

Primary Outcome Challenges

Sept. 26, 2016



Primary Outcome Challenges

Please take out your smartphones.

Open the web browser and go to www.sli.do and enter the event code 6199.

We have prepared a few polls to encourage interaction during the session.



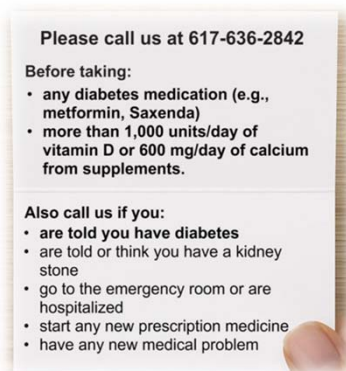
Case 1

- 63 y.o. woman, + FH diabetes, recruited via EMR
- BAS: A1c 6.1, FPG 110, 2hPG 178





Reviewed brochure with participant at randomization visit



Provided participant with D2d appointment card



Sent letter to PCP after randomization



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Case 1 (cont.)

- Just before M03, participant calls and states her PCP wants her to start Metformin
- She has not started yet 😊

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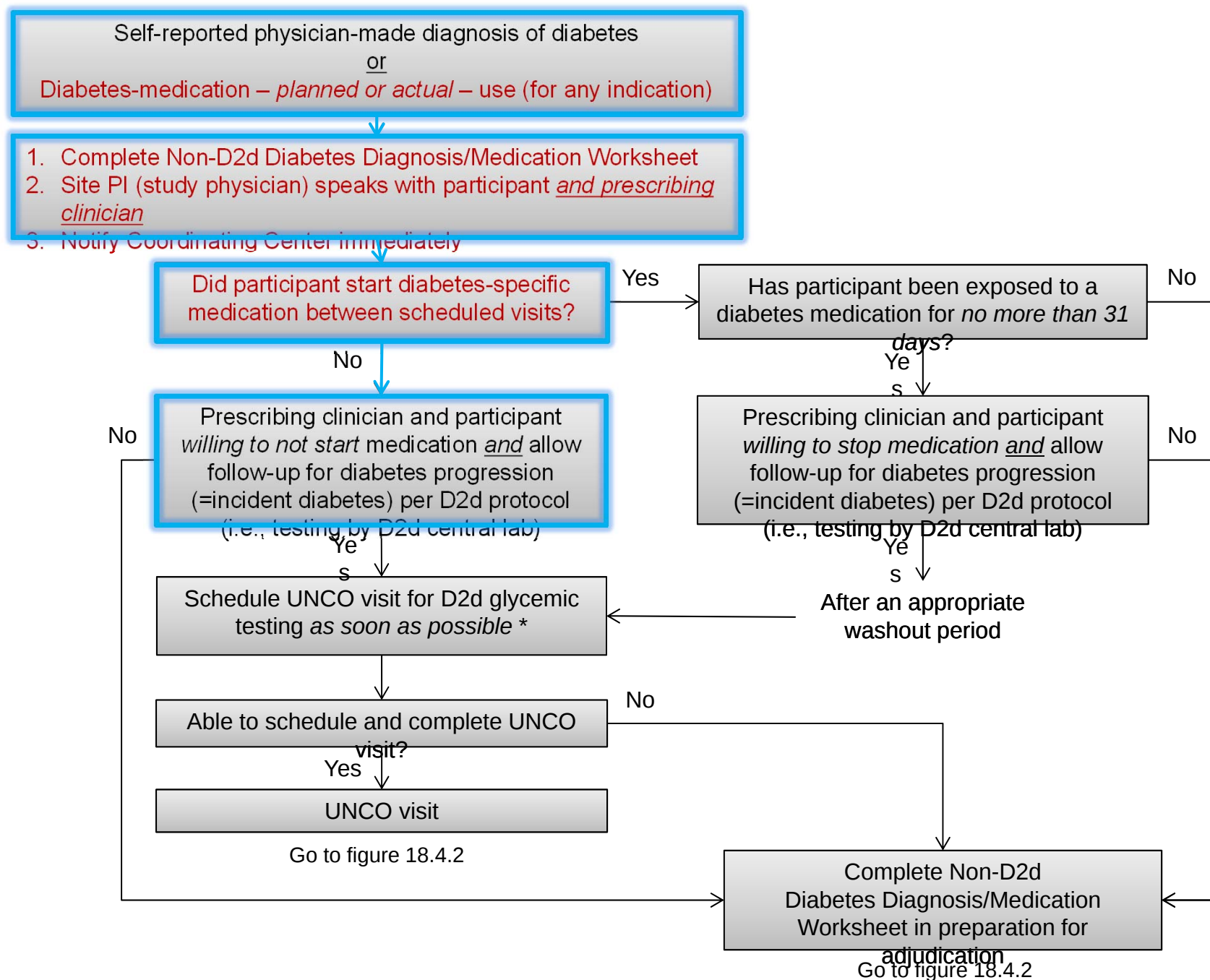


- Just before M03 visit, participant calls and states her PCP wants her to start metformin. She has not started yet. 😊

What is the next step?

1. Site PI and CC are informed immediately. No further action needed, except reinforcing study principles at M03
2. Site PI and CC are informed immediately. Site PI discusses study design and rationale with participant and PCP to assess intent to start metformin
3. No need to inform site PI. Coordinator collects records from PCP and sends to CC for adjudication.





- In lieu of an Unscheduled Confirmatory (UNCO) visit, a regular D2d visit may be done provided the visit window is approaching

Case 1 (cont.)

- What happened 🙅🙅
 - Site PI had conversation with PCP to assess intent
 - PCP's intent was to hold metformin until D2d confirms diabetes
- Per protocol, complete UNCO



Case 1 (cont.)

- Participant continues in D2d
 - At M12 participant has not met the outcome



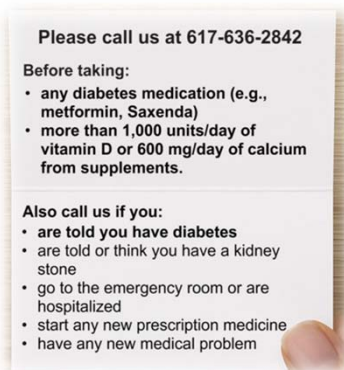
Case 2

- 48 y.o. man; BMI= 38.5; recruited via EMR
- BAS: A1c 6, FPG 112, 2hPG 188





Reviewed brochure with participant at randomization visit



Provided participant with D2d appointment card



Sent letter to PCP after randomization



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Case 2 (cont.)

