MAY 2019 NATIONAL REPORT

PAVING THE PATH FOR FAMILY-CENTERED DESIGN:

A NATIONAL REPORT ON FAMILY CAREGIVER ROLES IN MEDICAL PRODUCT DEVELOPMENT

National Alliance for Caregiving

IN PARTNERSHIP WITH

LEAD
Leaders Engaged on Alzheimer's Disease

ACKNOWLEDGMENTS

The National Alliance for Caregiving is proud to present "*Paving the Path for Family-Centered Design: A National Report on Family Caregivers' Roles in Medical Product Development*." The national Summit and this report were made possible through the contributions and direction of the following subject matter experts on caregiving and patient-focused medical product development:

Author

K. Kimberly McCleary, Founder & CEO, The Kith Collective

Project Directors

C. Grace Whiting, J.D., President and CEO, National Alliance for Caregiving

Ian Kremer, J.D., Executive Director, Leaders Engaged on Alzheimer's Disease (LEAD Coalition)

Reviewers and Subject-Matter Experts

Mousumi Bose, PhD, Assistant Professor, Nutrition and Food Studies, Montclair State University

Annie Kennedy, Senior Vice President of Legislation and Public Policy, Parent Project Muscular Dystrophy

Debra Lappin, J.D., Principal, Faegre BD Consulting

Schiffon Wong, M.P.H., Executive Director, Global Evidence & Value Development, Merck KGaA, Darmstadt, Germany | EMD Serono

The national Summit and this report were made possible through grant and contract funding from:

Leaders Engaged on Alzheimer's Disease Coalition (LEAD Coalition)

EMD Serono

The Allergan Foundation

Graphic Design and Layout

Julie Rathjens, Hello Brand | Design Creative

FOREWORD

Biomedical innovation is not a solitary endeavor; it is a team process. People living with various health conditions and their friends and family members are increasingly being viewed and treated as essential partners in the delivery of health care. Informed by their lived experiences, these citizen scientists often can provide remarkable and pivotal insights into what drugs and devices ("medical products") are needed, what therapeutic benefits matter and how much, what degree of risk or potential harms are tolerable, how clinical research should be conducted, and how safety and efficacy should be measured.

Starting in 2012, the U.S. Food and Drug Administration, in recognizing the critical role of patient-input, launched a series of meetings known as the "Patient Focused Drug Development (PFDD) initiative" throughout which the phrase "and caregiver" percolated. PFDD experts and multi-stakeholder groups issued written guidelines that rightly acknowledged roles that family and friends play in determining, facilitating, and providing care. Yet the word "caregiver" was often an afterthought; more than not, we've heard the phrase, "When I say 'patient,' I mean patient AND caregiver."

The person living with illness, disease, or disability may or may not have a caregiver and may or may not have clear communication with informal caregivers who can support them through the course of their medical conditions. Likewise, many caregivers often are unprepared to provide and sustain care, having received little training on how to use medical products and how to balance care responsibilities with other individual needs.

The person receiving care and the persons providing care offer complementary insights into the way that disease and disability impacts families and informal social structures. It is critical to define pathways for caregivers to provide additive input that does not replace the voice of the patient – input that provides new understanding into how medical products are used by informal partners in care delivery.

Improving health outcomes depends on scientists, regulators, payers, and clinicians knowing not only that a medical product is safe and effective, but also that a patient and caregiver will use the product and do so with fidelity. That requires understanding and addressing the views of patients and those of caregivers – as distinct and different from one another.

To start the dialogue on this vital topic, the National Alliance for Caregiving and the Leaders Engaged on Alzheimer's Disease (LEAD) Coalition convened a summit to explore salient roles for caregivers to participate in medical product development, a process that is – at last – becoming more patient-centered. We intend this report – the initial result of the summit – to catalyze even more robust discussion and action, some possibilities for which are outlined in these pages.

The demand for caregivers is fast outstripping the available supply. We must build a pathway for friends and relatives to provide care without sacrificing their own quality of life and that better recognizes and values their unique perspectives, always protecting the patient's autonomy and voice. Improving the care that people living with illness or disability receive depends on it.

Sincerely,

C. Grace Whiting, J.D.
President & CEO
National Alliance for Caregiving

Ian Kremer, J.D.
Executive Director
Leaders Engaged on Alzheimer's Disease (LEAD) Coalition

TABLE OF CONTENTS

In this report, the term "caregiver" refers to "a family member or other individual who has a significant relationship with, and who provides a broad range of assistance to, an individual with a chronic or other health condition, disability, or functional limitation," as defined in the RAISE Family Caregivers Act. Terms and definitions are addressed in more detail on page 8.

INTRODUCTION

Shifts in cultural expectations, advances in technology, and patient-driven policy changes have combined to expand opportunities for patients' perspectives to shape biomedical research and development, regulatory decision-making, and healthcare delivery.[1] It is the premise of this report that distinct roles for family caregivers should be formally included in these emerging opportunities.

The Food and Drug Administration Safety and Innovation Act (FDASIA)[2], signed into law in 2012, and the 21st Century Cures Act of 2016[3], have positioned the U.S. Food and Drug Administration (FDA) as a leader in defining methods and opportunities for capturing patients' views on the most burdensome aspects of their conditions as well as what matters most to them in terms of benefit expectations and tolerable harms or risks in exchange for those benefits. The Patient-Centered Outcomes Research Institute (PCORI) has helped fuel momentum to view patients as partners in research, rather than simply as subjects of it.

Efforts to establish a framework for scientifically valid "patient experience data,"[4] as described in the Cures Act (and addressed in more detail on page 20), have included unpaid family caregivers in the pool of participants building this new science of patient input. However, there has been limited attention paid to the roles that caregivers could play, as distinct from those of patients. With more than 43 million Americans serving as caregivers, there is a great deal to be gained by better understanding their perspectives and engaging them to improve outcomes for the recipients of their care as well as the betterment of their own health and wellbeing.

To recognize and explore possibilities for unpaid family caregivers to contribute to patient-focused medical product development, the National Alliance for Caregiving (NAC) and the Leaders Engaged on Alzheimer's Disease (LEAD) Coalition convened a one-day national summit on November 1, 2018 in Washington, D.C. This summit gathered 50 professionals from a range of disciplines, organizations, and therapeutic areas of interest, who were also encouraged to draw upon their personal experiences with family caregiving.

[1]Anderson, M., and McCleary, K. (2016). On the path to a science of patient input. Science Translational Medicine. Vol (8). Issue 336. doi; 10.1123/scitranslmed.aaf6730.
[2]Congress. (2012, July 9). Public Law 112 – 144. Retrieved from https://www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf
[3]Congress. (2016, January 4). Public Law 114 – 255. Retrieved from https://www.congress.gov/114/bills/hr34/BILLS-114hr34enr.xml
[4]Ibid.

The National Alliance for Caregiving (NAC) and the Leaders Engaged on Alzheimer's Disease (LEAD) Coalition convened a one-day national summit on November 1, 2018 in Washington, D.C. with 50 professionals representing numerous disciplines and organizations.

The express purposes of the Summit were to:

- share emerging practices and lessons learned from existing caregiver engagement;
- identify potential caregiver roles in medical product development;
- build consensus on the value of family caregiver engagement in the medical product development process; and,
- identify potential next steps and a call to action.

Section 1 of this report describes today's caregiver landscape. In Section 2, the activities of caregiving are viewed through the lens of medical product development, building on frameworks constructed to identify opportunities for patients to inform decision-making across a product's total lifecycle. Finally, potential actions to deepen caregiver engagement are identified in Section 3 as an outcome of both the November 1, 2018 Summit and broader lessons from patient-focused medical product development.

NAC and the LEAD Coalition have committed to pursue action steps that align with their missions and capabilities. It is vital that others committed to improved health for all join them or contribute in other ways to increase caregiver engagement in biomedical R&D and healthcare delivery.

The nature and prevalence of unpaid family caregiving is being reshaped by changes in 5 key aspects of American life:

- An aging population
- Changing family structures
- Widening care gap
- An increasingly complex and fragmented healthcare delivery system
- Increasing public health burden

SECTION 1

DEFINING TODAY'S CAREGIVER AND CAREGIVING ACTIVITIES

The unpaid family caregiver – supporting the physical, emotional, and social needs of those who are ill or impaired – has been a mainstay of human community, with each civilization and culture defining its own expectations and norms for the role. In the United States, the nature and prevalence of unpaid family caregiving is being reshaped by changes in five key aspects of present-day American life:

1. **An aging population**: Improved public health and medical advances increased average life expectancy from 47 years in 1900 to 75 years for males born in 2000. A woman's life expectancy is now 80 years for females born in 2000.[5] Continued gains mean that by 2030, 72.8 million Americans – more than one in five – will be age 65 or older, with the greatest population growth among "the oldest old" who are most likely to have physical, cognitive, and other functional limitations.[6] At the same time, the 2018 birth rate among U.S. women ages 15-44 reached an all-time low, with just 62 births per 1,000 women compared to 120 births per 1,000 in 1960.[7] Combining these trends, there will be fewer caregivers to support an aging population, as the caregiver ratio – the number of people theoretically available to support an older adult – declines from 7.2 in 2010 to 4.1 in 2030.[8]

2. **Changing family structures**: In 1963, roughly two-thirds of American households had a traditional nuclear family structure, with an employed father, a stay-at-home mother, and minor children. In 2014, only 20 percent of American households had this structure, with the other 80 percent reflecting a range of structures — from single parents to same-sex couples to dual-income couples, some of whom are married and some of whom are not.[9]

[5] *SeniorLiving. (n.d.). 1900-2000: Changes in Life Expectancy in the United States. Retrieved from https://www.seniorliving.org/history/1900-2000-changes-life-expectancy-united-states/*
[6] *The National Academies of Sciences, Engineering, and Medicine. (2016, September 13). Families Caring for an Aging America. Retrieved from http://www.nationalacademies.org/hmd/Reports/2016/families-caring-for-an-aging-america.aspx*
[7] *Pew Research Center. (2018, January 18). Is U.S. fertility at an all-time low? It depends. Gretchen Livingston. Retrieved from http://www.pewresearch.org/fact-tank/2018/01/18/is-u-s-fertility-at-an-all-time-low-it-depends/*
[8] *The Hastings Center. (nd.). Family Caregiving. Retrieved from https://www.thehastingscenter.org/briefingbook/family-caregiving/*
[9] *Anne Weisberg (2014). Changing families, changing work. Retrieved from https://www.dol.gov/wb/resources/changing_families_changing_work.pdf*

Since 1964, the percentage of women enrolling in college after graduating high school has risen from 41 percent to 70 percent and women now dominate every level of post-secondary educational attainment compared to men.[10] In 2010, 59 percent of women age 16 and older were employed or looking for work.[11] A survey of Millennials' aspirations indicates that today, young women and men expect to have "an egalitarian relationship at home that allows them to have both significant careers and meaningful, fulfilling roles at home."[12] So, mid-20th century expectations of the unemployed wife, mother, or daughter (-in-law) being available to provide care if and when serious illness, disability, or advanced age required full- or part-time unpaid family caregiving is necessarily shifting in response to new realities of the family unit itself. In fact, the impact of these changes are already being seen: according to "Caregiving in the U.S. 2015," 47 percent of family caregivers of the Millennial generation are male, compared to 40 percent of caregivers overall.[13]

3 **Widening care gap**: The most common family caregivers are living spouses and adult children who live within 10 miles of a parent (or parent-in-law). Between 1960 and 2014, U.S. Census data reflects that the share of single-person households doubled to 27.7 percent and the average number of people per household fell to 2.54, from 3.33.[14] This, coupled with higher rates of divorce and greater geographic distance between family members of successive generations led a University of Michigan research team to forecast that between 2010 and 2030 the number of 75-year-olds without a living spouse to provide care could double to 1.8 million. Those without an adult child nearby could increase by a multiple of six, to more than 600,000 by 2030.[15]

4 **An increasingly complex and fragmented healthcare delivery system**: Since the mid-1950s, the practice of medicine and delivery of care services has become ever more specialized and siloed with specialties and subspecialties forming around new technologies and a keener understanding of human biology. The notion of a family physician who would care for an individual from "cradle to grave" and was capable of treating most acute and chronic medical conditions was perhaps formally put to bed in 1969 when "family practice" itself was recognized as a medical specialty, rather than the norm.[16] The fragmented system in which healthcare is delivered in the United States, coupled with payment and public policy incentives to reduce hospital stays and shift procedures to outpatient and at-home settings, imposes great responsibility on the individual and family unit to coordinate care and support for those with acute, progressive, and chronic conditions that affect physical, cognitive, mental, and/or emotional functioning.

The demand for family caregivers is growing exponentially, while the supply is shrinking. The expectation for individuals who step into those roles is that they will be able to address ever-more complex tasks.

[10]Carnevale, A. P., & Smith, N. (2014). Women, jobs and opportunity in the 21st century. Retrieved from https://www.dol.gov/wb/resources/women_jobs_and_opportunity.pdf

[11]United States Department of Labor. (nd.). Women in the Labor Force in 2010. Retrieved from https://www.dol.gov/wb/factsheets/Qf-laborforce-10.htm

[12]Weisberg, 2014.

[13]NAC and AARP Public Policy Institute Research (2015). Caregiving in the U.S. 2015. Retrieved fromhttps://www.caregiving.org/wp-content/uploads/2015/05/2015_CaregivingintheUS_Final-Report-June-4_WEB.pdf

[14]Bachman, D. & Barua, A. (2015, November 12). Single-person Households: Another look at the changing American family. Deloitte Insights. Retrieved from https://www2.deloitte.com/insights/us/en/economy/behind-the-numbers/single-person-households-and-changing-american-family.html#endnote-sup-2

[15]Ryan L.H., Smith J., Antonucci T.C., Jackson JS. (2012) Cohort differences in the availability of informal caregivers: are the Boomers at risk? Gerontologist. 2012;52(2):177-88.

[16]American Board of Family Medicine. (n.d.) History of the specialty. Retrieved from https://www.theabfm.org/about/history.aspx

5 **An increasing public health burden**: The rates of major chronic conditions including heart disease, cancer, chronic lung disease, stroke, Alzheimer's disease, diabetes, and chronic kidney disease, continue to rise in the U.S. The U.S. Centers for Disease Control and Prevention (CDC) reports that presently 6 in 10 Americans have one of these conditions and 4 in 10 have two or more chronic conditions.[17] Pandemics have demonstrated the speed at which infectious diseases can spread across the globe, exerting periodic and sometimes substantially disruptive pressure on healthcare systems.[18] Additionally, with enhanced medical technology to detect and treat serious, life-threatening conditions, some diseases that were previously fatal are now manageable but require ongoing medical attention and care.[19] Healthcare resources are significantly strained and new ways to improve patient outcomes and support families experiencing these conditions are needed more than ever.

The changing caregiver landscape provides opportunities and challenges alike for expanding ways for caregivers to participate in medical product development.

To summarize, the demand for family caregivers is growing exponentially, while the supply is shrinking. The expectation for individuals who step into those roles is that they will be able to address ever-more complex tasks. The demographic profile of caregivers is changing as well. These combined forces prompt a need to rethink how caregivers are recognized for and supported in the tremendous work they do. As will be addressed later in this report, the changing caregiver landscape provides opportunities and challenges alike for expanding ways for caregivers to participate in medical product development.

TERMS AND DEFINITIONS

For purposes of this report, the term "caregiver" will refer to an "adult family member or other individual who has a significant relationship with, and who provides a broad range of assistance to, an individual with a chronic or other health condition, disability, or functional limitation," a definition codified in the RAISE Family Caregivers Act.[20] The term will also reflect features of FDA's definition of caregiver from its Patient-Focused Drug Development Glossary: "A person who helps a patient with daily activities, health care, or any other activities that the patient is unable to perform him/herself due to illness or disability, and who understands the patient's health-related needs. This person may or may not have decision-making authority for the patient and is not the patient's healthcare provider."[21] This blended definition is also intended to distinguish between family caregivers and professionals or para-professionals who are employed to provide caregiving services on an ongoing, periodic, or respite basis.

While these two sources provide useful definitions for the term caregiver for use in the context of this report, it is important to note that some object to the term itself because it suggests a particular dynamic between one who is giving and another who is receiving something of value, or for other cultural and linguistic reasons. Other terms used to represent roles similar to the one defined above are "care partner" or "carer." Use of the term "caregiver" throughout reflects these concepts as well.

(CONTINUES ON PAGE 10)

[17] *U.S Centers for Disease Control and Prevention. (2019, January 16). Chronic diseases in America. Retrieved from https://www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm*

[18] *PwC Global. (nd.) Chronic Diseases and Conditions Are on the Rise. Retrieved from https://www.pwc.com/gx/en/industries/healthcare/emerging-trends-pwc-healthcare/chronic-diseases.html*

[19] *Pharmaceutical Researchers and Manufacturers of America. (2016). A Decade of Innovation in Chronic Diseases, 2006-2016. Retrieved from http://phrma-docs.phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf*

[20] *Congress. (2018, January 22). Public Law 115-119. Retrieved from https://www.congress.gov/115/plaws/publ119/PLAW-115publ119.pdf*

[21] *U.S. Food and Drug Administration. (2018, December 6). Patient-Focused Drug Development Glossary. Retrieved from https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm610317.htm*

SNAPSHOT: CAREGIVING IN THE U.S. 2015

The most recent national study of caregiving, conducted in 2015 by the National Alliance for Caregiving (NAC) and AARP Public Policy Institute,* estimates that 43.5 million Americans, or 18.2 percent of adults, had provided unpaid care to an adult or child in the previous 12 months. The study found that 60 percent of caregivers are women and the average age of the caregiver is 49, while the average age of the care recipient is 69.4 years of age. Nearly half of caregivers provide care to someone 75 years old or older.

Eighty-two percent provide care for one person. A large majority, 85 percent, provide care for a relative, with 49 percent caring for a parent or parent-in-law and 10 percent providing care for a spouse. On average, caregivers have been in their role for five years or more; however, half of those surveyed were in their first year of caregiving. Six in 10 care for an adult with a long-term condition; 35 percent care for someone with a condition anticipated to be of shorter duration. Slightly more than one-third (35%) of caregivers live in the same household as the care recipient. Eighty-four percent of caregivers live in an urban/suburban setting, while 16 percent live in a rural area. Sixty percent report being employed in the past year while caregiving.

Two-thirds of survey respondents dedicate less than 20 hours per week to caregiving, and on average, caregivers spend 24.4 hours per week. The one-third of all caregivers who are “higher-hour caregivers,” providing more than 20 hours per week of care, are a more vulnerable population who report greater likelihood of experiencing emotional stress, physical and financial strain, and negative impacts on their health.

** NAC & AARP Public Policy Institute. (2015). Caregiving in the U.S.*

Many individuals who provide care, regardless of background, often resist self-identifying as "caregivers." Reasons include a lack of awareness of the expansive nature of caregiving activities (discussed below); cultural norms that do not attach a special label to activities expected of family members; stigma or other negative perceptions associated with the term or the role; a preference to retain a sole identity and relationship with the care recipient such as husband, wife, parent, sibling, daughter, or son; and many other reasons specific to individuals, relationships between individuals, and various conditions and diseases. At least one participant at the Summit had such an awakening. Introducing herself, **Teresa Brandt** of ACADIA Pharmaceuticals stated, "This is a relatively new area to me, but the other way I identify myself is as a mom of a child with Type 1 diabetes. Until today, I never really thought of myself as a caregiver."

There are also objections to use of the term "patient" to refer to an individual with a health condition or disability, especially when that label is applied outside the setting of healthcare delivery or clinical research. Resistance often stems from feeling the term demeans personhood and an individual's agency. For purposes of this report, the term patient is used because it is the term most commonly used in connection to patient-focused medical product development activities, including legislative and policy documents that create specific opportunities for members of the public who may be considered patients and/or caregivers.

AARP has estimated that in 2013, about 40 million family caregivers in the United States provided 37 billion hours of care to an adult with limitations in daily activities with an economic value of their unpaid contributions equal to $470 billion.

CAREGIVER ACTIVITIES AND TASKS

The current state of caregiving and caregivers in the U.S. is described in the "Snapshot" on page 9, based on research conducted by the NAC in partnership with the AARP Public Policy Institute and reported in "Caregiving in the U.S. 2015."[22] AARP has estimated that in 2013, about 40 million family caregivers in the United States provided 37 billion hours of care to an adult with limitations in daily activities with an economic value of their unpaid contributions equal to $470 billion.[23] That same year, the Congressional Budget Office placed the value of caregivers' services to older adults at $234 billion annually.[24] Both estimates must be viewed as minimum figures for the total value of caregivers' services, considering that the "Caregiving in the U.S. 2015" study indicates there are also approximately 10 million caregivers providing care to individuals under age 50, including children, the economic value of which is not reflected.

