



GLOBAL
DOWN SYNDROME FOUNDATION®

What Families & Clinicians Need to Know: **The 1st Evidence-based Medical Care Guidelines** **for Adults with Down Syndrome**

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GLOBAL Webinar Series
Wednesday, October 21, 2020

Welcome to the GLOBAL Webinar Series

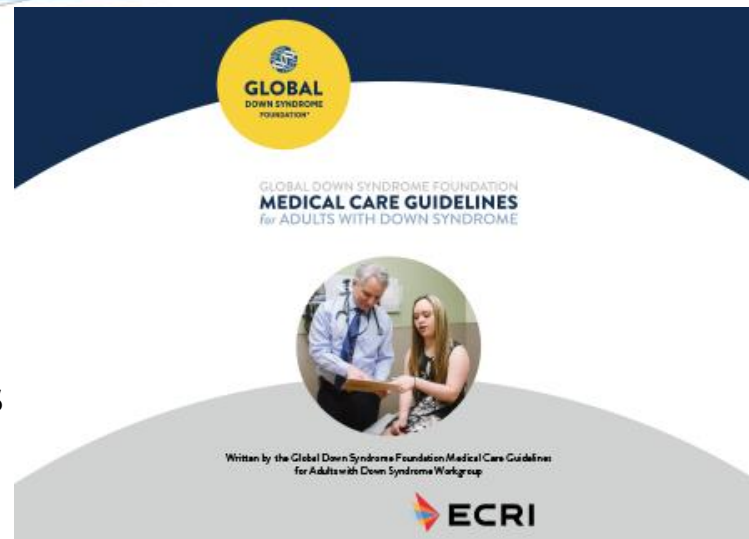
❖ Welcome & Housekeeping

❖ Global Down Syndrome Foundation

- Brief Overview & COVID-19 Update
- GLOBAL Medical Care Guidelines for Adults with Down Syndrome© Introduction
 - Brief History
 - Current Status
 - Future Plans

❖ Guideline Q&A with the Authors

- Questions emailed in advance
- Live chat questions



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The Inspiration behind Global



“Never doubt that a small group of thoughtful, committed citizens can change the world; indeed, it's the only thing that ever has.” -Margaret Mead

Global Overview: The Catalyst

People with DS have a Dramatically Different Disease Spectrum



The >350,000 Americans with trisomy 21 may hold the key to major medical conditions

Global Overview: The Catalyst

A life-threatening disparity

| Year | NIH Budget (Millions) | CF Research Funding | Fragile X Research Funding | Autism Research Funding | Ds Research Funding | Ds Research Funding to NIH Budget |
|------|-----------------------|---------------------|----------------------------|-------------------------|---------------------|-----------------------------------|
| 2000 | 17,840 | | | | 27 | 0.0015 |
| 2001 | 20,459 | | | | 29 | 0.0014 |
| 2002 | 23,321 | | | | 28 | 0.0012 |
| 2003 | 27,166 | | | | 23 | 0.0008 |
| 2004 | 28,037 | | | | 19 | 0.0007 |
| 2005 | 28,594 | | | | 15 | 0.0005 |
| 2006 | 28,560 | | | | 14 | 0.0005 |
| 2007 | 29,178 | | | | 16 | 0.0006 |
| 2008 | 29,607 | | | | 17 | 0.0006 |
| 2009 | 30,545 | | | | 18 | 0.0006 |
| 2010 | 31,238 | | | | 22 | 0.0007 |
| 2011 | 30,916 | | | | 20 | 0.0006 |
| 2012 | 30,860 | 86 | 27 | 192 | 20 | 0.0006 |
| 2013 | 29,129 | 78 | 30 | 186 | 18 | 0.0006 |
| 2014 | 30,019 | 77 | 36 | 186 | 18 | 0.0006 |
| 2015 | 30,293 | 80 | 38 | 208 | 24 | 0.0008 |
| 2016 | 30,293 | 83 | 40 | 216 | 25 | 0.0008 |

Global Down Syndrome Foundation

A Unique Affiliate Model



The Global Down Syndrome Foundation is the largest non-profit in the U.S. working to save lives and dramatically improve health outcomes for people with Down syndrome. Global has donated more than \$32 million to establish the first Down syndrome research institute supporting over 400 scientists and over 2,000 patients with Down syndrome from 28 states and 10 countries.

Working closely with Congress and the National Institutes of Health, Global is the lead advocacy organization in the U.S. for Down syndrome research and care.

