D2d Annual Meeting Breakout Session

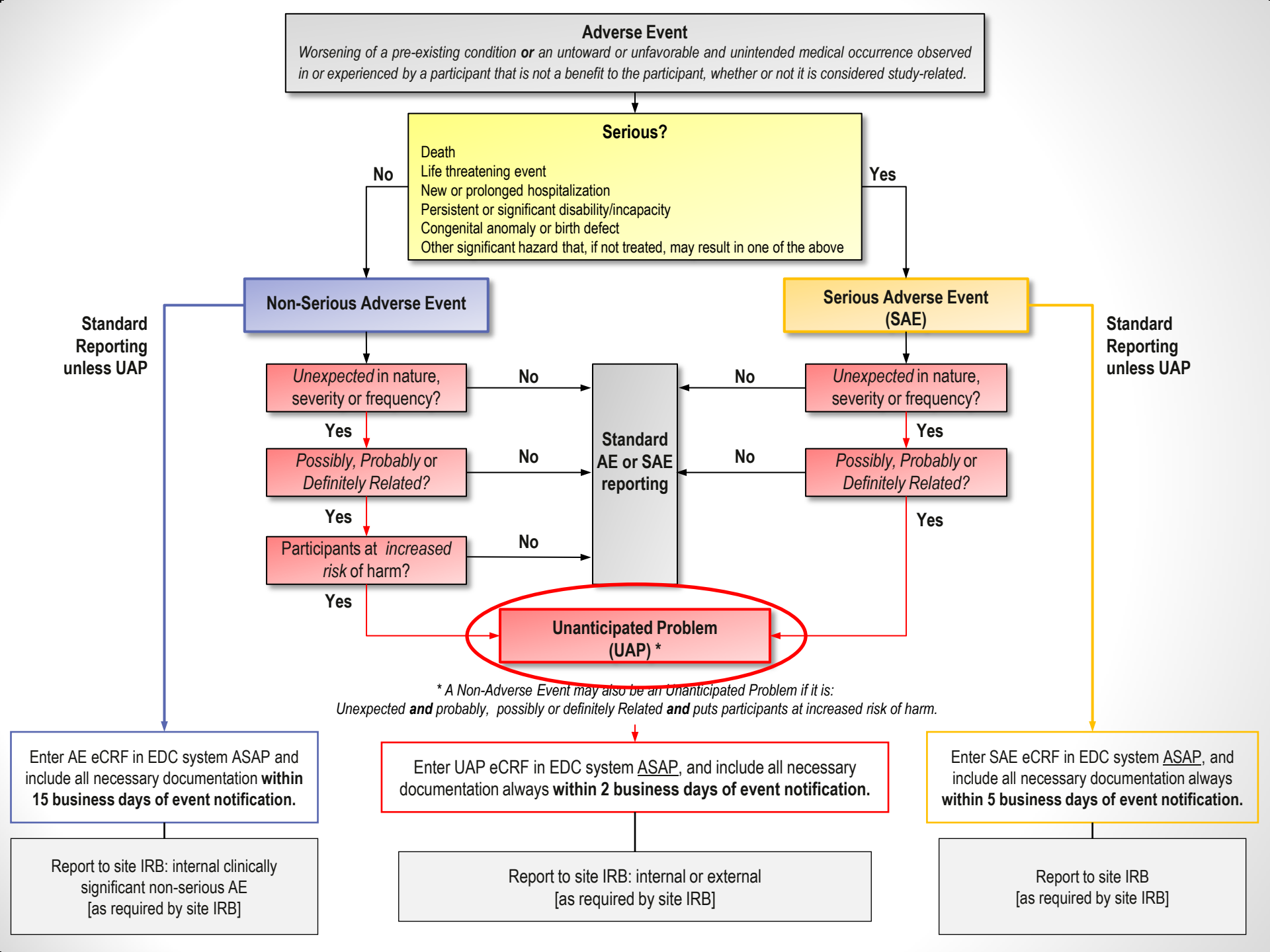
November 17, 2014

To Discuss

1. Adverse event documentation
2. Working with the Central Laboratory
3. CC-Site communications and reminders
4. D2d study outcome assessment