To deepen understanding of the nature of contemporary caregiving, it is useful to describe different categories and types of tasks that caregivers perform. Lists from two surveys of caregivers delineate the various actions taken on behalf of the care recipient as: Instrumental Activities of Daily Living (IADLs); Activities of Daily Living (ADLs); and Medical/Nursing Tasks (MNTs). They are presented in descending order from most commonly performed to least.

[22] NAC and AARP Public Policy Institute, Caregiving in the U.S. 2015.

[23] Reinhard S.C., Feinberg L.F., Choula R., Houser A. (2015, July). Valuing the invaluable: 2015 Update. AARP Public Policy Institute. Retrieved from https://www.aarp.org/content/dam/aarp/ppi/2015/valuing-the-invaluable-2015-update-new.pdf

[24] Congressional Budget Office. (2013). Rising demand for long-term services and supports for elderly people. Retrieved from https://www.cbo.gov/sites/default/files/113th-congress-2013-2014/reports/44363-ltc.pdf

Source: "Caregiving in the U.S. 2015" (NAC & AARP Policy Institute, see page 9)

Instrumental Activities of Daily Living (IADLs)[25]	Activities of Daily Living (ADLs)[26]	Medical/Nursing Tasks (MNTs)[27]
N=1,248 with 99% indicating having performed any IADL	N=1,248 with 59% indicating having performed any ADL	N=1,084, all of whom performed at least 1 MNT, of total sample of 2,089 caregivers surveyed
Transportation (78%)	Getting in and out of bed and chairs (43%)	Manage medications, including IV and injections (82%)
Grocery or other shopping (76%)	Getting dressed (32%)	Help with assistive devices for mobility like cane or walkers (51%)
Housework (72%)	Getting to and from the toilet (27%)	Prepare food for special diets (48%)
Preparing meals (61%)	Bathing or showering (26%)	Do wound care (bandages, ointments, prescription drugs for skin care, or to treat pressure sores or post-surgical wounds) and ostomy care (37%)
Managing finances (54%)	Feeding (23%)	Use meters/monitors (thermometer, glucometer, stethoscope, weight scales, blood pressure monitors, oxygen saturation monitors), administer test kits, use telehealth equipment (34%)
Giving medications, pills, or injections (46%)	Dealing with incontinence or diapers (16%)	Operate durable medical equipment (e.g., hospital beds, lifts, wheelchairs, scooters, toilet/bath chairs, geri-chairs) (27%)
Arranging outside services (31%)		Use incontinence equipment, supplies, administer enemas (25%)
		Operate medical equipment (mechanical ventilators, oxygen, tube feeding equipment, home dialysis equipment, suctioning equipment) (11%)

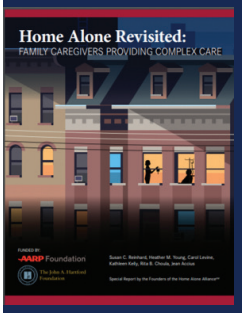
In the "Caregiving in the U.S. 2015" study, it was noted that caregivers' responsibilities frequently extend beyond these categories to include the following "other" tasks, such as:

- monitoring the health of the care recipient (66%);
- communicating with health care professionals (63%); and,
- advocating with providers, services, and agencies (50%).

[25] *NAC and AARP Public Policy Institute, Caregiving in the U.S. 2015.*
[26] *Ibid.*
[27] *Ibid.*

SNAPSHOT: MEDICAL/ NURSING TASKS PERFORMED BY CAREGIVERS

Source: "Home Alone Revisited" (AARP Public Policy Institute & Founders of the Home Alone Alliance; see sidebar at right)

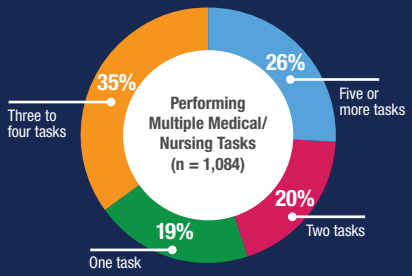


Recognizing an expansion of the role of family caregivers to include medical/ nursing tasks of a type and complexity once provided only in clinical settings, AARP Policy Institute and United Hospital Fund conducted a 2012 study to better understand what tasks were being performed and how well caregivers were being supported in this expanded role. A report titled, "Home Alone,"* reported their findings. In April 2019, results of a follow-up study were published in "Home Alone Revisited."**

The 2019 study found 50.1 percent of family caregivers performed medical/nursing tasks for care recipients with a variety of chronic physical and cognitive conditions, up from 46 percent in 2012. The medical/nursing tasks performed are listed in the table at left.

Fear of making a mistake was the reason most often given for rating a task as being difficult; 28 percent of family caregivers report experiencing this fear. It is highest for managing medications, using meters and monitors, and performing wound care. When asked what would make it easier to perform medical/ nursing tasks, caregivers' most common response across all tasks is more and/or better instruction, especially for suctioning, home dialysis, mechanical ventilators/ oxygen, urinary catheters, meters/monitors, telehealth equipment, and medications.

The study found choice is an important issue. (See also page 45.) Fifty-seven percent felt they did not have a choice in taking on these care responsibilities; 35 percent felt pressure to do so by other family members or health care professionals. Caregivers who are socially isolated or feel they have no choice about caregiving are more at risk for experiencing difficulties with complex care.

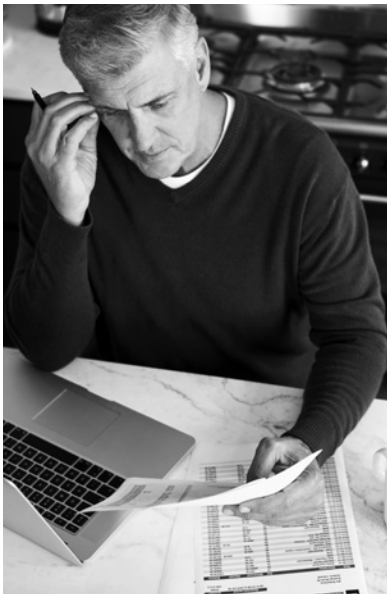


** Reinhard, S.C., Levine, C., & Samis, S. (2012). Home alone: Family caregivers providing complex chronic care. Retrieved from https://www.aarp.org/content/dam/aarp/research/public_policy_institute/health/home-alone-family-caregivers-providing-complex-chronic-care-rev-AARP-ppi-health.pdf*
*** Reinhard S.C., Young, H.M., Levine, C., Kelly K., Choula R.B., & Accius, J.C. (2019) Home alone revisited: Family caregivers providing complex care. Retrieved from: https://www.aarp.org/content/dam/aarp/ppi/2019/04/home-alone-revisited-family-caregivers-providing-complex-care.pdf*

The "Caregiving in the U.S. 2015" study also inquired about medical/nursing tasks that had once been performed solely by skilled nurses or technicians, building on findings from the "Home Alone" AARP/United Hospital Fund study issued in 2012.[28] The 2019 follow-up study is summarized in the Snapshot and right-hand column of the table on page 11. In the "Caregiving in the U.S. 2015" study, more than half (57%) of caregivers reported performing medical/nursing tasks, only 14 percent of whom had received prior preparation or training for these tasks.

Another set of activities which caregivers often assume relate to care recipients who participate in research studies and/or clinical trials. Caregivers may be involved in decision-making about whether to participate in research studies; they may also be instrumental in enabling the care recipient to take part. As highlighted in the NAC/Global Genes "Rare Disease Caregiving in America" study of caregiving for those with rare or orphan diseases (see the Snapshot on page 17),[29] caregivers help with tasks including trial-related paperwork (77%), transportation (65%), documenting trial response (62%), and care coordination (59%). Individuals with advanced progressive neurological conditions such as Alzheimer's disease and Parkinson's disease, and many other conditions, almost surely depend upon caregivers to facilitate participation in research studies.

Caregivers may be involved in decision-making about whether to participate in research studies; they may also be instrumental in enabling the care recipient to take part.



Finally, a 2016 report from the National Academies of Sciences, Engineering, and Medicine (NASEM)[30] identifies other practical, emotional, and social supports that caregivers of older adults can be called upon to provide, not otherwise addressed above. Some of these may also extend to younger care recipients as well. They include:

- home maintenance (e.g., installing grab bars, ramps, and other safety modifications; repairs; yardwork);
- management of behavioral symptoms;
- providing companionship;
- discussing ongoing life challenges with care recipient;
- facilitating and participating in leisure activities;
- helping care recipient manage emotional responses;
- managing family conflict;
- troubleshooting problems;
- encouraging healthy lifestyle, self-care, and treatment adherence;
- negotiating with other family member(s) regarding respective roles;
- ordering prescription medications;
- handling financial and legal matters;
- managing personal property;
- participating in advance care planning; and,
- participating in shared decision-making about treatments.

[28]Reinhard, S.C., Levine, C., & Samis, S. (2012). Home alone: Family caregivers providing complex chronic care. Retrieved from https://www.aarp.org/content/dam/aarp/research/public_policy_institute/health/home-alone-family-caregivers-providing-complex-chronic-care-rev-AARP-ppi-health.pdf

[29]National Alliance for Caregiving & Global Genes (2018). Rare disease caregiving in America. Retrieved from https://www.caregiving.org/wp-content/uploads/2018/02/NAC-RareDiseaseReport_February-2018_WEB.pdf

[30]The National Academies of Sciences, Engineering, and Medicine, Families caring for an aging America.

The activities listed above underscore the variety of skills called upon in caregiving. Cutting across specific tasks are cognitive and interpersonal faculties of problem solving, decision-making, communicating with others (family and healthcare and human service professionals), and vigilance over the care recipient's well-being.[31]

THE CAREGIVING JOURNEY

Each caregiving situation is unique, even if some common elements may be present across most caregiving situations. This report includes "Caregiver Spotlights," which consist of six real-life journeys that reveal some of the many factors impacting the caregiving journey. These lived experiences also enrich the academically oriented data and models presented in this section and the next, which 1) may oversimplify the dynamic nature of the conditions, 2) inadequately reflect the need for there to be one or more family members or friends to act as a caregiver, and 3) short-change the ways in which caregiving relationships may ebb, flow, and evolve over time.

The "entry-point" for caregiving is a key determinant in the caregiver's journey. For some, it will be quite sudden and unexpected, such as in the aftermath of a stroke, an acute infectious disease, or a vehicle accident. For others, there may be a period of preparation before the caregiving role begins, as may occur with a child born with a congenital condition detected during pregnancy or rare, heritable forms of Parkinson's or Alzheimer's diseases. For a large majority of those caring for aging adults, the caregiving role initiates with a gradual onset of support of a previously mostly independent person, or abruptly in response to a "wake up" call that the person who requires care is no longer able to be fully independent. Caregivers may be first to notice subtle changes in loved ones that signal a condition of new onset or progression of an existing one, prompting them to seek medical attention. They may also be providing additional support and/or care to a family member or friend in need well before a diagnostic label is applied to the individual, as can be the case for parents of children on the spectrum of autism disorders.

Gitlin and Wolff present one model of caregiving for a person with dementia,[32] mapping stages of caregiving and the types of activities that are required as the care recipient's condition advances (see Figure 1, page 15). In other caregiving situations, the journey may be more episodic than linear and with some conditions, such as curable cancers, the path may progress toward the care recipient's return to wellness and independence. The journey of a caregiver for a child with a serious physical or mental condition can be overlaid onto the activities of parenting a healthy same-age child to delineate the different types, duration, and/or intensity of tasks performed.

The ability of each caregiver to meet the demands of the caregiving situation will depend a great deal upon their own capabilities and capacities, and may vary over time in response to a large number of factors including their own physical and emotional health and well-being, education and literacy, financial situation, other family responsibilities, and interpersonal relationships with the care recipient and other members of the unpaid and paid caregiving team. The strain of caregiving

(CONTINUES ON PAGE 15)

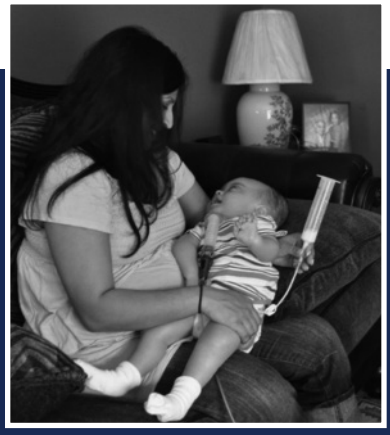
Caregivers may be first to notice subtle changes in the people they care for.

[31] *Gitlin, L. N., & Wolff, J. (2012). Family involvement in care transitions of older adults: What do we know and where do we go from here? Annual Review of Gerontology and Geriatrics, 31(1), 31-64. https://doi.org/10.1891/0198-8794.31.31*

[32] *Ibid.*

CAREGIVER SPOTLIGHT

This is the first in a series of six Caregiver Spotlights included throughout the report. It focuses on Mousumi Bose, PhD, of Montclair, NJ, and highlights the extent to which caregivers may be called upon to perform life-sustaining medical/nursing tasks (see page 11), their role in relaying crucial information to health care professionals, and the sometimes subtle signs and signals they detect that can escape notice by other members of the care team.



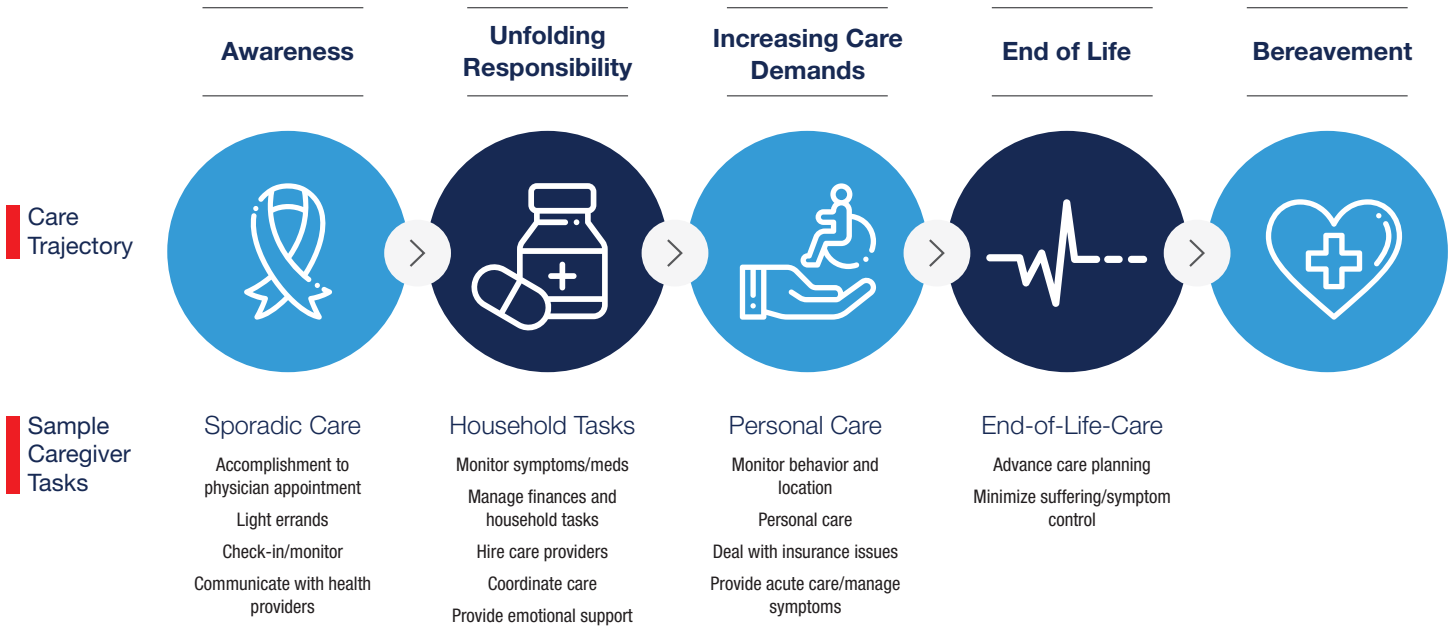
MOUSUMI BOSE

Mousumi Bose's first son, Ilan, was born with a severe form of a progressive genetic disorder called Zellweger spectrum disorder stemming from mutations in proteins found in every cell of the body. Nearly all organ systems are involved and children rarely survive into adulthood. Ilan's life was even shorter. "I was Ilan's full-time caregiver and the expert on how he was doing each day," Mousumi stated. She knew how many daily seizures he had and how long each one lasted. She managed his respiration with a tracheostomy and oxygen support, his nutrition and gastrointestinal health with the help of a feeding tube. She and her husband were methodical about administering Ilan's complicated medication regimen on schedule and in the correct dosages. "We were responsible for relaying all this information to the doctors and for making the call as to whether he needed to be hospitalized if his condition changed or an acute illness came on."

Ilan was deaf and had a lot of visual impairment; doctors told Mousumi that he wouldn't be able to communicate. "When he was about one month old and we were still in neonatal intensive care, I noticed he was pursing his lips in a way I had come to know meant something was wrong with him. Within an hour, he coded and almost died that night. It was the catalyst for getting a trach. Another time, when I was feeding him through the tube, he put his hand up, a sign I was feeding him too fast and that he was uncomfortable. These subtle signs helped me manage his care. I became an expert on this rare disease. More important, I became the expert on Ilan."

Ilan's life lasted just 14 months, but his mother took what she learned in caring for him and applied it to her research at Montclair State University in New Jersey. She now studies quality of life within families where one or more members have a rare disease. "I know from my own experience and that of the families that I work with, the caregiver holds a different, more comprehensive understanding of these rare diseases than the medical experts who study them. There is a lot that goes under the radar at the clinical level that family caregivers see on a day-to-day basis. Their viewpoint is essential."

FIGURE 1: EXAMPLE OF A DEMENTIA CARE TRAJECTORY; GITLIN AND WOLFF (2012)



and its dynamic intensity must be assessed against the backdrop of other life demands on the caregiver. Some risk factors for increased likelihood of high strain and adverse effects of caregiving include living in the same household as the care recipient; being a higher-hour caregiver (more than 21 hours per week); being the sole caregiver (with no other paid or unpaid help); and feeling as if they had no choice in taking on their caregiving role.[33] There is a vital need for contingency planning to accommodate changes in the caregiver's ability and willingness to meet the dynamic needs of the care recipient, yet studies suggest this issue is often not addressed in a direct manner. These varying abilities of each caregiver and the caregiver over time also have implications for their potential involvement in medical product development, as will be explored in the next section of this report.

The varying abilities of each caregiver and the caregiver over time have implications for their potential involvement in medical product development, as explored in Section 2.

SUPPORTING THE CAREGIVER

Studies of caregivers, including those cited here, often highlight policy and other recommendations to better support caregivers and adequately prepare those who will become caregivers. Indeed, the RAISE Family Caregivers Act[34] requires the U.S. Secretary of Health and Human Services (HHS) to develop, maintain, and update an integrated national strategy to support family caregivers. The Act is in the early stages of being implemented with formation of a federal advisory council. The law designates a broad range of caregiving stakeholders who will be represented on the

(CONTINUES ON PAGE 17)

[33] *NAC and AARP Public Policy Institute, Caregiving in the U.S. 2015.*
[34] *Congress. (2016, January 4). Public Law 114 – 255. Retrieved from https://www.congress.gov/114/bills/hr34/BILLS-114hr34enr.xml*

CAREGIVER SPOTLIGHT

This Spotlight on Alice and Brian Denger of Biddeford, Maine, depicts how families manage when more than one member requires ongoing care. It also illustrates how two people may divide caregiving responsibilities, the need to incorporate many different medical products (medications, medical devices, monitoring equipment, etc.) into home care routines, and the overarching outcomes of highest priority.

ALICE AND BRIAN DENGER

When the oldest of **Alice and Brian Denger**'s three children, Rachel, was diagnosed with type-1 diabetes at age 5, the couple thought they had their "family illness" and so they learned to test Rachel's blood, give her injections, and manage the ups and downs. Two years later, their 5-year-old son Matthew was diagnosed with Duchenne muscular dystrophy, a rare genetic disease that attacks all the muscles of the body. Soon after, their youngest, Patrick, was also diagnosed with Duchenne.

