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Anorexia Nervosa—Facts, Frustrations, and the Future

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IMPORTANCE Anorexia nervosa is a prevalent psychiatric illness associated with exceptionally poor outcomes, including high rates of morbidity and premature mortality. Current evidence-based treatments for anorexia nervosa were developed several decades ago and have limited efficacy. The anorexia nervosa field—and the eating disorders field more broadly—has yet to make significant scientific breakthroughs that lead to acceptable outcomes for people with anorexia nervosa.

FINDINGS This Special Communication highlights how the concurrent psychological and physical symptoms of anorexia nervosa contribute to 2 major problems that have held the anorexia nervosa research field back and hindered research innovations: (1) overspecialization and siloing of the field and (2) an overly narrow focus on weight restoration in treatment.

CONCLUSIONS AND RELEVANCE Specific recommendations are made to help progress the field, including taking a multidisciplinary and collaborative approach to research with colleagues from related disciplines, as well as taking a more holistic approach to understanding and treating anorexia nervosa.

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Facts

Anorexia nervosa (AN) is a serious mental illness characterized by disturbances in body image and disordered eating behaviors that lead to significantly low body weight.[1] The lifetime prevalence of AN is estimated to be as high as 4%, and while the overall incidence has remained relatively stable over time, the incidence of AN among youths has increased substantially in the last several decades.[2,3] Despite the high prevalence and increasing incidence among young people, treatment options for AN remain limited. Psychological therapies for AN include monitoring of eating and weight and generally aim to help patients build skills to manage cognitive, emotional, or environmental challenges that interfere with eating behaviors. These therapies are currently the only recommended evidence-based treatments for AN,[4] though this evidence base is marred by reliance on a small number of high-quality clinical trials whose findings show limited efficacy for these therapies.[5-7] Thus, AN remains an inadequately treated illness characterized by one of the highest premature death rates of any mental illness (standardized mortality ratio, 5.9; second only to opioid use) and a long-term recovery rate of only approximately 50% to 60% among surviving patients.[8-10]

Our current evidence-based treatments for AN were developed several decades ago and show efficacy for a proportion of patients. While international efforts are currently being made to improve our understanding and treatment of AN and other eating disorders, the field has yet to make the significant scientific breakthroughs that will lead to acceptable outcomes for people with AN. Here, we highlight several issues that have contributed to the limited progress experienced by the eating disorders field, with a particular focus on AN, and provide clear recommendations for the future of AN research. Although this article specifically focuses on AN, the obstacles are applicable to varying extents across the spectrum of eating disorders.

Frustrations

While AN is fundamentally defined as a psychiatric illness, the physical consequences directly associated with the disorder can be life-threatening. Together with the egosyntonic nature of the illness, this distinguishes AN from most other mental illnesses and makes it challenging for many clinicians to treat. Every organ and system within the body is affected by starvation, which is often exacerbated by pathological weight control behaviors, such as purging, excessive exercise, and misuse of medications.[11] Therefore, while patients are battling an all-consuming and overwhelming mental illness, they are also faced with a barrage of serious physical complications that need to be addressed. This complexity presents a unique challenge for many health care systems, with patients often falling in the gap between medical and mental health care when specialized eating disorder treatment is not accessible. In addition to complications accessing appropriate care to ensure both psychological and physiological needs are met (including restoring normal eating and weight), this division has contributed to 2 major problems impacting AN research: The field has become (1) overspecialized and siloed and (2) fixated on treatments that address weight restoration as the primary, or even singular, outcome.

The majority of health care systems around the world are not set up to facilitate appropriate multidisciplinary care across physi-

cal and mental health. Although physical complications are not uncommon in psychiatric conditions (eg, metabolic syndrome in schizophrenia[12]), they are not characteristic of the disorder in the same way as in AN, which is unique in having a physical symptom (ie, significantly low body weight) as a diagnostic criterion.[1] This distinctive feature of AN has contributed to the belief that AN is a niche disorder at the mind-body interface that requires specialized care and expertise. While it is true that comprehensive multidisciplinary care is warranted and that patients and families value specialist care,[13,14] we believe this mindset has contributed to overspecialization within the eating disorders field with the impact of siloing clinical care and research for eating disorders away from the rest of mental health.

