Chronic Overlapping Pain Condition Calculations

At baseline, when participants completed the CMSI (Complex Medical Symptoms Inventory) survey, positive responses to certain questions triggered the Research Coordinator to administer additional condition-specific questionnaires to determine if the participant has any of these six different COPCs (chronic overlapping pain conditions):

CFS = Chronic Fatigue Syndrome; variable name cfs_bin
FM = Fibromyalgia; variable name fm_bin
IBS = Irritable Bowel Syndrome; variable name ibs_bin
MIG = Migraine; variable names mi_bin and mi_ord
TMD = Temporomandibular Disorder; variable name tmd_bin
VUL = Vulvodynia (Females Only) ; variable name vdyn_bin

The table below shows the trigger questions for each condition:

CMSI Q#	SYMPTOM	CFS	FM	IBS	MIG	TMJ	VUL
4	Persistent fatigue not relieved with rest	X					
1	Muscle or joint pain	X	X				
19	Abdominal pain or discomfort			X			
33	Pulsating and/or one-sided headache pain or migraines				X		
23	Ear pain					X	
31	Jaw and/or face pain					X	
40	Constant burning or raw feeling at the opening of vagina (FEMALES ONLY)						X

The algorithms and resulting case report forms (CRFs) used to ascertain the presence or absence of each of these conditions changed partway through the MAPP I Study. Thus, below we present both the “old” and “new” criteria for each condition. The CRFs that correspond to the “new” criteria are reproduced at the end of each section.

Note that for MAPP I, we made the decision that missing values for each COPC would be treated as the absence of the condition, with the exception of Vulvodynia, which is always missing for men.

1. **CFS = Chronic Fatigue Syndrome**

    a. Old Criteria**:** Participant endorses 4 or more of the following:
        i. Impaired memory, concentration or attention
        ii. Sore throat
        iii. Muscle pain
        iv. Multi-joint pain without swelling
        v. New headaches
        vi. Unrefreshing sleep
        vii. Post-exertion malaise
        viii. Tender cervical or axillary lymph nodes

    b. New Criteria: Participant meets requirements for Major Fatigue Criteria PLUS 4 or more Ancillary Criteria as indicated on the CMSI-CFS2 CRF (Fukuda 1994 criteria)

        i. Major Fatigue Criteria: Must meet all 4 of the following requirements:
            1. Activity Reduced: YES response to Q#7 OR Q#8
            2. Fatigue present other than after exertion: NO response to Q#9
            3. Fatigue not relieved by rest: NO response to Q#10 OR Q#11
            4. Fatigue not lifelong: NO response to Q#2

        ii. Ancillary Symptoms Criteria: Participant must endorse 4 or more of the following:
            1. Q#12a AND Q#12b
            2. Q13a
            3. Q14a
            4. Q15a
            5. Q16a
            6. Q17a
            7. Q18a
            8. Q19a

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current Chronic Fatigue Symptoms (Fukuda 1994 criteria)

Instructions: The following questions are related to periods of fatigue lasting at least 6 months. An episode of fatigue or exhaustion is defined as "beginning" when you no longer felt that you had your normal amount of energy. An episode of fatigue or exhaustion is defined as "ending" when you felt basically back to normal.

1.	Have you ever had a period of ongoing fatigue or exhaustion lasting at least 6 months?	❑$_1$ Yes	❑$_0$ No **(Stop)**
2.	Do you consider your fatigue lifelong [from birth]?	❑$_1$ Yes	❑$_0$ No
3.	Are you currently experiencing such a period of ongoing fatigue or exhaustion lasting at least 6 months?	❑$_1$ Yes	❑$_0$ No
4.	During the last 6 months, have you experienced ongoing fatigue or exhaustion?	❑$_1$ Yes	❑$_0$ No **(Stop)**
5.	When did this period of fatigue begin?	YEAR _____ MONTH _____	
6.	Are you currently still experiencing this period of fatigue?	❑$_1$ Yes	❑$_0$ No **(Stop)**
7.	Compared to before the fatigue began, in the last 6 months have you substantially reduced your work or educational activities because of your fatigue?	❑$_1$ Yes	❑$_0$ No
8.	Compared to before the fatigue began, in the last 6 months have you substantially reduced your personal or social activities because of your fatigue?	❑$_1$ Yes	❑$_0$ No
9.	Is your fatigue present only following exertion, strenuous work, or exercise? That is, do you have fatigue at no other time except following exertion, strenuous work, or exercise?	❑$_1$ Yes	❑$_0$ No
10.	Is your fatigue substantially relieved by rest?	❑$_1$ Yes	❑$_0$ No
11.	After you rest, do you feel back to normal, that is, back to how you felt before the period of fatigue began?	❑$_1$ Yes	❑$_0$ No
12.	In the last 6 months, have you experienced ***impairment of short-term memory or concentration***?	❑$_1$ Yes	❑$_0$ No
	a. If **Yes**, have these ***memory or concentration problems*** been severe enough to cause you to substantially reduce your occupational, educational, social or personal activities?	❑$_1$ Yes	❑$_0$ No
	b. If **Yes**, have you had ***memory or concentration problems*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months?	❑$_1$ Yes	❑$_0$ No

