



## The ME/CFS Priority Setting Partnership

# The Long List of ME/CFS Research Questions

### Causes and prevention

1. Is there a genetic link to ME/CFS? If yes, how does this affect the risk of ME/CFS in families? Could this lead to new treatments?
2. Why do some people develop ME/CFS following an infection? Is there a link with long-COVID?
3. Is ME/CFS caused by a faulty immune system? Is ME/CFS an autoimmune condition?
4. Are there factors that increase the risk of developing ME/CFS (such as stress, trauma or exposure to toxic chemicals)?
5. Do hormonal imbalances (such as thyroid hormone or cortisol imbalances) cause ME/CFS and/or affect symptoms? Could this lead to new treatments?
6. Can ME/CFS be prevented?
7. Is ME/CFS infectious? Can it be transmitted to others?
8. What causes ME/CFS to become severe?
9. What can be learnt about the cause of ME/CFS from clusters of cases?

### Diagnosis

10. How can an accurate and reliable diagnostic test be developed for ME/CFS?
11. How can the current approach to diagnosing ME/CFS be improved, to reduce delays and include other conditions commonly linked to ME/CFS, such as Postural Orthostatic Tachycardia Syndrome (POTS), Ehlers-Danlos syndromes (EDS) and Mast Cell Activation Syndrome (MCAS)?

### Lifetime risks and course of the illness

12. What is the typical course of ME/CFS over a lifetime, for children and adults? What influences this?

13. Why do symptoms vary between people with ME/CFS? Why are there short term and long term changes in ME/CFS symptoms?
14. Why are women at greater risk of ME/CFS than men?
15. Are there different types of ME/CFS linked to different causes and/or how severe it becomes? Do different types of ME/CFS need different treatments and/or have different chances of recovery?
16. How do some people recover from ME/CFS? How might this understanding help others?
17. Do hormonal changes (such as during the menstrual cycle, pregnancy and menopause) affect ME/CFS symptoms? Does ME/CFS affect menstrual cycles, risks around pregnancy or menopause?
18. Which conditions are commonly linked with ME/CFS, such as Ehlers-Danlos syndromes (EDS), Postural Orthostatic Tachycardia Syndrome (POTS), gut disorders and Mast Cell Activation Syndrome (MCAS)? Do they have the same root cause or does one cause the other?
19. What causes people with ME/CFS to relapse and their symptoms to get worse? Are there ways to prevent or minimise relapses?
20. Does ME/CFS affect life-expectancy?
21. Are people from ethnic minorities at greater risk of developing ME/CFS? What barriers do they face to getting a diagnosis and treatment?
22. Are there long-term effects of repeated post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed)?

## Treatment and management

23. Can prompt treatment and advice when diagnosed prevent ME/CFS from getting worse over time? What does this mean for people whose illness starts gradually?
24. Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat Postural Orthostatic Tachycardia Syndrome (POTS)?
25. Do complementary and alternative therapies benefit people with ME/CFS?

26. How does ME/CFS impact on people's physical health, and does their physical health impact on their ME/CFS? What can people with ME/CFS safely do to maintain their physical health?
27. Does changing diet or taking supplements help people with ME/CFS?
28. Is there a way for people with ME/CFS to monitor and manage their activities (such as using a heart rate monitor) to avoid triggering post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed)?
29. Are there ways to objectively measure how severely someone is affected by ME/CFS and whether their symptom levels are changing over time?

## **Underlying mechanisms and their treatments**

30. What is the biological mechanism that causes post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed) in people with ME/CFS? How is this best treated and managed?
31. What causes the central and peripheral nervous systems (brain, spinal cord and nerves in the body) to malfunction in people with ME/CFS? Could this understanding lead to new treatments?
32. How are mitochondria, responsible for the body's energy production, affected in ME/CFS? Could this understanding lead to new treatments?
33. Does the immune system continue to over-function or under-function in some people with ME/CFS to cause symptoms? What does this mean for treatment and risks from infections and vaccinations, including COVID-19?
34. What happens to muscle function in people with ME/CFS?
35. What causes some people with ME/CFS to become intolerant to alcohol, chemicals and/ or medicines?
36. What are the links between nervous, digestive and immune systems that could cause ME/CFS symptoms?
37. How is the transport of nutrients/electrolytes in and out of cells affected in people with ME/CFS? Could this understanding lead to new treatments?
38. Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? If so, how is this best treated?

39. Does continuing viral or bacterial infection cause ME/CFS symptoms? If so, are antivirals or antibiotics effective treatments?

## Health services

40. What would be the make-up of a high-quality specialist service for people with ME/CFS? Would this improve the treatment and care of people with ME/CFS?
41. Why don't some health professionals accept ME/CFS is a serious illness? What would help them to recognise and respond appropriately to people's symptoms?
42. How can the needs of people with ME/CFS best be met when accessing and using health and social care services (for example while in hospital)?
43. Based on people's experiences, what does ongoing monitoring and care for people with ME/CFS need to include?

## Causes of symptoms and their treatment

44. What causes sensory problems in people with ME/CFS (such as sensitivity to light, noise, smell and touch)? How are these best managed and treated?
45. What causes orthostatic intolerance (e.g. feeling dizzy or unwell on standing or sitting up) or problems controlling body temperature? How are these best managed and treated?
46. What causes headaches and migraines in ME/CFS? How are these best treated and managed?
47. What causes skin problems in ME/CFS? How are these best treated and managed?
48. What causes sleep problems and sleep pattern changes in people with ME/CFS? How are these best managed and treated?
49. What causes ongoing fatigue (tiredness or exhaustion) in people with ME/CFS? How is this best treated and managed?
50. What causes gut problems, difficulties with swallowing and eating in people with ME/CFS? How are these best managed, for example with tube feeding for people who are very severely affected?
51. Do heart problems, changes to blood cells or blood/lymph circulation cause ME/CFS symptoms? If so, how are these best treated?

52. Do postural or structural problems in the head, neck and spine cause symptoms of ME/CFS? If so, how are these best treated?
53. What causes pain in people with ME/CFS? How is this best treated and managed?
54. What causes brain fog in people with ME/CFS? How is this best treated and managed?

## **Social and psychological impacts and support**

55. What are the impacts of ME/CFS on people's quality of life, including work, finances and family and social life? What practical support would be most effective, particularly in terms of social care and welfare benefits?
56. What are the psychological impacts of ME/CFS? How are these best treated and managed?
57. What harms do people with ME/CFS experience as a result of the lack of professional recognition and stigma from the condition? How can these best be addressed?
58. What practical and emotional support do carers/ parents of people with ME/CFS need and how can these needs be met?
59. What support do pupils and students with ME/CFS need to help them with their education?