"To keep up with the care of all three children and the household, Alice and I had to find an arrangement. For the most part, she was at home taking care of the kids and I was at work providing the financial support. I was the one more inclined to stay up 'til 2 a.m. searching the Internet for the latest information about clinical trials and treatment advances. Having separate focuses took a toll on our marriage," Brian acknowledged.

Matthew lost the ability to walk by age 8 and required surgeries to correct deformities in his back and feet stemming from muscle loss; he needed help from mechanical devices to breathe when he was 16. Yet he graduated from high school and was able to attend college. Patrick followed his older brother's lead, participating in student council, in extracurricular clubs, and going to college. "The boys encouraged each other," Brian recalled. "They helped each other understand there was more to life than dwelling on things that they couldn't change."

During Matthew's sophomore year in college, he succumbed to heart failure and died in 2013. Patrick graduated from college in 2017; he worked for University of New England until the position was eliminated last year. Now he's an entrepreneur, hosting subscribers to an online community of people with shared interests. Brian reflects, "Alice and I willingly cared for both boys at home and at college. We took them to physicians who were very experienced in Duchenne and explored life-extending interventions. Every measure was worth the burden or costs. Each new stage was preceded by fear and sadness followed by compensation and then acceptance. Stability at any stage becomes welcomed. For Patrick, I want him to experience life fully, for him to have some independence. Rachel has found her path in life, too. In spite of an early aversion to science, she earned her R.N. degree and is working at a major medical center."

advisory council, bringing together representatives from private and public sectors, such as family caregivers; older adults and persons with disabilities; veterans; providers of health care and long-term services and supports; employers; state and local officials; and others, to advise and make recommendations regarding this new strategy.

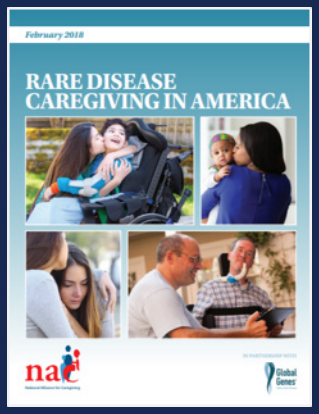
Additionally, the Caregiver Advise, Record, Enable (CARE) Act[35] passed by 36 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands and implemented administratively by several more states requires hospitals to:

- record the name of the family caregiver on the medical record of the care recipient;
- inform the family caregivers when their loved one is to be discharged; and,
- provide the family caregiver with education and instruction of the medical tasks he or she will need to perform for the patient at home.

The potential positive aspects of caregiving warrant mention as well. The NASEM study summarizes findings compiled from several caregiving surveys on the benefits: "For some, caregiving instills confidence, provides lessons on dealing with difficult situations, brings them closer to the care recipient, and assures them that the care recipient is well-cared for."[36] As reported in "Rare Disease Caregiving in America," (see page 17), nearly all caregivers (94%) took pride in better understanding their care recipient's condition and 91 percent felt satisfaction as a valued part of the care team; slightly more than half (56%) agreed that the role gives them a sense of purpose. As one caregiver stated, "I am motivated by seeing her progress in areas professionals told me I could never hope to see progress in because of all the work I do with her."[37]

As we will explore in the next section of this report, engaging willing and able caregivers more fully in opportunities to inform development of medical products that could improve the health and well-being of their loved ones might provide yet another benefit and avenue of personal satisfaction. At the Summit, **Mousumi Bose** shared her experience working with families that have one or more children with a rare disease which supports this possibility. "These parents don't have an opportunity to share what's going on in their kids' lives and the day-to-day experience of caring for them. They are eager to speak about it. In our structured interviews, we always run out of time because they have so much to offer," Mousumi reported. **Debra Lappin's** experience with the Alzheimer's community provides more evidence. "In an on-line cohort of more than 6,000 individuals called the A-LIST, 56 percent of whom are caregivers, the participants love to engage in rapid feedback surveys about their experience. We've done 17 "What Matters Most" insight surveys so far and have collected more than 20,000 responses," she stated. (See sidebar on 35 to learn more about A-LIST and AD PACE projects.)

[35] *AARP. (n.d.). New state law to help family caregivers. Retrieved from https://www.aarp.org/politics-society/advocacy/caregiving-advocacy/info-2014/aarp-creates-model-state-bill.html*
[36] *The National Academies of Sciences, Engineering, and Medicine. (2016) Families caring for an aging America.*
[37] *Rare caregiving in America, 2018.*



SNAPSHOT: CAREGIVING FOR THOSE WITH RARE DISEASES

To better understand the nature of caregiving for children and adults with rare diseases, NAC partnered with Global Genes to conduct a survey of 1,406 "rare caregivers" in the fall of 2017.* Most respondents (62%) were caring for a child under the age of 18 and most were immediate relatives of the care recipient, with 59 percent caring for their own child under 18; 17 percent caring for their own adult child; and 14 percent caring for a spouse or partner.

Caregiving for a person with a rare disease is time intensive. On average, rare caregivers of adults spend 12 hours more per week than caregivers of adults with more prevalent conditions. For children with rare diseases, caregivers spend 23 hours more per week than do caregivers for children with more prevalent conditions. Rare caregivers who perform medical/nursing tasks spend double the amount of time (51 hours per week) providing care as rare caregivers who do not perform these tasks (24 hours per week).

Rare caregivers are more likely than caregivers for other conditions to perform each of the Instrumental Activities of Daily Living and Activities of Daily Living, even when adjusted for those caring for young children. A defining feature of rare caregiving seems to be one of expertise: 84 percent help their care recipient with medical/nursing tasks.

** National Alliance for Caregiving & Global Genes (2018). Rare disease caregiving in America.*

Caregivers are an enormous – and largely untapped – reservoir of information and learned wisdom about the individuals they provide care for and the conditions their care recipients experience.

SECTION 2

POTENTIAL ROLES FOR CAREGIVERS IN PATIENT-FOCUSED MEDICAL PRODUCT DEVELOPMENT

While the demands on unpaid family caregivers are great, as described in Section 1, these caregivers are an enormous – and largely untapped – reservoir of information and learned wisdom about the individuals they provide care for and the conditions their care recipients experience. For at least a subset of caregivers, identifying a productive outlet for their observations would provide added meaning to their own lives. Following a brief description of patient-focused medical product development (PFMPD), this section explores opportunities for caregivers to participate, citing presentations and discussion from the Summit and other sources.

A PFMPD PRIMER

The 2012 reauthorization of the Prescription Drug User Fee Act (PDUFA-V) through the Food and Drug Administration Safety and Innovation Act (FDASIA)[38] launched a new era for patient engagement with regulators. One of FDA's commitments in PDUFA-V was to initiate a series of 20 meetings, known as the Patient-Focused Drug Development initiative, or PFDD. This meeting series provided FDA's Center for Drug Evaluation and Research (CDER) with a novel forum to hear directly from individuals with lived experience about what it is like to live with their medical conditions. Notably, PFDD meetings are broader than other types of public FDA meetings, such as Advisory Committee meetings held to gain expert and public

[38] *Congress. (2012, July 9). Public Law 112 – 144.*

opinion about selected evidence filed with the agency in support of a new drug application. PFDD meetings, of which there have been approximately 50 held to-date,[39] focus on the patient's experience of the symptoms of their conditions, the effects the condition has on their day-to-day lives and across their lifespans, ways in which they are treating the condition or its symptoms, their unmet medical needs, and the burdens of available therapies. In some meetings, FDA gathered input about hypothetical treatment options to better understand benefit-risk tradeoffs. A key observation FDA made through this meetings series is, "[The PFDD initiative] highlighted that what patients care most about may not always be factored into clinical trials or approved labeling."[40]

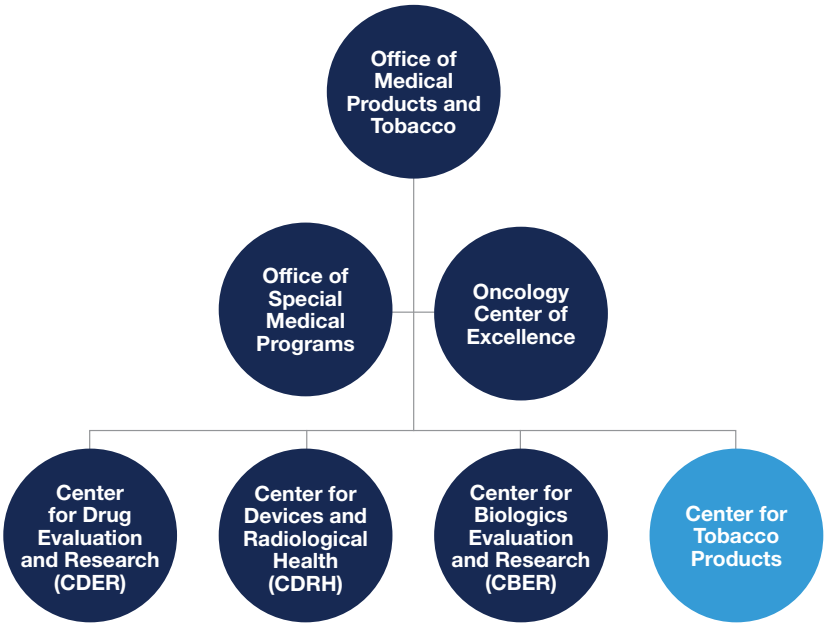


FIGURE 2:
FDA MEDICAL PRODUCTS CENTERS & OFFICES

As **Pujita Vaidya** explained at the Summit, FDA has learned a tremendous amount about specific conditions from these meetings. More importantly, the PFDD initiative has deepened the agency's respect for how much useful information can be gained via patients' perspectives to sharpen plans and decisions at every stage of the R&D process all the way through post-market surveillance for those products that receive regulatory approval, as depicted by the agency in Figure 3 below.

FIGURE 3: FURTHER INTEGRATING PATIENT PERSPECTIVE INTO MEDICAL PRODUCT DEVELOPMENT AND DECISION MAKING

Adapted from a May 8, 2018 presentation by Theresa Mullin, Associate Director for Strategic Initiatives, FDA Center for Drug Evaluation and Research, at meeting convened by the National Academies of Science, Engineering, and Medicine.

"The PFDD initiative highlighted that what patients care about most may not always be factored into clinical trials or approved labeling."

FDA

[39] *FasterCures. (2018, September 6). Patient-focused drug development tracker. Retrieved from https://www.fastercures.org/programs/patients-count/pfdd [Accessed January 1, 2019]*

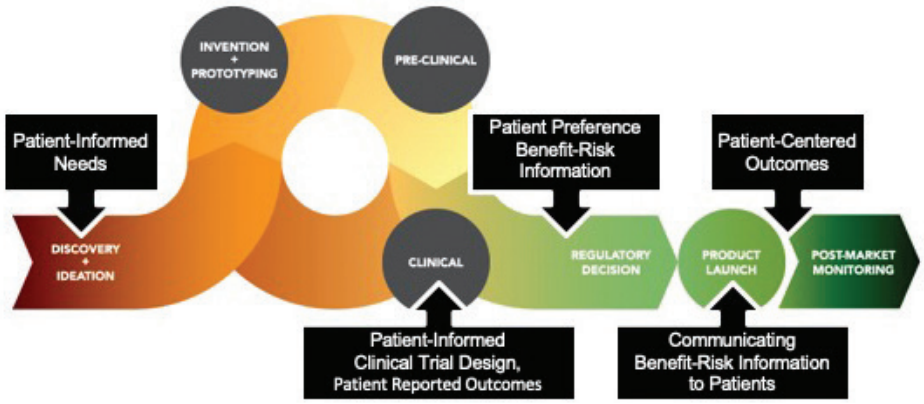
[40] *U.S. Food and Drug Administration. (2017). Plans for issuance of patient-focused drug development guidance. Retrieved from https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf*

To help foster more and better engagement with patients, CDER has compiled a glossary of PFDD-related terms,[41] created a repository for externally generated PFDD information/data,[42] and is working on a set of regulatory guidances to outline expectations and fit-for-purpose methods for systematically collecting patient experience data and submitting it as part of the evidence to support product-related applications.[43] These guidances are responsive to requirements under the 21st Century Cures Act of 2016[44] and PDUFA-VI, passed as part of the FDA Reauthorization Act (FDARA) in 2017.[45] (See Snapshot on page 30 for a description of "patient experience data" created under these Acts.)

In 2016, CDRH leadership established "partnering with patients" as one of its three strategic priorities and set – and then exceeded – aggressive goals to measure its progress.

At about the same time that CDER held the first PFDD meetings, FDA's Center for Devices and Radiological Health (CDRH) launched a complementary program known as the Patient Preference Initiative[46] to develop methods of understanding patients' preferences for benefits and tolerance for harms and risks related to interventions that involve medical devices. Working collaboratively with the Medical Device Innovation Consortium (MDIC), a framework for integrating patient preferences into the total product life cycle of medical devices, as depicted in Figure 4, below) was developed along with a catalog of methods.[47] These were published in May 2015 coincident with issue of draft guidance from CDRH and FDA's Center for Biologics Evaluation and Research (CBER) on voluntary submission of patient preference information; final guidance on this topic was issued in August 2016.[48] Also in 2016, CDRH leadership established "partnering with patients" as one of its three strategic priorities and set – and then exceeded – aggressive goals to measure its progress. In 2017, it convened the agency's first Patient Engagement Advisory Committee to guide continued interactions with patients and patient organizations.

FIGURE 4: INCORPORATING PATIENT PREFERENCES INTO THE MEDICAL DEVICE TOTAL PRODUCT LIFECYCLE



Source: FDA Center for Devices and Radiological Health (CDRH)

[41] *U.S. Food and Drug Administration. (2018, June 12). Patient-focused drug development glossary.*
[42] *U.S. Food and Drug Administration. (2018, November 20). External Resources or information related to patients' experience. Retrieved from https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579132.htm*
[43] *U.S. Food and Drug Administration. (2018, June 29). FDA patient-focused drug development guidance series for enhancing the incorporation of the patient's voice in medical product development and regulatory decision making. Retrieved from https://www.fda.gov/drugs/developmentapprovalprocess/ucm610279.htm*
[44] *Congress. (2018, January 22). Public Law 115-119.*
[45] *Congress. (2017, August 18). Public Law 115-52. Retrieved from https://www.congress.gov/115/plaws/publ52/PLAW-115publ52.pdf*
[46] *U.S. Food and Drug Administration. (2018, September 27). Patient preference initiative. Retrieved from https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhpatientengagement/ucm462830.htm*
[47] *Medical Device Innovation Consortium. (2015, May). Patient centered benefit-risk (PCBR) framework. Retrieved from https://mdic.org/resource/patient-centered-benefit-risk-pcbr-framework/*
[48] *U.S. Food and Drug Administration. (2015). Guidance for industry, Food and Drug Administration staff, and other stakeholders. Retrieved from https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf*

CDRH's efforts were apparent in the approval of the Maestro Rechargeable System, a surgically implanted device to aid weight loss for people with obesity. Although the clinical study did not meet its pre-specified endpoint, FDA's approval considered data from a patient preference study that indicated patients would accept risks associated with the intervention to achieve the level of benefit they experienced.[49] At the Summit, CDRH's **Michelle Tarver** described another example: "MDIC and the Michael J. Fox Foundation for Parkinson's Research recently conducted a patient preference study. Something we've never seen included in Parkinson's device studies was pain, but that came up as the number one issue patients were reporting. The review division said, 'Wow, we should be capturing this. This is important.' That is one of the ways something like this comes to people's attention and that you can bring about change in clinical trial approaches."

Another example showcased how CDRH worked to reduce burdens on patients and their caregivers. Michelle continued, "An FDA-approved home hemodialysis device required that a caregiver be present when performing dialysis, for safety reasons. Patients told us they didn't think they needed that, and requested they be able to make the decision about solo home hemodialysis. A patient preference study showed that they were willing to make certain benefit-risk trade-offs, which led to modification of the label. Now patients can do dialysis at home without having to enlist help from a caregiver, if this is deemed a suitable option by the patient and their physician."

These programs, which for the purposes of this report have been grouped under the term "patient-focused medical product development" (PFMPD), and others like them being conducted by the European Medicines Agency (EMA)[50], have created new opportunities for patient perspectives to inform decisions about the design and conduct of clinical trials and regulation of medical products, as shown below in Figure 5. They also have catalyzed dozens of multi-stakeholder projects to co-develop tools to facilitate meaningful patient engagement by medical product sponsors, payers, and healthcare delivery systems. Further, a growing number of life science companies have initiated or expanded initiatives to better understand patients' perspectives, with some naming experienced individuals to "chief patient officer" positions and others forming cross-functional teams to identify ways to integrate PFMPD concepts into internal workflows and practices. Likewise, patient organizations are expanding their outreach efforts and investing in registries and social-media-based research platforms to quantify their community's breadth of experience and expectations. The capacity for generating and making good use of patient experience information varies widely, but there is more interest than ever in scaling up.

(CONTINUES ON PAGE 23)

FDA's and EMA's patient-focused programs have created new opportunities for patient perspectives to inform decisions about the design and conduct of clinical trials and regulation of medical products.

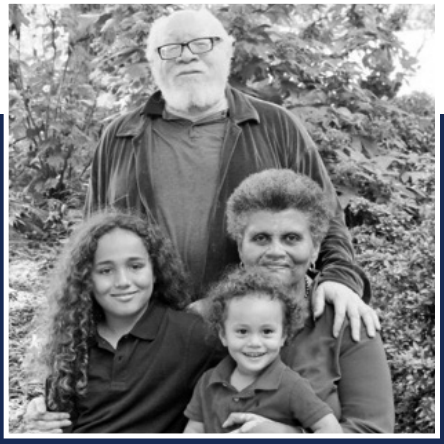
[49] *U.S. Food and Drug Administration. (2018, July 22). FDA's role in ensuring American patients have access to safe and effective medical device technology. Retrieved from https://wayback.archive-it.org/7993/20170722101552/https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm456969.htm*

[50] *European Medicines Agency. (n.d.). Patients and consumers. Retrieved from https://www.ema.europa.eu/en/partners-networks/patients-consumers*

CAREGIVER SPOTLIGHT

This Caregiver Spotlight reinforces the necessity of considering the individual patient's needs, expectations, and priorities in the context of their lives, including the medical condition(s) and concerns of those they rely upon for caregiving support. The progression and/or emergence of new conditions factors into perspectives on benefit-risk assessments and outcome prioritization, which may change over time.

WILHELMINA JENKINS AND HENRY NEAL



Henry Neal and Wilhelmina with their grandsons

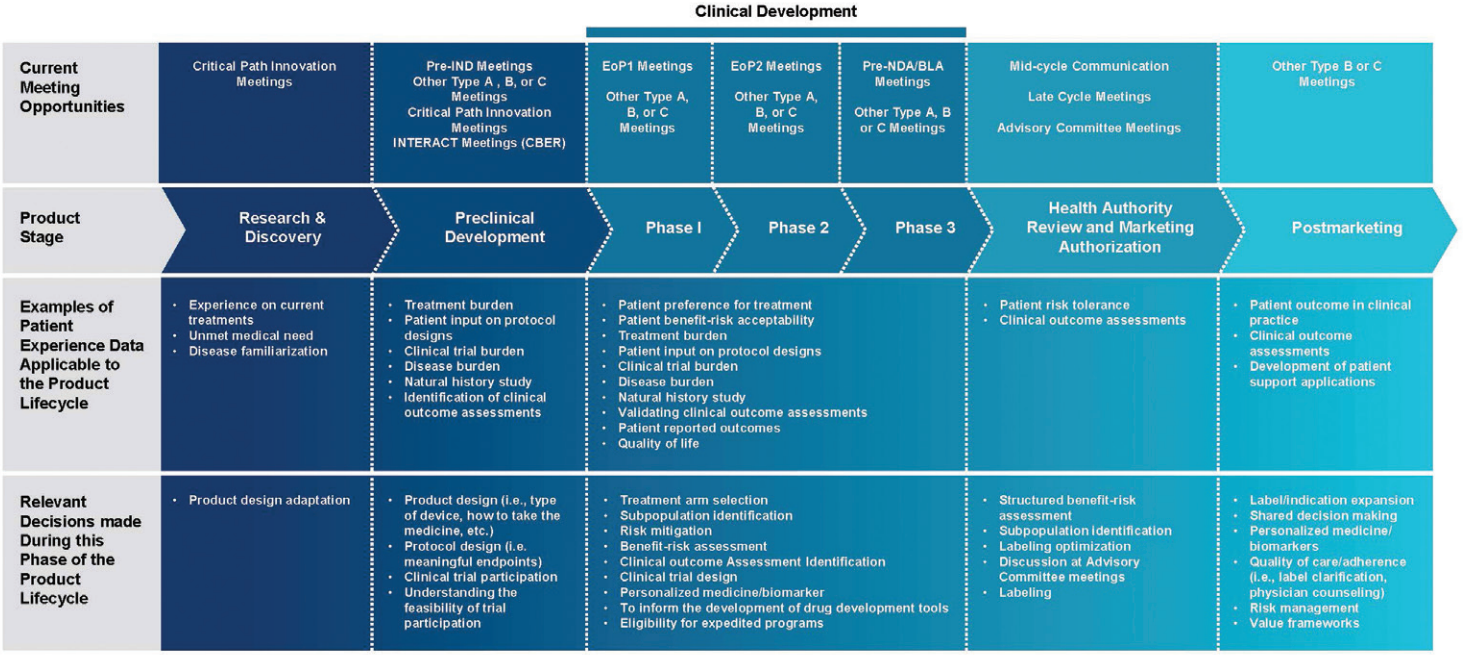
When the two physicists wed in 1987, they did so knowing they were taking on mutual caregiver roles to accommodate one another's complex medical conditions. **Henry Neal, PhD**, inherited albinism, a genetic condition that causes a reduction in melanin resulting in skin, vision, and other problems. Although his sight was already quite limited, he was working full-time, could manage independently in familiar surroundings, and was able to do light household tasks and prepare simple meals for them. **Wilhelmina Jenkins** had lived with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) since an abrupt onset in 1983 and was fully disabled from her profession due to the physical and cognitive toll it takes. She was severely limited in her ability to do household tasks and required extensive periods of rest; being upright aggravated orthostatic problems she experiences. With careful planning though, she was able to drive Henry the short distance to the Clark-Atlanta University campus at the beginning and end of each workday to meet his teaching and research schedule.

