

116TH CONGRESS  
1ST SESSION

# H. R. 3573

To increase research, education, and treatment for cerebral cavernous malformations.

---

## IN THE HOUSE OF REPRESENTATIVES

JUNE 27, 2019

Mr. LUJÁN (for himself, Ms. HAALAND, and Ms. TORRES SMALL of New Mexico) introduced the following bill; which was referred to the Committee on Energy and Commerce

---

## A BILL

To increase research, education, and treatment for cerebral cavernous malformations.

1 *Be it enacted by the Senate and House of Representa-*  
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Cerebral Cavernous  
5 Malformations Clinical Awareness, Research, and Edu-  
6 cation Act of 2019” or the “CCM–CARE Act”.

7 **SEC. 2. FINDINGS.**

8 Congress finds as follows:

9 (1) Cerebral cavernous malformations (referred  
10 to in this section as “CCM”), also known as cav-

1       ernous angioma, or cavernoma, is a devastating  
2       blood vessel disease characterized by vascular lesions  
3       that develop and grow within the brain and spinal  
4       cord.

5           (2) Detection of CCM lesions is achieved  
6       through costly and specialized medical imaging tech-  
7       niques, often not accessible or convenient to patients  
8       who need them.

9           (3) While CCM is a common type of vascular  
10      anomaly, many individuals are not aware they have  
11      the disease until the onset of serious clinical symp-  
12      toms. CCM is often inherited unknowingly.

13          (4) CCM affects an estimated 600,000 people  
14      in the United States.

15          (5) Individuals diagnosed with CCM may expe-  
16      rience neurological deficits, seizure, stroke, or sud-  
17      den death.

18          (6) Due to limited research, there is currently  
19      no treatment for CCM other than brain and spinal  
20      surgery, and only for certain patients.

21          (7) There is also a shortage of trained physi-  
22      cians to provide skilled and timely diagnosis and ap-  
23      propriate treatment for CCM.

24          (8) While the hereditary form of CCM may  
25      occur among any ethnicity, the presence of a muta-

tion called the “common Hispanic mutation”, has passed through 14 or more generations of American descendants from the original Spanish settlers of the Southwest in the 1590s. New Mexico has the highest population density of CCM in the world; Texas, Arizona, and Colorado also have high rates of CCM due to the common Hispanic mutation.

(9) A second mutation (CCM2 Common Deletion) originating in the Southeastern United States before 1800 has increased rates of the illness in South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Texas, Oklahoma, Kentucky, Kansas, and northern California.

**SEC. 3. EXPANSION AND COORDINATION OF ACTIVITIES OF  
NATIONAL INSTITUTES OF HEALTH WITH RE-  
SPECT TO CEREBRAL CAVERNOUS MAL-  
FORMATIONS RESEARCH.**

Part B of title IV of the Public Health Service Act (42 U.S.C. 284 et seq.) is amended by adding at the end the following:

**“SEC. 409K. CEREBRAL CAVERNOUS MALFORMATIONS RE-  
SEARCH ACTIVITIES.**

“(a) EXPANSION AND COORDINATION OF ACTIVITIES.—The Director of NIH, in coordination with the directors of the National Institute of Neurological Disorders

1 and Stroke, the National Center for Advancing Transla-  
2 tional Sciences, the National Heart, Lung, and Blood In-  
3 stitute, and other national research institutes, as appro-  
4 priate, for the purpose of conducting research and related  
5 activities concerning cerebral cavernous malformations  
6 (referred to in this section as ‘CCM’)—

7 “(1) shall strengthen and coordinate efforts of  
8 the National Institutes of Health; and

9 “(2) may award grants and cooperative agree-  
10 ments to public or nonprofit private entities (includ-  
11 ing State health departments, political subdivisions  
12 of States, universities, and other medical or edu-  
13 cational entities).

