

116TH CONGRESS
1ST SESSION

S. 2010

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

IN THE SENATE OF THE UNITED STATES

JUNE 27, 2019

Mr. UDALL (for himself and Mr. HEINRICH) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

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-

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

8 (9) A second mutation (CCM2 Common Dele-
 9 tion) originating in the Southeastern United States
 10 before 1800 has increased rates of the illness in
 11 South Carolina, Georgia, Florida, Alabama, Mis-
 12 sissippi, Louisiana, Texas, Oklahoma, Kentucky,
 13 Kansas, and northern California.

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

18 Part B of title IV of the Public Health Service Act
 19 (42 U.S.C. 284 et seq.) is amended by adding at the end
 20 the following:

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

23 “(a) EXPANSION AND COORDINATION OF ACTIVI-
 24 TIES.—The Director of NIH, in coordination with the di-
 25 rectors of the National Institute of Neurological Disorders

1 and Stroke, the National Center for Advancing
2 Translational Sciences, the National Heart, Lung, and
3 Blood Institute, and other national research institutes, as
4 appropriate, for the purpose of conducting research and
5 related activities concerning cerebral cavernous malforma-
6 tions (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) preclinical 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 symptom-
18 ology; 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 participa-
3 tion 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 1 or
6 more additional periods, not to exceed an addi-
7 tional 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.

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