

Key Question Medical Care for Adults with Down Syndrome

Background

The [Patient-Centered Outcomes Research Institute \(PCORI\)](#) is partnering with the Agency for Healthcare Research and Quality (AHRQ) to develop a systematic review on Medical Care for Adults with Down syndrome. The Global Down Syndrome Foundation (GLOBAL) plans to use this systematic evidence review to update and expand a related clinical practice guideline.

Down syndrome, a chromosomal condition in which individuals are born with an extra full or partial copy of chromosome 21, is the most prevalent genetic cause of intellectual disability.¹ Down syndrome occurs in 1 out of every 700 live births in the United States, a rate that has risen over the past years from 1 in 1,000.² This means that although an estimated 200,000 individuals with Down syndrome lived in the United States in 2010, adjusting for the rising birthrate suggests the population could far exceed 350,000.³⁻⁶

Down syndrome is characterized by a host of disparate medical, psychological, and social issues beyond intellectual disability, and individuals with Down syndrome face very different risks for many co-occurring health conditions compared with the general population.¹ In the case of Alzheimer's disease, for example, individuals with Down syndrome are at greatly increased risk, with a lifetime risk of up to 90%, and an earlier age of onset and mortality than those without Down syndrome.^{7,8} The increased risk is also apparent for a number of other conditions including thyroid disease, obstructive sleep apnea, and diabetes. Conversely, individuals with Down syndrome experience a decreased risk for some other diseases, such as solid tumor malignancies and atherosclerotic cardiovascular disease.^{3,9,10}

The unique health issues and considerations for individuals with Down syndrome pose a challenge to providing high quality, comprehensive medical care throughout their lifespan. The life expectancy for individuals with Down syndrome has significantly increased from past decades and is now at 60 years of age compared to just 25 years in the 1980's. Accordingly, there is an increased need for high quality, long term care (primary and specialty care) to support healthy aging, manage co-occurring conditions, and promote quality of life.^{1,3,5} However, a lack of funding and underrepresentation of individuals with Down syndrome in research has led to a lack of evidence on how best to manage their health and co-occurring conditions for this population.¹¹

As the number of individuals with Down syndrome grows and life expectancy continues to rise, the need to identify best practices for the medical management of adults with Down syndrome intensifies. In response to this need, the Global Down Syndrome Foundation (GLOBAL) published the 2020 clinical practice guideline, *Medical Care for Adults with Down Syndrome*, which is recognized as the first evidence-based guideline supporting clinicians caring for adults with Down syndrome.^{3,12} The guideline is cited by key clinical resources and organizations, including the National Institutes of Health, the Down Syndrome Medical Interest Group of the United States, the National Down Syndrome Congress, and the National Down Syndrome Society.¹³⁻¹⁵

The 2020 GLOBAL guideline provides recommendations for screening, diagnosis, and treatment of health conditions across nine clinical areas, identified as critically important for this population by experts and the wider Down syndrome community as part of guideline development: behavioral conditions, dementia, diabetes, cardiovascular disease, obesity, atlantoaxial instability, osteoporosis, thyroid, and celiac disease. The 2020 guideline's recommendations are based on limited evidence, however, with the guideline's underlying systematic review including only 22 studies published through 2020.^{3,12}

GLOBAL intends to update and expand the scope of their guideline to include four new clinical topic areas (e.g., sleep apnea, solid tumors, blood cancers/leukemias, and vision) and one considerable addition to the area of musculoskeletal conditions. A new systematic review in support of guideline development is warranted, as evidence has accumulated in the past few years, with many new studies mapping onto the four new clinical areas of interest in addition to the previously identified clinical areas and conditions. Additionally, while a few recent systematic reviews offer insights for specific health conditions in this population, including information on the estimated prevalence of co-occurring conditions like osteopenia and pharmacologic treatments for dementia among adults with Down syndrome, none comprehensively synthesize the evidence for adults with Down syndrome.^{9,10,16,17}

Given the lack of a recent and comprehensive systematic review in the face of accumulating evidence, this proposed systematic review will aim to inform the update and expansion of the GLOBAL guideline on medical care for adults with Down syndrome in order to inform decision-making for physicians, patients, and caregivers. The review will specifically address care for conditions commonly associated with Down syndrome that occur at increased risk or decreased risk among adults with Down syndrome.^{9,10,18}

Draft Key Questions

KQ1. What are the benefits, and harms, of *screening* for conditions occurring at increased or decreased prevalence in adults with Down syndrome?

KQ1a. Do adults with Down syndrome require a different approach to preventive screening (different screening timing/frequency/interval, or different instruments) than the general adult population?

KQ2. What are the benefits, and harms of *diagnostic approaches* for conditions occurring at increased or decreased prevalence in adults with Down syndrome?

KQ3. What are the benefits and harms of interventions to *treat* conditions occurring at increased or decreased prevalence in adults with Down syndrome?

