

115TH CONGRESS
1ST SESSION

S. 475

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

IN THE SENATE OF THE UNITED STATES

FEBRUARY 28, 2017

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 2017” 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 17 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 **SEC. 3. EXPANSION AND COORDINATION OF ACTIVITIES OF**
9 **NATIONAL INSTITUTES OF HEALTH WITH RE-**
10 **SPECT TO CEREBRAL CAVERNOUS MAL-**
11 **FORMATIONS RESEARCH.**

12 Part B of title IV of the Public Health Service Act
13 (42 U.S.C. 284 et seq.) is amended by adding at the end
14 the following:

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

17 “(a) EXPANSION AND COORDINATION OF ACTIVI-
18 TIES.—The Director of NIH, in coordination with the di-
19 rectors of the National Institute of Neurological Disorders
20 and Stroke, the National Center for Advancing Transla-
21 tional Sciences, the National Heart, Lung, and Blood In-
22 stitute, and other national research institutes, as appro-
23 priate, for the purpose of conducting research and related
24 activities concerning cerebral cavernous malformations
25 (referred to in this section as ‘CCM’)—

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

3 “(2) may award grants and cooperative agree-
4 ments to public or nonprofit private entities (includ-
5 ing State health departments, political subdivisions
6 of States, universities, and other medical or edu-
7 cational entities).

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

10 “(1) CLINICAL, TRANSLATIONAL, AND BASIC
11 RESEARCH.—The Director of NIH shall conduct or
12 support, through funding opportunity announce-
13 ments, grants, or cooperative agreements, basic, clin-
14 ical, and translational research on CCM, including
15 research on—

16 “(A) the identification and development of
17 biomarkers that fulfill the requirement of the
18 Food and Drug Administration for biomarker
19 qualification as proper measures of phenotypic
20 variation;

21 “(B) safety or efficacy for new or
22 repurposed currently approved drugs for CCM
23 treatment;

1 “(C) research related to improving the
2 quality of life for individuals with CCM and
3 their families;

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

6 “(E) early detection, diagnosis, and treat-
7 ment of CCM;

8 “(F) clinical training programs aimed at
9 increasing the number of scientists and clini-
10 cians who are trained to treat patients and
11 carry out the research described in this para-
12 graph;

13 “(G) continued development and expansion
14 of novel animal models for preclinical research
15 relating to CCM;

16 “(H) pre-clinical and clinical research re-
17 lated to repurposing currently approved drugs
18 for treatment of CCM;

19 “(I) proteomic, pharmacological, and cell
20 biological analysis of CCM molecules;

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

23 “(K) biological mechanisms for lesion
24 bleeding and symptomology; and

1 “(L) novel biomedical and pharmacological
2 interventions designed to inhibit new lesion de-
3 velopment, lesion growth, and lesion bleeding.

4 “(2) FACILITATION OF RESEARCH RESOURCES;
5 CLINICAL TRIAL PREPAREDNESS.—

6 “(A) IN GENERAL.—The Director of NIH
7 shall award grants and contracts to public or
8 nonprofit private entities to fund all or part of
9 the cost of planning, establishing, and providing
10 basic operating support for a network of CCM
11 Clinical Research Centers, including Coordin-
12 ating and Participating centers regarding re-
13 search on various forms of CCM.

14 “(B) CLINICAL AND RESEARCH COORDINA-
15 TION CENTERS.—

16 “(i) IN GENERAL.—The Director of
17 NIH shall identify and support the devel-
18 opment of 2 geographically distributed na-
19 tional clinical and research coordinating
20 centers with unique clinical expertise and
21 the potential for coordinating multi-site
22 clinical drug trials with respect to CCM.

23 “(ii) DUTIES.—The coordinating cen-
24 ters identified under clause (i) shall pro-
25 vide a model for the participation centers

1 described in paragraph (3), facilitate med-
2 ical research to develop a cure for CCM,
3 and enhance the medical care of individ-
4 uals with CCM nationwide, including by—

5 “(I) maintaining an institutional
6 infrastructure capable of hosting clin-
7 ical trials and facilitating translational
8 research projects and collaborations
9 for clinical trials;

10 “(II) implementing the programs
11 dedicated to patient education, patient
12 outreach, and awareness developed by
13 the Cerebral Cavernous Malformations
14 Consortium under subsection
15 (c)(3)(B);

16 “(III) developing the capacity to
17 establish and maintain communication
18 with other major CCM research and
19 care institutions internationally for in-
20 formation sharing and coordination of
21 research activities;