Later, Wilhelmina developed type-2 diabetes and severe joint pain and Henry was diagnosed with prostate cancer and lost his sight completely due to glaucoma. Henry also has developed balance problems following spinal surgery. The vow "to have and to hold, in sickness and in health" took on continual new meaning for the couple. Every treatment decision they made included re-evaluating its impact on the fragile balance between each of their abilities, as much as potential benefits and risks to each of them individually. "We rely on each other to take our medications on time and follow dietary restrictions. Whenever possible, I try to consolidate medical appointments and trips to the pharmacy. Outings require several days or more of recovery time," Wilhelmina reports.

After more than 30 years together, they're accustomed to constant recalibration, as acute illnesses, effects of aging, and other family caregiving roles have factored into daily life and demands on energy and abilities. Henry reflects on their journey, "For us, being realistic and honest about our limitations enables us to find ways to accomplish things together that we are unable to do separately. Loss is never easy and we have lost a great deal. But when we face our losses together, we can focus on all that we still have."

FIGURE 5: BIO'S FRAMEWORK FOR THE USE OF PATIENT EXPERIENCE DATA THROUGHOUT THE PRODUCT LIFECYCLE

Biotechnology Innovation Organization



DISTINGUISHING CAREGIVER PERSPECTIVES FROM PATIENT PERSPECTIVES

In settings where PFMPD is discussed, caregivers are regularly acknowledged as having a valuable perspective to contribute. It is quite common for a speaker to state at the outset of a presentation, "When I/we say 'patient,' we mean an individual with lived experience as the person diagnosed with a condition, caring for a person with a condition, or advocating on behalf of a person with a condition." This may be at least in part a courtesy, recognizing that in the setting of some medical conditions, it is challenging for patients to participate directly. It also may reflect a general sense that the caregiver has a close-up understanding of the condition and the patient's experience that – much like the patient's own perspective – has not been fully utilized as an R&D evidence source.

A 2015 white paper issued by the National Health Council addresses the need to consider each party separately: "…it is important to recognize that 'the patient perspective' is not monolithic, even within a disease or condition. Consumers, patients, family/caregivers, and patient advocacy organizations are all entities that can potentially provide valuable perspectives; however, those perspectives can vary widely."[51]

[51] *National Health Council & Genetic Alliance (2015). Dialogue/advancing meaningful patient engagement in research, development, and review of drugs. Retrieved from http://www.nationalhealthcouncil.org/sites/default/files/PatientEngagement-WhitePaper.pdf*

Consistent with a key pillar of medical ethics, the patient's moral right to express and act on his/her own perspective, preferences, and choices remains paramount.

At the Summit, **Pujita Vaidya** cited an example from a PFDD meeting on autism where many parents spoke on behalf of their children with autism, but one individual with autism spoke for himself, saying "We are autonomous people from our parents and often have different goals and needs than they do." Pujita observed, "Having this rich discussion is really helpful; it provides an understanding of both the patient's perspective and the caregiver's point of view on treatments and outcomes so we can integrate this information early on."

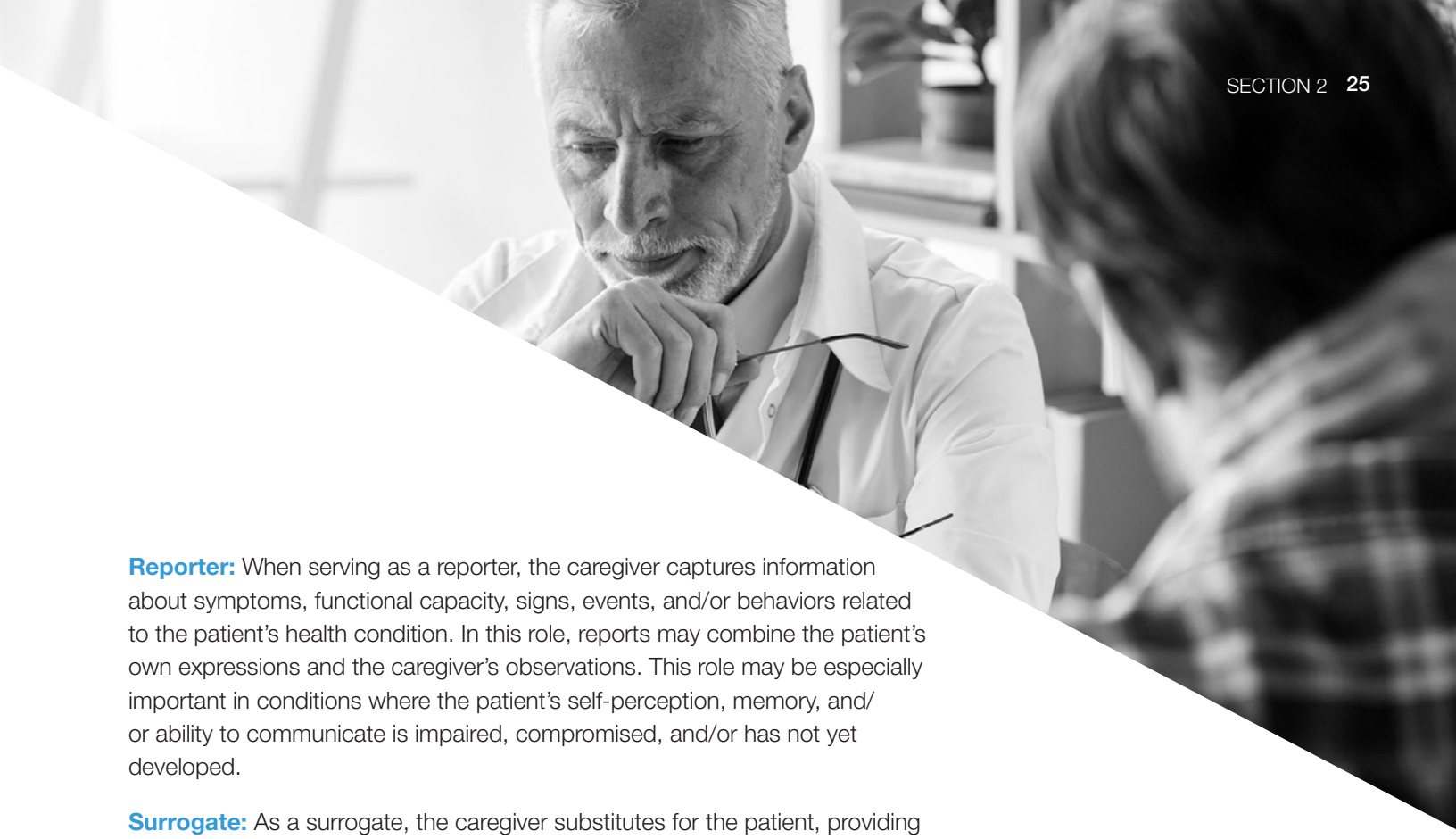
Annie Kennedy shared an example from studies conducted by Parent Project Muscular Dystrophy (PPMD). "In one study that involved both patients with Duchenne and their caregivers, we found differences among the boys' preferences for non-skeletal treatment targets compared to caregivers' preferences. The number of patients in that study was much smaller than the number of caregivers, so we are doing a much larger, global study to compare patient, caregiver, and physician treatment priorities and preferences." (See Snapshot on page 33.)

Building on these experiences, the Summit's exploration of distinct roles for caregivers can be viewed as a sign of progress in our collective understanding of patient-centricity. It also warrants a clear and direct statement about the relative importance of these viewpoints: consistent with a key pillar of medical ethics, the patient's moral right to express and act on his/her own perspective, preferences, and choices remains paramount. This initiative seeks to identify ways that caregivers can support patients' reports of their own preferences and experiences, supplement the patient's perspective, provide their own independent viewpoint, or, when needed, serve as a surrogate for a person not capable of articulating their own perspective. This information has the potential to inform clinical development plans, clinical trial operations, market access strategy, regulatory filings, commercial launch plans, healthcare utilization, ongoing safety monitoring, and other aspects of development and delivery. It may also yield improved understanding of the patient-caregiver dynamic that can be contextualized for the process of developing medical products for specific disease states. Later in this section, roles for the caregivers at each phase are explored in more detail.

DEFINING CAREGIVER ROLES

An important building block for this initiative is recognizing the different viewpoints of the caregiver as they relate to the care recipient. The following are working definitions intended to illuminate sometimes subtle differences in caregiver perspectives and roles. These will continue to evolve as more experience accrues and with more definition of the larger science of patient input.

Observer: As an observer, the caregiver makes independent observations about signs, events, and/or behaviors related to the patient's health condition. These observations do not require any medical judgement or interpretation.



Reporter: When serving as a reporter, the caregiver captures information about symptoms, functional capacity, signs, events, and/or behaviors related to the patient's health condition. In this role, reports may combine the patient's own expressions and the caregiver's observations. This role may be especially important in conditions where the patient's self-perception, memory, and/or ability to communicate is impaired, compromised, and/or has not yet developed.

Surrogate: As a surrogate, the caregiver substitutes for the patient, providing information about the patient's condition or perspective based on what the caregiver has heard directly from the patient or understands to be the patient's own experience or viewpoint.

Proxy: The role of proxy involves more agency of the caregiver acting on behalf of the patient, which may be legal authority (such as authority conveyed through a medical power of attorney or being the legal parent/guardian of a minor child) or simply the person who best knows the patient's wishes or values. As a proxy, the caregiver may interpret circumstances through their prior interactions, such as, "This is what I believe he/she would want, based on decisions made in the past."

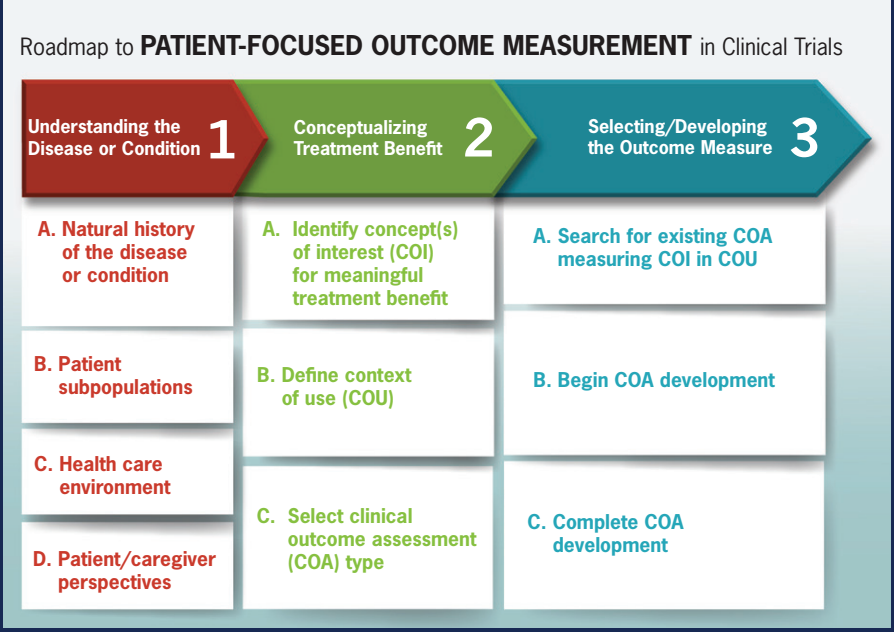
While these roles relate to the caregiver's direct or interpreted observations about the patient, there may be circumstances in which the caregiver's own experience is relevant to medical product decisions. EMD Serono's **Schiffon Wong** stated, "As medical product developers, we should be thinking about a holistic 'integrated' patient journey that includes the caregiver. In clinical trials we are really often enrolling 'dyads' of patients and one or more caregivers. Operational considerations that reduce the burden for both are important. Caregivers may need to understand how to administer a medicine or treatment, and we should think about caregiver-relevant labeling and support services so they can adequately perform any required medical or nursing tasks. Their preferences are often very important to understand."

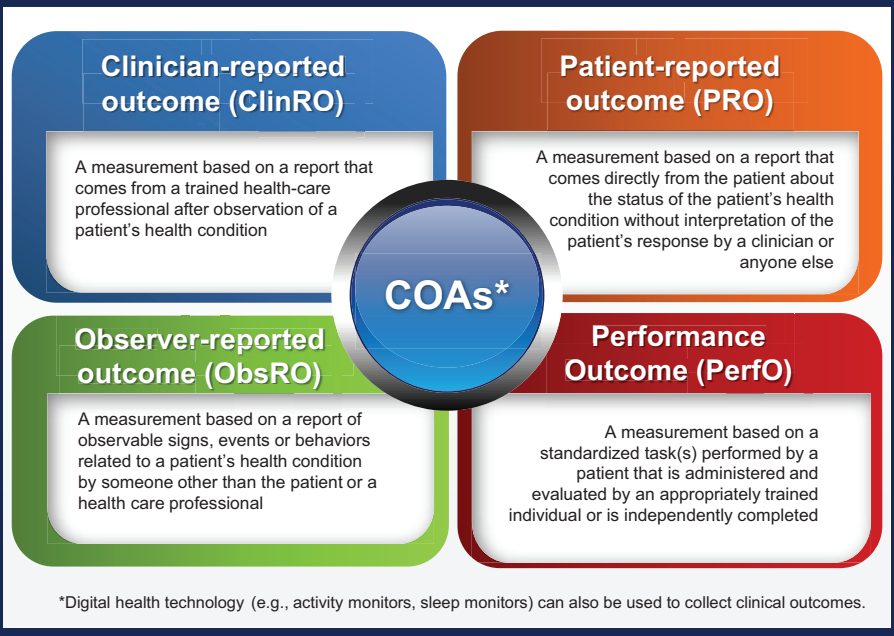
"As medical product developers, we should be thinking about a holistic 'integrated' patient journey that includes the caregiver."

Schiffon Wong

In addition, while the patient/care recipient is the person who experiences the disease/condition and the direct benefit and/or harm from a medical product, the condition and treatment may have consequences for the health and well-being of the caregiver, as discussed in Section 1. Therefore, products/services that reduce disease and treatment burden for both the patient and caregiver may have greater perceived benefit and value to patients, caregivers, clinicians, and payers.

(CONTINUES ON PAGE 27)





SNAPSHOT: CLINICAL OUTCOME ASSESSMENTS

The U.S. Food and Drug Administration (FDA) has defined different types of clinical outcome assessments (COAs) to measure how a patient feels, functions, or survives.* COAs can be used to assess the treatment benefits and/or safety of a medical product. Central to the COA is a "concept of interest," the thing measured by the COA – pain intensity, sensory acuity, or cognition, for example. A conclusion of treatment benefit can be described in product labeling in terms of the concept of interest, serving as useful information for the patient and prescribing physician about benefits the patient might experience in how s/he feels or functions.

There are four types of COAs, as described in the FDA's figure (at left).

Additionally, the FDA's 2009 guidance on PRO measures** includes a description of "proxy-reported outcomes" as "a measurement based on a report by someone other than the patient reporting as if he or she is the patient" and differentiated them from other COAs as follows: "A proxy-reported outcome is not a PRO. A proxy report also is different from an observer report where the observer (e.g., a clinician or caregiver), in addition to reporting his or her observation, may interpret or give an opinion based on the observation. We discourage use of proxy-reported outcome measures particularly for symptoms that can be known only by the patient."***

On October 15-16, 2018, FDA convened a workshop**** to examine methodological approaches that may be used to identify what is most important to patients and caregivers with respect to burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease or condition. The workshop also addressed best practices for selecting, developing, or modifying fit-for-purpose COAs to measure the patient experience in clinical trials. This dialogue will inform FDA's development of patient-focused drug development guidances, as described on page 30.

**U.S. Food and Drug Administration. (2018, December 17). Clinical Outcome Assessment (COA) Qualification Program. Retrieved from https://www.fda.gov/drugs/developmentapprovalprocess/drugdevelopmenttoolsqualificationprogram/ucm284077.htm*

***U.S. Food and Drug Administration. (2009). Guidance for industry Patient-Reported Outcome Measures: Use in medical product development to support labeling claims. Retrieved from https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf*

****Ibid, page 21.*

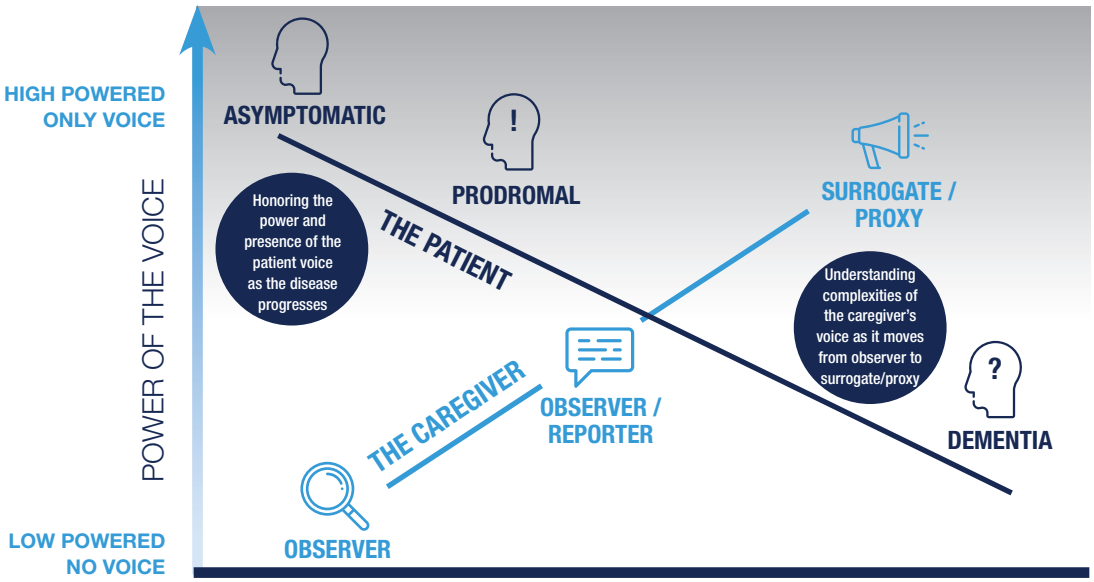
*****U.S. Food and Drug Administration. (2018, November 15). Patient-focused drug development guidance: methods to identify what is important to patients and select, develop or modify fit-for-purpose Clinical Outcome Assessments. Retrieved from https://www.fda.gov/Drugs/NewsEvents/ucm607276.htm*

CONCEPTUAL MODELS

To illustrate the various roles a caregiver might serve, both over time and across different disease states, **Debra Lappin** presented a series of conceptual models at the Summit. Initially developed for use with the dementia-Alzheimer's disease research project known as AD PACE (see Snapshot on page 35), she has drawn on her experience at Faegre Baker Daniels Consulting and work with a variety of patient advocacy organizations to develop working models for other groups of conditions and scenarios. She explained, "We can use these as a framework for understanding how we can honor the voice of the affected person as long (or as soon) as that's possible, while also recognizing the value of the caregiver's voice. In early stage Alzheimer's, the person with the disease can still reliably report on function and quality of life, so the caregiver's role is mainly as an observer. With progression of the disease, this shifts. [See Figure 6, below.] One of the early lessons of AD PACE has been how much earlier the patient begins to rely on the caregiver's observations and reporting ability than had been previously appreciated."