14 “(b) ACTIVITIES.—The research and related activi-  
15 ties described in subsection (a) shall include the following:

16 “(1) CLINICAL, TRANSLATIONAL, AND BASIC  
17 RESEARCH.—The Director of NIH shall conduct or  
18 support, through funding opportunity announce-  
19 ments, grants, or cooperative agreements, basic, clin-  
20 ical, and translational research on CCM, including  
21 research on—

22 “(A) the identification and development of  
23 biomarkers that fulfill the requirement of the  
24 Food and Drug Administration for biomarker  
25 qualification as proper measures of CCM patho-

1           genetic biology or response to clinical interven-  
2           tion;

3           “(B) safety or efficacy for new or  
4           repurposed currently approved drugs for CCM  
5           treatment;

6           “(C) research related to improving and  
7           measuring the quality of life for individuals  
8           with CCM and their families;

9           “(D) contributions of genetic variation to  
10          clinical presentation as targets for therapy;

11          “(E) early detection, diagnosis, and treat-  
12          ment of CCM;

13          “(F) clinical training programs aimed at  
14          increasing the number of scientists and clini-  
15          cians who are trained to treat patients and  
16          carry out the research described in this para-  
17          graph;

18          “(G) continued development and expansion  
19          of novel animal models for preclinical research  
20          relating to CCM;

21          “(H) pre-clinical and clinical research re-  
22          lated to repurposing currently approved drugs  
23          for CCM treatment;

24          “(I) proteomic, pharmacological, and cell  
25          biological analysis of CCM molecules;

1           “(J) biological mechanisms for lesion gen-  
2           esis, development, and maturation;

3           “(K) biological mechanisms for lesion  
4           bleeding and symptomology;

5           “(L) novel biomedical and pharmacological  
6           interventions designed to inhibit new lesion de-  
7           velopment, lesion growth, and lesion bleeding;

8           “(M) novel biomedical and pharmacological  
9           interventions designed to target existing lesions  
10          to reduce their size and clinical activity;

11          “(N) continued research related to under-  
12          standing better the natural history and clinical  
13          variation associated with CCM, particularly as  
14          it relates to the development of drug develop-  
15          ment tools and clinical outcome assessments;

16          “(O) the gut-brain axis and the effects of  
17          microbiome composition on clinical symptomolo-  
18          gy; and

19          “(P) the microbiome as a therapeutic tar-  
20          get for CCM treatment.

21          “(2) FACILITATION OF RESEARCH RESOURCES;  
22          CLINICAL TRIAL PREPAREDNESS.—

23          “(A) IN GENERAL.—The Director of NIH  
24          shall award grants and contracts to public or  
25          nonprofit private entities to fund all or part of

1 the cost of planning, establishing, and providing  
2 basic operating support for a network of CCM  
3 Clinical Research Centers, including Coordinating and Participating centers regarding re-  
4 search on various forms of CCM.  
5

6 “(B) CLINICAL AND RESEARCH COORDINA-  
7 TION CENTERS.—

8 “(i) IN GENERAL.—The Director of  
9 NIH shall build upon the network created  
10 by the U01 Clinical Trial Readiness Re-  
11 search Project to identify and support the  
12 development of 2 geographically distributed  
13 national clinical and research coordinating  
14 centers with unique clinical expertise and  
15 the potential for coordinating multi-site  
16 clinical drug trials with respect to CCM.

17 “(ii) DUTIES.—The coordinating cen-  
18 ters identified under clause (i) shall pro-  
19 vide a model for the participation centers  
20 described in paragraph (3), facilitate med-  
21 ical research to develop a cure for CCM,  
22 and enhance the medical care of individ-  
23 uals with CCM nationwide, including by—

24 “(I) maintaining an institutional  
25 infrastructure capable of hosting clin-

1 ical trials and facilitating translational  
2 research projects and collaborations  
3 for clinical trials;

4 “(II) implementing the programs  
5 dedicated to patient education, patient  
6 outreach, and awareness developed by  
7 the Cerebral Cavernous Malformations  
8 Consortium under subsection  
9 (c)(3)(B);

10 “(III) developing the capacity to  
11 establish and maintain communication  
12 with other major CCM research and  
13 care institutions internationally for in-  
14 formation sharing and coordination of  
15 research activities;

16 “(IV) demonstrating clinical ex-  
17 pertise in the management of CCM  
18 and appointing a director and support  
19 staff, including a trainee and patient  
20 representative, for CCM research pro-  
21 gramming;

22 “(V) treating a sufficient number  
23 of eligible patients for participation  
24 with particular focus on unique sub-  
25 populations, such as patients with the



1 common Hispanic mutation, Ash-  
2 kenazi Jewish mutation, CCM2 Com-  
3 mon Deletion, or CCM3 gene muta-  
4 tion carriers; and

5 “(VI) maintaining a telehealth  
6 infrastructure to support and provide  
7 clinical consultation for remote and  
8 underserved communities.

