#### SUPPLEMENTAL MATERIAL

Recruiting Control Participants into Stroke Biomarker Studies; Translational Stroke Research; Matthew A. Edwardson & Stephen J. Fernandez; Corresponding author: Matthew A. Edwardson, Georgetown University, Washington, DC, USA, email: mae97@georgetown.edu.

# Appendix 1. Example recruitment letter for controls identified by one-to-one matching through the electronic health record

Patient Name Patient Address Line 1 Patient Address Line 2

Dear MedStar Health Community Member,

We are writing to share information with you about a new research study which is being conducted at several MedStar hospitals and requires healthy participants. The study is looking at how well adults recover from stroke by identifying changes in the fats, proteins and DNA/RNA in the blood, which we hope will enhance our understanding as to why some patients recover well and others recover poorly. The objective is to develop better treatments for stroke in the future and understand the biological changes associated with brain recovery.

We are contacting you because your demographic information matches a participant already enrolled in the stroke research study. You can help with this important research by participating in the study as a matched control participant that has not had a stroke. As a study participant, you would provide two fasting blood draws 30 days apart and answer a few questions about your medical history. In exchange for your participation, we will offer you a \$50 Visa gift card at each visit, a voucher for breakfast at the hospital, and parking validation. We anticipate that participation would take no more than an hour of your time.

Thank you for considering being a part of this research effort. Participation in this study is optional and confidential. You will not receive any direct medical benefit from taking part in this research study. If you are interested in participating please contact our research coordinators, Jamal Smith or Juby Mathews, directly at the numbers below. Please also see our enclosed volunteer flyer for further information.

Sincerely,

Matthew A. Edwardson, MD (Principal Investigator), Jamal D. Smith and Juby Mathews (Clinical Research Coordinators) Comprehensive Stroke Trials Medstar Health Research Institute Office: XXX-XXX-XXXX Fax: XXX-XXX-XXXX Email: XXXXXXXX

### Appendix 2. Example online screening questionnaire for control participants

### **Questionnaire to determine eligibility**

### Principal Investigator: Matt Edwardson, MD

## Study Coordinators: Jamal Smith and Juby Mathews

Thank you for showing interest in the Biomarkers of Stroke Recovery Study with MedStar Health. Our goal is to find better ways to treat stroke patients in the future by measuring changes in the blood during recovery. Your participation will help us differentiate markers signaling neural repair from those found in the blood under normal conditions. We are recruiting healthy participants that can provide 2 blood draws one month apart who match our enrolled stroke patients with regard to age, race and medical history.

If your demographics match a patient already enrolled in the study and you are interested in participating, we will schedule a visit to your community that should take 30-45 minutes of your time. During the first visit you will sign a consent form. At each visit blood will be drawn between 7-9am before any meals or morning medications. You will provide your medical history and current medications. At the conclusion of each visit, we will provide you with a \$50 Visa gift card.

Please answer the questions below so that we can determine whether you are a match for a stroke patient already enrolled in the study.

What is your name? What is your date of birth? What is your race? What is your sex? What is your phone number or email address?	
Place an (x) in all that apply.	<ul> <li>Have you ever had a stroke?</li> <li>Are you able to live independently without assistance from others?</li> <li>Do you currently take statin drugs? (a cholesterol lowering agent)?</li> </ul>
Do you have any of the following? Place an (x) in all that apply.	<ul> <li>Active infection or cancer</li> <li>Anemia or fainting spells</li> <li>Neurological disorder such as dementia, multiple sclerosis, ALS, or Parkinson's?</li> <li>Psychiatric disorder including schizophrenia or alcohol abuse?</li> </ul>
Do you have any of the following risk factors for stroke? Place an (x) in all that apply	<ul> <li>High cholesterol</li> <li>High blood pressure</li> <li>Diabetes</li> <li>Heart Disease</li> <li>Smoking</li> </ul>
□ By checking this box I acknowledge that my de	emographic information will be sent securely

□ By checking this box I acknowledge that my demographic information will be sent securely to investigators who will determine whether I am eligible to participate in this study. This information will be stored on an encrypted database and will not be shared with any 3rd parties.