In terms of clinical care, this siloing has contributed to the attitude often expressed by general mental health services that they "don't do eating disorders"—an attitude that has arguably flowed into research with an apparent reluctance or disinterest regarding eating disorders research from the rest of the mental health field. This siloing, together with the stigmatizing attitude that AN only affects young, affluent White females,[15] has stymied collaboration with colleagues working in other areas of mental health research where greater advances in treatments have been made.[16,17] Indeed, the broader mental health field often excludes eating disorders research from large-scale initiatives (eg, Wellcome Trust Mental Health Funding). At the same time, the eating disorders field itself often contributes to the slow progress by not making specific efforts to partner with colleagues in related fields. This siloing and the consequent delays in progress are evident in the slow uptake by the eating disorders field of concepts and methodologies that are prominent in other areas of mental health, such as the early intervention model of mental illness, which promotes early identification and treatment before frank symptoms or illness have developed[18]; the use of a transitional aged youth model (ages 12-25 years) that recognizes the importance of consistent care across these developmental stages when mental illnesses are most likely to emerge (involving regular contact with clinicians and peer support in conjunction with skills training so recurrent pathology is caught early and treated before becoming entrenched)[19]; and the use of findings from basic research focused on understanding illness mechanisms to develop personalized, evidence-based treatments that target the underlying illness.[20]

Furthermore, this siloing, along with the stigma associated with eating disorders (eg, the misperception that they are not serious disorders and that they are a choice or about vanity in young females[21]), has challenged research funding, as eating disorders are often considered too niche or not serious enough for funding bodies to prioritize.[22,23] When research funding is directed toward eating disorders, the focus of funding bodies is often on translational research (eg, several National Health & Medical Research Council and Medical Research Future Fund opportunities in Australia). Together with this focus from funders, the very real and immediate threat of death from AN also creates a sense of urgency to (prematurely) focus research endeavors on treatment, which encourages researchers to submit proposals for underdeveloped interventional trials not adequately informed by mechanistic knowledge. Other areas of mental health have a modest but larger evidence base of mechanistic knowledge to back up their treatment studies (though it is noted that many successful treatment trials in other mental health conditions have relied on scant mechanistic knowledge, eg, the glutamate model of schizophrenia[24]); however, more foundational research is needed to determine what contributes to the development and maintenance of AN to adequately inform the creation of personalized or efficacious treatments.[25] Thus, while it is imperative to fund treatment trials that are informed by the limited existing mechanistic evidence, we underscore the parallel need for a greater focus on understanding how and what we should be targeting to support longer-term, impactful advancements in the treatment of AN.

The life-threatening nature of the physical consequences of AN leads to an understandable focus on medical stabilization and body weight restoration as the first priority in treatment. This focus has resulted in treatments, especially those delivered in intensive settings (inpatient, day patient, or residential), that center around first addressing the physical and behavioral components of the disorder in order to regulate eating behaviors before the underlying psychological components of the illness are addressed. These treatments often emphasize treating the psychological component of the illness in parallel (or aim to address psychological components indirectly by addressing behavioral components), but there is a clear prioritization of the disordered eating and low body weight associated with the illness (ie, arguably, the secondary and tertiary manifestations of the cognitions underlying AN). While this approach may be necessary for some, such as when psychological issues and cognitive distortions are a consequence of starvation, the prioritization of behavioral or physical symptoms over the psychological aspects of the illness that may drive disordered eating behaviors can feel like a misfit for many individuals with AN. To some, a narrow focus on weight restoration is experienced as distressing and invalidating if it does not feel to them like the most bothersome part of their illness and thus may also be prohibitive to adequately addressing the illness.[25] While a certain level of medical stabilization and weight restoration is required for individuals to have the cognitive capacity to engage in treatment, once medical stabilization is established, research is needed to investigate a more holistic approach to measuring and achieving wellness. Specifically, we advocate for an integrated approach from the outset that not only addresses the behavioral and physical symptoms of the illness but also explicitly addresses the psychological mechanisms that may drive the behavioral and physical manifestations of the disorder.

The current prioritization of the physical symptoms of AN is also evident in treatment programs that emphasize weight goals as a measure of treatment success and in the many AN clinical trials that report body mass index as the primary outcome. While weight is indisputably an important outcome, the focus on weight restoration as the main measure of treatment success is insufficient if there is not also a parallel focus on broader behavioral and physical symptoms and, above all, a shift in psychological symptoms as an outcome metric. Clinical trials in AN demonstrate that while weight restoration may be achieved at the end of treatment, psychological symptoms often endure and take longer to resolve. These persistent symptoms may drive a relapse to low weight, which frequently occurs.[26] Thus, treatments focusing on the psychological contributions to the disorder may be of particular importance, especially for individuals who do not respond to current evidence-based treatments. Furthermore, clinical trials in AN need greater focus on psychological outcomes (and mechanisms) leading up to,

during, and at the end of treatment. In addition, long-term follow-up studies are critical to evaluate the durability of progress and the relationship between physical, behavioral, and psychological progress across time.