9 “(3) PARTICIPATION CENTERS.—

10 “(A) IN GENERAL.—The Director of NIH  
11 shall build upon the network created by the  
12 U01 Clinical Trial Readiness Research Project  
13 to identify and support the development of ap-  
14 proximately 6 to 10 clinical and research par-  
15 ticipation centers to facilitate medical research  
16 to develop a cure for CCM and enhance the  
17 medical care of individuals with CCM, in part-  
18 nership with the coordinating centers under  
19 paragraph (2) and other national and inter-  
20 national entities, as appropriate.

21 “(B) ELIGIBILITY.—To qualify for selec-  
22 tion as a participation center under subpara-  
23 graph (A), an entity shall—

24 “(i) at the time of selection—

1           “(I) be affiliated with an estab-  
2           lished research network of the Na-  
3           tional Institutes of Health; and

4           “(II) have the potential to par-  
5           ticipate in a multisite clinical drug  
6           trial with respect to CCM;

7           “(ii) demonstrate—

8           “(I) an institutional infrastruc-  
9           ture capable of hosting a clinical trial  
10          site and facilitating translational  
11          projects and collaborations for clinical  
12          trials;

13          “(II) the capacity to maintain  
14          communication with other major CCM  
15          research and care institutions inter-  
16          nationally for information sharing and  
17          coordination of research activities, es-  
18          pecially through health information  
19          technology; and

20          “(III) clinical expertise in CCM  
21          management or complete the CCM  
22          clinical training program under sub-  
23          section (c)(4); and

24          “(iii) have a sufficient number of eli-  
25          gible patients with CCM.

1                   “(C) DURATION OF SUPPORT.—The Direc-  
2                   tor of NIH may provide support for partici-  
3                   pation centers under this section for a period not  
4                   to exceed 5 years. The Director of NIH may ex-  
5                   tend the period of support for a center for one  
6                   or more additional periods, not to exceed an ad-  
7                   ditional 5 years, if the operations of such center  
8                   have been reviewed by an appropriate technical  
9                   and scientific peer review group established by  
10                  the Director of NIH and if such group has rec-  
11                  ommended to the Director that such period  
12                  should be extended.

13               “(c) CEREBRAL CAVERNOUS MALFORMATIONS CON-  
14               SORTIUM.—

15               “(1) IN GENERAL.—The Director of NIH shall  
16               build upon the network created by the U01 Clinical  
17               Trial Readiness Research Project to convene a Cere-  
18               bral Cavernous Malformations Research Consortium  
19               (referred to in this section as the ‘consortium’).

20               “(2) MEMBERSHIP.—The consortium—

21                   “(A) shall include representatives of—

22                           “(i) the coordinating centers selected  
23                           under subsection (b)(2); and

24                           “(ii) at least 1 national CCM patient  
25                           advocacy organization, which may be an

1           entity that receives a grant or contract  
2           under subsection (b)(2)(A); and

3           “(B) may include representatives of the  
4           National Institutes of Health or the Food and  
5           Drug Administration, in an advisory or ex offi-  
6           cio role.

7           “(3) RESPONSIBILITIES.—Through a consensus  
8           based decisionmaking model, the consortium shall  
9           divide assignments and be responsible for—

10           “(A) developing and implementing training  
11           programs for clinicians and scientists in accord-  
12           ance with paragraph (4);

13           “(B) developing patient education, out-  
14           reach, and awareness programs and materials,  
15           which may be tailored for specific regional  
16           needs at coordinating centers, including—

17           “(i) a regional multimedia public  
18           awareness campaign;

19           “(ii) patient education materials for  
20           distribution by regional physician and sur-  
21           geon offices;

22           “(iii) an education program for ele-  
23           mentary and secondary school nurses to fa-  
24           cilitate early detection and diagnosis of

1 CCM in areas in which there is a high den-  
2 sity of cases of CCM;

3 “(iv) regular regional patient and  
4 family oriented educational conferences;  
5 and

6 “(v) nationally relevant electronic  
7 health teaching and communication tools  
8 and a network of professional capacity and  
9 patient and family support; and

10 “(C) preparing a biannual report to Con-  
11 gress, in accordance with paragraph (5).