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current Chronic Fatigue Symptoms - Continued

13. In the last 6 months, have you experienced a ***sore throat***? ❑1 Yes ❑0 No

    a. If **Yes**, have you had a ***sore throat*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

14. In the last 6 months, have you experienced ***muscle pain***? ❑1 Yes ❑0 No

    a. Have you had ***muscle pain*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

15. In the last 6 months, have you experienced ***joint pain involving more than one joint WITHOUT swelling or redness***? ❑1 Yes ❑0 No

    a. Have you had this ***joint pain*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

16. In the last 6 months, have you experienced ***headaches of a new type, pattern or severity***? ❑1 Yes ❑0 No

    a. Have you had this ***new type of headache*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

17. In the last 6 months, have you experienced ***non-refreshing sleep or not feeling rested when you wake up***? ❑1 Yes ❑0 No

    a. Have you had ***non-refreshing sleep or not feeling rested when you wake up*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

18 In the last 6 months, have you experienced ***fatigue or exhaustion***, after exertion, lasting more than 24 hours that you did not experience before the fatigue began? ❑1 Yes ❑0 No

    a. Have you had this ***new type of fatigue or exhaustion*** either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

19. In the last 6 months, have you experienced ***tender lymph glands in your neck or armpits***? ❑1 Yes ❑0 No

    a. Have you had ***tender lymph glands*** in your neck or armpits either persistently or recurrently (either continuously or off and on) over the entire last 6 months? ❑1 Yes ❑0 No

2. FM = Fibromyalgia

a. Old Criteria**:** Participant endorses all of the following:

i. Pain in the upper right quadrant of the body
ii. Pain in the upper left quadrant of the body
iii. Pain in the lower right quadrant of the body
iv. Pain in the lower left quadrant of the body
v. Pain in the axial skeleton (neck, chest, back, buttocks)

b. New Criteria: Participant meets ALL of the following as indicated on the CMSI-FM2 CRF:

i. Symptoms for 3+ months: YES response to Q#4
ii. No alternate explanation: NO response to Q#5
iii. Either:
1. Widespread Pain Index (WPI) >=7 AND Symptom Severity Score (SS) >=5 OR
2. Widespread Pain Index (WPI) between 3 and 6 AND Symptom Severity Score (SS) >=9