To Discuss

1. Adverse event documentation


Adverse Event
Worsening of a pre-existing condition or an untoward or unfavorable and unintended medical occurrence observed in or experienced by a participant that is not a benefit to the participant, whether or not it is considered study-related.
Serious?
Death
Life threatening event
New or prolonged hospitalization
Persistent or significant disability/incapacity
Congenital anomaly or birth defect
Other significant hazard that, if not treated, may result in one of the above
No
Yes
Non-Serious Adverse Event
Serious Adverse Event (SAE)
Standard Reporting unless UAP
Standard Reporting unless UAP
Unexpected in nature, severity or frequency?
Possibly, Probably or Definitely Related?
Participants at increased risk of harm?
Standard AE or SAE reporting
Unexpected in nature, severity or frequency?
Possibly, Probably or Definitely Related?
Unanticipated Problem (UAP) *
* A Non-Adverse Event may also be an Unanticipated Problem if it is:
Unexpected and probably, possibly or definitely Related and puts participants at increased risk of harm.
Enter AE eCRF in EDC system ASAP and include all necessary documentation within 15 business days of event notification.
Enter UAP eCRF in EDC system ASAP, and include all necessary documentation always within 2 business days of event notification.
Enter SAE eCRF in EDC system ASAP, and include all necessary documentation always within 5 business days of event notification.
Report to site IRB: internal clinically significant non-serious AE [as required by site IRB]
Report to site IRB: internal or external [as required by site IRB]
Report to site IRB [as required by site IRB]

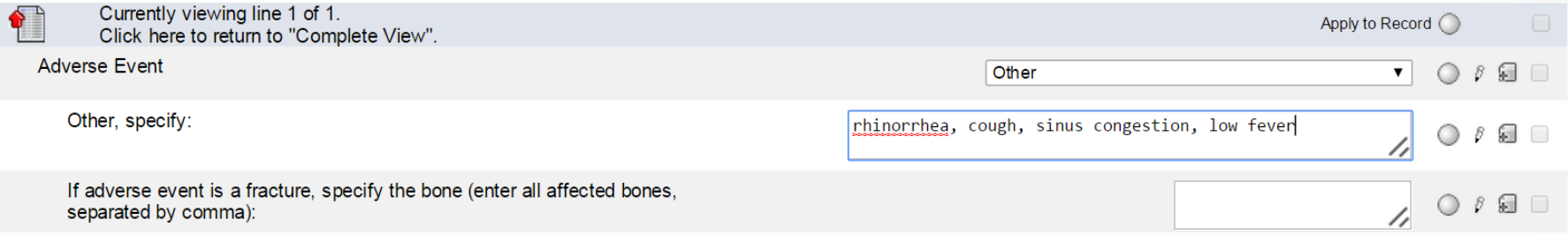
AE Term

Reminders and Tips:

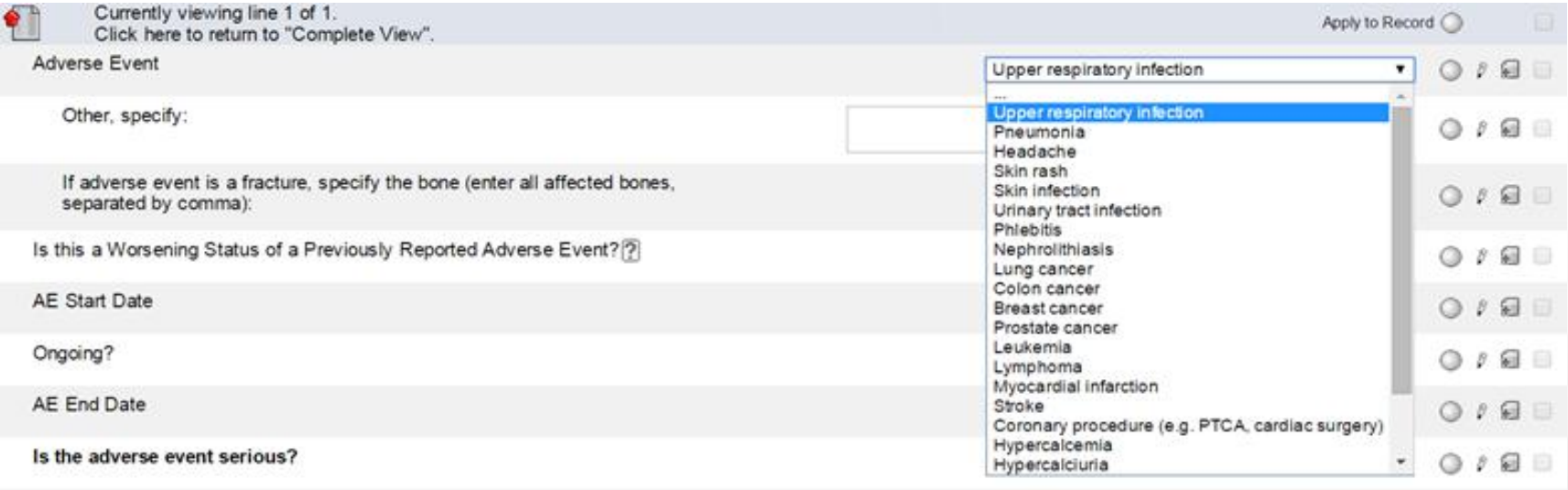
- Enter diagnosis, not symptoms if possible
- Review options in the dropdown before selecting Other
- Please, do not enter data using all UPPER CASE letters
- Refrain from entering explanations in the AE term
- Get as much detail as possible related to start date