- M12: HbA1c, FPG, 2hPG negative
- M15: Participant informed coordinator he had been taking metformin for 3 weeks 😞😞😞
- He saw a new PCP who prescribed it for A1c of 6%

This may sound familiar



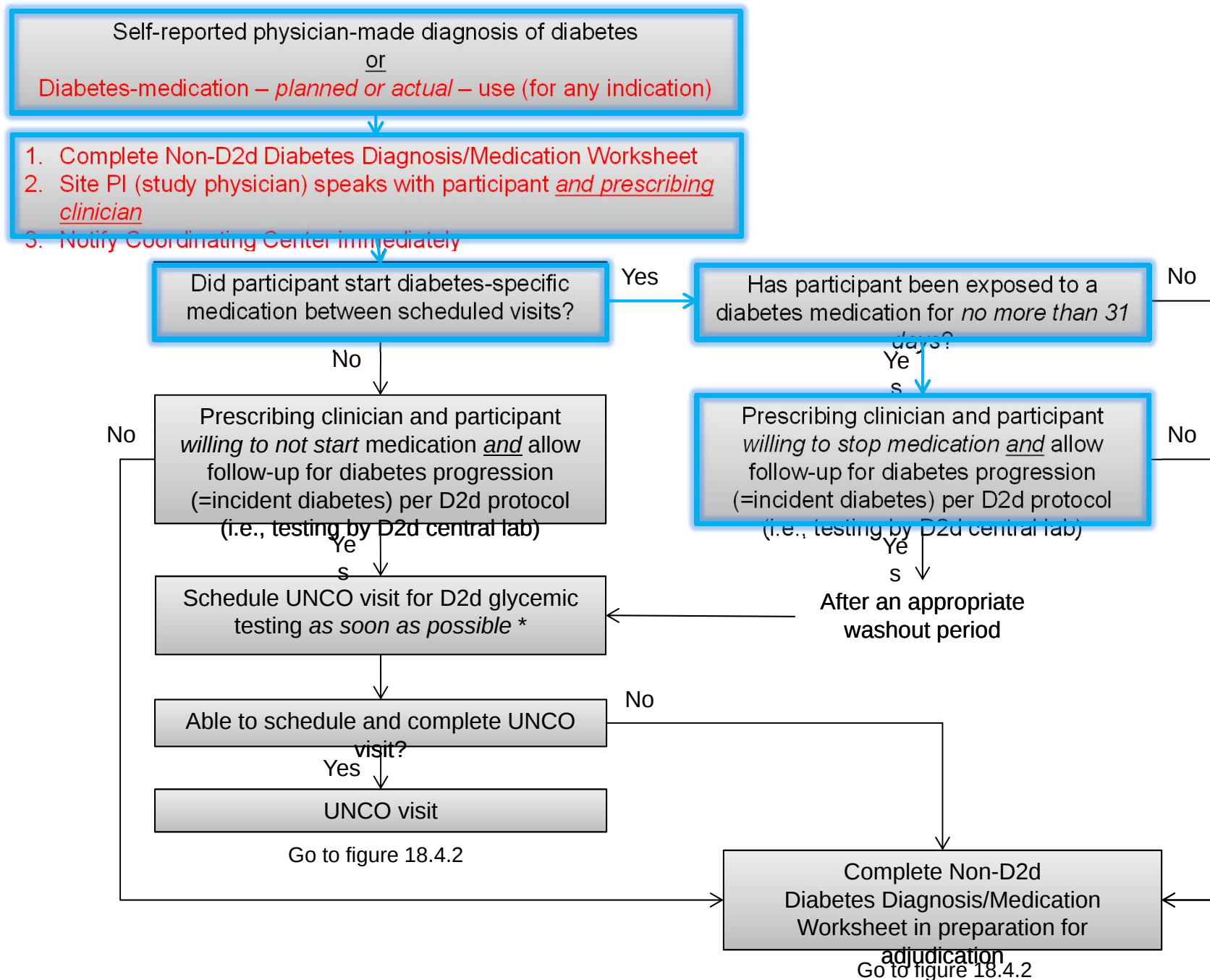
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M15 Phone call: Pt informed coordinator he had been taking Metformin for 3 wks. He saw a new PCP who prescribed it for A1c of 6%

What is the next step?

1. Panic, read protocol, inform CC.
2. Relax, the horse is out of the barn (i.e., participant already on metformin). No need to inform site PI. Inform the CC. Collect records from PCP and send to CC for adjudication.
3. Site PI and CC are informed immediately. Site PI discusses study design and rationale with participant and PCP to see whether PCP is willing to stop metformin.
4. Site PI is informed immediately. Schedule UNCO visit ASAP for FPG/HbA1c.



* In lieu of an Unscheduled Confirmatory (UNCO) visit, a regular D2d visit may be done provided the visit window is approaching

Case 2 (cont.)

- What happened 🙅🙅
 - Site PI had conversation with PCP to inform about D2d protocol and see whether metformin can be stopped
 - PCP agrees to stop metformin and not re-start until D2d confirms diabetes
- Per protocol, complete UNCO
- Participant continues in D2d
 - At M18, FPG positive, HbA1c negative



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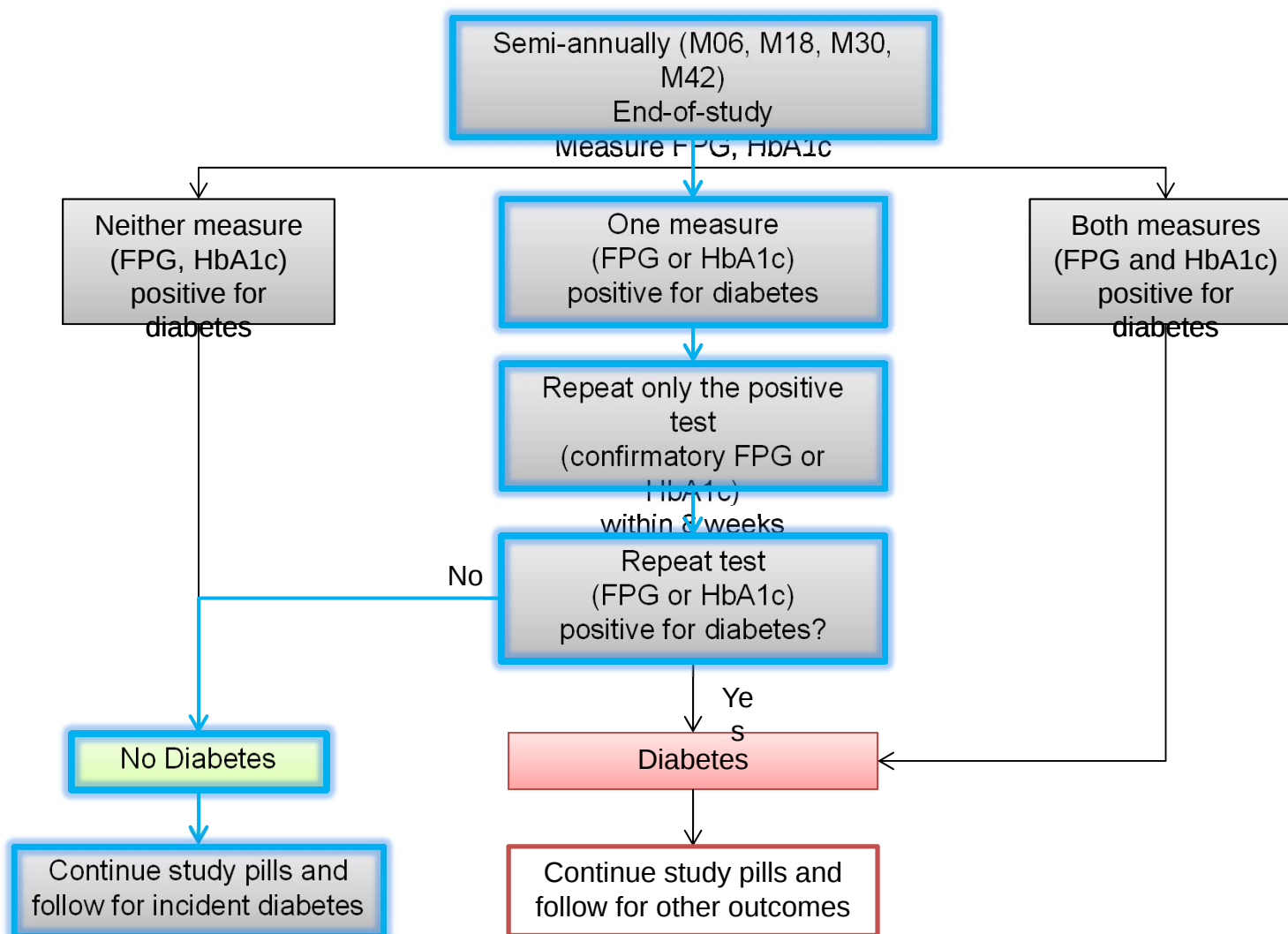
At M18, FPG is positive for diabetes, A1c negative

