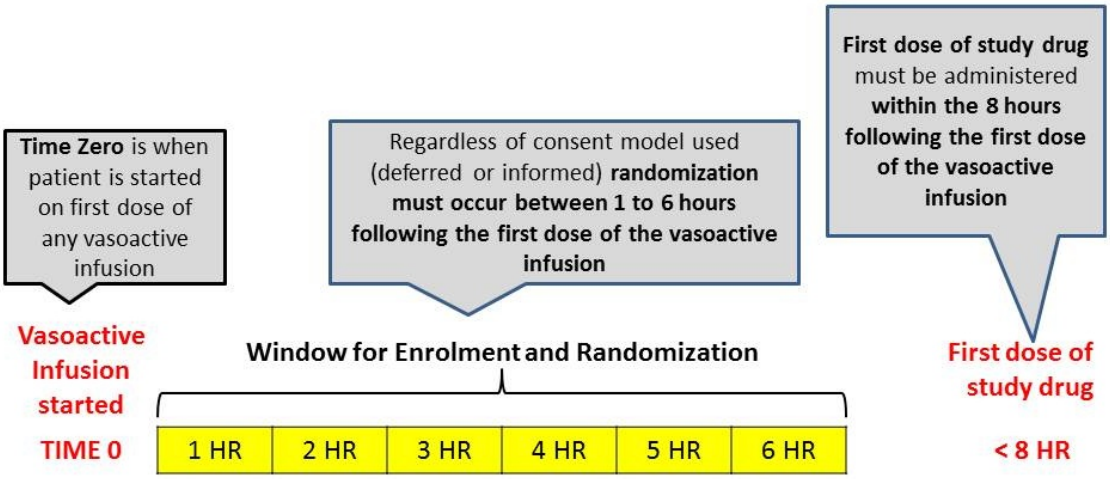
SOP Title:	STRIPES – Randomization Procedures (taken from STRIPES study SOP)
SOP Version:	Version 6
SOP Date:	24-Nov-2015

1. Randomization

1.1. Randomization Timeline

The timeline for enroling and randomizing a patient into the STRIPES study is shown below in Figure 1. Time Zero is the time when the patient is first started on a vasoactive infusion. **Patients must be enrolled and randomized within 6 hours of being started on a vasoactive infusion, and receive the first dose of study drug within 8 hours.**