12 “(4) TRAINING PROGRAM FOR CLINICIANS AND  
13 SCIENTISTS.—

14 “(A) IN GENERAL.—The consortium, in  
15 cooperation with the coordinating centers, shall  
16 establish or expand a physician training pro-  
17 gram, including information and education on  
18 advances in the diagnosis and treatment of  
19 CCM, and training and continuing education  
20 through programs for scientists, physicians,  
21 medical students, and other health professionals  
22 and care coordinators who provide care for pa-  
23 tients with CCM, telehealth, and research rel-  
24 evant to CCM, for the purpose of supporting  
25 the development of new participation centers

1 through educational programming to gain the  
2 expertise needed to become clinical and research  
3 participation centers with the potential to par-  
4 ticipate in clinical drug trials.

5 “(B) STIPENDS.—The Director of NIH  
6 may provide stipends for health professionals  
7 who are enrolled in the training programs de-  
8 scribed in subparagraph (A).

9 “(C) ELIGIBILITY.—To be eligible to par-  
10 ticipate in the training program, an individual  
11 shall be affiliated with an entity that is in an  
12 existing clinical research network of the Na-  
13 tional Institutes of Health.

14 “(5) REPORT TO CONGRESS.—The consortium  
15 shall biennially submit to the Committee on Health,  
16 Education, Labor, and Pensions of the Senate and  
17 the Committee on Energy and Commerce of the  
18 House of Representatives a report that describes the  
19 research, education, and other activities on CCM  
20 conducted or supported through the Department of  
21 Health and Human Services. Each such report shall  
22 include—

23 “(A) a research plan;

24 “(B) provisions specifying the amounts ex-  
25 pended by the Department of Health and

1 Human Services with respect to various forms  
2 of CCM, including those affected by the com-  
3 mon Hispanic Mutation, Ashkenazi Jewish mu-  
4 tation, CCM2 Common Deletion, CCM3 gene  
5 mutations, and other familial and sporadic  
6 forms of cerebral cavernous malformation; and  
7 “(C) recommendations for particular  
8 projects or types of projects that the national  
9 research institutes or other entities in the field  
10 of research should conduct on inherited or non-  
11 inherited forms of CCM.

12 “(d) PRIORITIZE CCM FUNDING FOR BIOTECH.—  
13 The Director of NIH, in coordination with the directors  
14 of the National Institute of Neurological Disorders and  
15 Stroke, the National Center for Advancing Translational  
16 Sciences, the National Heart, Lung, and Blood Institute,  
17 and other national research institutes, as appropriate,  
18 shall prioritize the provision of grant funding for small  
19 biotechnology entities that are working to develop treat-  
20 ments for CCM.”.

1 **SEC. 4. CENTERS FOR DISEASE CONTROL AND PREVEN-**  
2 **TION CEREBRAL CAVERNOUS MALFORMA-**  
3 **TIONS SURVEILLANCE AND RESEARCH PRO-**  
4 **GRAMS.**

5 Part B of title III of the Public Health Service Act  
6 (42 U.S.C. 243 et seq.) is amended by inserting after sec-  
7 tion 317T the following:

8 **“SEC. 317U. CEREBRAL CAVERNOUS MALFORMATIONS SUR-**  
9 **VEILLANCE AND RESEARCH PROGRAMS.**

10 “(a) IN GENERAL.—The Secretary, acting through  
11 the Director of the Centers for Disease Control and Pre-  
12 vention, may award grants in such sums as may be nec-  
13 essary and cooperative agreements to public or nonprofit  
14 private entities (including State health departments, polit-  
15 ical subdivisions of States, universities, and other medical  
16 or educational entities) for the collection, analysis, and re-  
17 porting of data on cerebral cavernous malformations (re-  
18 ferred to in this section as ‘CCM’).

