maisonneuve-Rosemont		15
8	Royal Victoria		10
9	Royal Alexandra		21
11	Grey Nun's		15
13	Victoria General		6
14	London HSC		14
16	Capital Health, QEII	1	14
19	Montreal General	1	17
20	L'Enfant Jesus		23
21	Liege, Belgium	1	7
22	CHUV, Switzerland		10
23	Royal Jubilee		8
25	Mount Sinai	3	33
26	U of Colorado		18
27	Miami Valley, Ohio	1	7
28	Fletcher Allen, Vermont	1	8
30	U of Louisville		10
31	U of Texas		5
32	University Hospital		6
33	Laval	1	9
34	Emory University	-	-
35	Kiel, Germany	1	3
36	Lubeck, Germany	-	-
37	Greifswald, Germany	-	6
38	Hamburg-Altona, Germany	1	4
39	Jewish Hospital	1	1
40	Atlanticare	*Starting to screen*	
41	Hershey Medical Center	*Starting to screen*	
	Intermountain Healthcare	*Starting Q2 2010*	
	Mayo Clinic, Arizona	*Starting Q2 2010*	
	*number patients from closed sites		18
	number patients enrolled in pilot		80
TOTALS		**22**	**750**

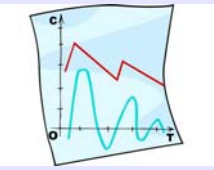


Enrollment Timelines

As illustrated by the chart below, the monthly enrollments for January, February and March 2010 have fallen short of those from 2009. It is imperative that we increase the rate of enrollment to meet our study timelines. **In order to complete the study within the next 12 months we must enroll 38 patients a month.** Given we have 34 sites screening patients, and another 2 sites anticipated to start soon, this works out to at least 1 pt/site/month. **We can do this!**



Interim Analysis: Next Steps



The interim analysis has been completed!

The following steps will now occur:

- It will be sent to the Data Monitoring Committee (DMC) within the next week.
- The DMC will review the data for safety and efficacy.
- The DMC will document the outcome of their review.
- The outcome of the DMC review will be communicated to all sites once it is available.

Dr. Heyland will be presenting the interim analysis results to the Canadian Critical Care Trials Group (CCCTG) at the June meeting in Prince Edward Island.

We plan to forward periodic quality reports to sites. Individualized reports will be sent to each site in early May.

A joint Steering Committee & DMC meeting will be held in May to review all safety data. Similar to previous meetings, a safety report will be sent to sites to submit to their local ethics board.

ICU Acquired Infection Adjudication

The site investigator or MD delegate is to make the determination of whether a newly acquired ICU infection exists based on antibiotic and microbiology data.

Part 1: Triggering a Suspicion of ICU Acquired Infection

We often receive questions from research coordinators asking how to answer the antibiotic and microbiology questions used to trigger a suspicion of infection.

First, the responses to the following questions require clinical inference from a physician. We strongly recommend that these questions be answered in consultation with the site investigator or MD delegate.

Next, a suspicion of ICU acquired infection can be triggered by an antibiotic **or** a positive culture.

Antibiotic Triggers: only for those antibiotics started greater than 72 hrs from ICU admission

Is this antibiotic prescribed for prophylaxis? □ YES □ NO

Is this antibiotic a substitute for an antibiotic previously ordered for an infection? □ YES □ NO

Answering 'NO' to both questions triggers a suspicion of infection.
An infection adjudication must be performed by the Site Inv/MD for this antibiotic.

Microbiology Triggers: only for those cultures taken greater than 72 hrs from ICU admission

Is this culture a manifestation of a previously diagnosed infection? □ YES □ NO

Is this a routine surveillance swab (i.e. nasal swab for MRSA or rectal swab for VRE)? □ YES □ NO

Answering 'NO' to both questions triggers a suspicion of infection.
An infection adjudication must be performed for this positive culture.

If a suspicion of infection has been triggered, the electronic data capture system (EDCS) generates an Infection Adjudication table pooling all relevant data for the site investigator or MD delegate to make their adjudication determination.
Refer to Part 2: Adjudicating a Suspicion of ICU Acquired Infection on the next page.