What is the next step?

1. Coordinator collects records from PCP and sends to CC for adjudication.
2. Inform the CC immediately. Schedule UNCO (unscheduled confirmatory) visit ASAP to collect FPG and HbA1c.
3. Schedule UNCO (unscheduled confirmatory) visit ASAP to collect FPG.
4. Schedule UNCO (unscheduled confirmatory) visit ASAP to collect HbA1c.



Diabetes diagnosis – semi-annual visit



Case 2 (cont.)

- UNCO: FPG negative for diabetes
- Participant did not meet the outcome, continues in D2d



- When site contacted participant to schedule M24, he reported having another new PCP who prescribed metformin, and he had been taking it for 2 months!

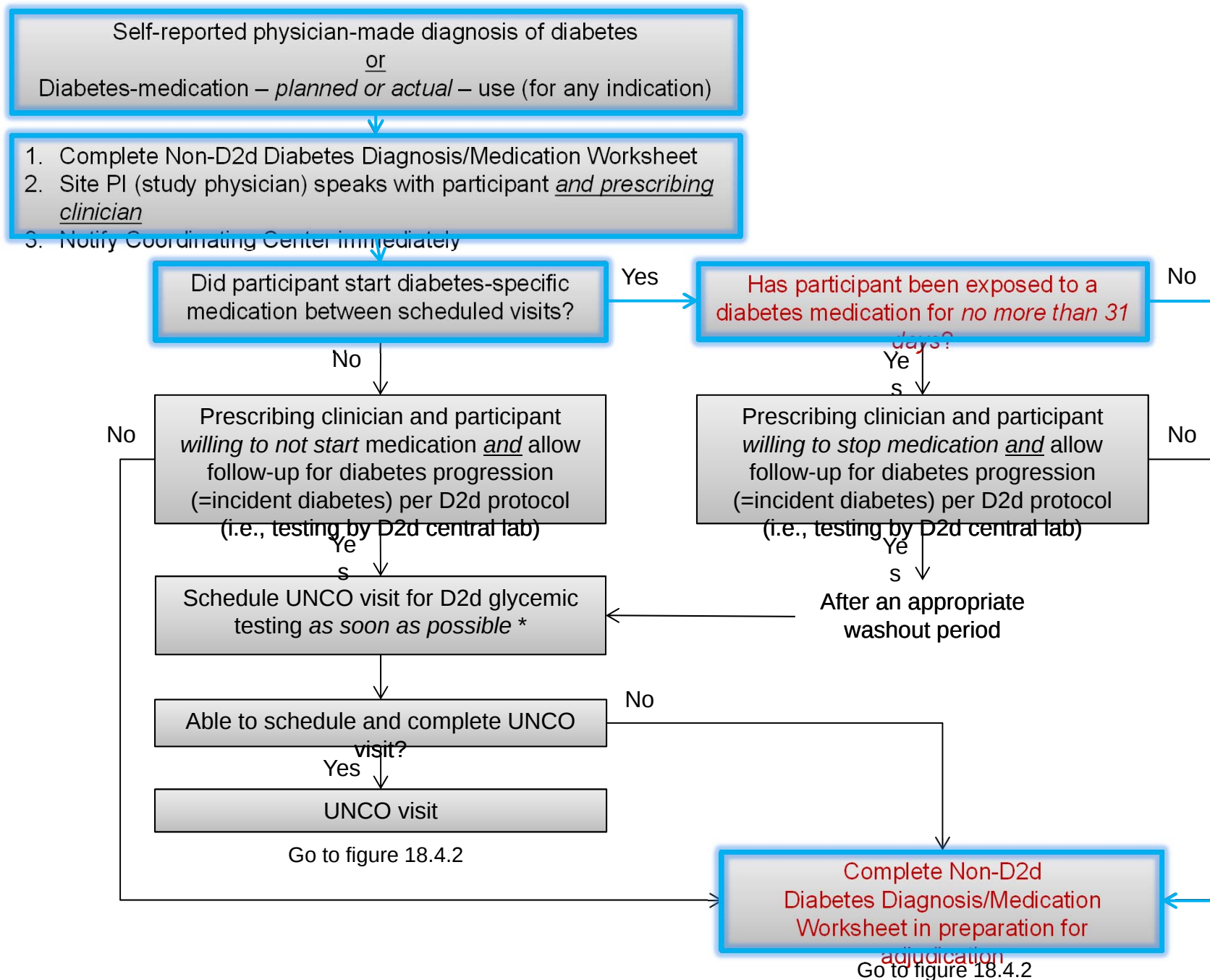
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Later, participant reported having another new PCP who prescribed metformin, and he had been taking it for 2 months!