22 “(IV) demonstrating clinical ex-
23 pertise in the management of CCM
24 and appointing a director and support
25 staff, including a trainee and patient

1 representative, for CCM research pro-
2 gramming;

3 “(V) treating a sufficient number
4 of eligible patients for participation
5 with particular focus on unique sub-
6 populations, such as patients with the
7 common Hispanic mutation, Ash-
8 kenazi Jewish mutation, or CCM3
9 gene mutation carriers; and

10 “(VI) maintaining a telehealth
11 infrastructure to support and provide
12 clinical consultation for remote and
13 underserved communities.

14 “(3) PARTICIPATION CENTERS.—

15 “(A) IN GENERAL.—The Director of NIH
16 shall identify and support the development of
17 approximately 6 to 10 clinical and research par-
18 ticipation centers to facilitate medical research
19 to develop a cure for CCM and enhance the
20 medical care of individuals with CCM, in part-
21 nership with the coordinating centers under
22 paragraph (2) and other national and inter-
23 national entities, as appropriate.

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

4 “(i) at the time of selection—

5 “(I) be affiliated with an estab-
6 lished research network of the Na-
7 tional Institutes of Health; and

8 “(II) have the potential to par-
9 ticipate in a multisite clinical drug
10 trial with respect to CCM;

11 “(ii) demonstrate—

12 “(I) an institutional infrastruc-
13 ture capable of hosting a clinical trial
14 site and facilitating translational
15 projects and collaborations for clinical
16 trials;

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

24 “(III) clinical expertise in CCM
25 disease management or complete the

1 CCM clinical training program under
2 subsection (c)(4); and

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

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

17 “(c) CEREBRAL CAVERNOUS MALFORMATIONS CON-
18 SORTIUM.—

19 “(1) IN GENERAL.—The Director of NIH shall
20 convene a Cerebral Cavernous Malformations Re-
21 search Consortium (referred to in this section as the
22 ‘consortium’).

23 “(2) MEMBERSHIP.—The consortium—

24 “(A) shall include representatives of—

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

3 “(ii) at least 1 national CCM patient
4 advocacy organization, which may be an
5 entity that receives a grant or contract
6 under subsection (b)(2)(A); and

7 “(B) may include representatives of the
8 National Institutes of Health or the Food and
9 Drug Administration, in an advisory or ex offi-
10 cio role.

11 “(3) RESPONSIBILITIES.—Through a consensus
12 based decisionmaking model, the consortium shall
13 divide assignments and be responsible for—

14 “(A) developing and implementing training
15 programs for clinicians and scientists in accord-
16 ance with paragraph (4);

17 “(B) developing patient education, out-
18 reach, and awareness programs and materials,
19 which may be tailored for specific regional
20 needs at coordinating centers, including—

21 “(i) a regional multimedia public
22 awareness campaign;

23 “(ii) patient education materials for
24 distribution by regional physician and sur-
25 geon offices;

1 “(iii) an education program for ele-
2 mentary and secondary school nurses to fa-
3 cilitate early detection and diagnosis of
4 CCM in areas in which there is a high den-
5 sity of cases of CCM;

6 “(iv) regular regional patient and
7 family-oriented educational conferences;
8 and

9 “(v) nationally relevant electronic
10 health teaching and communication tools
11 and a network of professional capacity and
12 patient and family support; and

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

15 “(4) TRAINING PROGRAM FOR CLINICIANS AND
16 SCIENTISTS.—

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

1 tients with CCM, telehealth, and research rel-
2 evant to CCM, for the purpose of supporting
3 the development of new participation centers
4 through educational programming to gain the
5 expertise needed to become clinical and research
6 participation centers with the potential to par-
7 ticipate in clinical drug trials.

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

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

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

1 “(A) a research plan;

2 “(B) provisions specifying the amounts ex-
3 pended by the Department of Health and
4 Human Services with respect to various forms
5 of CCM, including those affected by the com-
6 mon Hispanic Mutation, Ashkenazi Jewish mu-
7 tation, CCM3 gene mutations, and other famil-
8 ial and sporadic forms of cerebral cavernous
9 malformation; and

10 “(C) recommendations for particular
11 projects or types of projects that the national
12 research institutes or other entities in the field
13 of research should conduct on inherited or non-
14 inherited forms of CCM.”.