Part 2: Adjudicating a Suspicion of ICU Acquired Infection

The site investigator or MD delegate should perform an infection adjudication as follows:

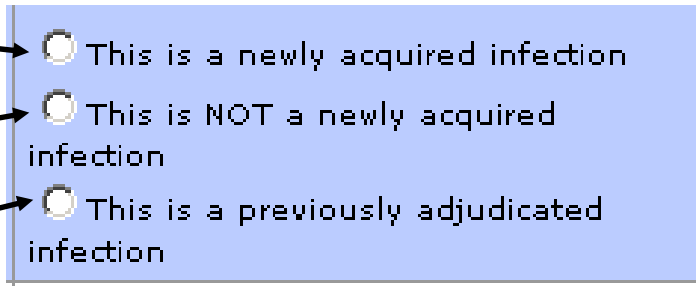
18 Dec 2009	38.1	252.0	High=13.0 Low=13.0	YES	YES			Vancomycin	1.5	g	q48 hrs	IV	
								Metronidazole	500.0	mg	BID	IV	
								Meropenem	1.0	g	q12 hrs	IV	○ This is a newly acquired infection ○ This is NOT a newly acquired infection ○ This is a previously adjudicated infection

For each triggered suspicion there are 3 options:

If 'YES' to infection, refer to the Categories of Infection to determine whether YES -Definite, YES - Probable or YES - Possible

If 'NO' to infection, refer to the Definitions to determine whether NO - Probable or NO - Possible

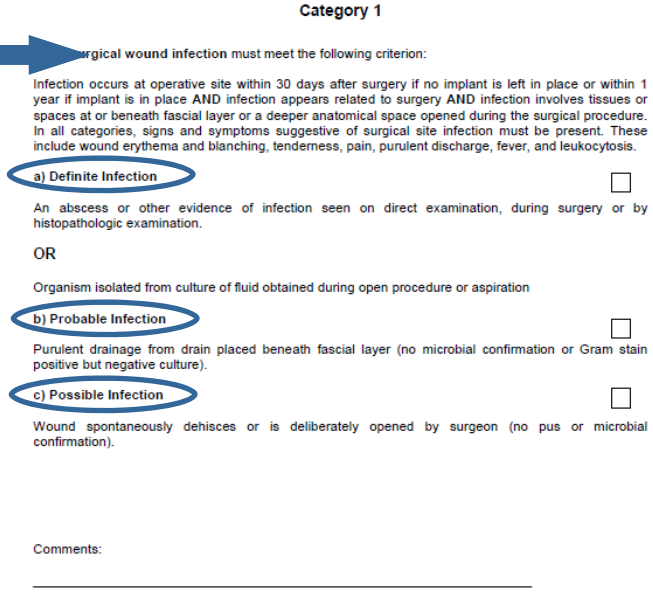
This suspicion has already been adjudicated



For 'YES' to newly acquired infection, there are 12 Categories of Infection for the site investigator to choose from. Refer to Implementation Manual Appendix 10.2.

categories of infection are as follows:

Category 1	Deep surgical wound infection
Category 2	Incisional (or superficial) surgical wound infection
Category 3	Skin and soft-tissue infection (non-surgical) (SSTS)
Category 4	Catheter-related blood stream infections (CRI)
Category 5	Primary blood stream infections (BSI)
Category 6	Lower urinary tract infection
Category 7	Upper urinary tract infection
Category 8	Intra abdominal infection
Category 9	Sinusitis
Category 10	Lower respiratory tract infection (excluding pneumonia)
Category 11	ICU Acquired Pneumonia
Category 12	Other



Category 1

rgical wound infection must meet the following criterion:

Infection occurs at operative site within 30 days after surgery if no implant is left in place or within 1 year if implant is in place **AND** infection appears related to surgery **AND** infection involves tissues or spaces at or beneath fascial layer or a deeper anatomical space opened during the surgical procedure. In all categories, signs and symptoms suggestive of surgical site infection must be present. These include wound erythema and blanching, tenderness, pain, purulent discharge, fever, and leukocytosis.

a) Definite Infection ☐

An abscess or other evidence of infection seen on direct examination, during surgery or by histopathologic examination.

OR

Organism isolated from culture of fluid obtained during open procedure or aspiration

b) Probable Infection ☐

Purulent drainage from drain placed beneath fascial layer (no microbial confirmation or Gram stain positive but negative culture).

c) Possible Infection ☐

Wound spontaneously dehisces or is deliberately opened by surgeon (no pus or microbial confirmation).

Comments: _____

For 'NO' to infection, there are two definitions for the site investigator to choose from.
Refer to Implementation Manual Appendix 10.3.

For further information regarding the infection adjudication process please refer to the Implementation Manual pgs. 58-60 & Appendix 10. Contact the Project Leader if you have any questions.

STUDY CHAIR	PROJECT LEADERS	DATA MANAGEMENT	PROJECT ASSISTANTS
Daren Heyland	**Janet Overvelde**	**Jennifer Korol**	**Suzanne Biro**
dkh2@queensu.ca	overvelj@kgh.kari.net	korolj@kgh.kari.net	biros@kgh.kari.net
	Rupinder Dhaliwal	**Shawna Froese**	**Susan Campbell**
	dhaliwar@kgh.kari.net	froeses@kgh.kari.net	campbes3@kgh.kari.net