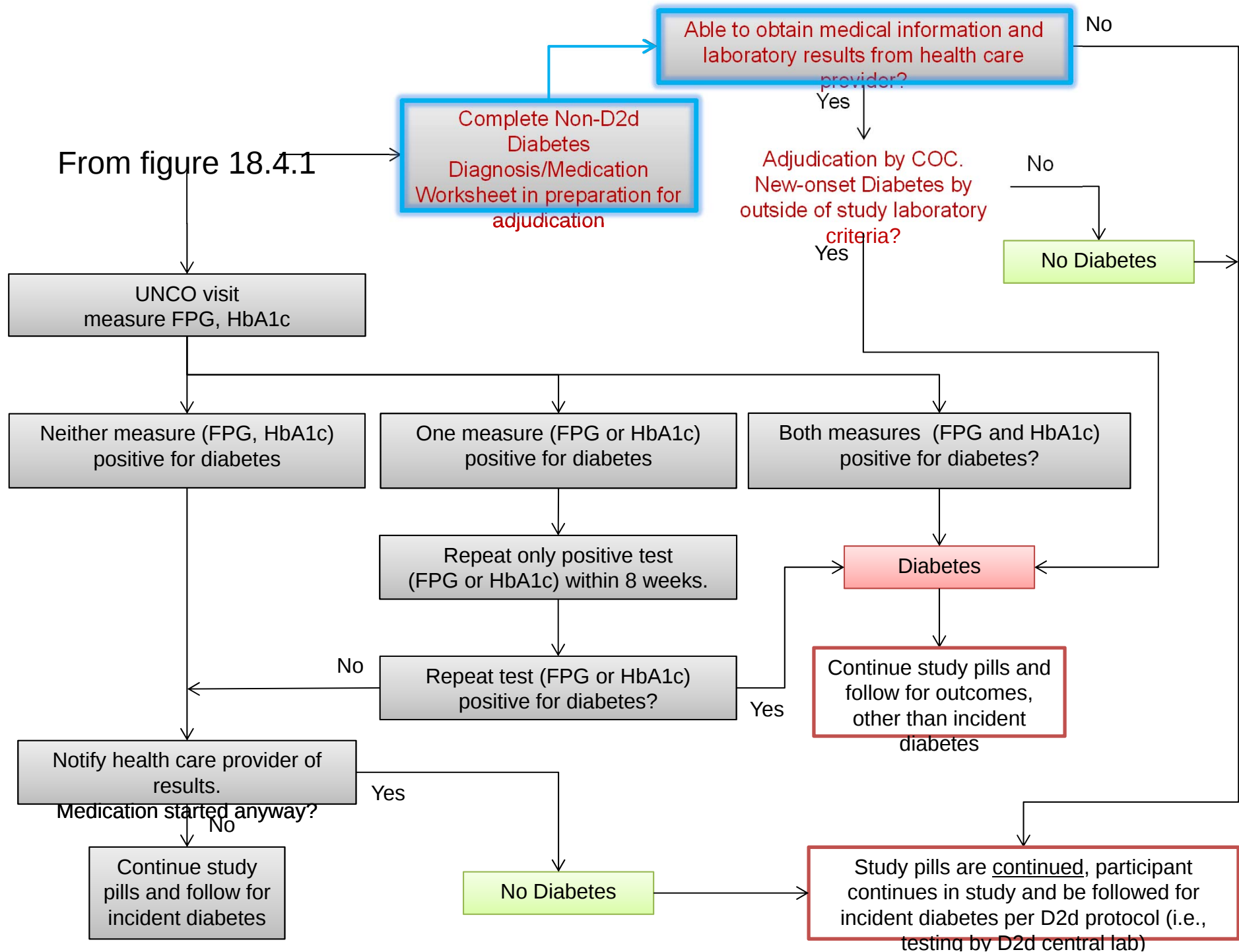
What is the next step?

1. Coordinator collects records from PCP and sends to CC for adjudication. Site staff discuss if this could have been prevented.
2. Ask participant to hold metformin for one week and schedule UNCO (unscheduled confirmatory) visit to collect FPG and HbA1c.





- In lieu of an Unscheduled Confirmatory (UNCO) visit, a regular D2d visit may be done provided the visit window is approaching



Case 2 (cont.)

- Site collected records from PCP office to send to CC for adjudication
- Clinical Outcomes Committee review

Date medical records received

06/Jul/2016

Provide a narrative summary of the medical records relevant to the diagnosis of diabetes or prescribing or start of diabetes-specific medication.

laboratory testing

Enter outside of study glycemia measures

	Date of test	Test	Result	Lab name or site of testing	
1	05/May/2016	Hemoglobin A1c (%)	6.6	Baton Rouge Clinic	
2	05/May/2016	Fasting plasma glucose (mg/dl)	138	Baton Rouge Clinic	

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This section is to be completed by the Clinical Outcomes Committee.

Choose one of the following:

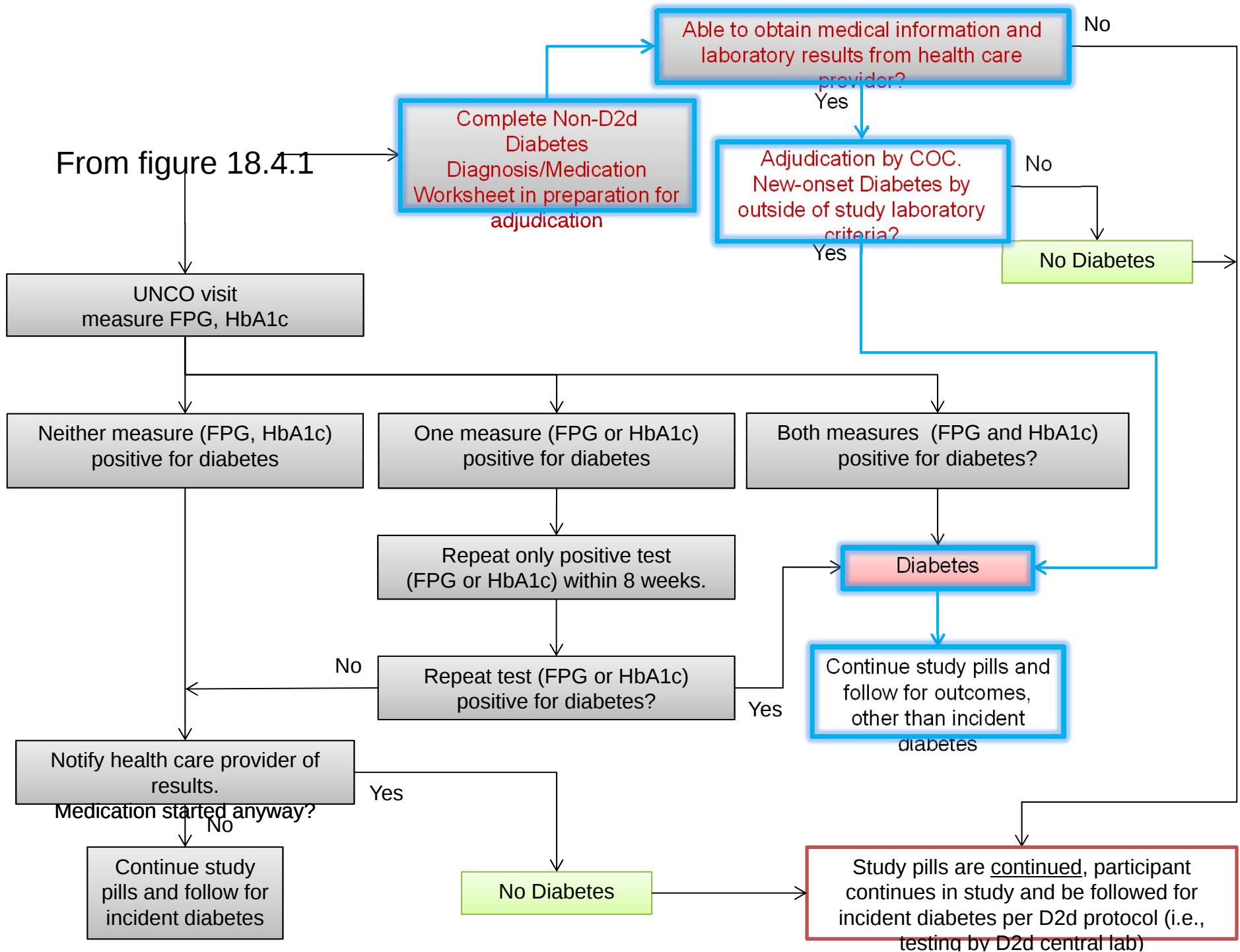
If new onset diabetes, indicate date of onset

Participant experienced new-onset diabetes

05/May/2016



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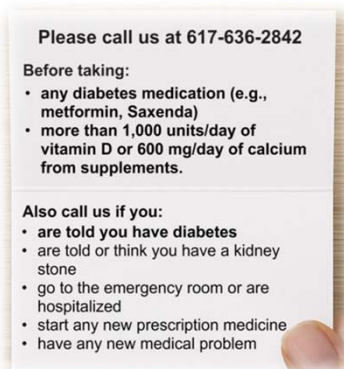
Case 3

- 70 y.o. woman, BMI 28.5, FH of diabetes, recruited via EMR
- BAS: A1c 6.2, FPG 114, 2hPG 186





Reviewed brochure with participant at *screening and randomization* visit



Provided participant with D2d appointment card



Letter sent via EMR to PCP about enrollment in study



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Case 3 (cont.)

