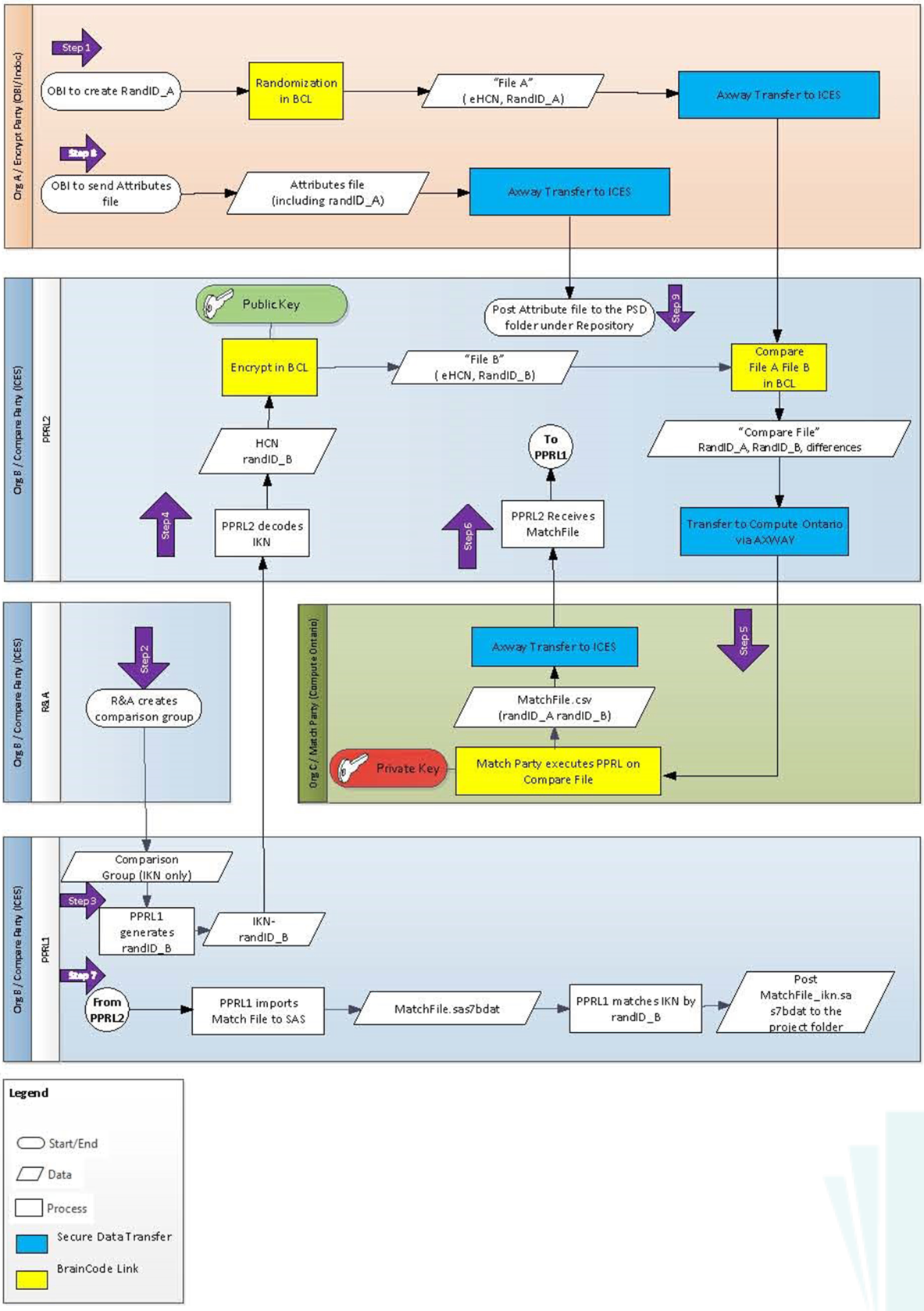
Supplementary Appendix 1

Supplementary Figure 1: Data Flow and Process for Brain-CODE Link (BCL) at ICES



The detailed algorithm (Supplementary Figure 1):

1. OBI: Ontario Health Insurance Plan (OHIP) numbers were entered into the Subject Registry at Brain-CODE over several years. These values were encrypted using a public key in the browser via JavaScript, and only the encrypted text left the user's computer to be stored in Brain-CODE. The encryption technique is such that the encrypted text is highly-variable, even if the same OHIP number is entered repeatedly. For a specific linkage study, a set of test subjects within Brain-CODE was identified for linking. Their encrypted OHIP numbers were extracted and paired with randomized subject IDs (RandID_A) via the 'link-randomize' utility of the BCL package, while the original participant IDs were retained on the central system. This extracted data was transmitted to ICES via the Axway secure transfer system.