19 “(b) NATIONAL CEREBRAL CAVERNOUS MALFORMA-  
20 TIONS EPIDEMIOLOGY PROGRAM.—The Secretary shall  
21 award grants and cooperative agreements, including tech-  
22 nical assistance, to public or nonprofit private entities  
23 for—

24 “(1) the collection, analysis, and reporting of  
25 data on CCM; and



1           “(2) epidemiological activities, including encour-  
2           aging consistency in ICD–10 coding, collecting and  
3           analyzing information on the number, incidence, cor-  
4           relates, and symptoms of cases and the clinical util-  
5           ity of specific practice patterns.

6           “(c) NATIONAL SURVEILLANCE PROGRAM.—The  
7           Secretary shall—

8           “(1) provide for a national surveillance program  
9           for the purpose of carrying out epidemiological ac-  
10          tivities regarding CCM, including collecting and ana-  
11          lyzing information on the number, incidence, cor-  
12          relates, and symptoms of cases of CCM and the clin-  
13          ical utility (including costs and benefits) of specific  
14          practice patterns; and

15          “(2) wherever possible, ensure that the surveil-  
16          lance program is coordinated with the data and sam-  
17          ple collection activities of the National Institutes of  
18          Health under section 409K.

19          “(d) TECHNICAL ASSISTANCE.—In making awards  
20          under this section, the Secretary may provide direct tech-  
21          nical assistance, including personnel support.

22          “(e) COORDINATION WITH CLINICAL CENTERS.—  
23          The Secretary shall ensure that epidemiological informa-  
24          tion is made available to clinical centers as supported by

1 the Director of the National Institutes of Health under  
2 section 409K.

3 “(f) AUTHORIZATION OF APPROPRIATIONS.—There  
4 are authorized to be appropriated such sums as may be  
5 necessary to carry out this section.”.

6 **SEC. 5. FOOD AND DRUG ADMINISTRATION CEREBRAL CAV-**  
7 **ERNOUS MALFORMATIONS CLINICAL TRIAL**  
8 **PREPAREDNESS AND SUPPORT PROGRAM.**

9 (a) BIOMARKER QUALIFICATION PROGRAM.—The  
10 Secretary of Health and Human Services, acting through  
11 the Commissioner of Food and Drugs, shall coordinate  
12 with clinical centers, investigators, and advocates to sup-  
13 port the qualification of appropriate surrogate biomarkers  
14 in an effort to hasten the pace of clinical trials for cerebral  
15 cavernous malformation.

16 (b) CLINICAL OUTCOME ASSESSMENT QUALIFICA-  
17 TION.—The Secretary of Health and Human Services, act-  
18 ing through the Commissioner of Food and Drugs, shall  
19 coordinate with clinical centers, investigators, and advo-  
20 cates to support the qualification of newly developed pa-  
21 tient reported outcome measures for quality of life as a  
22 clinical outcome in an effort to hasten the pace of clinical  
23 trials for cerebral cavernous malformation.

24 (c) INVESTIGATIONAL NEW DRUG APPLICATION.—  
25 The Secretary of Health and Human Services, acting

1 through the Commissioner of Food and Drugs, shall co-  
2 ordinate with clinical centers, investigators, and advocates  
3 to support appropriate investigational new drug applica-  
4 tions under section 505(i) of the Federal Food, Drug, and  
5 Cosmetic Act (21 U.S.C. 355(i)) in an effort to hasten  
6 the pace of clinical trials for cerebral cavernous malforma-  
7 tion.

8 (d) ADAPTIVE TRIAL DESIGN AND EXPEDITED RE-  
9 VIEW PATHWAYS.—The Secretary of Health and Human  
10 Services, acting through the Commissioner of Food and  
11 Drugs, shall coordinate with clinical centers, investigators,  
12 and advocates to support appropriate adaptive trial de-  
13 signs for rare disease research and expedited peer review  
14 mechanisms for including Orphan Drug Designation, Fast  
15 Track, Breakthrough Therapy Designation, Priority Re-  
16 view or Accelerated Review, where appropriate, in an ef-  
17 fort to hasten the pace of clinical trials for cerebral cav-  
18 ernous malformation.

○