Global has a membership of over 100 Down syndrome organizations worldwide, and is part of a network of Affiliates - the Crnic Institute for Down Syndrome, the Sie Center for Down Syndrome, and the University of Colorado Alzheimer's and Cognition Center - all on the Anschutz Medical Campus.

GLOBAL's Lobbying, Advocacy & Outreach

- ❖ **Tripling of the DS Research Budget at NIH**
 - \$27M in FY2016
 - \$35M in FY2017
 - \$60M in FY2018 (\$23M from INCLUDE)
 - \$77M in FY2019 (\$36M from INCLUDE)
 - \$113M in FY2020 (TBD from INCLUDE)
- ❖ **Global's Long-standing 2 Goals are Being Met:**
 - (1) Move DS research from NICHD to a trans-NIH model
 - (2) Dramatically increase funding for DS research at NIH
- ❖ **A Trans-NIH Model: The NIH INCLUDE Project**
 - Establishment of INCLUDE (Investigation of Co- occurring conditions across the Lifespan to Understand Down syndromE) Project Research - 18 Participating Institutes



GLOBAL's Groundbreaking Research

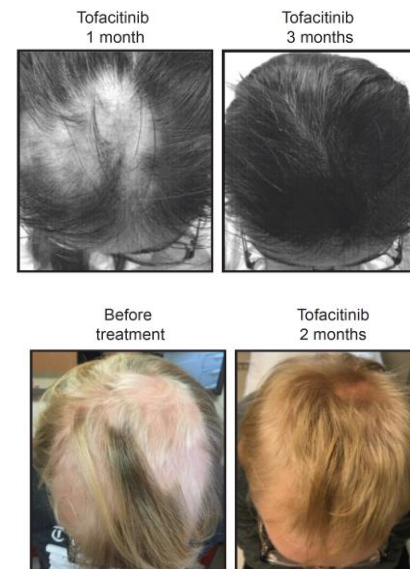
*Linda Crnic Institute for Down Syndrome at
CU SOM/Anschutz Medical Campus*

- ❖ 200+ scientists working on DS research
- ❖ Breakthrough Discovery - Down syndrome can be categorized as an immune system disorder
 - Crnic Institute Human Trisome Project™
 - Interferon Pathway is key! **JAK Inhibitors bring Interferon down!**
- ❖ Crnic Institute NIH Funding
 - 23% of NIH INCLUDE DS Research Funding FY2019
 - 1st NIH-funded Clinical Trial aimed at curing certain autoimmune diseases in people with DS
 - Primary Research Areas:
 - Immunology
 - Alzheimer's disease
 - Cognition, Autism, & Brain Function; Leukemia
 - Stem Cells & Development
 - Advanced Genetics & Genomics
 - New/Young Investigators

Trisomy 21 consistently activates the interferon response

Kelly D Sullivan^{1,2,3,4*}, Hannah C Lewis^{1,2}, Amanda A Hill^{1,2}, Ahwan Pandey^{1,2,3,4}, Leisa P Jackson^{1,3,4}, Joseph M Cabral^{1,3,4}, Keith P Smith¹, L Alexander Liggett^{1,5}, Eliana B Gomez^{1,3,4}, Matthew D Galbraith^{1,2,3,4}, James DeGregori^{1,5,6,7,8,9}, Joaquín M Espinosa^{1,2,3,4*}

JAK inhibitors are being heavily tested for immune-driven skin conditions more prevalent in people with Down syndrome (e.g. alopecia areata, vitiligo, atopic dermatitis, hidradenitis suppurativa)



XELJANZ
[tofacitinib]

GLOBAL's Groundbreaking Research

Linda Crnic Institute for Down Syndrome at
CU SOM/Anschutz Medical Campus

LINDA CRNIC INSTITUTE
for DOWN SYNDROME

RESEARCH TO DEVELOP THE
HUMAN TRISOME PROJECT BIOBANK



PURPOSE OF THE STUDY

The purpose of this study is to provide qualified and approved researchers with access to biological samples and health information to answer specific research questions. This project will significantly increase the speed of Down syndrome research and the understanding of associated medical conditions such as leukemia and Alzheimer's disease.

WHO CAN PARTICIPATE?

Anyone who is 6 months – 89 years old who:

1. Has Down syndrome (any type, including mosaic or partial Down syndrome/trisomy 21)
2. Has a family member with Down syndrome but does not him/herself have Down syndrome
3. Does not have Down syndrome and does not have a family member with Down syndrome (this would be a "control" group to compare with those affected by Down syndrome)

MAIN PROCEDURES INVOLVED

Participation would include a single successful blood draw, a mouth swab and allowing researchers to look at your health information. It is optional to give a stool sample and take part in the study for a longer time frame.