Emerging evidence demonstrates that the physiological and neurological impacts of weight loss and low weight in AN can play a role in illness persistence.[27] While this underscores the importance of reversing weight loss and low weight, it also introduces the possibility that there are important—and as yet understudied—markers of or mechanisms involved in low weight in AN that could represent novel treatment targets. A narrow focus on weight as the primary treatment target or marker of successful treatment may be clouding our treatment innovations.

The Future

It is time for the eating disorders field to make purposeful and strategic efforts to break down the barriers that have held us back. First, we need to break down the silo that we have created around eating disorders. We need to make concerted efforts to learn from other areas of mental health and apply these learnings to eating disorders research. We need to undertake multidisciplinary research and actively collaborate with researchers from other areas of mental health and related disciplines (eg, Xie et al,[28] Robinson et al,[29] Phillipou et al,[30] Becker et al,[31] and Bulik et al[32]). Furthermore, we need to attend—and encourage our trainees to attend—scientific meetings outside the eating disorders field and recruit individuals from unconventional disciplines to join our work. We need to put eating disorders at the forefront of funding agendas by demonstrating that we can apply learnings from other areas of mental health to produce high-quality research worth investing in without reinventing the wheel—specifically around personalized, evidence-based treatments and early intervention (eg, Dwyer et al[33] and McGorry et al[34]). To encourage funders to take eating disorders seriously, we need to educate them and the general public on the misconception that eating disorders are not worth investing in because they are seen as trivial or too niche.[35]

Second, although we must of course continue caring for patients with the best treatments currently available, we need to shift our focus away from body weight as the sole or preeminent primary treatment goal and outcome measure in clinical trials and instead also include (and validate) comprehensive indicators of physical recovery (including body weight) concurrently with psychological aspects of the illness, which may take longer to resolve and should continue to be monitored long term.[36,37] Importantly, while we must continue trialing treatments that have a strong theoretical or mechanistic rationale, the focus on translation to treatment when we do not have sufficient knowledge to promote the development of effective treatments is illogical and potentially harmful to patients. To treat patients more effectively, we need to understand the underlying mechanisms and factors that contribute to the development and maintenance of the disorder so that we can appropriately target treatments. This understanding is a critical and foundational step that will surpass the immediate impacts of most clinical trials in the field. Without a deep, data-driven understanding of AN, attempts to design and implement clinical trials may be premature and potentially misaligned with the needs of patients. As researchers, we need to accept this reality and advocate to funding bodies to support research that will have longer-term translational applicability, be more impactful, and push the field forward.

To make significant advances to the field of AN research that will lead to meaningful improvements in patient outcomes, we specifically recommend the following:

- Comprehensive multidisciplinary and collaborative research studies across biological, psychological, and sociocultural factors and mechanisms involved in the development and maintenance of AN to better tailor prevention and treatment efforts in the future.
- Development of interventions that are based on the evidence, are personalized to individuals, and are applicable in real clinical practice.
- Establishment of markers for early identification and treatments that focus on early intervention to alter the illness course so AN does not become chronic, entrenched, and more difficult to treat.
- Assessment of comprehensive physical, behavioral, cognitive, and psychological symptoms and their dynamic relationship at multiple points during, at the end of, and following treatment to better inform what is working in which treatments, how, and for whom.

It is of course important to note that while the eating disorders field may be behind other areas of mental health in terms of efficacious treatment options, significant contributions have been made to our understanding, prevention, and treatment of AN and other eating disorders, and there are several initiatives led by research groups around the world that focus on the priority areas we have described (eg, Walsh[38]). While the field has experienced a unique set of circumstances resulting from dealing with a disorder at the mind-body interface, which has contributed to the modest progress of our field, we must recognize these historical barriers and push past them. We need to reevaluate our understanding of AN and make concerted efforts to invest in studying the foundations of AN, which will set ourselves up to produce the high-quality and effective treatments that individuals with AN deserve.

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