One of the early lessons of AD PACE has been how much earlier the patient begins to rely on the caregiver's observations and reporting ability than had been previously appreciated.

FIGURE 6: DEMENTIA-ALZHEIMER'S MODEL



Lappin, 2016

Debra then described the model for some pediatric conditions, as shown in Figure 7 on page 29. "In rare genetic conditions like Duchenne, we can imagine the slope being inverted, with the adult parent or guardian having the high or only voice, and the child's own voice gaining strength as the child ages and their capacity to articulate needs, expectations, and preferences increases, moving toward the point where the child becomes a young adult and can consent to clinical trials and make independent treatment decisions. While the parent can still be a valuable reporter and observer in this context, the parent may need to learn how to yield.

(CONTINUES ON PAGE 29)

CAREGIVER SPOTLIGHT

In this Spotlight, Los Angeles native Kim Ridley's story emphasizes the benefits of family dialogue and advance care planning to guide decisions about treatment, clinical trial participation, and end-of-life care. It also illustrates that the patient-caregiver "dyad" may actually be more "flower-shaped," with multiple caregivers supporting an individual's needs, each with their own role to play and viewpoint to contribute.

KIM RIDLEY

Kim with her mother, Hazel Arch, and Hazel with her seven living children

Kim Ridley was the ninth of 10 children born to her mother, Hazel Arch. While the responsibilities of planning for a parent's declining health in later years often fall to the eldest children in family, Hazel named Kim as her medical power of attorney when she was still in very good health in her 70s. She also made sure Kim understood that when the time came for Kim to make decisions on her behalf, preserving her pride and dignity were of utmost importance.

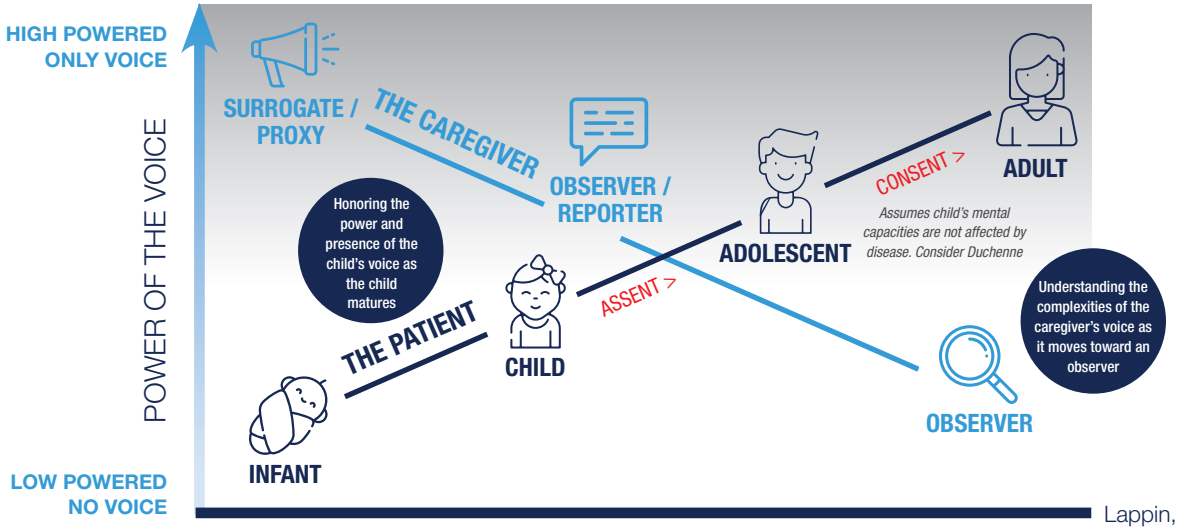
A few years earlier, the large family had made a commitment to meet monthly for Sunday dinner at their mother's house. "There would be 30-40 of us together at these dinners. The bonds we renewed as adults helped my sisters, brothers, and me navigate the family dynamics that inevitably occur when our mother was diagnosed with early Alzheimer's at age 85. Each of us took the news differently, but they recognized that Mom trusted that I knew what she'd want," Kim said.

Hazel was fiercely independent and insisted on living alone. She had osteoarthritis which limited her mobility and made it hard to get around. That, coupled with her age and a sensitive stomach, made them decide together not to pursue clinical trials or experimental therapies. "We decided to love what time we had left together," Kim reminisced, reporting it wasn't easy to get everyone to go along with that at first.

Kim set a schedule for Hazel's seven living children and two of her adult grandchildren to take turns staying overnight. Kim also sought support and education from Alzheimer's Los Angeles; some of her fellow family caregivers participated in sessions with counselors and family programs; others didn't. "Each of us did what we could manage," Kim acknowledged.

One day in August of 2017, Hazel fell in the bathroom after her two eldest sons brought her home from a dental appointment. She hit her head badly and was taken by ambulance to the hospital; her brain swelled and she remained unconscious. "Mom had already signed a 'Do Not Resuscitate' order prohibiting extraordinary measures, which took the guesswork out of decision-making when this occurred." Kim described the rather cut-and-dried circumstances at the end of her mother's long life – and those monthly family dinners – as being pivotal to preserving family relationships among her siblings. "We're all still talking to each other. We all understood what Mom wanted."

FIGURE 7: PEDIATRIC DISEASE MODEL

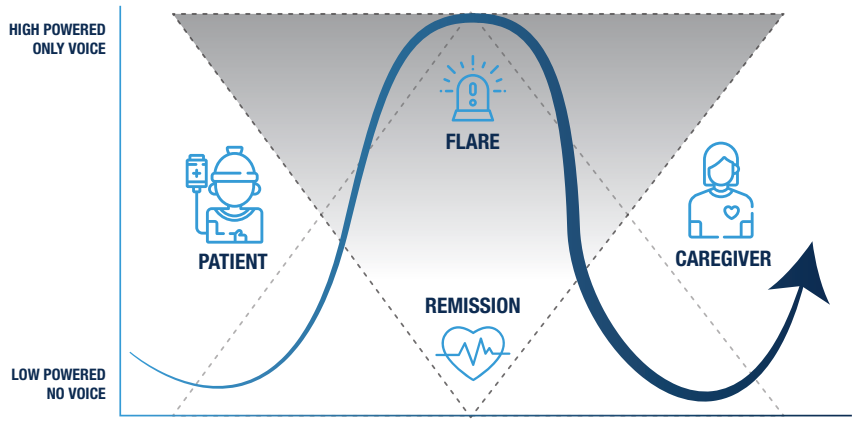


Lappin, 2018

Annie Kennedy commented on this depiction, explaining that the significant impairments young men with Duchenne experience require ongoing dependence on family (and paid) caregivers. "Until very recently, the caregiver voice was really the only voice in our community, because our patients weren't living long enough to be able to express their own voices. Now we're trying to understand through our preference studies how the personal preferences and priorities of boys and their parents contribute to decision-making around interventions, clinical trial participation, etc.," she stated, acknowledging the complexities. (See Snapshot on page 33.)

One final model illustrated the dynamic interplay of patient and caregiver roles in conditions that may wax and wane or remit and relapse, either as a part of the natural history, in response to therapeutic interventions, or as an outcome of treatment adherence, as shown in Figure 8. As Debra indicated, "In mental health and other types of conditions, the parent or spouse/partner's role may be one of observer/reporter until there is a flare, when their role becomes more prominent as a surrogate until the disease comes back under control and the power of each voice flips back."

FIGURE 8: REMITTING & RELAPSING MENTAL HEALTH AND CHRONIC CONDITION MODEL



Lappin, 2018

(CONTINUES ON PAGE 31)

"In mental health and other types of conditions, the parent or spouse/partner's role may be one of observer/reporter until there is a flare, when their role becomes more prominent as a surrogate until the disease comes back under control and the power of each voice flips back."

Debra Lappin

SNAPSHOT: PATIENT EXPERIENCE DATA

The FDA's Patient Focused Drug Development (PFDD) initiative launched in 2013 has, as **Pujita Vaidya** stated at the Summit, "been a monumental time for elevating the patient voice." It contributed greatly to overwhelming support – not only from Congress, but from industry and the patient advocacy community – for passage of provisions of the 21st Century Cures Act which further strengthens opportunities for patients and caregivers to inform the medical product development process.

Title III, Section 3001 of the 21st Century Cures Act describes a new type of information collected to inform regulatory decision-making called "patient experience data." It is defined as:

> "Data collected by any person (including patients, family members, and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers) that are intended to provide information about patients' experiences with a disease or condition. The term specifically includes data regarding (a) the impact of the disease or condition, or a related therapy, on patients' lives; and (b) patient preferences with respect to treatment of the disease or condition."*

FDA's plan for four guidance documents it is developing in response to the Act identifies the following purposes for collecting patient experience data:

> "Ideally, these patient-identified disease impacts, and potential measures of benefit and burden, would be explicitly considered from the early stages of drug development. In addition, these patient-identified key impacts and elements of disease experience could be translated into a measurement set that is validated for clarity to patients, reliability in capturing their reported experience, and responsiveness of the reporting scale to reflect changes in experience. For a given disease the set of elements used in different clinical studies would ideally reflect those that patients have identified as mattering most to them."**

Section 3004 of the statute mandates that as of June 13, 2017, all new drug approvals must include a brief statement summarizing any patient experience data that was submitted and reviewed as part of the application.***

As a report issued by contract research organization Evidera states, these statutory requirements and FDA's guidance plan, "…suggest that we have entered a new era of drug development where systematic inclusion of patients' perspectives and experiences across the drug development cycle are an integral part of drug development and approval process."****

Congress. (2016, January 4). Public Law 114 – 255.

**U.S. Food and Drug Administration. (2017). Plan for issuance of patient-focused drug development guidance. Retrieved from https://www.fda.gov/downloads forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf*

***Congress. (2016, January 4). Public Law 114 – 255, Subtitle B - Advancing new drug therapies. Retrieved from https://www.congress.gov/114/bills/hr34/BILLS-114hr34enr.xml#toc-H4B1DD3D645DA41BDA35C039B96801922*

****Wilson, H., Anatchkova, M., & Gelhorn, H. (2017). A perspective on the 21st Century Cures Act: Patient-focused drug development. Retrieved from https://www.evidera.com/wp-content/uploads/2017/11/04-A-Perspective-on-The-21st-Century-Cures-Act-Patient-Focused-Drug-Development_2017Nov-1.pdf*

In the discussion that followed the presentation of these conceptual models, additional variations were described. **Margaret Longacre** of Arcadia University suggested another dynamic, based on her prior experience as director of research for the Cancer Support Community and personal experience as a caregiver for her father who had Lewy Body Disease, a common cause of dementia. "How could we reflect the more continuous involvement of the caregiver in decision-making for treatment and clinical trials, like we see in cancer? Some cancers, like brain cancer, follow a similar transition pattern to the one presented for Alzheimer's, while others might look more like the other two models. The treatment period may be shorter than some other conditions, but it's very intense and the caregiver is often the one who has to absorb and process a lot of the information," Margaret said.

Rachel Cannady of the American Cancer Society agreed. "The trajectory of caregiving distress in cancer spikes at the time of diagnosis, during treatment, and then, as treatment comes to an end, there may be added anxiety about moving away from the medical setting and losing the ongoing surveillance (and support) from the medical team. A recurrence of the cancer or onset of a second primary diagnosis spikes that distress again. We are trying to educate and empower caregivers so they are better prepared."

Jenna McDavid of the Diverse Elders Coalition raised the important need to ensure that models are inclusive of diverse experiences: "Rates of participation in clinical trials by people of color and the LGBT community are extremely low. We need to understand how their potentially different experience can be reflected in these types of conversations and research efforts." Generational differences were mentioned as well, with older individuals perhaps according greater respect to medical professionals' views than young people, who place more reliance on their own research and peers' experiences.

Bringing in her work with HIV-positive adolescents, **Maureen Lyon** of Children's National Medical Center shared key insights from a five-year study to determine the effect of family-centered advance care planning (FACE pACP) with 105 patients and their family members, 93 percent of whom were African-American.[52] While this example related to an interpersonal process, rather than a medical product, it underscores the value of understanding perspectives of both patients and caregivers. "We asked teenagers with HIV, 'Would you like to have a voice in your own end-of-life care if you couldn't speak for yourself?' We asked bereaved parents, 'Would you have liked to have had the opportunity to talk to your dying child about death and dying?' With feedback from both groups, we adapted the Respecting Choices adult model for advance care planning (see page 36) to be a three-session intervention. Teens said that one meeting wasn't enough and that going down to age 12 was too young, so we started at age 14. Parents told us they didn't want us coming to their homes. There is still a lot of stigma about disclosing the diagnosis outside the family, so we met at the hospital," Maureen recounted.

Maureen continued, reporting their findings, "FACE pACP increased and maintained agreement about the goals of care over time, which also had the effect of lowering teens' physical symptoms and suffering as measured by very well-validated scales.

Learnings from a study of family-centered advance care planning underscore the value of understanding perspectives of both patients and caregivers.

[52] *AAP News & Journals Gateway. (2018, November). Advance care planning and HIV symptoms in adolescence. Retrieved from http://pediatrics.aappublications.org/content/142/5/e20173869.long?sso=1&sso_redirect_count=1&nfstatus=401&nftoken=00000000-0000-0000-0000-000000000000&nfstatusdescription=ERROR%3a+No+local+token*

"Parents are very effective reporters of pain in their young children, yet our findings showed that parents were not as accurate at reporting pain in adolescents; caregivers both under-reported and over-reported their teen's pain."

Maureen Lyon

Truly, these outcomes were equivalent to what we'd hope to see in a drug intervention trial. By having the family in the room and increasing communication, we were able to get families on the same page and have this very significant symptom relief." (See Snapshot on page 36 for information about advance care planning tools.)

Two additional points Maureen made relate to a similar study of adults with HIV, another study in cancer, and her work with aged adults. "First, the literature suggests that parents are very effective reporters of pain in their young children. Our findings among these teens and their family caregivers showed that parents were not as accurate at reporting pain in adolescents; caregivers both under-reported and over-reported their teen's pain. Second, 90 percent of the people with HIV who were eligible to participate as a patient in our adolescent and adult studies could not identify a family caregiver or a surrogate decision-maker whom they trusted enough to make decisions for them. Part of that was based on not having disclosed their HIV status. In our cancer trial, however, we never had a situation where a teenager or an adult couldn't identify somebody to speak for them. Yet, we do find this in older populations, and there's more literature coming out about the 'unbefriended.' We need to be creative in how we include unbefriended people in our research," Maureen advocated.

Discussion of these models and scenarios prompted **Cynthia Bens** of the Personalized Medicine Coalition to add, "We tend to think of 'personalized medicine' as targeting the molecular underpinnings of a disease with a specific treatment, but we also consider it to mean matching treatment to the preferences, values, and circumstances of the patient and their family. We're getting better at matching on biology, but we have a long way to go to be successful with preferences and values. Some of our work suggests that it's not until well into treatment that people feel informed and empowered enough to weigh in with those."

Cynthia's comment about there being a long way to go resonated with other aspects of the discussion. There was general consensus about the tremendous opportunity that lies ahead if patients and caregivers were meaningfully engaged in all aspects of medical product development and healthcare delivery.

ACKNOWLEDGING CHALLENGES

Summit participants were enthusiastic about opportunities to more fully engage caregivers in medical product development; they were also realistic about some of the challenges in doing so. Chief among them, was a concern about adding more weight to caregivers' responsibilities and the risk of increasing strain on taxed resources of time, energy, and emotional reserves. There was general recognition that some individuals would be more immediately capable of contributing to medical product development and that others would be inclined but might need

training and other forms of support to help build confidence and skills.

The discussion of ethical issues (see page 45) raised the importance of balancing the patient's privacy with the caregiver's full knowledge of medical history, current condition, and treatment decisions; in some cases a more limited view of the total picture may compromise the caregiver's ability to participate effectively. In other circumstances, the patient's perspective/priorities and the caregiver's may not agree, as early research from PPMD and others has illustrated, and, as FDA's Pujita Vaidya stated, is not necessarily the objective in eliciting perspectives from both.

One challenge that may require more exploration to address is how to discern which of the roles described on pages 24-25 the caregiver is performing. The lines may not always be clear, especially in conditions where there are waxing and waning features, or where progression or ascension of intellectual capacity is not linear. A 2018 study conducted by Mayo Clinic, Weill Cornell Medical School, and UsAgainstAlzheimer's interviewed caregivers of and individuals with cognitive impairment (CI) identified through the A-List (see page 35). One of its findings was, "Both people with CI and caregivers expressed that people with CI should maintain decisional authority within the health care setting as long as possible. However, navigating the shift from a competent to incompetent decision maker is fraught with challenges."[53] Additionally, there may be some aspects of a condition – or times in the lifespan of a patient – that the caregiver's perspective is more accurate and crucial than others, as Maureen's observations about pain levels (page 32) illustrate.

Additionally, there are pragmatic issues to overcome, such as identifying new resources to support the studies needed to document methods to effectively elicit and utilize caregivers' perspectives. Life science companies may need to be convinced of the business or regulatory "return on engagement" for such information in order to make it a budgetary priority. MDIC helped advance a tool to help identify "preference sensitive decisions" in medical product development that could be adapted to help discern the need and appropriateness of caregiver input, as posited on page 50.

PHASE-BY-PHASE POSSIBILITIES

These and other challenges notwithstanding, there are numerous specific ways in which caregivers could inform medical product development. Figure 9 is a model of patient engagement developed by the Clinical Trials Transformation Initiative (CTTI), a public-private partnership, that provides a useful framework and starting point.

Discovery & Pre-Clinical Phase: Caregivers can provide meaningful observations to help build a holistic understanding of the natural history of a condition and can weigh in with their own impressions of research priorities, as well as articulating those as reporters, surrogates, or proxies for their care recipients, when appropriate. **Christina SanInocencio** of the Lennox-Gestaut Syndrome Foundation indicated that caregivers of people with rare epilepsies are actively engaged in helping document the natural history of these conditions through the Rare Epilepsy Network. They can also inform the understanding of unmet medical

SNAPSHOT: PREFERENCE STUDIES INFORM DECISION-MAKING IN DUCHENNE

Parent Project Muscular Dystrophy (PPMD) was among the first patient advocacy organizations to conduct scientifically rigorous preference studies to aid therapy development. PPMD's first study published in 2012* revealed a willingness of caregivers to accept considerable risk and uncertainty on behalf of their child for a therapy that stops or even slows the progression of Duchenne. These findings have been useful in both the regulatory and therapeutic access context based on community interest in accessing the first two drugs approved to treat Duchenne.

A second preference study of both caregiver and patients' preferences for non-skeletal muscle benefits** demonstrated the high value both groups placed on cardiac and pulmonary benefits, such as a stronger cough and fewer lung infections. The study results also provided drug developers with data about symptom treatment priorities not associated with skeletal muscle, and the heterogeneity of those priorities based on the patient's experience.***

In 2018, PPMD launched a global study of benefit-risk preferences in patients and caregivers and a study focused on risk tolerance in gene therapy interventions. Both are being conducted in collaboration with industry, academia, and federal agencies and results will be reported in 2019.