DURATION OF PARTICIPATION

A single visit to collect blood and mouth swab, fill out a health survey, with the option of a stool sample and repeat visits for a longer term study.

INTERESTED?

Contact Angela Rachubinski at 303-724-7366 or <http://ucdenver.edu>

Compensation will be provided.
COMIRB #: 15-2170 PI: Joaquin Espinosa



Research opportunity for people with Down syndrome with immune skin conditions



LINDA CRNIC INSTITUTE
for DOWN SYNDROME™

Scientists at the Linda Crnic Institute are recruiting for a new clinical trial funded by the National Institutes of Health.



The purpose of this clinical trial is:

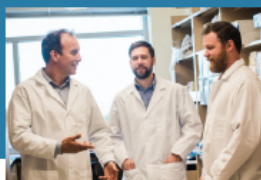
1. To better understand immune system dysregulation in people with Down syndrome
2. To see if a drug called Tofacitinib is a safe and effective treatment for immune skin conditions

You may qualify if you:

1. Have Down syndrome and are 18-60 years old
2. Have an active immune skin condition, including moderate-to-severe
 - atopic dermatitis (eczema)
 - alopecia areata (hair loss)
 - hidradenitis suppurativa (boils)
 - psoriasis (scaly, itchy skin)
 - vitiligo (pigmentation loss)
3. Have a study partner who can participate with you

Main study procedures involve:

1. Taking oral medication twice per day
2. Blood draws and physical exams
3. Completion of interactive tasks designed to measure cognition
4. Attending 8 study visits over ~5 months in Denver



COMIRB #19-1362
NCT04246372

PI: Dr. Joaquin Espinosa

To learn more, please email: dsresearch@ucdenver.edu



SCHOOL OF MEDICINE
Linda Crnic Institute for Down Syndrome
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS



Dermatology
UNIVERSITY OF COLORADO MEDICINE



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DOWN SYNDROME FOUNDATION™

*Photos credit of
the Global Down
Syndrome Foundation

GLOBAL's Pediatric Medical Care

Sie Center for DS at Children's Hospital Colorado

❖ Established and Support the Sie Center

- 1,800+ unique patients from 28 states and 10 countries
- 14 FTE, 8 Clinics - Mental Wellness; School Age/Education
- Dr. Fran Hickey, Dr. Lina Patel, Patricia C. Winders and Dee Daniels

❖ Specialty Areas

- DS and Aspiration, Infantile Spasms, Autism, Sleep apnea, Morphine for surgery, Behavior and regression
- PT, Speech, Feeding/Swallowing, and more

❖ Publish the Pamphlet - 'Prenatal Testing & Information About Down Syndrome

- With NDSC, Spanish & Icelandic, FREE downloads & print copies



Excerpts from the Pamphlet



What is Down syndrome?

Down syndrome, also known as Trisomy 21, is a condition where a person is born with three copies of chromosome 21 instead of two. In the United States, 1 in every 691 babies is born with the condition.³ There are hundreds of thousands of people with Down syndrome in the United States, and an estimated six million people with Down syndrome worldwide.



How will Down syndrome affect my baby?

There is no way to know what the future holds for any baby. In many ways, babies with Down syndrome are just like other babies. All babies need to be fed, have their diapers changed, and have playtime, but, most of all, they need to be loved. These needs are the same for a baby with Down syndrome.

GLOBAL's COVID-19 RELATED WORK

People with DS are High Risk AND Vulnerable

❖ COVID-19 Emergency Relief GLOBAL GRANTS

- Family Grants - 140 families served
- Small DS Org Grants - 20+ supported

❖ COVID-19 & Down Syndrome Q&A Resource

- GLOBAL is helping spearhead a national consortium & is a lead author; A NEW update in January 2021

❖ GLOBAL provided PPE to ever person with IDD in CO

- ❖ Who are wards of the state - Group/Host homes

❖ Fighting discrimination against people with DS and IDD when it comes to COVID-19 care

- GLOBAL led 140 social justice and disability organizations in CO to ensure equitable care
- AL, TN, WA, NY, PA, and others - people with chromosomal disorders/disabilities are targeted



**COVID-19
Emergency Relief
GLOBAL Grants**



GLOBAL/CRNIC Institute CO-founded the International Consortium for JAK inhibition in COVID-19