2. ICES - Research and Analysis department (R&A): A cohort of potential individuals was identified and their encoded OHIP numbers (called ICES Key Numbers or IKNs) extracted from ICES data repository. This list was passed to the group 'PPRL1', which represents the group of individuals within the ICES Data Quality (DQ) team that are only permitted to work with encoded information.

3. ICES – Data Quality (PPRL1): PPRL1 assigns a random ID (RandID_B) to each IKN and passes the two variables to the group 'PPRL2'. The PPRL2 is the group of individuals within Information Management (IM) team that are authorized to view and process direct personal identifiers (DPI), such as the OHIP number. To respect the privacy-preserving aspect of the process the creation of random ID must not be shared with PPRL2.

4. ICES – IM (PPRL2): PPRL2 group decodes IKNs to raw, original OHIP numbers. The raw OHIP numbers are then encrypted in BCL using the public key (provided by the 'Match Party'). The resulting file (File B) is ready for the Compare Process. The PPRL2 group will import File A and File B into the BCL application to create the Compare file. The Compare file which will be a Cartesian match product of file A and file B will contain RandID_A, RandID_B, and the differences (generated by the software). When the size of the compare file is greater than the size limit of an Axway transfer, an adequate number of splits must occur and steps 4 and 5 will need to be repeated iteratively.

5. Trusted third-party (CS): The difference file was transferred securely via SFTP to an autonomous server run by a trusted third party. Once the file transfer was complete, the file integrity was verified by the server, which proceeded to run the Link utility 'link-match' against the encrypted differences, decrypting these values using the Brain-CODE secret key. When decrypted, the values were either 0, indicating a match, or a random value, indicating a non-match. An output file consisting of the lists of matched ID pairs is created by 'link-match,' which also creates a flag file when the run has finished.

6. ICES – IM (PPRL2): The PPRL2 group receives the encrypted MatchFile via Axway and passes it to the PRL1 group.

7. ICES – DQ (PPRL1): The PPRL1 group retrieves the study subject IKN by merging with the RandID_B and posts the file directly to the project folder.

8. OBI: OBI sends the clinical variables (attributes file) for the matched RandID_A (received from CS) to ICES via the Axway secure transfer system.

9. ICES – IM (PPRL2): The PPRL2 group receives the attributes file(s) (clinical variables) and makes them available to the project team through the ICES Data Repository. This attributes data will be linkable to ICES repository by the research team through the crosswalk posted under project folder in step 6.

Supplementary Appendix 2 – DOC Screen

DOC SCREEN PART 1

Date: _____

Patient of: _____

Completed by:
- ☐ RN
- ☐ MD
- ☐ RA
- ☐ Medical Student
- ☐ Other_____

Language:
- ☐ English 1st language
- ☐ ESL, fluent
- ☐ ESL, not fluent

Sex:
- ☐ M
- ☐ F

Unable to complete due to:
- ☐ Language
  - ☐ Aphasic/Dysphasic
  - ☐ Unable to translate
- ☐ Motor
- ☐ Vision
- ☐ Too ill
- ☐ Other: _____

Resides at:
- ☐ Home
- ☐ Nursing Home/ LTC/CCC
- ☐ Inpatient rehab facility
- ☐ Retirement Home
- ☐ Other Residential Facility
- ☐ No Fixed Address
- ☐ UTD

Education: highest grade (1-13) _____ # of undergraduate years _____ # of graduate years _____

Systolic BP: _____

Diastolic BP: _____

Height: _____

Weight: _____

Waist/Hip Circumference: _____ /_____

Modified Rankin Scale: _____

0 – No symptoms
1 – No significant disability despite symptoms; able to carry out all usual duties and activities
2 – Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3 – Moderate disability; requiring some help, but able to walk without assistance (**with or without cane or walker)**
4 – Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5 – Severe disability; bedridden, incontinent and requiring constant nursing care and attention