3/24/2016 M03 Study principles reinforced

- ~3 weeks later participant informed coordinator that she saw her PCP and was told she has diabetes 😞
- She was given prescription for metformin, but wanted to try diet and exercise first. Metformin not started.



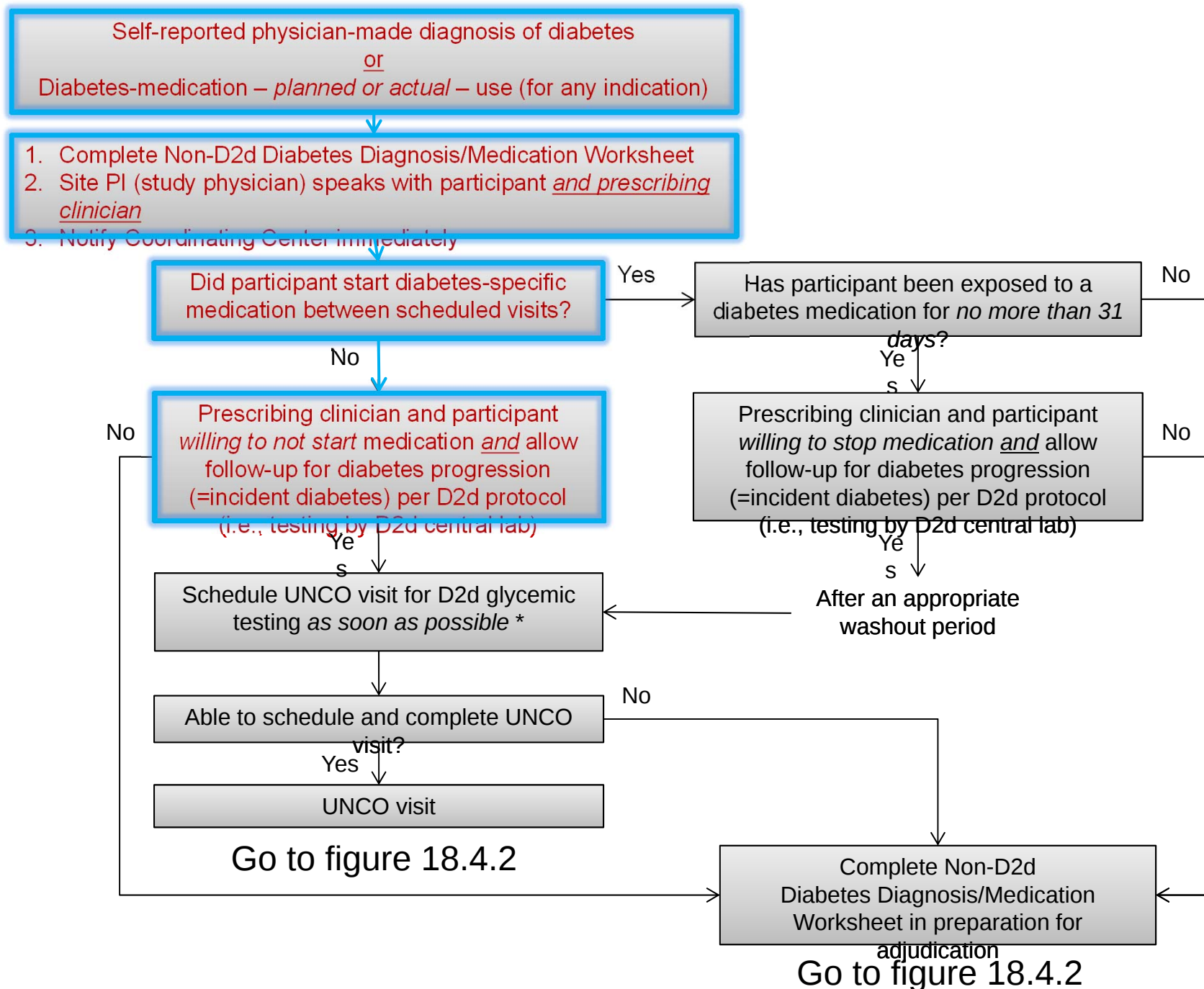
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Participant informed coordinator that she saw her PCP and was told she has diabetes. She was given Rx for Metformin, but wanted to try diet and exercise first. Metformin not started.

What is the next step?

1. Not sure, call the CC
2. Site PI and CC are informed immediately. Site PI discusses study design and rationale with participant and PCP to elicit PCP's intent for using diabetes medication.
3. Schedule UNCO to do OGTT
4. None of the above