• HOME / • INVESTORS / • LILLY BEGINS CLINICAL TESTING OF THERAPIES FOR COVID-19

Lilly Begins Clinical Testing of Therapies for COVID-19

04/10/2020

- Baricitinib Research Commences in NIH-led Adaptive COVID-19 Treatment Trial



Download PDF

2020 Be Beautiful Be Yourself Fashion Show

Saturday, November 14, 2020

The largest fundraiser for people with Down syndrome in the world

- Raised over \$20M in 11 years
- Quincy Jones Exceptional Advocacy Honorees each year
- Sold out with 1,400 attendees (in 2019 25 states, 10 countries, 22 self-advocate models including one from England and one from India)
- Strong Celebrity Presence
- Strong Press Results

2020 NEW VIRTUAL FORMAT

- NEW \$25 Tickets
- Largest number of celebrities
- Largest number of models & self-advocates



GLOBAL Medical Care Guidelines for Adults with Down Syndrome©

An Important Legacy for our Community



GLOBAL Medical Care Guidelines for Adults with Down Syndrome©

An Important Legacy for our Community

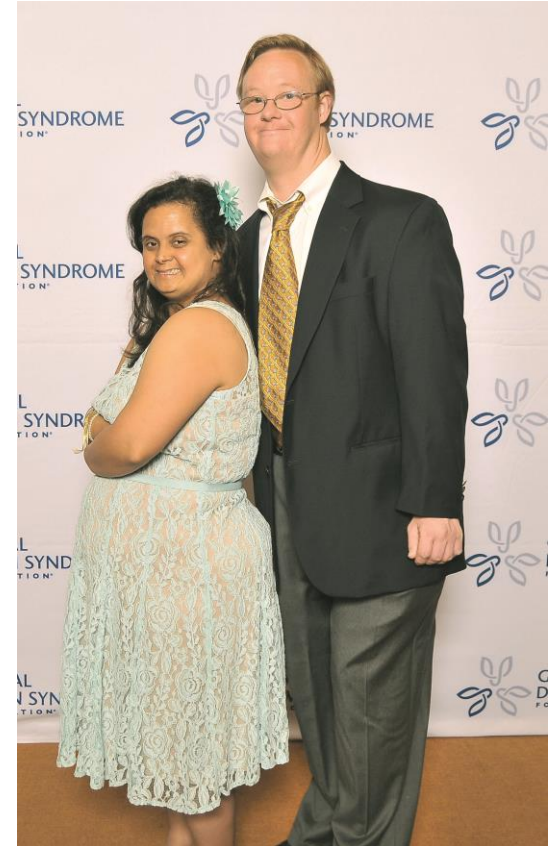


The Critical & Timely Need

- ❖ **There is a population explosion of people with Down syndrome in the U.S. that requires dramatically *more* funding not less**
 - **Population** - is somewhere between 250,000 to 430,000
 - **Live Births** - have increased to 1 in 691 today from 1 in 1,000 in 2002
 - **Lifespan** - has more than doubled to 60 years from 28 years in the 1980s
 - **A Mini Population Explosion** - will happen over the next several decades due to increased live births and lifespan
 - **Societal Trends** - include a small but growing number of people with Down syndrome participating in college programs, choosing to get married, and living independently or semi-independently
- ❖ **There is a “eugenics framework” in countries like Iceland and Denmark...**

Why did it take so long? The Challenges

- ❖ **Down syndrome was the least funded genetic condition by NIH**
 - ❖ Funding was stuck between \$14-24 million funding for over two decades, which limited the number of researchers drawn to the field as well
- ❖ **Fewer than 12 adult focused DS clinics across the US**
 - ❖ Most adults with DS receive care from general PCP
 - ❖ Relatively few experts available
- ❖ **The complexity of Down syndrome**
 - ❖ Not a “single system condition”
 - ❖ Complexity of multiple comorbidities
- ❖ **Creating guidelines requires a significant amount of time on the part of clinicians and families!**