Clinical Frailty Scale: _____

1 – Very fit - Robust, active, energetic, well-motivated and fit
2 – Well - Without active disease, but less fit than those in 1
3 – Well, with treated comorbid disease - Disease symptoms well controlled
4 – Apparently vulnerable - Not dependent, but common complaints about being 'slowed up' or having disease symptoms
5 – Mildly frail - Limited dependence for IADLs
6 – Moderately frail - Help required for both IADLs/ADLs
7 – Severely frail - Completely dependent on others for ADLs, or terminally ill

Please see reverse side!
Version Date Mar 13 2014

Please see reverse side!
Version Date Mar 13 2014

DOC SCREEN PART 2

Time to complete: _____ min _____ s

Memory (Registration)						
Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED
	1st trial					
	2nd trial					

DOC Mood[1] "Over the last 2 weeks, how often have you been bothered by any of the following problems?"				
	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
Little interest or pleasure doing things				
Feeling down, depressed or hopeless				

Score (D): /6

DOC Apnea[2]	**Yes**	**No**
Do you snore loudly (louder than talking, heard through a door, or bother other people)?		
Do you often feel tired, fatigued or sleepy during the daytime?		
Has anyone observed you stop breathing during your sleep?		
Do you have, or are you being treated for high blood pressure?		

Score (O): /4

Draw a Clock (Ten Past Eleven)

Contour [ ]
Numbers [ ]
Hands [ ]

Score (C): /3

Abstraction "What is the similarity between: (e.g. banana – orange = fruit)"
A train and a bicycle? [ ] A watch and a ruler? [ ]

Score (C): /2

Memory (Delayed Recall)						
What were those 5 words?	WITHOUT CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]
	Category cue					
	Multiple choice cue					

Score (C): /5

D (DOC-Mood) : /6	**O (DOC-Apnea) : /4**	**C (DOC-Cog[3]) : /10**
TOTAL DOC SCORE = D + O + (10 – C) = /20		

Modified/Combined from: [1]**PHQ-2**: Hajek VE et al. Brief assessment of cognitive impairment in patients with stroke. Arch Phys Med Rehabil. 1989 Feb;70(2):114-7. [2]**STOP**: Chung F et al. STOP questionnaire: A tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008 May;108(5):812-21. 74. [3]**MoCA**: Nasreddine ZS et al. The montreal cognitive assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005 Apr;53(4):695-9. MoCA copyright of the adapted version: Z. Nasreddine MD. Adapted by Swartz et al., 2013.

Supplementary Appendix 3 – DOC Case Report Form

DOC 2.0 CASE REPORT FORM Ver. Aug 13 2014

Initial Visit Date: _____

❑ 1st visit to Clinic
❑ Assessed at F/U for OBI Eligibility

Age at Visit: _____

Date of Referral: _____

Source of Referral (check only one):
❑ Emergency Department **Institution:** _____
❑ Post-admission Inpatient Follow-up
❑ Community/ Family Physician (GP)
❑ Other Subspecialties **Specify:**
□ Ophthalmology □ Orthopedics □ Cardiology □ Obstetrics
□ Neurosurgery □ Vascular Surgery □ Neurology □ Surgeon
□ Nephrology □ GIM □ Other: _____

Reason for Referral:
Date of event: _____
❑ New/Recent (≤180 days) ❑ Remote > 180 days
Type of event (check only one):
❑ Ischemic Stroke ❑ Hemorrhagic ❑ TIA/Minor Stroke
❑ Sinus Venus Thrombosis ❑ Asymptomatic Carotid Artery Disease
❑ Asymptomatic Abnormal Imaging ❑ Other: _____ ❑ UTD
Symptoms (check all that apply):
□ Left □ Right □ Bilateral □ UTD □ Not Applicable
□ Weakness □ Speech □ Sensory □ Monocular Visual Symptoms
□ Diplopia □ Vertigo □ Headaches/Migraines
□ Other: _____