Appendix 3. Sample SAS code to identify matched control participants for a 79yo African American male stroke patient with a history of hypertension, hyperlipidemia, diabetes, coronary artery disease, smoking and statin use

SELECT DISTINCT P.PERSON\_ID P.NAME\_LAST\_KEY P.NAME\_FIRST\_KEY P.BIRTH\_DT\_TM ,AD.STREET\_ADDR ,AD.STREET\_ADDR2 ,AD.STREET\_ADDR3 ,AD.STREET\_ADDR4 ,AD.CITY ,AD.STATE ,AD.ZIPCODE ,PH.PHONE\_NUM

FROM PERSON P JOIN ENCOUNTER ENC ON P.PERSON\_ID=ENC.PERSON\_ID LEFT JOIN ADDRESS AD ON AD.parent\_entity\_ID=P.PERSON\_ID LEFT JOIN V500.PHONE PH ON PH.PARENT\_ENTITY\_ID = P.PERSON\_ID

WHERE

------ RACE P.RACE\_CD IN ( 5048372, 5045710, 309315, 1327505661 ------ AA/Black ) ------ Gender AND P.SEX\_CD IN ( 363 ------ Male ) ------ AGE AND P.birth\_dt\_tm BETWEEN TO\_DATE('02/07/1941','mm/dd/yyyy') AND AD.active\_ind=1

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AND AD.STATE in ('DC', 'MD', 'VA')
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----- HTN