AE Term

Instead of this

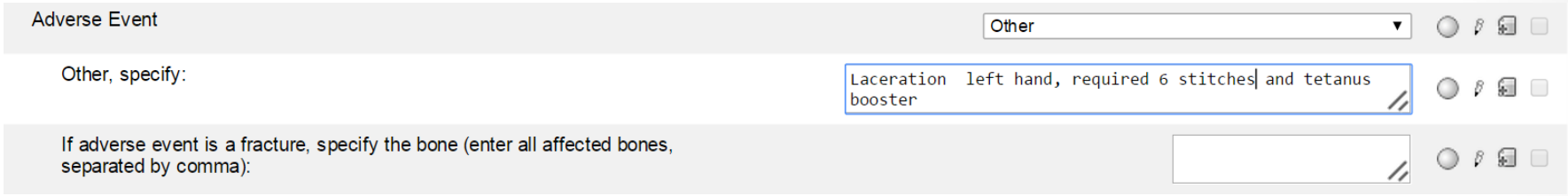


Consider this



AE Term

Instead of this



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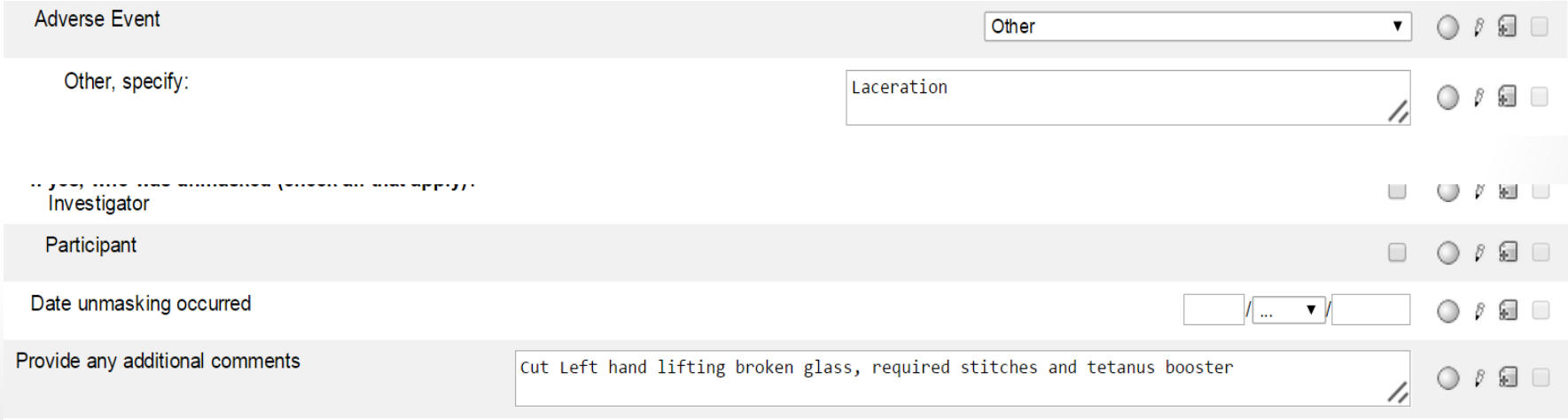
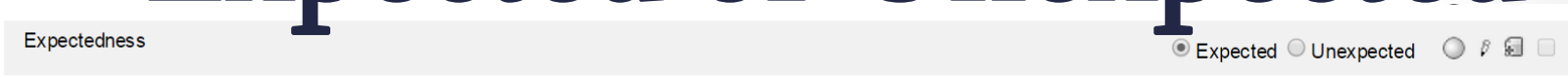