Vascular Risk Factors (check all that apply):
❑ Previous Stroke **Specify:**
□ Ischemic □ ICH □ SAH □ IVH □ UTD
Most recent occurred: □ ≤ 3months □ > 3months □ UTD
❑ Previous TIA
Most recent occurred: □ ≤ 3months □ > 3months □ UTD
❑ Hypertension (HTN)
❑ Diabetes (DM) **Specify:** □ Type I □ Type II □ UTD
Specify End-organ damage: □ Yes □ No □ UTD
❑ Dyslipidemia/Hyperlipidemia
❑ Family History of Vascular Disease
❑ Carotid Stenosis (Extra Cranial)
□ **Right Side Specify:** □ Symptomatic □ Asymptomatic
□ Trace (<30%) □ Mild (30-49%) □ Moderate (50-69%)
□ Severe (70-99%) □ Occluded (100%)
□ **Left Side Specify:** □ Symptomatic □ Asymptomatic
□ Trace (<30%) □ Mild (30-49%) □ Moderate (50-69%)
□ Severe (70-99%) □ Occluded (100%)
□ **UTD**
❑ Symptomatic Intracranial Arterial Disease (e.g. Moya-moya, Atherosclerosis, Vasculitis, RCVS, Fibromuscular Dysplasia)
❑ Peripheral Vascular Disease (PVD)
❑ Carotid Endarterectomy (CEA)/ Stenting **Specify:**
□ Right □ Left □ Both □ UTD
❑ Deep Venous Thrombosis (DVT) or Pulmonary Embolism(PE)

Smoker Status (check only one):
❑ Life-long non-smoker ❑ Current non-smoker (hist. unknown)
❑ Non-smoker (including quit >5yrs) ❑ Reformed smoker (quit > 1 mo to 5 years) ❑ Current (including quit <30 days) ❑ UTD

Cardiac Disease (check all that apply):
❑ Angina ❑ Prior MI ❑ Prior CABG (triple bypass)
❑ Prior PTCA (angioplasty) ❑ Congestive Heart Failure (CHF)
❑ Valve Replacement ❑ Atrial Fibrillation (A-fib)/Flutter
❑ Significant Murmur (grade ≥3/6 for systolic, any diastolic)
❑ Left Ventricular Hypertrophy (LVH)
❑ Other Cardiac Source of Emboli **Specify:**
□ Poor LV function (low EF) □ Abnormal Aortic or Mitral Valve (Valvular Heart Disease) □ Cardiomyopathy □ PFO or other Shunt □ Intracardiac Thrombosis
❑ CAD type not specified

Others (check all that apply):
❑ Obesity
❑ Prothrombotic State
❑ Known Pregnancy **Specify:**
□ N/A □ 1st trimester □ 2nd trimester □ 3rd trimester
❑ Post-partum **Specify:**
□ N/A □ <6 weeks □ 6 – 12 weeks
❑ Known Obstructive Sleep Apnea (OSA) **Specify:**
□ Using CPAP □ Not using CPAP □ Using other therapy: _____
❑ History of Migraines

Alcohol Consumption (check only one):
❑ Never ❑ Not currently (hist. unknown) ❑ Rare/Social
❑ < 2 drinks/day ❑ > 2 drinks/day ❑ UTD

Systemic Disease (check all that apply):
❑ Dementia
❑ Chronic Renal disease **Specify any of:**
□ Mild (Cr < 256) □ Moderate - Severe (Cr ≥ 256) □ Dialysis
□ Transplantation
❑ Cancer **Specify:**
□ Breast □ Lung □ Leukemia □ Lymphoma □ Metastatic □ UTD
□ Other: _____
❑ COPD/Asthma
❑ Connective Tissue Disease
❑ Peptic Ulcer Disease (PUD)
❑ Liver Disease **Specify:**
□ Mild (Cirrhosis without PHT, Chronic Hepatitis) □ Moderate □ Severe (Cirrhosis with PHT +/- Variceal Bleeding) □ UTD
❑ Hemiplegia or Paraplegia
❑ AIDS
❑ Autoimmune Disease **Specify:**
□ CNS (MS, Vasculitis etc.) □ Rheumatological (Lupus/ SLE, RA etc.)
□ Other: _____

Most Responsible Diagnosis after Initial Visit:
❑ Ischemic Stroke **Specify:**
□ Definite Stroke □ Possible/Query Stroke
❑ Hemorrhage
□ ICH □ SAH □ IVH □ SDH
❑ TIA **Specify:**
□ Definite TIA □ Possible/Query TIA
❑ Sinovenous Thrombosis
❑ Asymptomatic Carotid Artery Disease
❑ Abnormal CT/MRI scan
❑ Other Vascular: _____
❑ Other Non-Vascular: Specify
□ BPPV/Vertigo □ Migraine/Aura □ Seizure/Aura
□ Other: _____