AND( P.person\_id IN ( SELECT person\_id FROM DIAGNOSIS WHERE nomenclature\_id in (SELECT nomenclature ID FROM nomenclature WHERE ((source\_identifier like '401%' --Essential Hypertension OR source\_identifier like 'I10%'--Essential Primary Hypertension, HTN (Hypertension) ) AND active ind=1))) OR P.person\_id in ( SELECT person id FROM PROBLEM where annotated\_display IN ('Hypertension', 'HTN (hypertension)', 'HTN - Hypertension', 'HYPERTENSION', 'HYPERTENSION, BENIGN ESSENTIAL', 'ESSENTIAL HYPERTENSION, BENIGN', 'HYPERTENSION, BENIGN', 'HYPERTENSION BENIGN', 'Benign hypertension', 'H/O: HTN (hypertension)', 'HT - Hypertension', 'ESSENTIAL HYPERTENSION', 'HTN [Hypertension]', 'Essential hypertension', 'Benign essential hypertension', 'hypertension', 'BP+ - Hypertension', 'BENIGN ESSENTIAL HYPERTENSION', 'H/O: hypertension', 'Essential (primary) hypertension', 'HYPERTENSION, ESSENTIAL NOS', 'UNSPECIFIED ESSENTIAL HYPERTENSION', 'History of HYPERTENSION', 'HYPERTENSION, ESSENTIAL', 'Hypertension NOS', 'HYPERTENSION NEC', 'HTN (hypertension), benign') and active\_ind=1)) ----- No Stroke -----and (p.person\_id not in ( Select person\_id from **DIAGNOSIS** where nomenclature\_id in (select nomenclature ID from nomenclature where (( source\_identifier like '430%' --Subarachnoid Hemorrhage or source\_identifier like '431%' --Intracerebral Hemorrhage or source\_identifier like '432%' --Other and Unspecified Intracranial Hemorrhage

```
or source_identifier like '433%' --Carotid artery stenosis
or source_identifier like '434%' --Cerebral Thrombosis, without Mention of Cerebral Infarction
or source identifier like '435%' -- Basilar Artery Syndrome
or source_identifier like '436%'
or source identifier like '437%'
or source_identifier like '438%'
or source identifier like 'I60%'
or source_identifier like 'I61%'
or source identifier like 'I62%'
or source identifier like 'I63%'
or source_identifier like 'I64%'
or source identifier like 'I65%'
or source identifier like 'I66%'
or source_identifier like 'I67%'
or source identifier like 'I68%'
or source_identifier like 'I69%'
or source identifier like 'G45%'
)
and active_ind=1
))))
----- HIV
and (
p.person_id not in (
Select person id
from DIAGNOSIS
where
nomenclature id in
(select nomenclature_ID
from nomenclature
where ((
source_identifier like '042%' --Human Immunodeficiency Virus [HIV] Disease
or source_identifier like 'B20%'-- Human immunodeficiency virus [HIV] disease
or source identifier like 'B21%'
or source identifier like 'B22%'
or source identifier like 'B23%'
or source identifier like 'B24%'
or source identifier like 'V08%'
or source_identifier like 'Z21%'
)
and active_ind=1))))
----- HLD
and
(p.person_id in (
Select distinct person_id
```

```
from DIAGNOSIS
where
nomenclature id in
(select distinct nomenclature_ID
from nomenclature
where
((
source_identifier like 'E78.0%' --Pure hypercholesterolemia
or source_identifier like 'E78.1%' --Pure hyperglyceridemia
or source identifier like 'E78.2%'--Mixed hyperlipidemia
or source_identifier like 'E78.3%'--Hyperchylomicronemia
or source identifier like 'E78.4%'
or source identifier like 'E78.5%'
or source_identifier like '272.0%'
or source identifier like '272.1%'
or source_identifier like '272.2%'
or source identifier like '272.3%'
or source_identifier like '272.4%'
)
and active_ind=1)))
or p.person id in
(Select distinct person_id
from PROBLEM
where
annotated_display
In
('Hyperlipidemia', 'HYPERLIPIDEMIA', 'HLD (hyperlipidemia)', 'HLD - Hyperlipidemia',
'Hyperlipemia', 'Mixed hyperlipidemia', 'H/O hyperlipidemia', 'HYPERLIPIDEMIA, MIXED',
'HYPERLIPIDEMIA, OTHER UNSPECIFIED', 'Hyperlipidemia, Group A', 'MIXED
HYPERLIPIDEMIA', 'Hyperlipidemia NOS', 'HYPERLIPIDEMIA NEC/NOS', 'OTHER AND
UNSPECIFIED HYPERLIPIDEMIA', 'HYPERLIPIDEMIA MIXED', 'Hyperlipidemia,
unspecified', 'Hyperlipidemia, mixed', 'hyperlipidemia')
and active ind=1))
----- DM
and
(p.person_id in (
SELECT person_id
from DIAGNOSIS
where
nomenclature id in
(SELECT nomenclature_ID
from nomenclature
where
((
```

```
source_identifier like '250._0' --Diabetes mellitus, new onset
or source_identifier like '250._2' --Diabetes Mellitus without Mention of Complication, Type II
or Unspecified Type, Uncontrolled
or source_identifier like 'E11%'
or source identifier like 'E13%'
)
and active_ind=1
))))
----- CAD
and
(
p.person_id in (
Select distinct person_id
from DIAGNOSIS
where
nomenclature_id in
(select distinct nomenclature_ID
from nomenclature
where
((
source identifier like '414.0%' -- Coronary Atherosclerosis
or source_identifier like '414.2%' --Chronic Total Occlusion of Coronary Artery
or source_identifier like '414.3%'
or source_identifier like '414.4%'
or source identifier like 'I25.82%'
or source identifier like 'I25.83%'
or source_identifier like 'I25.84%'
or source_identifier like 'I25.1%'
or source identifier like 'I25.4%'
or source_identifier like 'I25.7%'
)
and active_ind=1
))))
----- PVD
and
(
p.person_id not in (
Select distinct person id
from DIAGNOSIS
where
nomenclature_id in
(select distinct nomenclature_ID
from nomenclature
where
```

```
((
source_identifier like '440.2%' -- Atherosclerosis of Native Arteries of the Extremities
or source_identifier like 'I70.2%'
or source_identifier like 'I73%'
or source identifier like '443%'
)
and active_ind=1
))))
----- Afib
and (
p.person_id not in (
Select distinct person_id
from DIAGNOSIS
where
nomenclature_id in
(select distinct nomenclature ID
from nomenclature
where
((
source_identifier like '427.31%'
or source identifier like 'I48%'
)
and active_ind=1
))))
----- CHF
and
(
p.person_id not in (
Select distinct person_id
from DIAGNOSIS
where
nomenclature_id in
(select distinct nomenclature_ID
from nomenclature
where
((
source_identifier like '428%' --Heart Failure
or source identifier like 'I50%'
)
and active_ind=1))))
----- DVT/PE
and (
p.person_id not in (
```

```
Select distinct person_id
from DIAGNOSIS
where
nomenclature_id in
(select distinct nomenclature ID
from nomenclature
where
((
source_identifier like '453.4%' --Acute Venous Embolism and Thrombosis of Deep Vessels of
Lower Extremity
or source_identifier like 'I82.4%'
or source identifier like '451.1%'
or source identifier like 'I26%'
)
and active_ind=1))))
----- SMOKING
and
(
p.person_id in (
Select distinct person_id
from PROBLEM
where
annotated_display
in
('Tobacco use and exposure - finding', 'Tobacco and nicotine', 'Tobacco abuse', 'Tobacco Use
Disorder', 'Tobacco dependence syndrome', 'Tobacco', 'Tobacco - substance', 'Tobacco use',
'Tobacco chewing', 'Tobacco dependence, continuous', 'Tobacco use and exposure', 'Tobacco
dependence', 'Tobacco use disorder', 'Tobacco user', 'Tobacco smoking consumption', 'Personal
History of Tobacco Use')
and active_ind=1))
and p.active ind=1
-----STATIN
SELECT DISTINCT PERSON ID
FROM [AmalgaV2].[dbo].[CernerMedRec]
WHERE
(ORDER_MNEMONIC like '% statin%' or hna_order_mnemonic like '% statin%' or Categories
like '%HMG-CoA reductase inhibitors%') AND ORDER_MNEMONIC not like '%nystatin%'
AND PERSON ID in (Person Id's of patients that have met the criteria for Race, Gender, Age,
and Comorbidity's is included here to check for statin matches )
```