Wanted the Best Experts

- ❖ Jarrett Barnhill (MD DFAPA FAACAP) Professor and Director, UNC Developmental Neuropsychopharmacology Clinic
- ❖ Donald Bodenner (MD, PhD) Professor, Department of Geriatrics, University of Arkansas for Medical Sciences, Director of Thyroid Center and Chief of Endocrine Oncology
- ❖ Paul Camarata (MD) Professor and Chairman, Vascular & Skull Base Neurosurgery, University of Kansas Medical Center
- ❖ Kamala Gullapalli Cotts (MD) Associate Professor of Medicine, Director, Adult Developmental Disabilities Clinic, Section of General Medicine, Department of Medicine, The University of Chicago
- ❖ Robert Eckel (MD) Charles A. Boettcher II Endowed Chair in Atherosclerosis Professor of Medicine - Division of Endocrinology, Metabolism and Diabetes, and Cardiology, Professor of Physiology and Biophysics, Director of Lipid Clinic, University of Colorado Hospital
- ❖ Anna Esbensen (PhD) Associate Professor of Pediatrics, Cincinnati Children's Hospital
- ❖ James Hunt (MD) Assistant Professor of Anesthesiology, UAMS COM, Division of Pediatric Anesthesiology and Pain Medicine, Arkansas Children's Hospital
- ❖ Seth Keller (MD) Co-Chair, National Task Group on Intellectual Disabilities and Dementia Practices; Chair, Special Interest Group Adult IDD, American Academy of Neurology Past President, American Academy of Developmental Medicine and Dentistry
- ❖ Judy Kim (MD) Assistant Professor, Department of Medicine, Transition Medicine, Baylor College of Medicine

Wanted the Best Experts

- ❖ Ira Lott (MD) Pediatric Neurologist, Emeritus Professor, University of California, Irvine and CHOC Children's Hospital
- ❖ Michael McDermott (MD) Professor of Medicine and Clinical Pharmacy, Division of Endocrinology, Diabetes Metabolism, University of Colorado School of Medicine
- ❖ Joan Medlen (MEd, RD, LD) Nutrition Counseling and Registered Dietitian
- ❖ Micol Rothman (MD) Associate Professor of Medicine, Director of the Metabolic Bone Program, Department of Medicine, Division of Endocrinology, University of Colorado Denver
- ❖ Stephanie Santoro (MD) Director of Quality Improvement Research, Down Syndrome Program, MassGeneral Hospital
- ❖ Mary Stephens (MD, MPH) Family Medicine and Jefferson Continuing Care Program, Jefferson Health and Down syndrome Consult Program, Christiana Care Center for Special Health Care Needs
- ❖ Elizabeth Yeung (MD) Associate Professor of Clinical Practice, Pediatric and Adult Congenital Cardiology, University of Colorado School of Medicine

- ❖ ***PLUS Additional Contributors to Future Research Needs...***
 - ❖ Lina R Patel (PsyD)
 - ❖ Joaquin M Espinosa (PhD)
 - ❖ Michael S. Rafii (MD, PhD)

Wanted the Most Advanced Methodology

❖ PICOT Questions

- Key questions asked directly inform the literature review and the types of recondition statements that can be created
- PICTOS is the evidence-based framework each key question must follow



❖ GRADE Evidence-to-Decision Making

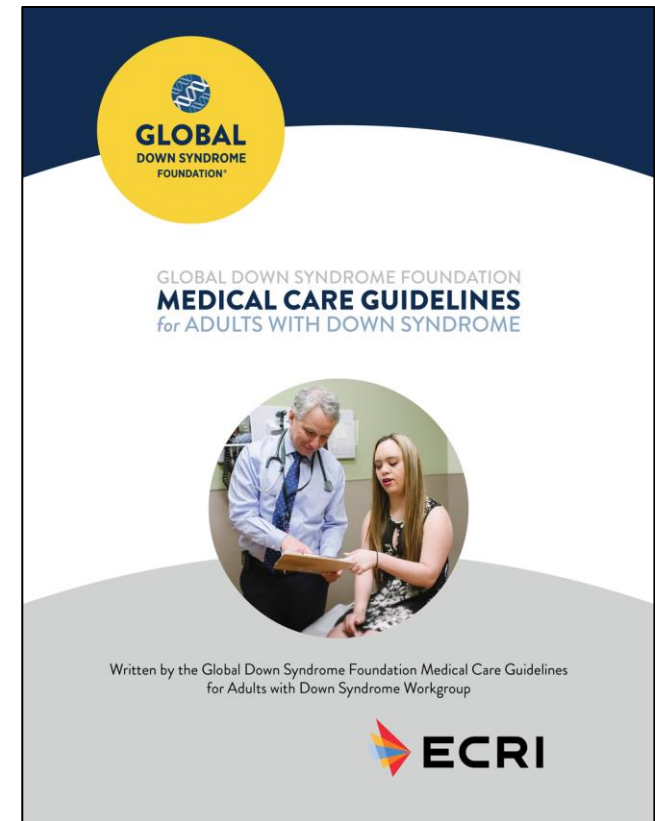
- Process for translating evidence into recommendations
- Ensure rigorous, evidence based, and transparent
- Standardizing quality of evidence

| Recommendation Text | | Strength | | |
|------------------------------------|-------------------------------------|---|---|---|
| "We recommend/suggest offering..." | | Strong For Weak For Neither for or against Weak against Strong against | | |
| | Relevant outcome (s) | | | |
| | e.g. ADLs (Critical outcomes) | | | |
| | Confidence in quality of evidence | Balance of desirable and undesirable outcomes | Values and preferences | Other implications |
| Judgement | High Moderate Low Very Low | Benefits outweigh harms/burdens Benefits slightly outweigh harms/burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits | Similar values Some variation Large variation | Resource use Equity Acceptability Feasibility Subgroup considerations |
| Justification | | | | |
| Notes | | | | |