Figure 1. Randomization timeline for the STRIPES Study

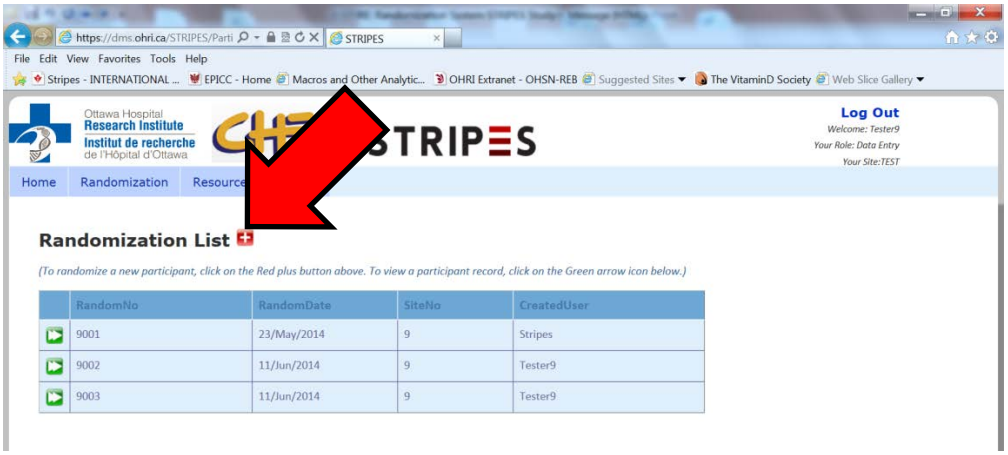


1.2. Randomization Process

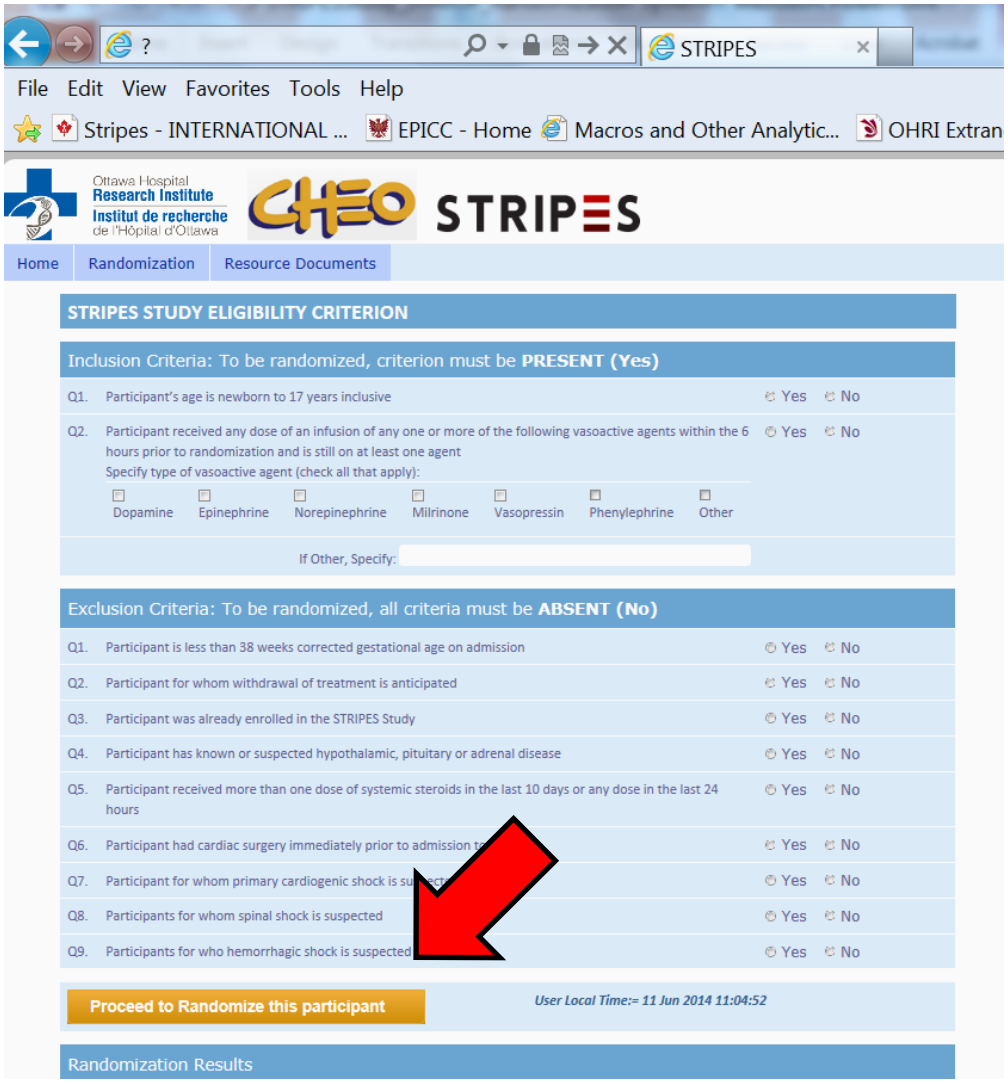
Once a patient's eligibility has been confirmed (and for sites not using a deferred consent model, once informed consent has been obtained), the Site Research Coordinator will call the pharmacy to make sure the study drug can be dispensed within the 8 hour time frame. The 8 hours starts from the time that the patient was first started on a vasoactive infusion. **Do not randomize the patient unless you have confirmed that the pharmacy can dispense the study drug on time.** The Site Research Coordinator will then logon to the study randomization webpage at https://dms.ohri.ca/Stripes/ and complete the randomization process as described below:

a. Log into the randomization system using your site randomization login.

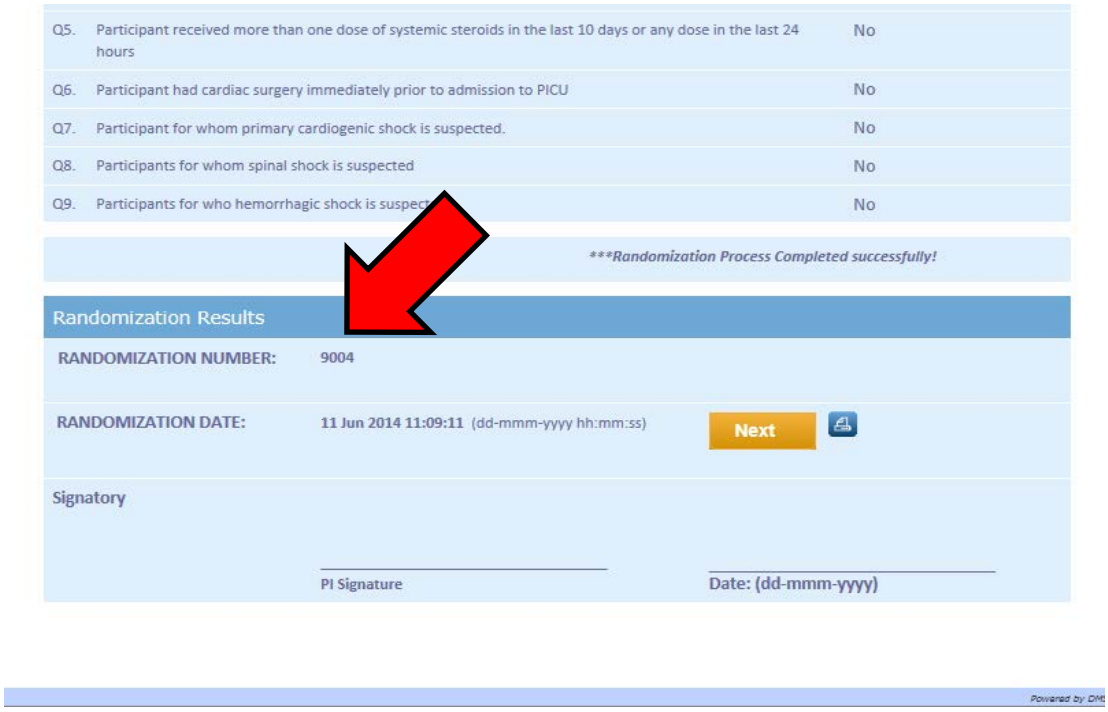
b. Click on the red "+" sign to add a new participant.