*Adapted from PPMD's website*****

**Peay, H. L., Hollin, I., Fisher, R., & Bridges J. F. P. (2014). A community-engaged approach to quantifying caregiver preferences for the benefits and risks of emerging therapies for Duchenne muscular dystrophy. Clinical Therapeutics. Vol (36), No. 5. Retrieved from https://www.parentprojectmd.org/wp-content/uploads/2018/07/Preference_Study_Pilot_Study_Quantifying_Caregiver_Preferences_-_Publication_1.pdf*

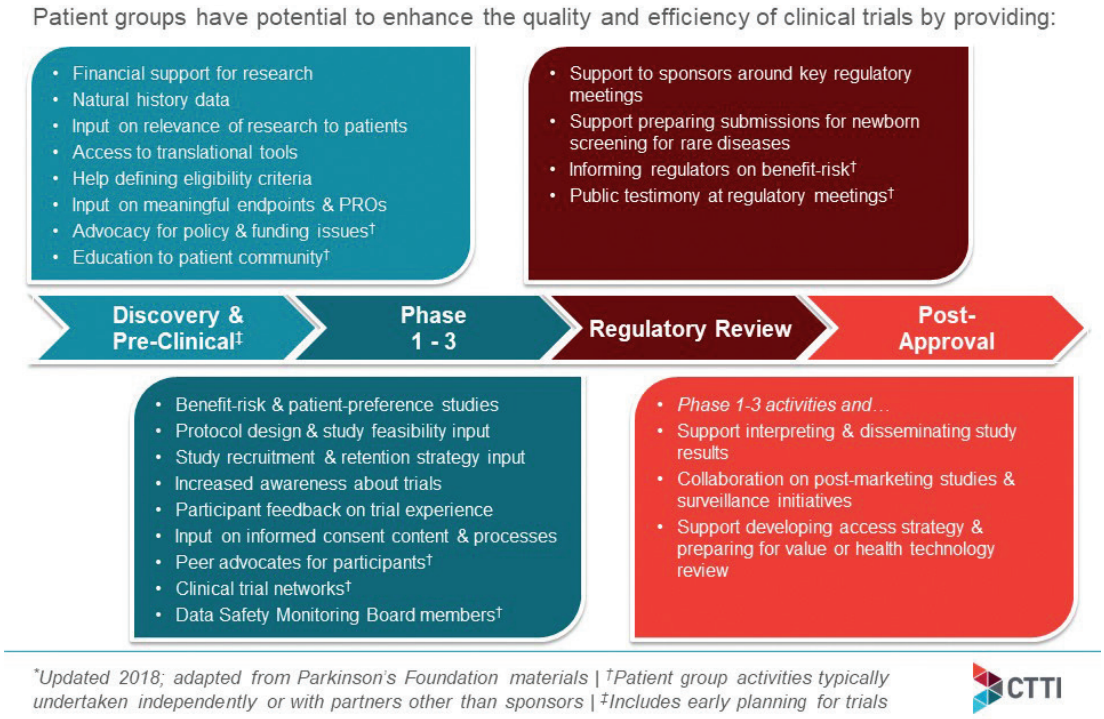
***Hollin, L. I., Peay, H. L., Apkon, S. D., & Bridges, J. F. P. (2016). Patient-centered benefit-risk assessment in Duchenne muscular dystrophy. Retrieved from https://www.parentprojectmd.org/wp-content/uploads/2018/07/Preference_Study_Second_Study_on_treatment_targets_and_meaningful_benefit_Publication_1.pdf*

****Hollin, I. L., Peay, H., Fisher, R., Janssen, E. M., & Bridges J. F. P. (2018). Engaging patients and caregivers in prioritizing symptoms impacting quality of life for Duchenne and Becker muscular dystrophy. Quality of Life Research. Retrieved from https://www.parentprojectmd.org/wp-content/uploads/2018/07/Preference_Study_Second_Study_prioritizing_treatment_targets_-_Publication_2.pdf*

*****Parent Project Muscular Dystrophy. (n.d.). Regulatory Advocacy. Retrieved from https://www.parentprojectmd.org/advocacy/our-strategy-and-impact/regulatory-advocacy/*

[53]Griffin J.M., Bangerter L., Havyer, R., et al. November 2018. Gerontological Society of America Annual Scientific Meeting (presented poster). Integrating family caregivers into health care delivery: The building blocks for potential best practices."

FIGURE 9: PATIENT GROUP ENGAGEMENT ACROSS THE CLINICAL TRIAL CONTINUUM



needs and identify targets that align best with a patient-centered view of medical needs. Their perspective can be used to continually refine the target product profile and design features of the product, including dosing and mode of administration.

As **Mousumi Bose** explained at the Summit, caregivers can be valuable partners in crafting development tools like trial endpoints, PROs, and ObsROs. (See Snapshot on page 26 for a description of these tools.) "Speaking mainly from the experience of pediatric rare diseases where the patient is not able to communicate directly, parent caregivers are the experts about the symptoms of these conditions and how their child is experiencing them. Often the natural history is not well documented, and parents notice things that go under the radar of clinical observations and records. They are the best source of information about which aspects of the disease impact their child's day-to-day life. They can help with the phrasing of survey instrument questions, testing the instrument, and helping determine how it can be used to measure treatment benefits in clinical trials," Mousumi stated, based on her studies conducted at Montclair State University. (See also Mousumi's Caregiver Spotlight on page 12.) **Debra Lappin** suggested that caregivers are positioned to advise on creating COAs that are both patient-centered and relevant to caregivers. This might have particular importance in conditions where the caregiver is helping to keep the patient at home, rather than receiving care (temporarily or permanently) in an acute- or long-term care facility.

"Caregivers can help with the phrasing of survey instrument questions, testing the instrument, and helping determine how it can be used to measure treatment benefits in clinical trials."

Mousumi Bose

Phase 1-3: As a medical product moves into clinical trials, caregivers can participate in many of the same ways as patients. As in the earlier stage of research, their viewpoints might be sought as an observer, reporter, surrogate, and/or proxy for the care recipient, or their independent perception of benefit-risk tradeoffs and preference may be of interest as well. **Schiffon Wong** made this point at the Summit: "We need to keep expanding our conceptualization of clinical

benefit and societal value and recognize the caregiver as an extension of the patient who is impacted by clinical benefit from a societal and healthcare outcome standpoint." Particularly in conditions where individuals rely on a family caregiver to enable their participation in a clinical trial, obtaining caregiver input on protocol design, informed consent content and processes, and recruitment and retention strategies will improve acceptability, enrollment, and retention. Their participation in clinical trial simulations would be vital as well, with special contributions they can make to trial requirements that will take place outside the clinical setting, such as post-clinic visit care or follow-up. Caregivers also can serve on data safety monitoring boards, assess communications with potential and enrolled clinical trial participants (and caregivers), and help to make sense of trial data. Their input on early or expanded access programs can be vital, especially for products that may serve individuals for whom the caregiver will be likely to act as a surrogate or as a proxy for care recipients.

Regulatory Review: Building on the opportunities in earlier phases, as a product approaches the point of filing for marketing approval, caregivers can provide support in key regulatory meetings; articulate the unmet medical needs of patients; validate the desirability of benefits experienced by clinical trial participants; and evaluate the tolerability of tradeoffs represented by potential or experienced side effects, adverse events, or other harms, based on their observations and interaction with patients and other caregivers. Their testimony at public meetings such as Advisory Committee sessions convened by FDA to consider evidence from the sponsor's submission can be useful as well. Caregivers may also be valuable to include in focus groups or other market research conducted to assess

(CONTINUES ON PAGE 37)

> "We need to keep expanding our conceptualization of clinical benefit and societal value and recognize the caregiver as an extension of the patient who is impacted by clinical benefit from a societal and healthcare outcome standpoint."
>
> Schiffon Wong

SNAPSHOT: ALZHEIMER'S DISEASE PATIENT AND CAREGIVER ENGAGEMENT (AD PACE) INITIATIVE

AD PACE is a ground-breaking patient and caregiver-led precompetitive collaboration among industry, academics, government agencies, and advocates. It was launched in May 2018 to build a sustainable research platform that will deliver new insights to research, regulatory, and payer authorities on preferred treatment and health outcomes sought by those living with Alzheimer's disease and their caregivers.

AD PACE studies will become an authoritative "patient voice" to inform product and clinical trial design, regulatory submissions, payer value models, coverage and payment determinations, and research on care and services in Alzheimer's disease. They will also become part of a shared data commons.

One component of AD PACE is the A-LIST, a first-of-its kind online community of people with or at risk for Alzheimer's disease, other dementias, and Mild Cognitive Impairment, along with current and former care partners. Its 6,265 members (as of January 2019) are regularly invited to respond to "What Matters Most" Insight Surveys. There have been 17 surveys fielded to date with more than 20,000 responses; more surveys are in development. Topics have included clinical trial participation, at-home care, technology, and caregiver-physician relationships.

Survey results are helping inform the two-part "What Matters Most" study, a mixed-methods research project to better understand the treatment-related needs, preferences, and priorities of people with Alzheimer's disease and their care partners.

Adapted from UsAgainstAlzheimer's website and a poster presentation at the 2018 Alzheimer's Association International Conference.***

**UsAgainstAlzheimer's. (n.d.). About Us. Retrieved from https://www.usagainstalzheimers.org/networks/ad-pace*
***Vrandenberg, G., Callahan L.F., Comer M., et al. Alzheimer's Association International Conference. (2018, July). Alzheimer's Disease Patient and Caregiver Engagement Initiative (AD PACE): Determining what matters most to Alzheimer's patients and caregivers to inform the development of new therapies, payment and coverage determinations, and delivery of care services*

SNAPSHOT: TOOLS FOR ADVANCE CARE PLANNING

These two programs are beneficial adjuncts to the dialogue about caregiving roles; they are also instructive in terms of how to scale a new practice involving patients and caregivers from inception to broad adoption.

Respecting Choices

In 1985, clinical ethicist Bud Hammes observed that families and physicians frequently experience moral distress when faced with critical choices about treatments for patients and loved ones who lack decision-making capacity to participate in their healthcare decisions. Although his experience related mostly to older patients who had prolonged periods of worsening health with ample opportunity to engage in planning, health professionals had no training or workflows to help make advance care planning happen. Bud developed the "If I Only Knew" program to provide an organized system of educating nurses to facilitate conversations with patients and families, starting first with kidney dialysis patients. From those origins has grown an international, evidence-based curriculum and training model of advance care planning used in 12 countries, 27 U.S. states, and 287 U.S. healthcare centers that creates a healthcare culture of person-centered care honoring an individual's goals and values for current and future healthcare.

*Adapted from the Respecting Choices website**

Five Wishes

After serving as legal counsel for Mother Teresa of Calcutta for 12 years, Jim Tomey founded a nonprofit organization, Aging With Dignity, to improve end-of-life care by encouraging people to make medical decisions in advance of a serious illness. With help from the American Bar Association and end-of-life experts, and support from The Robert Wood Johnson Foundation, in 1998 Aging with Dignity developed the Five Wishes advance directive document. It was designed to be accessible, legal, and easy-to-understand tool for helping people discuss and document their wishes in a non-threatening, life-affirming way. The Five Wishes advance directive document has been distributed by over 40,000 organizations and has reached over 30 million individuals, and Five Wishes has grown into a comprehensive program with robust tools for healthcare providers, businesses, and communities, as well as individuals and families.

*Adapted from the Five Wishes website***

**Respecting Choices. (n.d.). About Respecting Choices. Retrieved from https://respectingchoices.org/*
***Five Wishes. (n.d.). Five Wishes is Changing the way we talk about advance care planning. Retrieved from https://fivewishes.org/Home*

packaging and patient-facing materials (including product labels, inserts, and direct-to-consumer (DTC) advertising) being developed for a commercial launch, in anticipation of regulatory approval. For conditions where there is an interplay between the product and newborn screening programs, caregivers have a clear role to play in helping guide communication materials and processes. Similarly, for products that may require special Risk Evaluation and Mitigation Strategies (REMS), caregiver input can be very helpful.

Post-Approval: For products that are approved with post-marketing study requirements (often referred to as Phase IV studies) or where a label change or new indication is being considered, caregivers will be able to participate in the same manner as described in Phase 1-3 studies, above. They also can collaborate on evidence collection and other surveillance activities. Their viewpoints will have great importance for some conditions in developing and supporting market access strategies and health technology assessment (HTA), especially where there is a home care delivery component. As in the regulatory stage, in preparation for commercial launch, the ongoing involvement of caregivers in public- and patient-facing materials is advised.

Several Summit participants drew attention to the importance of caregivers in developing tools to facilitate shared-decision-making about initiating therapy and adhering to it. FDA's **Michelle Tarver** recognized the importance of this point as well. "There are certain diagnostics and therapeutics where payers have insisted on a shared decision-making process in order for them to cover that product. We are looking at some of the preference assessment tools to explore whether they can inform shared-decision-making tools, too. If we can create tools that help inform regulatory and payment decisions, it will be a win-win," she forecasted.

Ian Kremer from the LEAD Coalition related the importance of involving caregivers for individuals with Alzheimer's disease and other forms of dementia early in the process of developing shared decision-making supports, stating, "If caregivers do not fully buy into the value proposition about safety, efficacy, and benefit of a newly approved therapy, then they are not going to seek a diagnosis for their loved one as readily. If given a diagnosis, they're less likely to ask the physician for the product. If the product is ordered by the prescribing physician and if they can get their payer to cover it, their support is crucial to make sure their loved one is using the product appropriately and adhering to the optimal regimen. That all will be diminished if caregivers don't appreciate the value proposition and both understand and agree with the safety and efficacy that underlies it. Their engagement is going to be critical to the innovator's success in providing effective therapy."

Moving from product development and approval into healthcare delivery, the vital role of the caregiver in helping to optimize care and achieve the best possible outcomes is described in detail in Section 1. Throughout the Summit, discussion among participants crossed into providing more support to caregivers in their expansive roles as well as the means by which all stakeholders in the biomedical ecosystem could come to better appreciate the opportunity they have to learn and benefit from increased interaction with caregivers. Some of the recommendations that emerged from the Summit are presented in Section 3.

Throughout the Summit, discussion among participants crossed into providing more support to caregivers in their expansive roles as well as the means by which all stakeholders in the biomedical ecosystem could come to better appreciate the opportunity they have to learn and benefit from increased interaction with caregivers.

Some of the ideas presented here are possible for single organizations to pursue; others would benefit from multi-disciplinary, multi-stakeholder collaboration.

SECTION 3

ACTION STEPS TO CATALYZE INCREASED CAREGIVER PARTICIPATION IN MEDICAL PRODUCT DEVELOPMENT

The Summit dialogue surfaced a wide variety of ideas and recommendations for further defining the caregiver's role in medical product development, contextualizing it for different disease states and medical settings, and engaging caregivers at various stages of research, development, and delivery of medical products and services. While this section is intended to present an initial set of potential actions to advance caregiver participation in PFMPD, it is by no means exhaustive, nor does it reflect emerging possibilities as other PFMPD-related initiatives are implemented and as adoption continues to spread.

Some of these ideas are possible for single organizations to pursue, contextualizing for their disease, therapeutic area, or product type of interest. It is important to underscore again the need to be sensitive to cultural, ethnic, gender, educational, social, and economic factors that may require attention in implementation plans. Other ideas would benefit from multi-disciplinary, multi-stakeholder collaboration. Finally, some projects can stand alone; others could be viewed as stepping stones to more ambitious multi-year initiatives.

The National Alliance for Caregiving and the LEAD Coalition have committed to pursue action steps that align with their missions and capabilities. They strongly encourage others to join them or contribute in other ways to enhancing caregiver engagement in biomedical R&D and healthcare delivery.

LEVERAGING POLICY

A number of federal policies related to caregiving and PFMPD create opportunities to introduce the concepts and opportunities outlined in this report, as outlined below.

- **FDARA & 21st Century Cures:** As described in Section 2, implementation of these two Acts requires FDA to issue a set of regulatory guidances that will shape expectations for and the practice of patient-focused medical product development. FDA's plan for meeting these requirements states, "…FDA intends to issue a series of four guidance documents to focus on approaches and methods to bridge from initial patient-focused drug development meetings to fit-for-purpose tools to collect meaningful patient and caregiver input for ultimate use in regulatory decision making. FDA plans to conduct a public workshop prior to the issuance of each of the draft guidances, to gather input from the wider community of patients, parents, caregivers, patient advocacy organizations, academic and medical researchers, expert practitioners, industry, and other stakeholders and inform the draft guidance."[54] It will also involve development and adoption of new and/or updated Manuals for Policies and Procedures (MAPPs), Standard Operating Practices and Procedures (SOPPs), clinical review templates, and other tools intended for use by FDA review staff and management.

- FDARA also includes a requirement for FDA to continue efforts to enhance benefit-risk assessment and communication in the human drug review process. In fulfillment of requirements under PDUFA-V and FDASIA, FDA developed a Benefit-Risk Framework (BRF) to provide a "structured, qualitative approach focused on identifying and clearly communicating key issues, evidence, and uncertainties in FDA's benefit-risk assessment and how those considerations inform regulatory decisions. FDA recognizes the importance of enabling meaningful patient input in helping to inform the context for drug development and regulatory decision-making, including FDA's benefit-risk assessment."[55] The plan for continued enhancement of the BRF includes providing "training and other resources to review staff on the fundamental concepts of benefit-risk assessment, the Benefit-Risk Framework, and its use to support drug review." The plan also states that, "by the end of FY 2019, FDA will convene and/or participate in, at least one meeting, conducted through a qualified third party, to gather industry, patient, researcher, and other stakeholder input on applying the BRF throughout the human drug lifecycle and best approaches to communicating FDA's benefit-risk assessment. Input from this meeting will support development of the draft guidance on benefit-risk assessment for

The National Alliance for Caregiving and the LEAD Coalition have committed to pursue action steps that align with their missions and capabilities. They strongly encourage others to join them or contribute in other ways to increase caregiver engagement in biomedical R&D and healthcare delivery.

[54] *U.S. Food and Drug Administration. (2017). Plans for issuance of patient-focused drug development guidance. Retrieved from https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf*

[55] *U.S. Food and Drug Administration. (2018). Benefit-risk assessment in drug regulatory decision-making. Retrieved from https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM602885.pdf*

Those interested in deepening roles for caregivers in PFMPD must follow closely and engage early and often as FDARA and the 21st Century Cures Act are implemented.

new drugs and biologics [in FY 2020]." Finally, in response to a third-party assessment of actions taken in response to FDASIA, FDA has committed to explore additional opportunities to make BRFs for approved products more accessible to the public, to more systemically incorporate BRFs into product-specific discussions at advisory committee meetings, and to expand use of BRFs to inform pre-market or post-market review.

Those interested in deepening the understanding of possibilities for distinct roles for caregivers in PFMPD must provide FDA with new evidence as it becomes available, participate actively in workshops as they are planned and conducted, submit comments on drafts, and otherwise follow closely and engage early and often as opportunities arise in the implementation of these plans and the Acts themselves.

- **Upcoming PDUFA-VII & MDUFA-V Negotiations:** FDA's reauthorization every five years is preceded by an extended period of negotiation between the agency and industry representatives organized by the trade associations: Pharmaceutical Research and Manufacturers of America (PhRMA), Biotechnology Innovation Organization (BIO), and the Medical Device Manufacturers Association (MDMA). These negotiations cover user fees by paid industry and agency performance benchmarks for the review of new applications and related activities. For the first time, negotiations for PDUFA-V and MDUFA-III included a parallel set of public meetings to engage patient and consumer representatives in discussions about agency programs; such meetings were pivotal to the development of PFDD activities enacted in PDUFA-V through FDASIA. Patient and consumer representatives also participated in agency discussions about PDUFA-VI and MDUFA-IV that were

enacted with FDARA. Congress will reauthorize FDA's user fee programs next by the end of FY 2022; closed-door negotiations and public meetings generally begin two years prior to the deadline. These meetings provide another opportunity to strengthen the attention paid to caregiver participation in PFMPD, and those committed to increased participation should actively engage in public opportunities and through various coalition efforts that form and mobilize. It is not too early to begin dialogues with the trade associations that will drive discussions of external stakeholders' expectations for the agency and its Centers. Gaining active commitment from patient and consumer groups that have traditionally been fully engaged (including *FasterCures*, National Consumers League, National Health Council, National Organization for Rare Disorders, Public Citizen, and many disease-specific organizations, etc.) would further galvanize support.

- **DHHS-led National Family Caregiving Strategy:** The RAISE Family Caregivers Act requires that the Secretary of Health and Human Services "shall develop a national family caregiving strategy to identify recommended actions that federal, state, and local governments, communities, health care providers, long-term services and supports providers, and others are taking, or may take, to recognize and support family caregivers."[56] The central intent of the plan is to promote greater adoption of patient-centered care, with "the person receiving services and the family caregiver (as appropriate) at the center of care teams." As indicated in Section 1, a new Family Caregiving Advisory Council is being formed to shape development of and monitor implementation of this plan. Its public meetings, required under the Act to be held at least three times per year, represent key opportunities to raise and reinforce the importance of caregiver input into medical product development as a means of achieving patient-centered care. Once the national strategy is issued, there will be future opportunities to influence it; the law requires the strategy be reviewed every two years. It should be noted that although more than one year has passed since enactment of this law, as of this publication date, the Secretary has not yet announced the composition of the Advisory Committee or plans for its first meeting. The Act itself currently sunsets in January 2021, so the window of opportunity may be fairly limited.