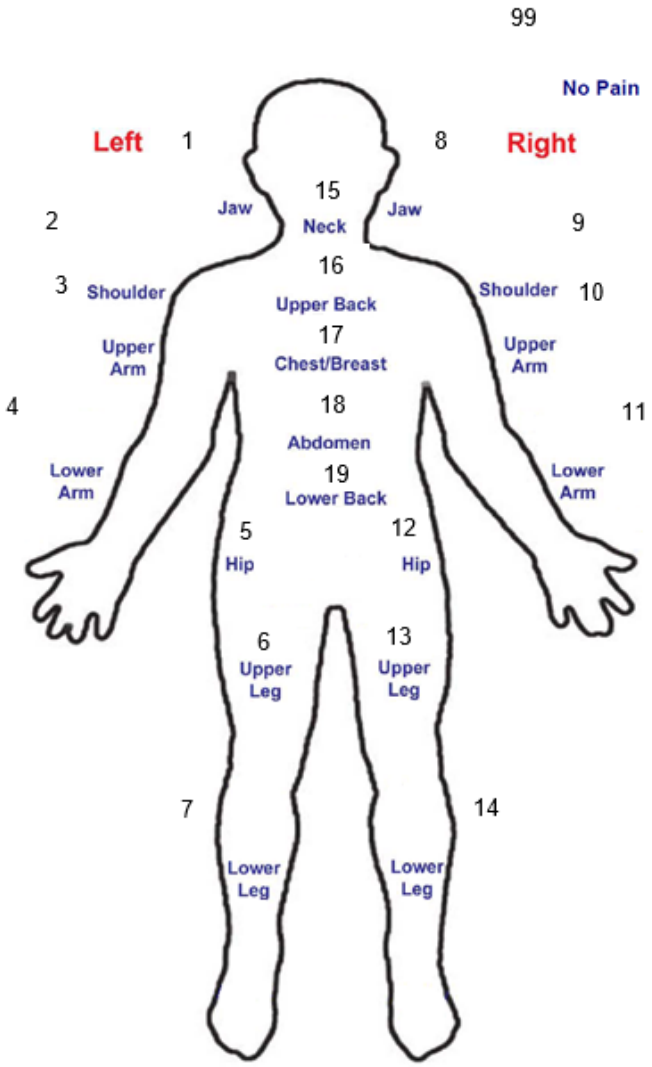
Where**:**

- WPI = Number of body areas with pain (0-19 as per diagram)
- SS = Sum of responses to questions 2a, b, and c (0-3 each) PLUS 3a, b, and c (0-1 each), for a total range of 0-12

COMPLEX MEDICAL SYMPTOMS INVENTORY

Fibromyalgia Symptoms Modified (ACR 2010 Fibromyalgia Diagnostic Criteria)

1. Please indicate below if you have had pain or tenderness over the past 7 days in each of the areas listed below. Check the boxes below for each area on the body diagram if you have had pain or tenderness. Be sure to ***mark both right side and left sides separately***.



- ☐99 No Pain
- ☐1 Left Jaw
- ☐2 Left Shoulder
- ☐3 Left Upper Arm
- ☐4 Left Lower Arm
- ☐5 Left Hip
- ☐6 Left Upper Leg
- ☐7 Left Lower Leg
- ☐8 Right Jaw
- ☐9 Right Shoulder
- ☐10 Right Upper Arm
- ☐11 Right Lower Arm
- ☐12 Right Hip
- ☐13 Right Upper Leg
- ☐14 Right Lower Leg
- ☐15 Neck
- ☐16 Upper Back
- ☐17 Chest/Breast
- ☐18 Abdomen
- ☐19 Lower Back

COMPLEX MEDICAL SYMPTOMS INVENTORY

Fibromyalgia Symptoms Modified (ACR 2010 Fibromyalgia Diagnostic Criteria) – Cont.

2. Using the following scale, indicate for each item your severity over the past week by checking the appropriate box.

   No problem
   Slight or mild problems: generally mild or intermittent
   Moderate: considerable problems; often present and/or at a moderate level
   Severe: continuous, life-disturbing problems

	No Problem	Slight or Mild	Moderate	Severe
a. Fatigue	❑0	❑1	❑2	❑3
b. Trouble thinking or remembering	❑0	❑1	❑2	❑3
c. Waking up tired (unrefreshed)	❑0	❑1	❑2	❑3

3. During the past 6 months have you had any of the following symptoms?

a. Pain or cramps in lower abdomen	❑1 Yes	❑0 No
b. Depression	❑1 Yes	❑0 No
c. Headache	❑1 Yes	❑0 No

4. Have the symptoms in questions 2-3 and pain been present at a similar level for at least 3 months? ❑1 Yes ❑0 No

5. Do you have a disorder that would otherwise explain the pain? ❑1 Yes ❑0 No

3. **IBS = Irritable Bowel Syndrome**

   a. **Old Criteria:** Participant endorses "Recurrent abdominal pain or discomfort (at least 3 days each month during the last 3 months with symptom onset at least 6 months prior to diagnosis)" which meets at least 2 of the following conditions:
      i. Is relieved with bowel movement (at least sometimes)
      ii. Has onset associated with a change in stool frequency (at least sometimes)
      iii. Has onset associated with a change in stool form or appearance (at least sometimes)

   b. **New Criteria:** Participant endorses abdominal pain at least 2-3 days per month (Q#1>2) AND at least two of the following sets of requirements:
      i. NO or N/A response to Q#2 (females only) AND Q#4 >0 AND Q#5 >0
      ii. Q#6 >0 AND Q#7 >0
      iii. Q#8 >0 AND Q#3 = 1

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current IBS Symptoms (Rome III Criteria)

1. In the last 3 months, how often did you have discomfort or pain anywhere in your abdomen?
   - ❑0 Never **(STOP)**
   - ❑1 Less than one day a month
   - ❑2 One day a month
   - ❑3 Two to three days a month
   - ❑4 One day a week
   - ❑5 More than one day a week
   - ❑6 Everyday

2. For women: Did this discomfort or pain occur only during your menstrual bleeding and not at other times?
   - ❑1 Yes
   - ❑0 No
   - ❑99 Does not apply (either due to menopause or male)