RESULTS: Guideline Topics & Questions

- ❖ 40 topics had to be narrowed down to nine for these initial guidelines:
 1. Behavior/Mental Health
 2. Dementia
 3. Metabolic Disorders
 4. Cardiac Metabolism
 5. Obesity-Lifestyle Activity-Special Diets
 6. Muscular Skeletal
 7. Bone Density
 8. Thyroid-Immunology
 9. GI-Immune-Special Diets

- ❖ Other important topics such as Sleep Apnea and Cancer should be covered in the future



Global's Focus Groups

❖ Focus groups

- 27 family members or caregivers
- 7 self advocates
- 10 states
- 7 DAYS of online discussion forum format
- 10 participants recommended

❖ Ensuring Diversity!

- Gender: 57% Female, 43% Male
- Race & Ethnicity:
 - Caucasian 69%
 - Black 9%
 - Latino 14%
 - Asian 9%

❖ Results

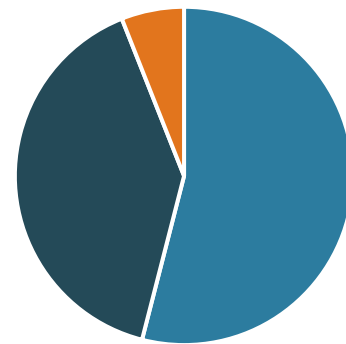
- 82% were satisfied
- Unsatisfied was associated with technical terms and unhappiness that these didn't exist before
- We need a layperson's glossary & toolkits



Special Thanks:

DSA Jacksonville
DSA Central FL
Rocky Mountain DSA
DSA of Greater Cincinnati
DS Connection of the Bay Area
DSA of Greater Richmond
DSA of Minnesota
DS Alliance of the Midlands
DSF of SE New Mexico
NDSC

Age of Participants



■ 18-29 yrs ■ 30-49 yrs ■ 50+ yrs

Questions & Qualifying Studies

A Daunting Task

11,295 possible
citations Identified



7,200 abstracts
reviewed



1,929 Articles
reviewed round 1



199 Articles
reviewed round 2



**22 Studies
Qualify**

❖ 26 different key questions address the 9 medical topic areas

❖ Only 22 Studies Qualified!!
FINAL Product

❖ Final Product

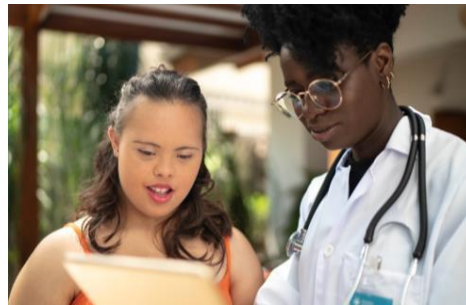
- Statements of Good Practice: 4
 - Obesity
 - GI-Immune
 - Behavior (2)
- Recommendation Statements: 14
 - 1 “Strong” recommendation (dementia)
 - 12 “Weak” recommendations
 - 1 Neither for nor against recommendation

Evidence by Question

Our Desperate Need for Research

FOURTEEN have “No Evidence” – what does that mean?

| Question # | Category Question | Evidence Found | Question # | Category Question | Evidence Found |
|------------|------------------------|--------------------|------------|-------------------|---------------------------|
| 1 | Behavior/Mental Health | 2 Low | 14 | Musculoskeletal | No Evidence |
| 2 | Behavior/Mental Health | No Evidence | 15 | Bone Density | 6 Low |
| 3 | Dementia | 1 High, 2 Moderate | 16 | Bone Density | No Evidence |
| 4 | Metabolic Disorders | 2 High, 3 Moderate | 17 | Bone Density | 2 Low |
| 5 | Metabolic Disorders | No Evidence | 18 | Bone Density | 1 Moderate |
| 6 | Metabolic Disorders | No Evidence | 19 | Thyroid | 1 High, 1 Moderate, 1 Low |
| 7 | Cardiac Metabolism | 1 High, 1 Low | 20 | Thyroid | No Evidence |
| 8 | Cardiac Metabolism | 1 Low | 21 | Thyroid | No Evidence |
| 9 | Cardiac Metabolism | No Evidence | 22 | Thyroid | No Evidence |
| 10 | Obesity-Lifestyle | 2 Low | 23 | GI-Immune | 2 Low |
| 11 | Obesity-Lifestyle | No Evidence | 24 | GI-Immune | No Evidence |
| 12 | Obesity-Lifestyle | No Evidence | 25 | GI-Immune | No Evidence |
| 13 | Musculoskeletal | 2 Moderate | 26 | GI-Immune | No Evidence |