- **Reauthorization of PCORI:** The Patient-Centered Outcomes Research Institute (PCORI) was established in 2010 under provisions of the Affordable Care Act as an independent entity. Its primary purpose is to assist patients and providers to make better health decisions by conducting comparative clinical effectiveness research (CER). Indeed, its very name preordained PCORI to play a vital role in defining and shaping the conduct of patient-centered research programs and initiatives. PCORI is one of the first large research funding institutions to require involvement of patients and other stakeholders in the prioritization and conduct of studies it funds. It has also created important infrastructure to equip patients and caregivers with tools for engagement and to facilitate the collection of patient experience data, including the National

(CONTINUES ON PAGE 43)

A new Family Caregiving Advisory Council is being formed by the Secretary of Health and Human Services to shape development and monitor implementation of a national family caregiving strategy.

[56] *Congress (2018). Public Law 115 – 119.*

CAREGIVER SPOTLIGHT

The caregiver's role in prompting medical attention to new or unusual symptoms or changes in function, as well as adhering to and monitoring treatment, is highlighted in this Spotlight on Gail Achin of North Attleboro, Massachusetts. Her story also reveals how each partner's perspective, shaped by past and present experiences, may factor into decisions about new therapy approaches.

GAIL ACHIN

In 2006, Mike's little finger started quivering. His doctor thought he had some minor nerve damage but didn't recommend any particular treatment. A couple years later, around the time Mike was abruptly laid off after 25 years and the family was dealing with other stressful events, **Gail Achin** noticed some unusual changes in her husband. She recalled, "He was walking like an old man, with his arms at his side, shuffling his feet. He had trouble getting out of the car." When these new symptoms appeared, Gail was concerned, but they didn't have medical insurance so she just kept a close eye on him. She also did some online research and, as soon as they had coverage, she made an appointment with their primary care physician. Mike was referred to a neurologist who diagnosed Parkinson's disease, but didn't offer any treatment recommendations and suggested they seek a second opinion.

The second neurologist confirmed the diagnosis and started Mike on standard medications. Gail got him to add high-intensity exercise to his weight-lifting routine, after reading about its benefits. "Six months into the new regimen I was in denial. I kept hoping Gail and the doctor were wrong. Most of the time I took the advice we were given, but nothing seemed to help much. At times I just wanted somebody to shoot me in the head," Mike admitted.

When the doctor suggested adding more meds, they decided to explore other options. Mike joined "Rock Steady Boxing," a program designed for people with Parkinson's, and they sought help from a nutritionist. Two people at the gym had benefited from deep brain stimulation and Mike wanted to try it, too. "At first I thought it was a middle-school-type reaction – 'they're doing it and I want to do it too,'" Gail said. "My father had passed away after battling Alzheimer's and I was worried Mike would lose his brain function with the surgery." Testing showed Mike was a good candidate and Gail went along with Mike's desire to get the implant. "He's so much better now than he was before," she remarks. "He has been able to cut back on medications and the side effects are less of a problem. I tend to overthink things, but Mike can be too hasty, so we're a good pair."

"If it wasn't for Gail, I'd still be in denial about having Parkinson's. She's been my shepherd through all this," Mike says lovingly.

"We're getting through this together," they state in near-perfect unison.

Patient-Centered Clinical Research Network, or PCORnet.[57] PCORI reports that caregivers have engaged in 63 percent of research projects it has funded.[58]

A PCORI Reauthorization Primer, published by the Partnership for Improved Patient Care (PIPC), states, "PCORI receives income from three funding streams: appropriations from the general fund of the U.S. Treasury; transfers from Centers for Medicare and Medicaid (CMS) trust funds; and a fee assessed on private insurance and self-insured health plans (the PCOR fee). PCORI's initial (current) authorization expires on September 30, 2019; funding for new research commitments and infrastructure will lapse without Congressional action."[59]

At PCORI's most recent annual meeting, held in early November 2018 (prior to the midterm elections), a panel discussion revealed that members of Congress had already begun discussing PCORI's reauthorization. Panelist Jeff Lucas, health policy advisor to Sen. Bill Cassidy, MD (R-LA), invited public input, saying, "Any feedback you have on how we can help in the next iteration of the legislation, we'd love to hear."[60] Leaders of PIPC and the Alliance for Aging Research have convened a coalition of organizations as "Friends of PCORI Reauthorization" working to coordinate legislative requests and action. This would be an ideal group to approach with opportunities to recognize caregiver involvement as somewhat distinct from patient "and other stakeholder" involvement in authorizing language for PCORI's future activities.

- **Federal Acts Related to Particular Diseases and Conditions**: There are a number of research- and care-related activities governed by federal laws such as the National Alzheimer's Project Act,[61] the Paul D. Wellstone Muscular Dystrophy Community Assistance, Research and Education (CARE) Amendments of 2014,[62] the Rare Diseases Act,[63] and the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act.[64] Some of these Acts create federal advisory committees and may also authorize funding for research networks, training programs, and other programs. Working in close collaboration with the advocacy organizations representing patients and caregivers affected by the condition the law addresses, the topic of caregiver participation in medical product development could be advanced through these venues and vehicles. Reauthorization of these Acts, as they occur, represent additional opportunities for formal recognition of caregiver roles in medical product development.

Reauthorization of PCORI and federal acts related to particular diseases and conditions represent additional opportunities.

[57] PCORnet. (n.d.). PCORnet, the National Patient-Centered Clinical Research Network. Retrieved from https://pcornet.org/

[58] PCORI. (2018, October). Better research through engagement. Retrieved from https://www.pcori.org/sites/default/files/PCORI-Better-Research-Through-Engagement.pdf

[59] PIPC. (2018, October 25). Primer: PCORI background, funding streams, and reauthorization. Retrieved from http://www.pipcpatients.org/blog/primer-pcori-background-funding-streams-and-reauthorization

[60] MEDPAGETODAY. (2018, November 1). Outcomes research group likely to be reauthorized. Retrieved from https://www.medpagetoday.com/publichealthpolicy/healthpolicy/76081

[61] Congress. (2011). Public Law 111 – 375. Retrieved from https://www.congress.gov/111/plaws/publ375/PLAW-111publ375.pdf

[62] Congress. (2014, September 26). Public Law 113 – 166. Retrieved from https://www.govinfo.gov/content/pkg/PLAW-113publ166/html/PLAW-113publ166.htm

[63] Congress. (2002, November 6). Public Law 107 – 280. Retrieved from https://history.nih.gov/research/downloads/PL107-280.pdf

[64] Congress. (2018, January 3). Public Law 115 -- 180. Retrieved from https://www.congress.gov/bill/115th-congress/senate-bill/292/text?q=%7B%22search%22%3A% 5B%22s292%22%5D%7D&r=1

ENHANCING THE PRACTICE OF PFMPD

Throughout the day, Summit participants highlighted numerous existing programs and venues where the importance of incorporating caregiver perspectives could be introduced or emphasized. Pursuing a combination of strategies to "push" information about potential opportunities for caregiver participation in PFMPD and efforts to "pull" caregivers into shaping this field would accelerate momentum.

Pursuing a combination of strategies to "push" information about potential opportunities for caregiver participation in PFMPD and efforts to "pull" caregivers into shaping this field would accelerate momentum.

- **Partner with Existing Collaborative Initiatives Shaping the PFDD/PFMPD Field:** As described in Section 2, FDA's momentum to integrate patient perspectives following passage of FDASIA has generated dozens of formal and informal collaborative endeavors to define methods and further shape practice. These include public-private partnerships such as the Clinical Trials Transformation Initiative (CTTI) and the European Union's Innovative Medicines Initiative (IMI), multi-stakeholder consortia such as Transcelerate and Patient-Focused Medicines Development (PFMD), and distinct collaborative projects led by Center for Medical Technology Policy (CMTP), DIA, *FasterCures*, Food and Drug Law Institute (FDLI), and National Health Council, among others. Professional societies, including the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and International Society for Quality of Life Research (ISOQOL), have activities related to caregiver burden and family "spillover" as well. All of these entities and others would benefit by gaining a deeper understanding of the concepts addressed in this report and could be important advocates for spurring adoption and advancing practice.

- **Encourage Caregiver Participation in Externally-led PFDD Meetings:** FDA has outlined a process for patient organizations to "expand the benefits of FDA's PFDD initiative…by [organizing] patient-focused collaborations to generate public input on other disease areas, using the process established by FDA-led PFDD meetings as a model." Their guidelines recognize caregivers as one of the groups FDA is interested in hearing from at these meetings. Additional direction to applicants regarding the distinct role of caregivers, as well as a suggestion to applicants to consider how caregivers might complement patient perspectives, could serve to stimulate more inclusion of caregivers in externally-led meetings, where appropriate.

- **Enlist Other Research Funders Requiring Patient Engagement:** PCORI (see pages 4 and 41) and the NIH Clinical and Translational Science Awards (CTSA) funded through the National Center for Advancing Translational Science (NCATS) both require grantees to actively engage patients as partners in the conduct of their studies. Additionally, the Department of Defense, through its Congressionally Directed Medical Research Program (CDMRP), has involved patients in the prioritization and review of grant awards. These and other funders (such as philanthropies, industry, and academic institutions) that have recognized the benefits of patient involvement may be primed to promote distinct roles for caregivers to inform treatment-related research and development projects.

(CONTINUES ON PAGE 46)

SNAPSHOT: ETHICAL CONSIDERATIONS FOR CAREGIVER ROLES IN PFMPD

At the Summit, **Michele Mathes** of the Center for Advocacy of the Rights and Interests of the Elderly (CARIE), reviewed the four principles of medical ethics and contributed observations about the caregiver's role in patient-focused medical product development. These were based on the day's discussion and work she has done in her current role and former position with the Center for Ethics and Professionalism at the American College of Physicians.

The four moral principles of biomedical ethics,* which are of equal weight, are generally defined as:

- Justice – concerns the distribution of scarce health resources, decisions about who gets what treatment, as well as protection of vulnerable persons
- Respect for autonomy – the patient's right to refuse or choose their treatment
- Non-maleficence – a practitioner or treatment should not be a cause of harm, should promote more good than harm, and should understand the likelihood of harm to the person being treated
- Beneficence – a practitioner should act in the best interest of the patient

Michele connected the emphasis on women in discussions about caregiving to issues of justice. She observed, "This morning someone commented that the pediatrician always spoke to the woman, even when a (heterosexual) couple came in with their child, making an assumption that the woman is the caregiver. This automatically imposes a burden on the woman that she might or might not be suited to, might or might not want, and might or might not reflect who is actually doing the caregiving. It also marginalizes the man and denies him the care and attention for his role as a caregiver." Changing norms and expectations for family-related gender roles, as described in Section 1 (see page 6), make this an increasingly important issue.

Continuing with several issues tied to the principle of respect for autonomy, Michele emphasized the importance of the individual giving truly informed consent for care and treatment. "Consent is clearly an important part of making decisions for oneself. Clinicians and researchers are required to get the consent of the person whom they treat or with whom they are testing drugs or devices as an essential regard for that person's individuality and their dignity." Referencing the conceptual models discussed earlier

(see pages 27-29), she cautioned, "Working with individuals who have fluctuating capacity to make decisions, dementia, or a decline in the ability to make decisions presents real challenges. Insisting that people who can't process the information must make decisions is not really respecting them. We call this 'information dumping' – you give them all this information just to get a signature on a line. That may meet the legal requirement, but it doesn't really address the ethical issues behind the regulation. Ethics and regulations are not always in sync. What's important is respecting the individual and finding a way to ensure that." This role of receiving and integrating information with personal values and preferences can be an important role for the caregiver to play, as described in Section 1 and as illustrated in several of the Caregiver Spotlights.

Policies designed to promote and protect confidentiality and privacy, such as HIPAA,** impact both autonomy and beneficence and the caregiving role. Michele highlighted the difficulty of keeping these sometimes competing rights in balance. "How do we do what's good for the patient, respect their right to make decisions, and respect their right (and in some cases, legal protection) to keep information confidential? Personal information may involve issues of sexuality, drug or alcohol use, or other things that a person may not want their caregiver to know." She posited that perhaps there was an opportunity to think about partial disclosure – to provide the caregiver with adequate information for making or supporting decisions about care and treatment without violating the patient's privacy. This may also affect the extent of their participation in medical product development (see page 32).

This dilemma around privacy and confidentiality was discussed by **Maureen Lyon** in her work with HIV-positive teens and adults and their inability to name a person whom they would trust to make decisions on their behalf as a consequence of not having disclosed their HIV status (see page 32). **Marquitta Magnini** expressed frustration with not having access to information about her adult son's schizoaffective disorder during the interview for her Caregiver Spotlight (see page 52). She shared, "I understand the doctor can't tell me everything I want or might need to know about Paul's condition, but I can share my observations with him. I write his providers detailed letters so they have a window into what's happening with Paul between appointments." The discussion of challenges around sensitive and stigmatized

ETHICAL ISSUES TO CONSIDER

- Effect of gender-based assumptions about caregiving roles
- Caregiver's role as it relates to informed consent, especially with fluctuating capacity and competence to make autonomous decisions
- Caregiver's role to ensure true informed consent
- Challenges related to privacy and confidentiality and effect on caregiving roles/expectations
- Need to separate issues of morality from illness, especially in context of stigmatized conditions
- Respect for an individual's right to choose becoming (and continuing as) a caregiver

conditions prompted Michele to urge, "We must move away from the idea that illness has a moral implication to it. People used to think cancer was a moral failing and more recently believed that about HIV. Even alcoholism is increasingly recognized as a disease, rather than a moral issue."

Michele continued, "Ethics operate at the boundary between choice and behavior. This raises an important issue in caregiving: We rarely ask, 'Do you want to be a caregiver?' Yet, we are asking a person to be a moral agent, to act ethically on someone else's behalf, but we're not respecting them and their own agency to choose. Do we avoid that question for fear the answer would almost certainly be 'no'? If we treated caregivers as moral agents who can make that choice, I believe the parent would say 'yes;' the spouse would say 'yes.' If someone doesn't want to be a caregiver, can we rely on them to adhere to a protocol, to pay careful attention to what we're asking them to observe, to report regularly, to administer treatments accurately, etc.? This is not simply an ethical issue, but a practical one as well. Giving the caregiver that initial agency allows what follows to be their choice. They have taken it on, and then the burdens are ones they have willingly accepted, as opposed to feeling that 'it has all landed on my head.' "

Oxford University Press. (2013). Principles of biomedical ethics. Retrieved from https://global.oup.com/ushe/product/principles-of-biomedical-ethics-9780199924585?cc=us&lang=en&

***Health Insurance Portability and Accountability Act of 1996. Retrieved from https://www.hhs.gov/hipaa/index.html*

At the Summit and in many other venues, there has been a resounding call for PROs to be patient-centered as well as patient-reported, meaning focused on domains and functions that truly matter to patients.

- **Engage Via Established Caregiver Networks:** There are several existing networks of caregivers through which information about patient-focused medical product development (in general, and specific opportunities) could potentially be disseminated, including Caregiver Connect (hosted by the Family Caregiver Alliance),[65] Caregiver Action Network (hosted by the National Family Caregivers Association), [66] Military and Veteran Caregiver Network (hosted by the American Red Cross), [67] and SibNet (hosted by the Sibling Support Project),[68] to name just a few. Adding links to this report and other PFMPD-related information to "caregiver-rich" websites, such as AARP, and resource libraries would also help to raise awareness and generate interest.

- **Refine and Contextualize Models:** At the Summit, there was great interest in the initial models depicting the relationship of patient and caregiver insights (see pages 27-29). Participants suggested other scenarios, such as may be the case for an adult with cancer whose spouse or partner is actively involved as a caregiver, with each having a perspective, preferences, and voice in decisions. These models can be adapted for use by various organizations to better understand the separate and connected roles of patients and their caregivers, helping stimulate a deeper appreciation for their perspectives, needs, and expectations, with the goal of more fully engaging patients and caregivers in medical product development.

- **Document and Disseminate Case Studies:** Summit presentations given by Annie Kennedy and Debra Lappin highlighted two key initiatives where caregiver perspectives are being utilized to inform medical product development: PPMD's preference studies (see page 33) and AD PACE (see page 35). Developing and circulating case studies about projects like these could stimulate greater awareness of opportunities to engage caregivers, as well as the rationale for doing so, for a specific disease or groups of conditions (e.g., progressive neuromuscular diseases or end-stage cancers of all types).

- **Assess Existing Observer Reported Outcomes (ObsROs) for Relevancy to Patient and Caregiver:** At the Summit and in many other venues, there has been a resounding call for PROs to be patient-centered as well as patient-reported, meaning focused on domains and functions that truly matter to patients. Similarly advancing the importance of patient- and/or caregiver-relevant ObsROs could begin with a review of existing ObsROs in the FDA's COA Compendium,[69] enlisting appropriate expertise from related patient advocacy groups to help assess whether the tool or instrument measures meaningful concepts of interest to patients and/or caregivers and the ease of understanding and using the tool/instrument by caregivers. For example, the patient diary said to capture seizure frequency by observers of patients with Lennox-Gastaut Syndrome (LGS) (see page 18 of the COA Compendium) could be assessed by the LGS Foundation. This exercise would help establish a baseline understanding of these measures as well as provide a starting point for initiatives to enhance COAs so they reflect high-value domains to both patients and caregivers.

[65] Family Caregiver Alliance. (n.d.). Caregiver Connect. Retrieved from https://www.caregiver.org/caregiver-connect
[66] Caregiver Action Network. (n.d.). Home. Retrieved from https://caregiveraction.org/
[67] American Red Cross. (n.d.). Home. Retrieved from https://milvetcaregivernetwork.org/
[68] SiblingSupportProject. (n.d.). SibNet. Retrieved from https://www.siblingsupport.org/connect-with-others-sibs/meeting_other_sibs_online/sibnet
[69] U.S. Food and Drug Administration. (2015). Clinical Outcome Assessment compendium. Retrieved from https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM481225.pdf

- **Review Caregiver-Related Mobile Applications:** The importance of encouraging development and use of technology tools to aid the caregiver was a recurring theme at the Summit. These tools are still relatively new and experience is mixed, yet the trend is toward greater consumer use of medical sensors and monitors and more mobile-enabled clinical trials and research efforts. For example, the FDA-approved Embrace SmartWatch detects seizure activity in people with epilepsy and the Apple Watch 4 has FDA-approved medical features for detecting falls and atrial fibrillation. Enlisting expertise from advocacy organizations to inventory and assess condition-related digital tools and mobile apps that are designed to aid the caregiver in performing care-related tasks and documenting information about the care-recipient, would be an important step toward encouraging use and developing improved technology tools.
- **Query Other Regulatory Authorities:** While the discussion at the Summit was focused mostly on the United States, there are global opportunities to involve caregivers in medical product development. First it would be helpful to understand current practice and interest among other regulatory authorities in patient engagement, to help gauge their readiness. For instance, the European Medicines Agency (EMA) has multiple initiatives to encourage PFMPD[70] and the FDA and EMA participate in a joint Patient Engagement Cluster, enabling them to share best practices.[71] It is therefore reasonable to think that they may have greater receptivity to involving caregivers, as compared to a regulatory authority that has not yet made formal provisions for patient engagement.

(CONTINUES ON PAGE 49)

The trend is toward greater consumer use of medical sensors and monitors and more mobile-enabled clinical trials and research efforts.

[70] *European Medicines Agency. (n.d.). Partners & networks. Retrieved from https://www.ema.europa.eu/en/partners-networks/patients-consumers/getting-involved*

[71] *U.S. Food and Drug Administration. (2018, January 8). FDA and European Medicines Agency Patient Engagement Cluster. Retrieved from https://www.fda.gov/ForPatients/PatientEngagement/ucm507907.htm*

SNAPSHOT: WHERE TO START WITH COAS, LEGACY OR NOVEL MEASURES?