3. Have you had this discomfort or pain 6 months or longer?
   - ❑1 Yes
   - ❑0 No

4. How often did this discomfort or pain get better or stop after you had a bowel movement?
   - ❑0 Never or rarely
   - ❑1 Sometimes
   - ❑2 Often
   - ❑3 Most of the time
   - ❑4 Always

5. When this discomfort or pain started, did you have more frequent bowel movements?
   - ❑0 Never or rarely
   - ❑1 Sometimes
   - ❑2 Often
   - ❑3 Most of the time
   - ❑4 Always

6. When this discomfort or pain started, did you have less frequent bowel movements?
   - ❑0 Never or rarely
   - ❑1 Sometimes
   - ❑2 Often
   - ❑3 Most of the time
   - ❑4 Always

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current IBS Symptoms (Rome III Criteria) – Continued

7. When this discomfort or pain started, were your stools (bowel movements) looser?

- ❑0 Never or rarely
- ❑1 Sometimes
- ❑2 Often
- ❑3 Most of the time
- ❑4 Always

8. When this discomfort or pain started, how often did you have harder stools?

- ❑0 Never or rarely
- ❑1 Sometimes
- ❑2 Often
- ❑3 Most of the time
- ❑4 Always

9. In the last 3 months, how often did you have hard or lumpy stools?

- ❑0 Never or rarely
- ❑1 Sometimes
- ❑2 Often
- ❑3 Most of the time
- ❑4 Always

10. In the last 3 months, how often did you have loose mushy or watery stools?

- ❑0 Never or rarely
- ❑1 Sometimes
- ❑2 Often
- ❑3 Most of the time
- ❑4 Always

4. **MIG = Migraine**

   a. **Old Criteria:** Participant meets all of the following criteria:
      i. Headache attacks last for 4-72 hours
      ii. Two or more of the following are true:
         1. Unilateral pain
         2. Pulsating quality to the pain
         3. Moderate to severe intensity which inhibits or prohibits normal daily activities
         4. Aggravated by walking up stairs or similar routine physical activity
      iii. One or more of the following are true:
         1. Nausea and/or vomiting during the headache attack
         2. Sensitivity to light and sound
      iv. Headache is NOT associated with any of the following:
         1. Head trauma
         2. Vascular disorders
         3. Non-vascular intracranial disorders
         4. Substances or withdrawal
         5. Non-cephalic infection
         6. Metabolic disorder
         7. Disorder of the cranium, neck, eyes, ears, nose, sinus, teeth, mouth or other cranial structure

   b. **New Criteria:** Participants are first assigned to a 4-level ordinal variable, mi_ord:
      i. 0 : Not Migraine:
         1. No headaches longer than 4 hrs (Q#1c AND Q#1d NOT checked)
         2. Q#2 AND Q#3 are both 0 or missing
      ii. 3: Definite:
         1. Endorses headaches longer than 4 hours (Q#1c and/or Q#1d checked)
         2. Q#2 >1 AND Q#3 >1
      iii. 2: Probable: Meet criteria for duration/frequency OR symptom/intensity:
         1. Q#1c and/or Q#1d endorsed AND Q#2 = 1 or 2 AND Q#3 = 1 **OR**
         2. YES responses to one or more of (Q4a, Q4b, Q4c, Q4d) AND YES responses to two or more of (Q4e, Q4f, Q4l, Q4n, Q4p)
      iv. 1: Doubtful: Participants who don't meet the criteria listed in I, ii, or iii above are assigned to 1: Doubtful.

   Participants assigned a value of 2: Probable or 3: Definite for the ordinal variable as defined above meet the criteria for Migraine (mi_bin = 1)

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current Migraine Symptoms (HIS 2nd edition criteria, 2004)

1. How long is your typical headache? ***(Choose all that apply)***
   - ❑$_1$ Less than 30 Minutes
   - ❑$_1$ Between 30 Minutes and 4 Hours
   - ❑$_1$ Between 4 Hours and 3 Days? (untreated or unsuccessfully treated)
   - ❑$_1$ Longer than 3 days
2. How often do you have these headaches?
   - ❑$_0$ Never
   - ❑$_1$ Once or twice a year
   - ❑$_2$ Every few months
   - ❑$_3$ Monthly
   - ❑$_4$ Weekly
3. How many severe headaches (lasting more than 4 hours) have you had in the <u>past 6 months</u>?
   - ❑$_0$ None
   - ❑$_1$ 1-2
   - ❑$_2$ 3-5
   - ❑$_3$ More than 5
4. Do any of the following accompany your typical headache?