Expected or Unexpected



Reminders :

- Expected events are listed in Data Safety Monitoring Plan (MOP 14).
- If it is not on the list it is unexpected.

"Expected" AE related to the *intervention, vitamin D supplementation* (uncommon).

- Hypercalcemia
- Hyperphosphatemia
- Nephrolithiasis
- Hypercalciuria
- Nephrotoxicity
- Anemia
- Polyuria
- Nausea
- Vomiting
- Poor appetite
- Weakness
- Fatigue
- Insomnia
- Headache
- Metallic taste

"Expected" AE related to *study procedures for outcome assessment (testing)*

Related to blood draws

- Minor discomfort from introducing the needle/catheter under the skin or skin bruise (common)
- A skin infection from the needle/catheter (rare)
- Mild anemia from repeated blood draws (rare)
- Syncope (uncommon)

Related to the OGTT

- Risks associated with insertion of needle/catheter and mild anemia as described above
- Phlebitis (rare)
- Nausea, vomiting and symptoms or signs of hypoglycemia following the oral glucose load (uncommon)

Other risks related to overall trial participation

Social-psychological risk due to inadvertent disclosure of confidential medical information (rare)

58 year old man arrives for his M03 visit. You ask him:

"Have you had any changes in your health since your last visit in August?"

He responds:

"No" "Except this eczema is driving me crazy" (note he is scratching his arm)

Is it an AE?

You then ask:

"When did that start?"

"Have you seen your primary care about it?"

He responds:

"No, I have had eczema since I was a kid, it always gets worse when I turn the heat on"

Is it an AE?

To Discuss

2. Working with the Central Laboratory

Central Laboratory Issues

- **Mix Ups:**
  - **Serum and EDTA specimens in wrong transfer tubes**
  - **30 minute and 120 minute put in the wrong tubes**
- **Unlabeled tubes sent to Lab**
- **Inconsistent visit date information on the Central Lab e-CRF versus the visit date e-CRF**
- **Biorepository specimens collected and sent to lab when participant did not provide repository consent**
- **Central Lab e-CRF not included in the shipping box**

Site Lab issues?

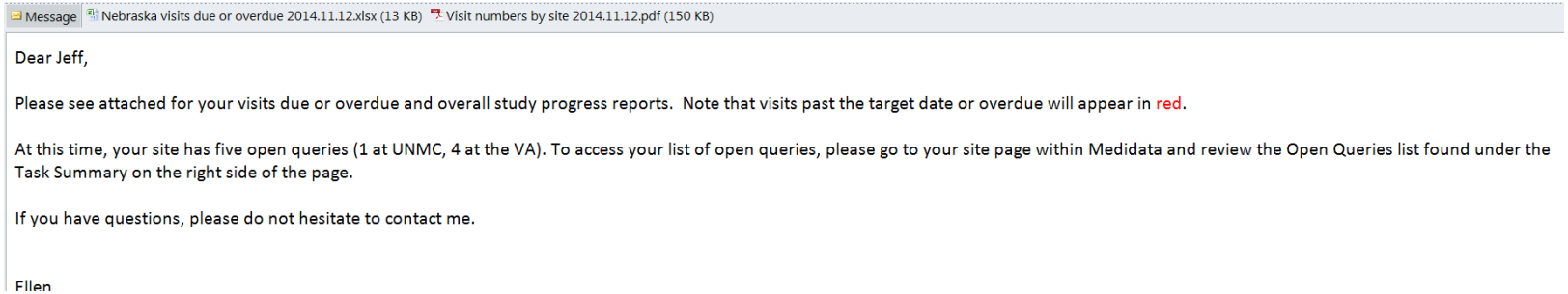
- Shipping?
-

To Discuss

3. CC-Site communications and reminders

CC-Site communications

- Weekly data management e-mails


Message Nebraska visits due or overdue 2014.11.12.xlsx (13 KB) Visit numbers by site 2014.11.12.pdf (150 KB)