Presentations by **Mousumi Bose** and **Maureen Lyon** about creating patient- and caregiver-relevant outcome measurement tools generated debate about whether to start with and/or adapt existing measurement tools (including PROs and ObsROs – see page 26), or to develop novel outcomes and tools to measure them. Here are some advantages and drawbacks to each approach, as summarized from Summit participants' comments:

"There are good tools out there including the POS* and the MOS** for symptom measurement, PROMIS measures,*** and the Carer Needs Assessment Tool.**** Look at those measures first; otherwise you face five or more years to build reliability, validity, construct validity, concordant validity, and face validity." – **Maureen Lyon**

"As someone who worked on MOS, many of those tool developers consulted doctors first. Some – but not all – items in the PROMIS pool came from asking doctors, 'What do you ask your patients?' I fear a 'validated tool' may have been validated for the wrong concept of interest, when assessed from the perspective of the patient or caregiver. I strongly encourage everyone to work with the patient and caregiver populations first to figure out what the true high-priority concepts of interest are, and then see if the tools and item banks exist before jumping to those tools first." – **Eleanor Perfetto**

"My experience relates to PROMIS. When I was at the Alliance for Aging Research, we were taking a new performance outcome measure for sarcopenia through the COA qualification process. FDA encouraged us to see if we could adapt a functional item bank from PROMIS for use in that population. In talking with the PROMIS investigators, however, the research required to 'retrofit' the functional item bank was going to cost as much as continuing to pursue qualification of our novel tool. Plus, we were finding ours was probably going to be more acceptable to our population. So in my experience, if you can take something off the shelf and retrofit it, great. But we spent eight months figuring out that it wouldn't be appropriate." – **Cynthia Bens**

**Palliative Care Outcome Scale, (n.d.). Home. Retrieved from https://pos-pal.org/*
***RAND Health Care. (n.d.). RAND Medical Outcomes Study: Measures of quality of life core survey from RAND Health Care. Retrieved from https://www.rand.org/health-care/surveys_tools/mos.html*
****HealthMeasures. (n.d.). Why use PROMIS? Retrieved from http://www.healthmeasures.net/explore-measurement-systems/promis*
*****Carer Support Needs Assessment Tool. (n.d.). The Carer Support Needs Assessment Tool (CSNAT). Retrieved from http://csnat.org/*

Each of the possibilities explored below attempts to utilize existing programs or make use of tools developed for other purposes, to generate early momentum and foster broader adoption.

PURSUING NEW POSSIBILITIES

Many ideas for novel projects arose at the Summit, in conversations leading up to it and in the weeks after; some of the most salient are described below. Additionally, potential action steps outlined above may have follow-on activities that would represent new initiatives, such as undertaking design and development of a new or improved ObsRO, if one does not exist or if existing ones fail to measure concepts of high priority to patients and/or caregivers. Each of the possibilities explored below attempts to utilize existing programs or make use of tools developed for other purposes, to generate early momentum and foster broader adoption.

- **Host PFDD Meeting on Caregiver Involvement:** To showcase ways in which caregivers can inform medical product development in different disease states and to further illustrate the models and frameworks shared in Section 2 of this report, application could be made to FDA to convene an externally-led PFDD meeting that focuses on different roles for the caregiver in PFMPD, as described by caregivers themselves and, when possible, patients as well. The meeting would address many different conditions and life stages, helping to depict the full range of ways in which caregivers could contribute evidence and perspectives to medical product development and regulatory decisions, for the benefit of FDA review staff, life science companies, and other stakeholders.
- **Prepare Draft Guidance:** Following the model pioneered by Parent Project Muscular Dystrophy and now codified under Section 3002(c)(5) of the 21st Century Cures Act,[72] a multi-stakeholder group could develop draft guidance to describe objectives for and methods to involve caregivers in medical product development. Such a crafting process would follow the practices outlined in FDA's draft guidance on submitting guidance, issued December 2018.[73]

[72] *Congress. (2016, January 4). Public Law 114 – 255*
[73] *Food and Drug Administration. (2018). Developing and submitting proposed draft guidance relating to patient experience data. Retrieved from https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM628903.pdf.*

- **Explore Development of "Caregiver-Sensitive" Concept:** The Medical Device Innovation Consortium's Patient-Centered Benefit-Risk Framework defined a set of conditions to help establish which types of product-related decisions might be particularly "preference sensitive," as shown in Figure 10[74], below. Using this as a model, a set of conditions that might point to the need for caregiver input could be similarly defined. This would help prioritize when and how to optimally elicit and integrate caregiver perspectives. Illustrating such concepts with real-world experiences would help to advance utilization and refine the model over time.

FIGURE 10: THE VALUE OF PATIENT PREFERENCE INFORMATION AS A FUNCTION OF BENEFIT AND RISK

Adapted from MDIC's Patient-Centered Benefit Risk Framework.

- **Conduct a Literature Review and Compile a Resource Library:** There does not appear to be a complete listing of published studies of caregiver-related contributions to medical product development, including participation in developing PROs or ObsROs, preference studies, etc. Collecting such references and identifying which disease states and product types have most effectively engaged caregivers would be illuminating and would also point to future opportunities. Building a repository for those references would be an additional boost to the field. One model for this is the Health Preference Study and Technology Registry (or "Hipster"),[75] a service of the International Academy of Health Preference Research, where the public can easily locate information about publicly and privately supported health preference studies and technologies on a wide range of diseases and conditions.

- **Engage Evidence Generation Networks:** Over the last decade, three partnership-driven networks have been constructed to amass clinical and administrative health-related data and to generate evidence for medical product decision-making (including safety surveillance). These networks are FDA CDER's Sentinel network; [76] FDA CDRH's National Evaluation System for Health

[74] *Medical Device Innovation Consortium (2015). MDIC patient centered benefit-risk framework report. Retrieved from http://mdic.org/wp-content/uploads/2015/05/MDIC_PCBR_Framework_Web1.pdf*
[75] *Health Preference Study and Technology Registry. (nd.). Retrieved from https://hpstr.org/landing*
[76] *U.S. Food and Drug Administration. (2019, January 09). FDA's Sentinel Initiative. Retrieved from https://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm*
[77] *U.S. Food and Drug Administration. (2018, November 16). National Evaluation System for Health Technology (NEST). Retrieved from https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhreports/ucm301912.htm*

Technology (NEST); [77] and the National Patient-Centered Clinical Research Network (PCORnet), [78] initially funded by PCORI and now under direction of the People Centered Research Foundation.[79] The growing emphasis on real-world evidence will require the development of evidentiary requirements for data that might come from caregivers, rather than directly from patients. It is also worth noting that each of these networks depends heavily on electronic health records (EHR); in the 39 states/jurisdictions that have passed the Caregiver Advise, Record, Enable (CARE) Act (as described in Section 1, see page 17), the name of the family caregiver is recorded in the EHR. Dialogue with network leaders would help uncover whether this creates any new possibilities worthy of further exploration.

There is a need to greatly expand the number of patients and caregivers capable of taking active roles to contribute to medical product development.

- **Educate and Train Caregivers About Medical Product Development Materials:** There is a need to greatly expand the number of patients and caregivers capable of taking active roles to contribute to medical product development. Many of the programs designed to inform patients and their advocates about medical product development and regulation (such as Friends of Cancer Research's training course[80]) could be repurposed or distributed through caregiver-rich networks, including the networks identified above. There may also be a need for materials that describe the distinct role for caregivers and equip caregivers with knowledge and know-how to participate effectively. Additional distribution points for these materials would be through state training programs under CARE Act provisions, through federal programs created under the RAISE Family Caregivers Act, and by organizations and entities fostering PFDD/PFMPD.

- **Develop a "White Label" (Unbranded) Toolkit Template:** To aid organizations interested in engaging their caregiver communities to take active roles in medical product development, a toolkit template could be created. Such a toolkit could include the conceptual models (see pages 27-29), the National Health Council's "Patient Perspectives on Disease Impact and Treatment Options: A Stratification Tool"[81] (possibly adapted for use in better understanding caregivers), and other resources that would serve to spur greater or more meaningful engagement with those caring for the patients they serve. These resources would then be contextualized and branded by the organization for use in their specific community.

- **Construct a "Science of Caregiver Input" Research Agenda:** In May 2018, the National Academy of Science, Engineering, and Math (NASEM) Forum on Drug Discovery, Development, and Translation hosted a workshop to "examine the state of the science of patient input, explore gaps in the knowledge base, and discuss potential components of a research agenda to address gaps and barriers."[82] Learnings from this session, as well as from a "Science of Caregiving Summit" hosted by the NIH's National Institute of Nursing Research in 2017,[83] would be useful to review. Although a parallel effort to evaluate the state of the science of caregiver input is unlikely to be ripe for some time, having this longer term need in mind from the start can help to clarify a path forward.

(CONTINUES ON PAGE 53)

[78] *Pcornet. (n.d.). PCORnet, the National Patient-Centered Clinical Research Network. https://pcornet.org/*
[79] *People-Centered Research Foundation. (n.d.). About PCRF. Retrieved from https://pcrfoundation.org/about_pcrf*
[80] *Friends of Cancer Research (2018). Progress for patients advocacy education course. Retrieved from https://www.progressforpatients.org/education*
[81] *National Health Council (2012). Patient perspective on disease impact and treatment options: A stratification tool. Retrieved from http://www.nationalhealthcouncil.org/sites/default/files/NHCPatientInformationToolandinstructions_0.pdf*
[82] *The National Academies of Sciences, Engineering, and Medicine. (2018, May 9). Advancing the science of patient input in medical product R&D: Towards a research agenda – A workshop. Retrieved from http://www.nationalacademies.org/hmd/Activities/Research/DrugForum/2018-MAY-09.aspx*
[83] *National Institute of Nursing Research. (January 2018). The science of caregiving: Bringing voices together. Retrieved from https://www.ninr.nih.gov/sites/files/docs/Caregiving-Summit-Summary-508c.pdf*

CAREGIVER SPOTLIGHT

The final Spotlight on Marquitta Magnini of Hot Springs, Arkansas, portrays the continuous yet dynamic nature of some caregiving relationships and how they can be punctuated by periods in which an observer/reporter role is replaced by surrogate and/or proxy roles. It also illustrates the challenges associated with access that can interrupt treatment and its benefits, burdening the patient, the caregiver, and the medical system. Finally, Marquitta's ability to attach meaning to her experience is a reminder of the potential individual and collective good that can come from deeper involvement of caregivers in medical product development and care delivery.

MARQUITTA MAGNINI

A recent photo of Marquitta and Paul

Marquitta Magnini has faced a lot of challenges in her life, but nothing prepared her for the challenges of parenting her son, Paul, these past 19 years since he experienced a complete mental breakdown at age 18.

Looking back, she knew Paul was different from other children and his sister. "He could be moody and he cried more than other kids. There were odd behaviors, but he was loving, kind, smart, and did well in school, as long as there was structure and predictability. During his junior year in high school he started skipping class and his grades fell. A psychiatrist we consulted didn't offer much insight; his father said he just needed to 'be a man.' I regret not doing more at that point to help him."

A few years later when Paul was enrolled in a local college, he didn't have as much structure or support as he had been used to. Marquitta recalls, "On March 31, 2001, Paul left a voicemail saying 'It's more than I can handle. I just can't do it anymore.' I went searching for him, not knowing whether it was drugs, psychological problems, or both. It took three days to find him. After a few days in detox, the treatment center released him, telling us he'd have to hit rock bottom on the street."

Over the next few months he bounced in and out of treatment. He jumped out of a moving car and was treated in the hospital for his injuries, where Marquitta lay down next to him, praying for help. A physician who treated Paul there recognized he had untreated kidney stones, along with addiction and mental health issues, likely schizoaffective disorder.

Fighting the insurance and health care system to get him appropriate ongoing medical attention, in 2003 she gained guardianship and had to commit Paul to residential treatment. Medication combined with other therapeutic approaches helped him stabilize; he's been able to live on his own from time to time.

In September 2018, Paul lost his Medicaid benefits without explanation. Without these benefits, he lost access to his doctor, his therapist, and his medication; this upset his highly structured life and triggered a return of many symptoms. It also impaired his ability to communicate effectively with his parents about what was happening. When Marquitta realized he wasn't on treatment, she sprung into intense advocacy on her son's behalf. "I was acting on Paul's two requests – that he not be labeled a danger to himself or others, and that he be treated like a human and not an animal," she said. She was able to get him admitted to a local hospital so he could get back on medication under medical supervision.

"Our system of health 'care' isn't much better today than it was in 1986 when my father tried to commit suicide," Marquitta laments. She's grateful that Paul has retained his sweet nature and much of what he learned before the breakdown at 18. "When I had knee surgery, he was my caregiver. Recently, he took me on a date to celebrate my birthday. If our experience and work we do with our state chapter of the National Alliance on Mental Illness (NAMI) can lead to lasting change, then that is God's purpose for my life."

CONCLUSION & CALL TO ACTION

The National Summit on Family Caregiver Roles in Patient-Focused Medical Product Development has launched a productive dialogue about the myriad ways that family caregivers can make (and are making) important – and distinctive – contributions to the development and delivery of medical products that their care recipients depend upon. Regulators in the U.S. and Europe are setting expectations that patients' priorities and preferences will be integrated from the earliest stages of medical product development. Now is the time to illuminate a new dimension in the science of patient input, by distinguishing the role of caregiver as a vital resource and stakeholder. Building a field of study and experience around how to effectively mobilize the knowledge and insights of 43 million family caregivers in the U.S., alone, will yield benefits for the care recipient and the caregiver as well as at the product level, the disease level, and the system level.

As NAC CEO Grace Whiting stated at the beginning of the Summit, "Today we hope to build a roadmap for future action. This is a big topic. The road will be long." The intent of this report, and in particular the recommendations described above, is to energize interest among diverse stakeholders to set off on the journey. There is much work that can be done in small increments, perhaps initially yielding modest progress but, over time, fueling more interest and uptake. There is also great potential in collaborative undertakings that bring unexpected partners together to create the synergy necessary to build something truly novel. Everyone has an opportunity to participate, for if we are not already either a patient or a caregiver, the chances are great that we will be some day. Active involvement in pioneering this work now may have personal benefits in addition to those it promises to bring to the healthcare system and public health.

Now is the time to illuminate a new dimension in the science of patient input, by distinguishing the role of caregiver as a vital resource and stakeholder.

"TODAY WE HOPE TO BUILD A ROADMAP FOR FUTURE ACTION. THIS IS A BIG TOPIC. THE ROAD WILL BE LONG."

C. GRACE WHITING, J.D.
PRESIDENT AND CEO OF THE NATIONAL ALLIANCE FOR CAREGIVING

SUMMIT ATTENDEE LIST

Meagan Bates
Associate Director, Patient Advocacy and Strategic Partnerships, Global Healthcare
EMD Serono, Inc./Merck KGaA

Cynthia Bens
Senior Vice President, Public Policy
Personalized Medicine Coalition

Mary Bordoni
Director, Alliance Development
Biotechnology Innovation Organization

Mousumi Bose, Ph.D.
Assistant Professor, Nutrition and Food Studies
Montclair State University

Teresa Brandt, Ph.D.
Senior Director, Regulatory Affairs
ACADIA Pharmaceuticals

Rachel Cannady
Strategic Director, Cancer Caregiver Support
American Cancer Society

Lauren Chiarello, M.P.H.
Associate Director, Patient Advocacy
Biogen

Rita Choula, M.A.
Senior Advisor, Public Policy Institute
AARP

Dayna Cooper, R.N., M.S.N.
Director, Home and Community Care
U.S. Department of Veterans Affairs

Danielle Friend, Ph.D.
Director, Science and Regulatory Affairs
Biotechnology Innovation Organization

Cynthia Grossman, Ph.D.
Director
FasterCures

Kristi Guillory, J.D., M.S.
Senior Associate Director
Alzheimer's Association

James Ingram
Senior Manager, US Advocacy Relations
Amgen

Missy Jenkins
Vice President, Public Policy
Alliance for Aging Research

Annie Kennedy
Senior Vice President, Legislation & Public Policy
Parent Project Muscular Dystrophy

Mike Knaapen
Director, Patient and Caregiver Programs
Pulmonary Hypertension Association

Ian Kremer, J.D.
Executive Director
Leaders Engaged on Alzheimer's Disease

Debra Lappin, J.D.
Principal
Faegre Baker Daniels Consulting

Margaret Longacre, Ph.D.
Assistant Professor
Arcadia University/Department of Public Health

Maureen Ellen Lyon, Ph.D.
Clinical Health Psychologist
Children's National Health System
Associate Research Professor of Pediatrics
George Washington University School of Medicine and Health Sciences

Michele Mathes, J.D.
Development Director
Center for Advocacy for the Rights and Interests of the Elderly (CARIE)

Kim McCleary
Founder & CEO
Kith Collective

Jenna McDavid
National Managing Coordinator
Diverse Elders Coalition

Lisa McGuire, Ph.D.
Lead, Alzheimer's Disease and Healthy Aging
U.S Centers for Disease Control and Prevention

Janet McUlsky, M.B.A.
Senior Director, National Alliance Development
Pfizer, Inc.
Chair, National Alliance for Caregiving

Stacy Meisberger Holdsworth, Pharm.D.
Senior Advisor, U.S. Regulatory Policy and Strategy
Eli Lilly & Co.

Lisa Miller Noel, B.S.N., M.P.H.
Patient Engagement Lead, CDRH, OCD
U.S. Department of Veterans Affairs

Hazel Moran
Senior Director, International Patient Advocacy and Strategic Partnerships
EMD Serono, Inc./Merck KGaA

Ann Moravick
President
Rx4good

Chinyelum (Chi-Chi) Olele, Pharm.D.
Patient Engagement Advisory Committee Manager
U.S. Food and Drug Adminstration

Michele Oshman
Director, Advocacy and Alliance Development, Corporate Affairs
Eli Lilly and Company
Vice Chair, National Alliance for Caregiving

Dorothy Ouchida
Government Affairs and Advocacy
Avanir

Eleanor Perfetto, M.S., Ph.D.
Senior Vice President, Strategic Initiatives
National Health Council

Meagan Perry
Associate Director
EMD Serono

Amanda Pratter
Coordinator, Alliance Development
Biotechnology Innovation Organization

Kara Rogers
Meeting Facilitator

Christina Sanlnocencio, Ph.D.
Executive Director
Lennox Gastaut Syndrome Foundation

Alicia Subasinghe, M.A.
Director, Strategic Alliance Development
Novartis

Michelle Tarver, M.D., Ph.D.
Director, Patient Science & Engagement Program, Office of the Center Director, CDRH
U.S. Food and Drug Administration

Pujita Vaidya, M.P.H.
Senior Advisor, Patient-Focused Drug Development Program, Office of the Center Director, CDER
U.S. Food and Drug Administration

C. Grace Whiting, J.D.
President & CEO
National Alliance for Caregiving

Scott Williams, M.P.A.
Vice President, Head of Global Patient Advocacy & Strategic Partnerships, Global Healthcare, Government & Public Affairs
EMD Serono, Inc./Merck KGaA

Lisa Winstel
Chief Operating Officer
Caregiver Action Network

Schiffon Wong, M.P.H.
Executive Director
EMD Serono

National Alliance for Caregiving Staff:

Rachael Gass; Special Assistant to the C.E.O.

Mike Wittke, BSW, MPA; Director of Advocacy

National Alliance for Caregiving

4720 Montgomery Lane, Suite 205
Bethesda, MD 20814

301.718.8444 phone
301.951.9067 fax
info@caregiving.org

caregiving.org

National Alliance for Caregiving

About the National Alliance for Caregiving

Established in 1996, the National Alliance for Caregiving is a non-profit coalition of national organizations focusing on advancing family caregiving through research, innovation, and advocacy. The NAC conducts research, does policy analysis, develops national best-practice programs, and works to increase public awareness of family caregiving issues. Recognizing that family caregivers provide important societal and financial contributions toward maintaining the well-being of those they care for, the NAC supports a network of more than 80 state and local caregiving coalitions and serves as Secretariat for the International Alliance of Carer Organizations (IACO). Learn more at **www.caregiving.org**.

LEAD
Leaders Engaged on Alzheimer's Disease

About the Leaders Engaged on Alzheimer's Disease (LEAD Coalition)

Leaders Engaged on Alzheimer's Disease (LEAD Coalition) is a diverse and growing national coalition of 100 member organizations committed to stopping Alzheimer's disease and other forms of dementia, including vascular disease, Lewy body dementia, and frontotemporal degeneration. The coalition works collaboratively to focus the nation's attention on accelerating transformational progress in: (1) care and support to enrich the quality of life of those with dementia and their caregivers; (2) detection and diagnosis; and (3) research leading to prevention, effective treatment, and eventual cures. LEAD Coalition members include patient advocacy organizations and health non-profits, philanthropies and foundations, trade and professional associations, academic research and clinical institutions, home and residential care providers, and biotechnology and pharmaceutical companies. Learn more at **www.leadcoalition.org**.