15 **SEC. 4. CENTERS FOR DISEASE CONTROL AND PREVEN-**
16 **TION CEREBRAL CAVERNOUS MALFORMA-**
17 **TIONS SURVEILLANCE AND RESEARCH PRO-**
18 **GRAMS.**

19 Part B of title III of the Public Health Service Act
20 (42 U.S.C. 243 et seq.) is amended by inserting after sec-
21 tion 317T the following:

22 **“SEC. 317U. CEREBRAL CAVERNOUS MALFORMATIONS SUR-**
23 **VEILLANCE AND RESEARCH PROGRAMS.**

24 “(a) IN GENERAL.—The Secretary, acting through
25 the Director of the Centers for Disease Control and Pre-

1 vention, may award grants in such sums as may be nec-
2 essary and cooperative agreements to public or nonprofit
3 private entities (including State health departments, polit-
4 ical subdivisions of States, universities, and other medical
5 or educational entities) for the collection, analysis, and re-
6 porting of data on cerebral cavernous malformations (re-
7 ferred to in this section as ‘CCM’).

8 “(b) NATIONAL CEREBRAL CAVERNOUS MALFORMA-
9 TIONS EPIDEMIOLOGY PROGRAM.—The Secretary shall
10 award grants and cooperative agreements, including tech-
11 nical assistance, to public or nonprofit private entities
12 for—

13 “(1) the collection, analysis, and reporting of
14 data on CCM; and

15 “(2) epidemiological activities, including col-
16 lecting and analyzing information on the number, in-
17 cidence, correlates, and symptoms of cases and the
18 clinical utility of specific practice patterns.

19 “(c) NATIONAL SURVEILLANCE PROGRAM.—The
20 Secretary shall—

21 “(1) provide for a national surveillance program
22 for the purpose of carrying out epidemiological ac-
23 tivities regarding CCM, including collecting and ana-
24 lyzing information on the number, incidence, cor-
25 relates, and symptoms of cases of CCM and the clin-

1 ical utility (including costs and benefits) of specific
2 practice patterns; and

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

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

10 “(e) COORDINATION WITH CLINICAL CENTERS.—
11 The Secretary shall ensure that epidemiological informa-
12 tion is made available to clinical centers as supported by
13 the Director of the National Institutes of Health under
14 section 409K.

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

18 **SEC. 5. FOOD AND DRUG ADMINISTRATION CEREBRAL CAV-**
19 **ERNOUS MALFORMATIONS CLINICAL TRIAL**
20 **PREPAREDNESS AND SUPPORT PROGRAM.**

21 (a) BIOMARKER QUALIFICATION PROGRAM.—The
22 Secretary of Health and Human Services, acting through
23 the Commissioner of Food and Drugs, shall coordinate
24 with clinical centers, investigators, and advocates to sup-
25 port the qualification of appropriate surrogate biomarkers

1 in an effort to hasten the pace of clinical trials for cerebral
2 cavernous malformation.

3 (b) CLINICAL OUTCOME ASSESSMENT QUALIFICA-
4 TION.—The Secretary of Health and Human Services, act-
5 ing through the Commissioner of Food and Drugs, shall
6 coordinate with clinical centers, investigators, and advo-
7 cates to support qualification of newly developed patient
8 reported outcome measures for quality of life as a clinical
9 outcome in an effort to hasten the pace of clinical trials
10 for cerebral cavernous malformation.

11 (c) INVESTIGATIONAL NEW DRUG APPLICATION.—
12 The Secretary of Health and Human Services, acting
13 through the Commissioner of Food and Drugs, shall co-
14 ordinate with clinical centers, investigators, and advocates
15 to support appropriate investigational new drug applica-
16 tions under section 505(i) of the Federal Food, Drug, and
17 Cosmetic Act (21 U.S.C. 355(i)) in an effort to hasten
18 the pace of clinical trials for cerebral cavernous malforma-
19 tion.

20 (d) ADAPTIVE TRIAL DESIGN AND EXPEDITED RE-
21 VIEW PATHWAYS.—The Secretary of Health and Human
22 Services, acting through the Commissioner of Food and
23 Drugs, shall coordinate with clinical centers, investigators,
24 and advocates to support appropriate adaptive trial de-
25 signs for rare disease research and expedited review mech-

1 anisms for including Fast Track, Breakthrough Therapy
2 Designation, Priority and/or Accelerated Review, where
3 appropriate, in an effort to hasten the pace of clinical
4 trials for cerebral cavernous malformation.

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