Published in JAMA!

Journal of the American Medical Association

- ❖ Featured in October 20, 2020 issue print and online
- ❖ One of the largest issues
- ❖ High impact and wide distribution
 - ❖ Prestigious *and* trusted
 - ❖ Reaches across disciplines
- ❖ Includes list of experts, donors, PLUS: Guideline Checklist!!!
- ❖ Featured on JAMA Podcast

Clinical Review & Education

JAMA | Special Communication

Medical Care of Adults With Down Syndrome A Clinical Guideline

Amy Y. Tsou, MD, MSc; Peter Bulova, MD; George Capone, MD; Brian Chicoine, MD; Bryn Gellaro, MA, LSW; Terry Odell Harville, MD, PhD, DABIMB, DABH; Barry A. Martin, MD; Dennis E. McGuire, PhD, LCSW; Kent D. McKelvey, MD; Moja Peterson, PhD, APRN, FNP-BC; Carl Tyler, MD, MSc; Michael Wells, BS; Michelle Sie Whitten, MA; for the Global Down Syndrome Foundation Medical Care Guidelines for Adults with Down Syndrome Workgroup

IMPORTANCE Down syndrome is the most common chromosomal condition, and average life expectancy has increased substantially, from 25 years in 1983 to 60 years in 2020. Despite the unique clinical comorbidities among adults with Down syndrome, there are no clinical guidelines for the care of these patients.

OBJECTIVE To develop an evidence-based clinical practice guideline for adults with Down syndrome.

EVIDENCE REVIEW The Global Down Syndrome Foundation Medical Care Guidelines for Adults with Down Syndrome Workgroup (n = 13) developed 10 Population/Intervention/Comparison/Outcome (PICO) questions for adults with Down syndrome addressing multiple clinical areas including mental health (2 questions), dementia, screening or treatment of diabetes, cardiovascular disease, obesity, osteoporosis, atlantoaxial instability, thyroid disease, and celiac disease. These questions guided the literature search in MEDLINE, EMBASE, PubMed, PsychINFO, Cochrane Library, and the TRIP Database, searched from January 1, 2000, to February 26, 2018, with an updated search through August 6, 2020. Using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology and the Evidence-to-Decision framework. In January 2019, the 13-member Workgroup and 16 additional clinical and scientific experts, nurses, patient representatives, and a methodologist developed clinical recommendations. A statement of good practice was made when there was a high level of certainty that the recommendation would do more good than harm, but there was little direct evidence.

FINDINGS From 11 295 literature citations associated with 10 PICO questions, 20 relevant studies were identified. An updated search identified 2 additional studies, for a total of 22 included studies (3 systematic reviews, 19 primary studies), which were reviewed and synthesized. Based on this analysis, 14 recommendations and 4 statements of good practice were developed. Overall, the evidence base was limited. Only 1 strong recommendation was formulated: screening for Alzheimer-type dementia starting at age 40 years. Four recommendations (managing risk factors for cardiovascular disease and stroke prevention, screening for obesity, and evaluation for secondary causes of osteoporosis) agreed with existing guidance for individuals without Down syndrome. Two recommendations for diabetes screening recommend earlier initiation of screening and at shorter intervals given the high prevalence and earlier onset in adults with Down syndrome.

CONCLUSIONS AND RELEVANCE These evidence-based clinical guidelines provide recommendations to support primary care of adults with Down syndrome. The lack of high-quality evidence limits the strength of the recommendations and highlights the need for additional research.

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CME Quiz at
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Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: A complete list of the members of the Global Down Syndrome Foundation Medical Care Guidelines for Adults with Down Syndrome Workgroup appears at the end of this article.

Corresponding Author: Amy Y. Tsou, MD, MSc, Evidence-Based Practice Center, Center for Clinical Excellence and Guidelines, ICH, 5200 Butler Pike, Plymouth Meeting, PA 19062 (atsou@ICH.org).