Dear Jeff,

Please see attached for your visits due or overdue and overall study progress reports. Note that visits past the target date or overdue will appear in red.

At this time, your site has five open queries (1 at UNMC, 4 at the VA). To access your list of open queries, please go to your site page within Medidata and review the Open Queries list found under the Task Summary on the right side of the page.

If you have questions, please do not hesitate to contact me.

Ellen

Are these useful?

What other information do you want or need?

- CC-Site scheduled phone meetings

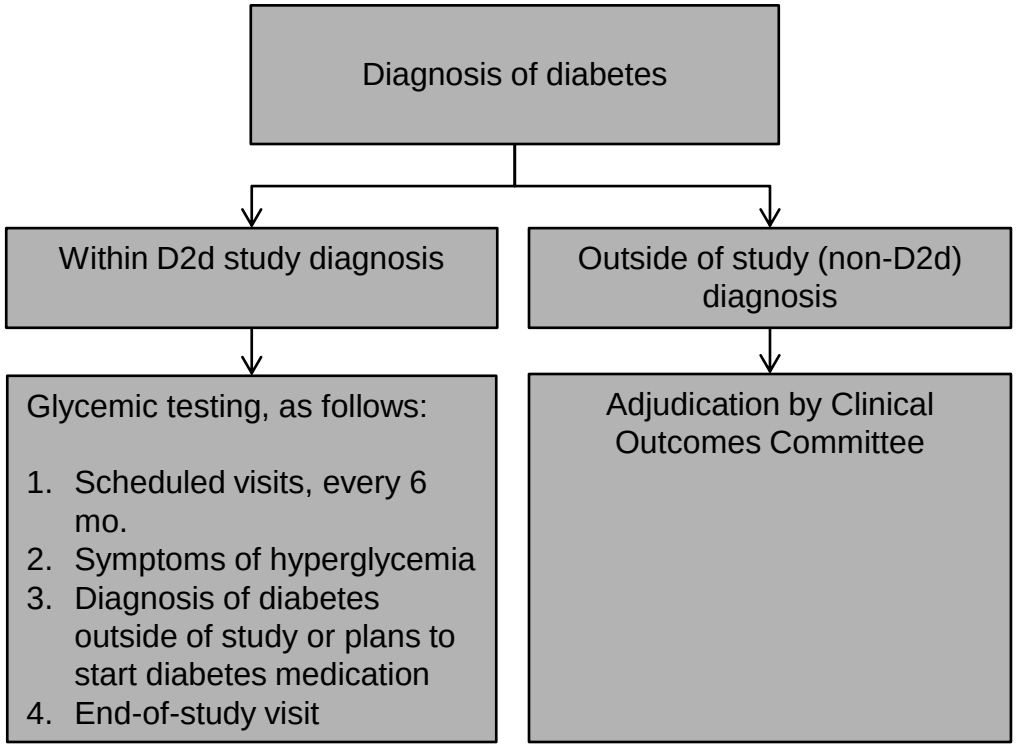
Are these helpful?

- What can the CC do to increase efficiency or make recruiting, enrolling and managing the D2d?