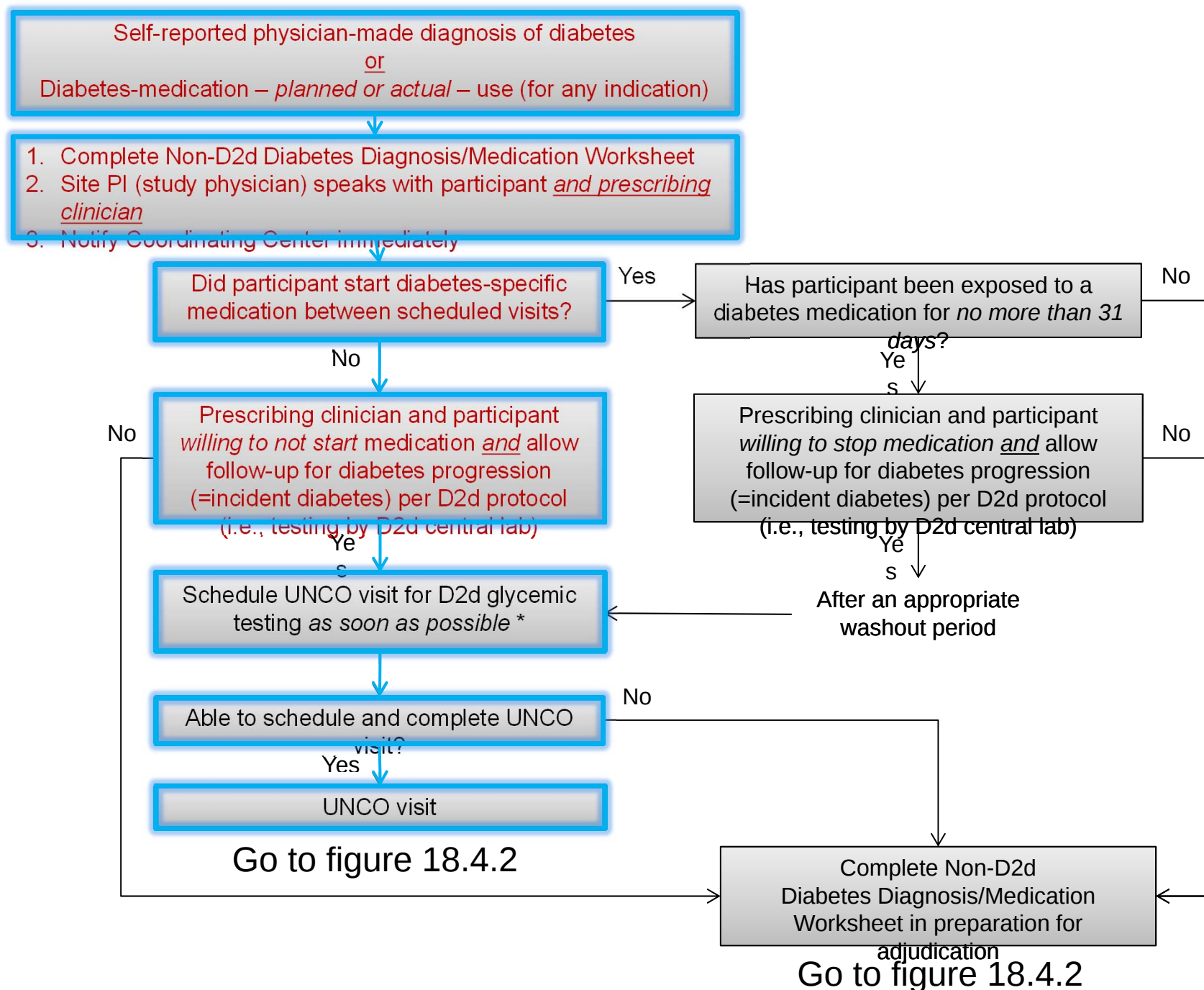


* In lieu of an UNCO visit, a regular D2d visit may be done provided the visit window is approaching

Case 3 – What Happened?

- Site PI informed
- Site PI communicated with PCP to determine intent. PCP agreed to hold off on metformin and allow participant to be followed by D2d.
- Participant scheduled for UNCO



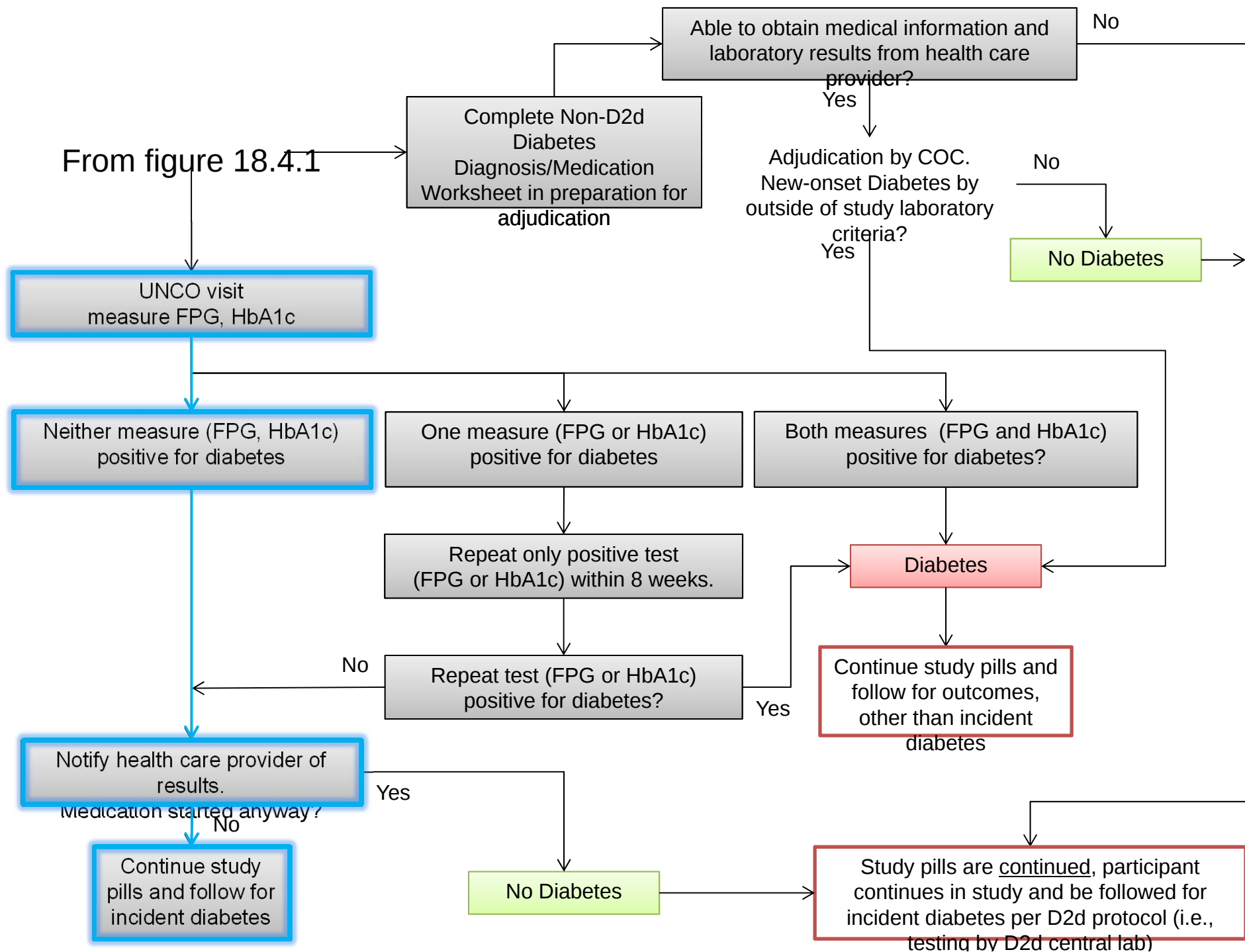


* In lieu of an UNCO visit, a regular D2d visit may be done provided the visit window is approaching

Case 3 – What Happened? (cont)