Contextual Questions

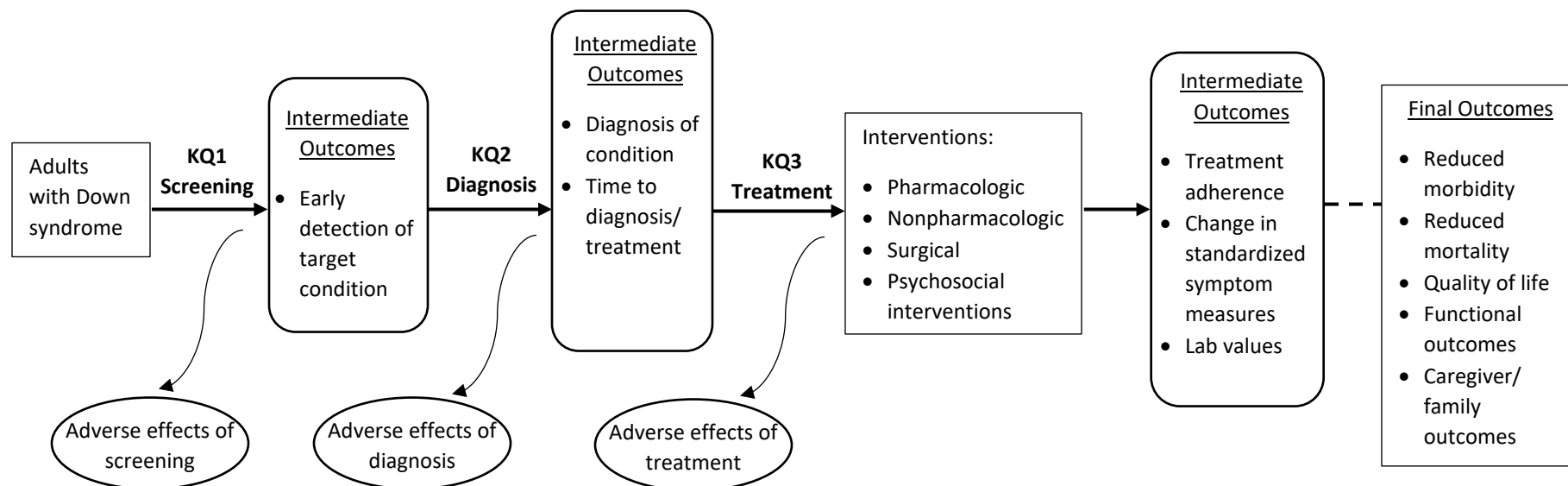
CQ1. What is the prevalence of conditions occurring more frequently in adults with Down syndrome compared to the general population and how does this vary by age/decade of age, gender, setting (rural) and race/ethnicity?

CQ2. How do clinical symptoms and the presentation of common mental health conditions such as anxiety and depression differ among adults with Down Syndrome compared to their presentation in the general adult population?

Table 1: Key Questions and PICOs for Medical Care for Adults with Down Syndrome

Key Questions	Population	Intervention	Comparator	Outcomes
<p>KQ1. What are the benefits, harms of <i>screening approaches</i> for conditions occurring at increased prevalence in adults with Down syndrome?</p> <p>KQ1a. Do adults with Down syndrome require a different screening timing/frequency interval, or a different approach or instrument than the general population?</p>	Adults with Down syndrome	Screening for conditions occurring at increased prevalence for adults with Down syndrome	<p>For all conditions, compared with no screening or alternative approach to screening</p> <p>Standard recommended screening approach for adults (non-pregnant)</p>	<ul style="list-style-type: none"> • Benefits: accurate diagnosis, time to diagnosis or intervention • Harms: adverse events related to screening
<p>KQ2. What are the benefits, harms of <i>diagnostic approaches</i> for conditions occurring at increased prevalence in adults with Down syndrome?</p>	Adults with Down syndrome	Diagnostic approach/(es) for conditions associated with Down syndrome (non-pregnant)	For all conditions, compared with no diagnostic approach or alternative approach to diagnosis	<ul style="list-style-type: none"> • Benefits: Time to intervention/treatment • Health and quality of life outcomes • Harms: Misdiagnosis/adverse effects of diagnosis
<p>KQ3. What are the benefits and harms of interventions to <i>treat</i> conditions occurring at increased prevalence in adults with Down syndrome?</p>	Adults with Down syndrome	Treatment approach/(es) for adults with Down syndrome-associated conditions	For all conditions, compared with usual care or alternative approach to treatment	<p>Intermediate outcomes</p> <ul style="list-style-type: none"> • Treatment adherence • Change in standardized symptom measures • Lab values • Adverse treatment effects <p>Final outcomes</p> <ul style="list-style-type: none"> • Morbidity/mortality (e.g., Years of life saved) • Quality of life • Functional outcomes (e.g., Activities of daily living, assisted living/nursing home status) • Caregiver or family outcomes (including caregiver health and quality of life)

Figure 1. Preliminary Analytic Framework – Medical Care for Adults with Down Syndrome



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