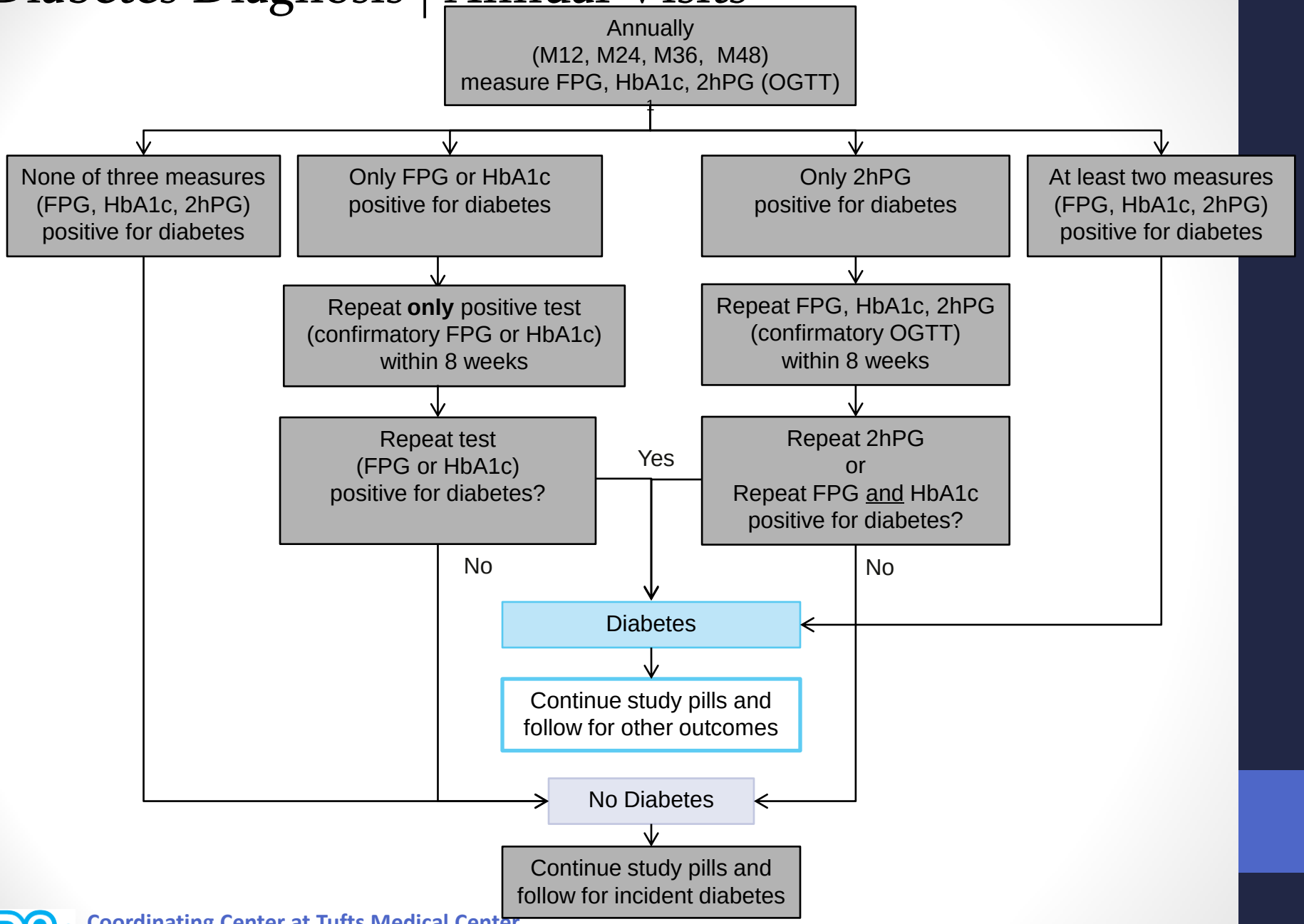
To Discuss

4. D2d study outcome assessment