- UNCO
 - FPG and HbA1c negative





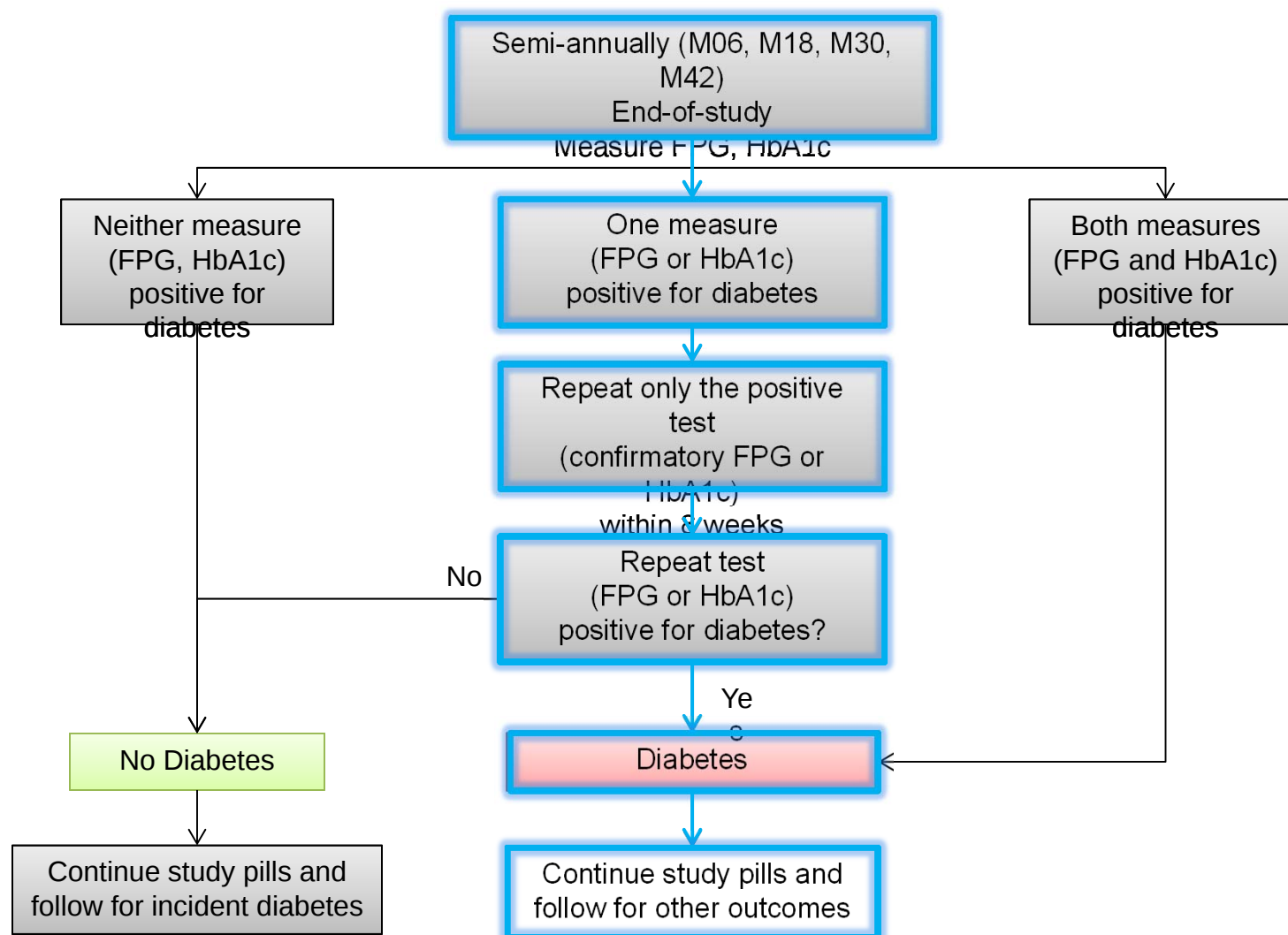
Case 3 (cont.)

At M06 visit:

- FPG negative
- HbA1c positive
- Participant scheduled for an UNCO visit to run HbA1c only
 - HbA1c positive => diabetes



Diabetes diagnosis – semi-annual visit



Case 3 – What Happened? (cont)

	Baseline 12/10/2015	UNCO 4/19/2016	M06 7/7/2016	UNCO 7/29/2016 (confirmation)
HbA1c (%)	6.2	6.4	6.5	6.5
FPG (mg/dL)	114	121	120	
2hPG (mg/dL)	186			



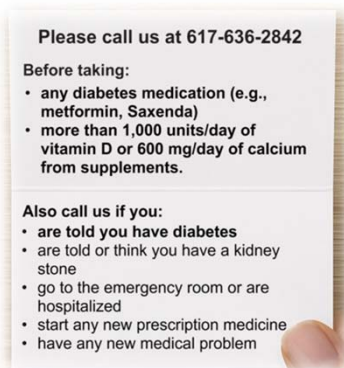
Case 4

- 76 y.o. man, BMI 35.6 , FH of diabetes, recruited via EMR
- BAS: A1c 6.4, FPG 109, 2hPG 159





Reviewed brochure with participant at randomization visit



Provided participant with D2d appointment card



Sent letter to PCP after randomization



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Case 4 (cont.)

- M09 phone call: participant states his new PCP diagnosed diabetes at his yearly physical exam and prescribed Metformin

“Oh, by the way...”

Between M03 and M09, participant changed PCP



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- M09 phone call, participant states his PCP diagnosed diabetes and prescribed him Metformin at his yearly physical exam

What is the next step?

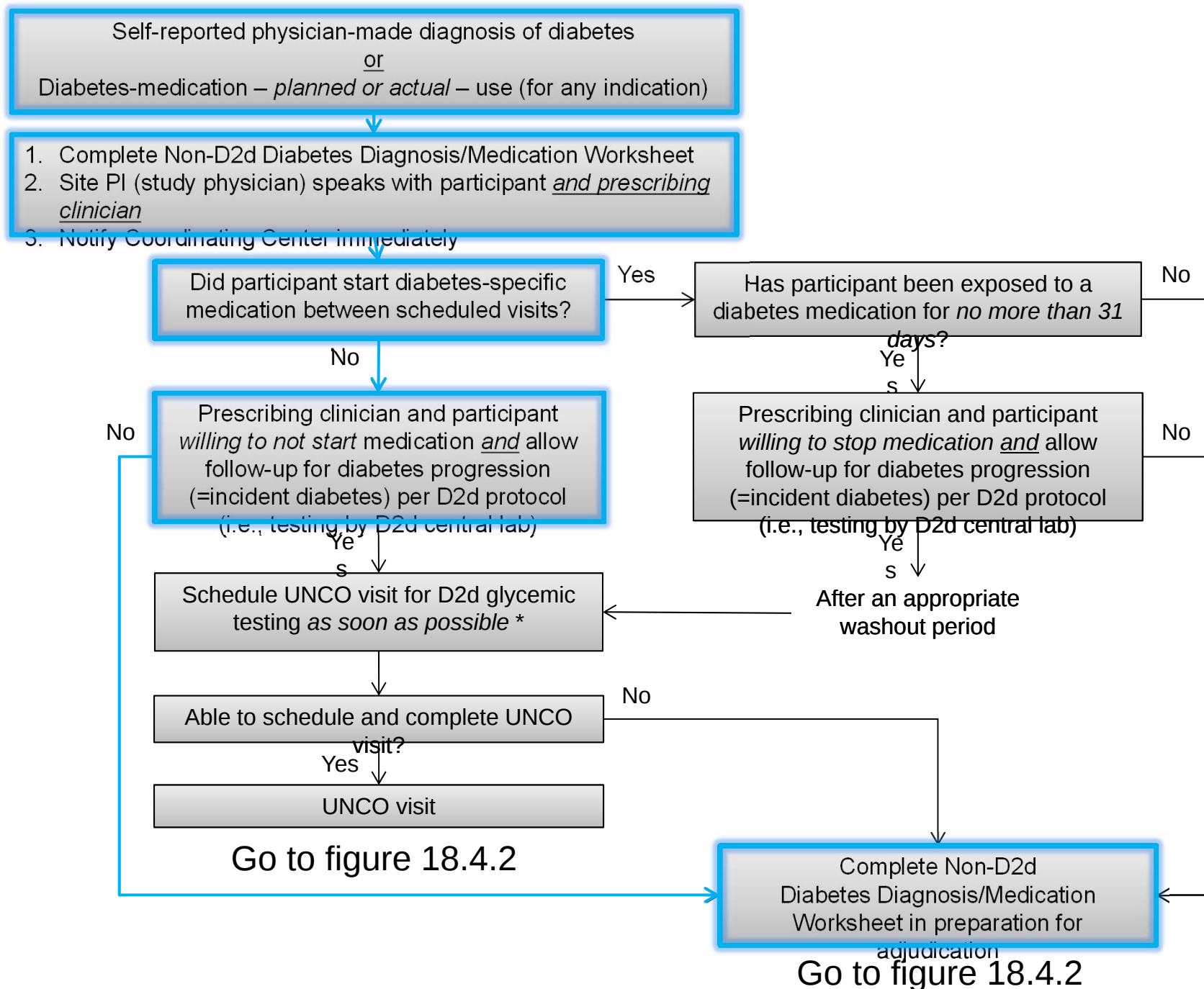
1. Not sure, call the CC
2. Site PI and CC are informed immediately. Site PI discusses study design and rationale with participant and PCP to elicit PCP's intent for using diabetes medication.
3. Schedule participant for an UNCO visit to do OGTT
4. None of the above