c. Enter the participant inclusion and exclusion criteria. Once all criteria has been entered, click on “Proceed to Randomize this Participant” at the bottom of the screen.



d. Note the randomization number on the screen and record the number on the pre-printed order for the study drug. This is the participant's study ID number that will be used to de-identify the participant on study documentation (e.g. eCRF). The Site Research Coordinator and the research pharmacist will also receive an email with the randomization ID number.



e. Each site pharmacy will be given a randomization schema list. Pharmacy staff will match the study randomization number recorded on the pre-printed order to the site randomization schema list to determine the patient's allocated treatment.

The randomization site will be generated and maintained by the Methods Centre at OHRI. The Methods Centre will generate a randomization list stratified by site. Patients will be randomized 1:1 using random variable block sizes (2-4 patients/block).

If you experience technical difficulties with the randomization system, contact the Methods Centre.

During office hours: 8:30 - 4:30 ET.

Please email dms@ohri.ca and phone (613) 737-8899 Ext. 73804

If no one can be reached after 10 minutes, please call Douglas McGuire at (613) 737-8899 Ext. 73802

Outside business hours:

Please email dvo@ohri.ca

Please have the following information ready for the Methods Centre staff (if contacting by phone) or include the following information in the email:

- Study name
- Full name
- Username
- User role (e.g. coordinator, pharmacist)
- Site name
- Site ID (Site number for the randomization system)
- Information on the issue(s)

2. Randomization Back-Up

In the event that the randomization system does not work, and the issue cannot be quickly resolved by the Methods Centre, the participant should still be enrolled and randomized manually according to the following steps:

a. Bring the pre-printed order form to pharmacy, and inform pharmacy staff that the randomization system is not working.

b. Pharmacy staff will assign the patient the next sequential randomization ID number on the site randomization list and allocate treatment

c. Note: Please ensure that you get the ID number from pharmacy for use on study documents and eCRF

d. Notify the Methods Centre at dms@ohri.ca as soon as possible after enroling patient and inform them of the randomization number that was used.

e. The Methods Centre will adjust the web-based system so the manually assigned number will not be re-assigned at a later date.

3. Randomization with Pre-Made Study Packages

For sites that pre-make study drug packages for off-hour enrolment, please proceed as follows:

a. Pharmacy should pre-make study drug packages for the next sequential patient number on the master randomization list.

b. To enroll the patient, the Site Coordinator should still enter the patient into the web-based randomization system as described above at the time of enrolment.

c. The randomization system will assign the next sequential patient number on the randomization list. This number should match the number on the pre-made study drug package. All other enrolment and study drug procedures are unchanged.

d. If the randomization system does not function at the time of enrolment, the Site Coordinator should proceed with administering the pre-made study drug package to patient. As soon as possible, contact the study coordinator and let them know the patient number that was manually assigned so that the web-based randomization system can be updated by the Methods Centre.

4. Blinding

The randomization list will only be accessible to the Methods Centre at the OHRI and to the pharmacy staff at each site, and will not be seen by anyone directly involved with the study. All study personnel (the Study Coordinator, Site Research Coordinators, Site Investigators, Principal Investigator, Co-Investigators, Data Management personnel and statisticians), members of the health care team (treating physicians, and bedside nurses) and patients/families will be blinded to the study group assignment. If possible at your site, the clinical pharmacist should also be blinded to the study group assignment. If the clinical pharmacist cannot be blinded, please ensure that they are aware of the importance of not revealing the patient's allocated study treatment.