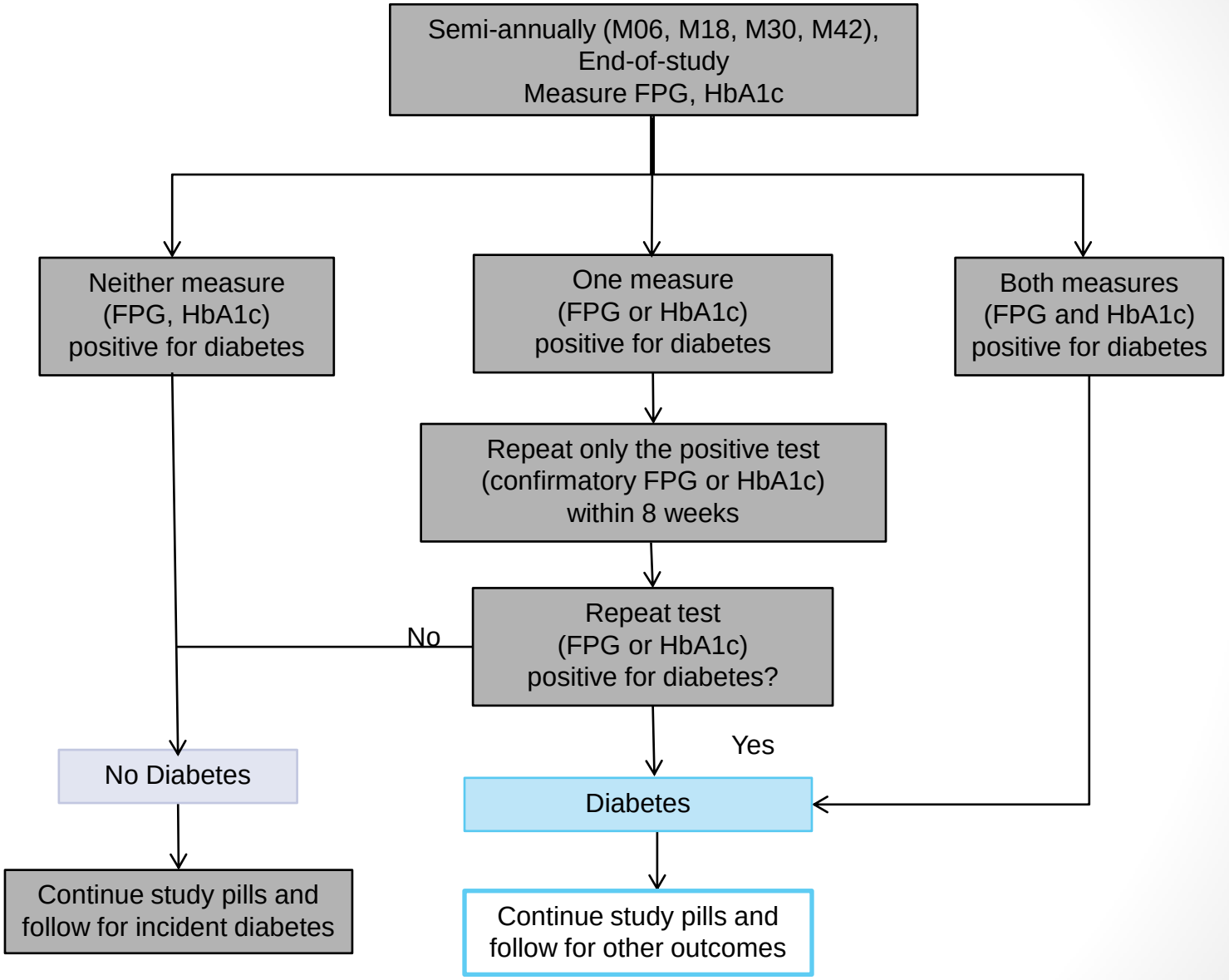
Primary Outcome: Incident Diabetes | Overview