Case 4 (cont.)

- What happened
 - Site PI had conversation with PCP to inform about D2d protocol and see whether metformin can be stopped
 - PCP willing to stop metformin until D2d testing could be done, but did not commit to holding metformin for the duration of D2d because it is his practice to start metformin in cases like this
- UNCO not needed because long-term intent of the PCP to hold metformin is questionable, so case goes to adjudication
- Participant continues in D2d (regardless of results of adjudication)





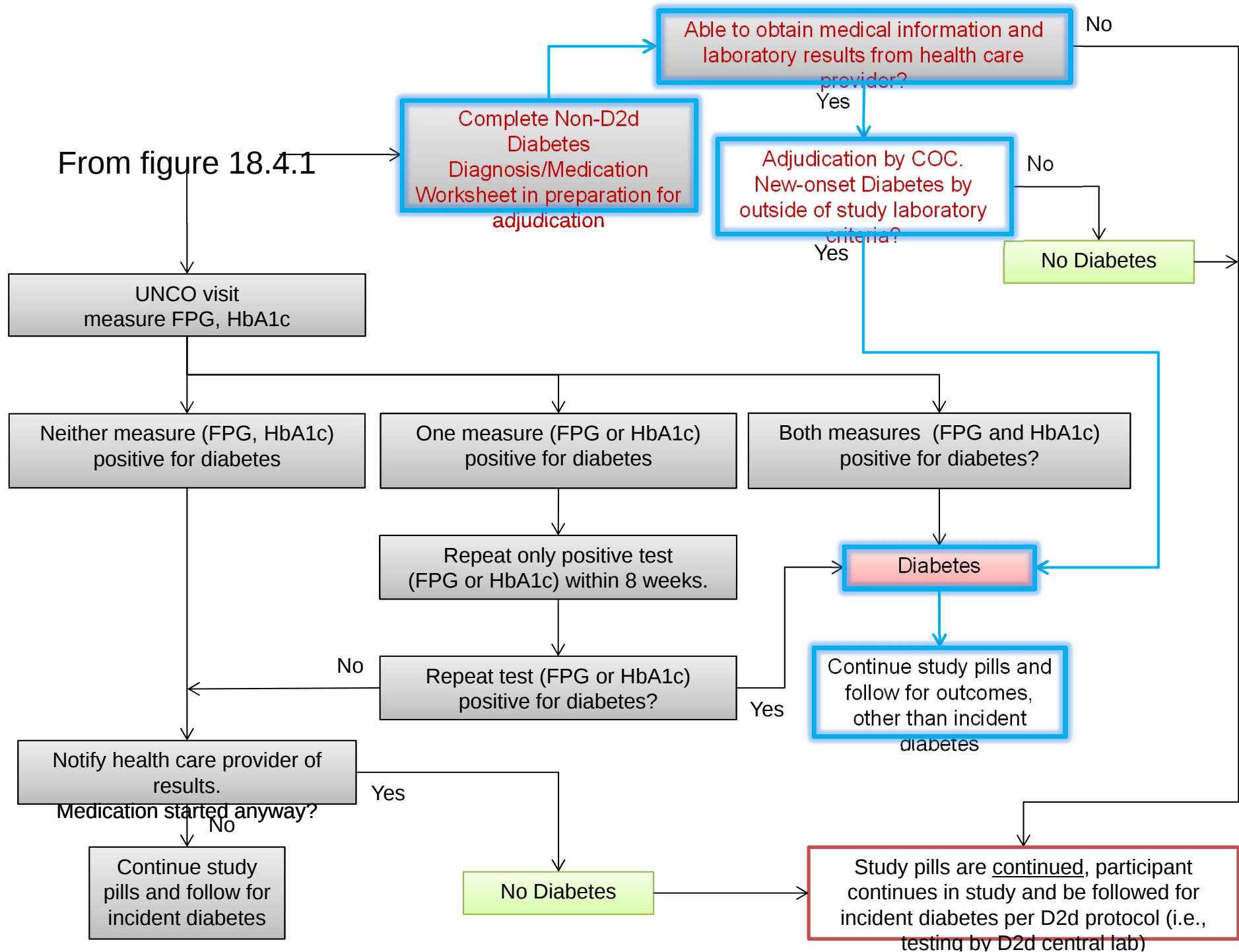
*In lieu of an UNCO visit, a regular D2d visit may be done provided the visit window is approaching

Case 4 (cont.)

- Site collected records from PCP office to send to CC for adjudication.
- Clinical Outcomes Committee review

Date medical records received					21/Jul/2016
Provide a narrative summary of the medical records relevant to the diagnosis of diabetes or prescribing or start of diabetes-specific medication.					
Enter outside of study glycemia measures					
#	Date of test	Test	Result	Lab name or site of testing	
1	19/May/2016	Hemoglobin A1c (%)	6.8	nordx	
2	19/May/2016	Fasting plasma glucose (mg/dl)	127	nordx	
=====					
This section is to be completed by the Clinical Outcomes Committee.					
Choose one of the following:					
If new onset diabetes, indicate date of onset					
Participant experienced new-onset diabetes					19/May/2016





If a case needs to be adjudicated:

1. Complete Diabetes Adjudication eCRF
2. Submit relevant medical records including lab results to CC
3. CC submits case to COC for review
4. When results are in, CC notifies site
5. Site completes Outcomes eCRF

Note: date of diabetes diagnosis is determined by COC



Discussion