a.	Feeling sick to your stomach	❑$_1$ Yes	❑$_0$ No
b.	Vomiting	❑$_1$ Yes	❑$_0$ No
c.	More sensitive to light	❑$_1$ Yes	❑$_0$ No
d.	More sensitive to sound	❑$_1$ Yes	❑$_0$ No
e.	A throbbing feeling in your head	❑$_1$ Yes	❑$_0$ No
f.	Pain on only one side of your head	❑$_1$ Yes	❑$_0$ No
g.	Pain on both sides of your head	❑$_1$ Yes	❑$_0$ No
h.	A preceding warning such as problems with vision, speech, hearing, swallowing, strength or sensation	❑$_1$ Yes	❑$_0$ No ***(If No, skip to Q#4k)***
i.	Does this warning last less than 60 minutes?	❑$_1$ Yes	❑$_0$ No
j.	Do you have a headache less than 60 minutes following the warning?	❑$_1$ Yes	❑$_0$ No
k.	A decrease in your normal daily activity	❑$_1$ Yes	❑$_0$ No
l.	A pressing or tightening feeling	❑$_1$ Yes	❑$_0$ No
m.	Aggravated by routine physical activity	❑$_1$ Yes	❑$_0$ No
n.	Not aggravated by routine physical activity	❑$_1$ Yes	❑$_0$ No

5. **TMD = Temporomandibular Disorder**

    a. **Old Criteria:** Participant endorses one or more of the following:
        i. Jaw and/or face pain
        ii. Temple pain
        iii. Ear pain

    b. **New Criteria:** YES response to Q#1: Have you had persistent or recurrent pain in the face, jaw, temple, in front of the ear or in the ear in the past month?

COMPLEX MEDICAL SYMPTOMS INVENTORY
Current TMD Symptoms (TMD/RDC 2002)

1. Have you had persistent or recurrent pain in the face, jaw, temple, in front of the ear or in the ear in the past month? ❑$_1$ Yes ❑$_0$ No **(Stop)**

2. How would you rate your facial pain right now?

No Pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

3. In the past 6 months, how intense was your *worst* pain?

No Pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

4. In the past 6 months, on the *average*, how intense was your pain?
[That is, your usual pain at times you were experiencing pain.]

No Pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

5. About how many days in the past 6 months have you been kept from your usual activities (work, school or housework) because of facial pain? ___ ___ # of Days

6. In the past 6 months, how much has facial pain interfered with your daily activities?

No Interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

7. In the past 6 months, how much has facial pain changed your ability to take part in recreational, social and family activities?

No Change										Extreme change
0	1	2	3	4	5	6	7	8	9	10

8. In the past 6 months, how much has facial pain changed your ability to work (including housework)?

No Change										Extreme change
0	1	2	3	4	5	6	7	8	9	10

6. **VUL = Vulvodynia (Females Only)**

   a. **Old Criteria:** All of the following are true:
      i. Constant burning or raw feeling at the opening of the vagina AND/OR tender to the touch or pain with tampon insertion and/or intercourse
      ii. No itching at the opening of the vagina
      iii. No relief from anti-candidal therapy

   b. **New Criteria:** All of the following are true:
      i. YES response to Q#1 AND/OR Q#2
      ii. YES response to Q#3
      iii. YES response to Q#4
      iv. NO response to Q#6
      v. NO response to Q#7
      vi. NO response to Q#8

COMPLEX MEDICAL SYMPTOMS INVENTORY

Current Vulvodynia Symptoms – Females Only

1.	On the survey you indicated that you experience constant burning or raw feeling at the opening of the vagina – is this correct?	❑$_1$ Yes	❑$_0$ No
2.	Is your vaginal area tender to touch, or do you experience pain with tampon insertion and/or intercourse?	❑$_1$ Yes	❑$_0$ No
3.	Have these pain symptoms persisted for 3 months or more?	❑$_1$ Yes	❑$_0$ No
4.	Are you experiencing pain currently (w/in the last week)?	❑$_1$ Yes	❑$_0$ No
5.	On the survey you indicated that you experience itching at the opening of the vagina – is this correct?	❑$_1$ Yes	❑$_0$ No
6.	Could this pain be caused by a rash or lesion in the area?	❑$_1$ Yes	❑$_0$ No
7.	Is there a discharge, the onset of which can be associated with the onset of the pain or discomfort?	❑$_1$ Yes	❑$_0$ No
8.	Is this itching and discomfort relieved by the use of anti-candidal therapy (ie Monistat)?	❑$_1$ Yes	❑$_0$ No