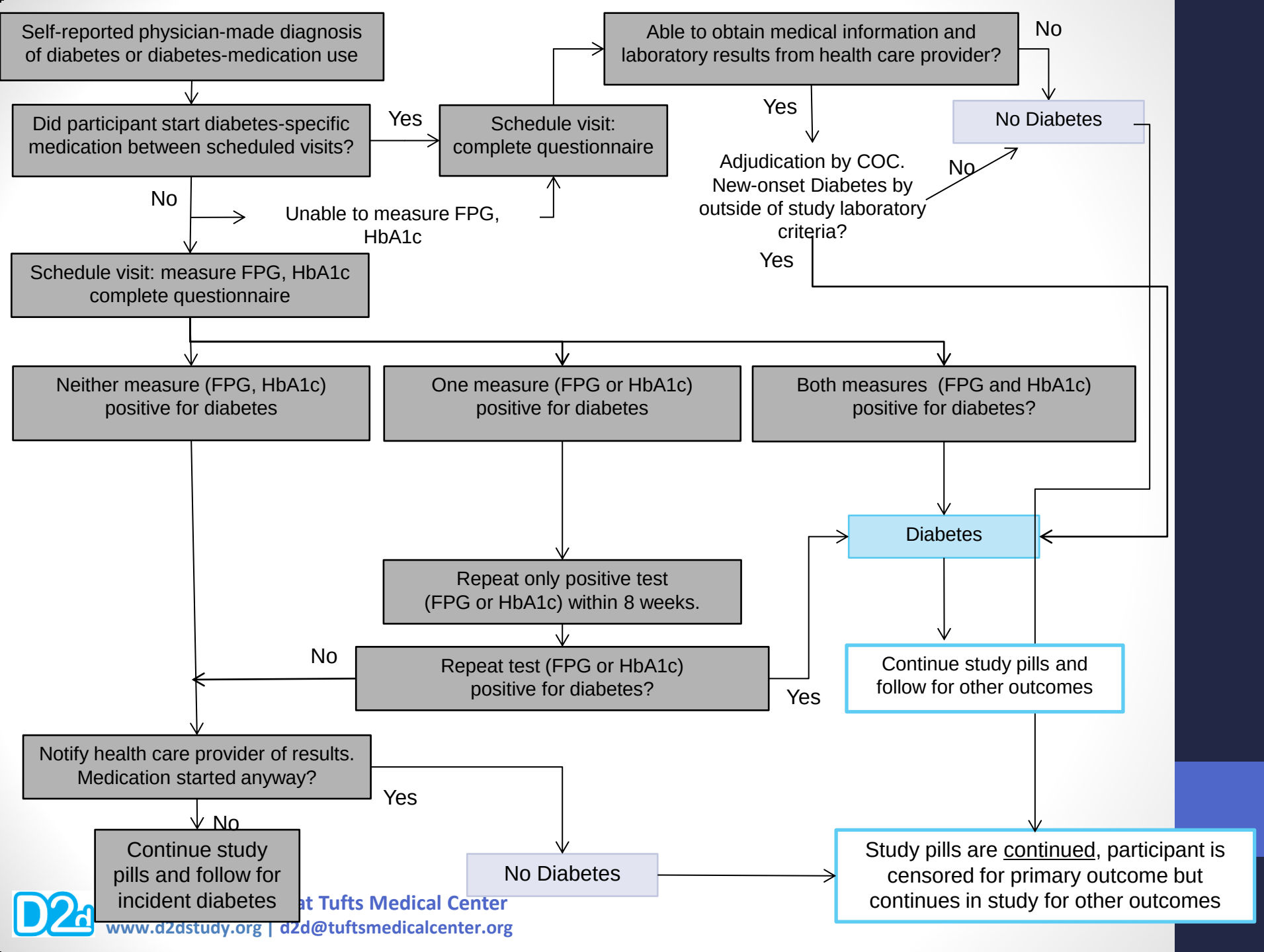


Diabetes Diagnosis | Annual Visits



Diabetes Diagnosis | Semi-annual Visits




Self-reported physician-made diagnosis of diabetes or diabetes-medication use
Did participant start diabetes-specific medication between scheduled visits?
Yes
Schedule visit: complete questionnaire
Able to obtain medical information and laboratory results from health care provider?
No
Yes
No Diabetes
Adjudication by COC. New-onset Diabetes by outside of study laboratory criteria?
No
Yes
No
Unable to measure FPG, HbA1c
Schedule visit: measure FPG, HbA1c complete questionnaire
Neither measure (FPG, HbA1c) positive for diabetes
One measure (FPG or HbA1c) positive for diabetes
Both measures (FPG and HbA1c) positive for diabetes?
Diabetes
Repeat only positive test (FPG or HbA1c) within 8 weeks.
No
Repeat test (FPG or HbA1c) positive for diabetes?
Yes
Continue study pills and follow for other outcomes
Notify health care provider of results. Medication started anyway?
Yes
No
Continue study pills and follow for incident diabetes
No Diabetes
Study pills are continued, participant is censored for primary outcome but continues in study for other outcomes
at Tufts Medical Center
www.d2dstudy.org | d2d@tuftsmedicalcenter.org