1543

The Final Product as Published in JAMA

| Recommendations | | Strength |
|-----------------|--|------------|
| Behavior | | |
| 1. | When concern for a mental health disorder in adults with Down syndrome is present, medical professionals should refer to a clinician knowledgeable about the medical, mental health disorders, and common behavioral characteristics of adults with Down syndrome. | Weak For |
| 2. | When concern for a mental health disorder in adults with Down syndrome is present, medical professionals should follow guidelines for diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (5 th Ed; DSM-5). ²⁶ The Diagnostic Manual-Intellectual Disability 2 (DM-ID-2) ²⁷ also may be used to adapt diagnostic criteria from the DSM-5. | Weak For |
| Dementia | | |
| 3. | Caution is needed when diagnosing age-related, Alzheimer's-type dementia in adults with Down syndrome younger than age 40 due to its low prevalence before this age. | Weak For |
| 4. | Medical professionals should assess adults with Down syndrome and interview their primary caregivers about changes from baseline function annually beginning at age 40. Decline in the following six domains as per the National Task Group - Early Detection Screen for Dementia (NTG-EDSD), ²⁸ should be used to identify early-stage age-related Alzheimer's-type dementia and/or a potentially reversible medical condition: <ul style="list-style-type: none"> Cognition, memory, and executive function Behavior and personality Communication Adaptive functioning Ambulation and motor skills General decline in established skills | Strong For |

| | | |
|---|--|----------|
| Diabetes | | |
| 5. | For asymptomatic adults with Down syndrome, screening for type 2 diabetes mellitus (T2DM) using hemoglobin A1c (HbA1c) or fasting plasma glucose should be performed every 3 years beginning at age 30. | Weak For |
| 6. | For any adult with Down syndrome and comorbid obesity, screening for T2DM using HbA1c or fasting plasma glucose should be performed every 2–3 years beginning at age 21. | Weak For |
| Cardiovascular Disease | | |
| Atherosclerotic Cardiovascular Disease | | |
| 7. | For adults with Down syndrome without a history of atherosclerotic cardiovascular disease (ASCVD), the appropriateness of statin therapy should be assessed every 5 years starting at age 40 and using a 10-year risk calculator as recommended for adults without Down syndrome by the U.S. Preventive Services Task Force. ²⁹ | Weak For |
| Stroke | | |
| 8. | For adults with Down syndrome, risk factors for stroke should be managed as specified by the American Heart Association/American Stroke Association's Guidelines for the Primary Prevention of Stroke. ³⁰ | Weak For |
| 9. | In adults with Down syndrome with a history of congenital heart disease, given the elevated risk of cardioembolic stroke, a periodic cardiac evaluation and a corresponding monitoring plan should be reviewed by a cardiologist. | Weak For |
| Obesity | | |
| 10. | Monitoring for weight change and obesity should be performed annually by calculating body mass index (BMI) in adults with Down syndrome. The U.S. Preventive Services Task Force (USPSTF) Behavioral Weight Loss interventions to Prevent Obesity-Related Morbidity and Mortality in Adults should be followed. ³¹ | Weak For |

The Final Product as Published in JAMA

| Recommendations | | Strength |
|---------------------------------|---|-------------------------|
| Atlantoaxial Instability | | |
| 11. | In adults with Down syndrome, routine cervical spine X-rays should not be used to screen for risk of spinal cord injury in asymptomatic individuals. Instead, annual screening of adults with Down syndrome should include a review of signs and symptoms of cervical myelopathy using targeted history and physical exam. | Weak Against |
| Osteoporosis | | |
| 12. | For primary prevention of osteoporotic fractures in adults with Down syndrome, there is insufficient evidence to recommend for or against applying established osteoporosis screening guidelines, including fracture risk estimation; thus, good clinical practice would support a shared decision-making approach to this issue. | Neither for nor Against |
| 13. | All adults with Down syndrome who sustain a fragility fracture should be evaluated for secondary causes of osteoporosis, including screening for hyperthyroidism, celiac disease, vitamin D deficiency, hyperparathyroidism and medications associated with adverse effects on bone health. | Weak For |
| Thyroid | | |
| 14. | Screening adults with Down syndrome for hypothyroidism should be performed every 1–2 years using a serum thyroid-stimulating hormone test beginning at age 21. | Weak For |

| Statements of Good Practice | |
|-----------------------------|---|
| Behavior | |
| 1. | Statement of Good Practice 1: A review of behavioral, functional, adaptive, and psychosocial factors should be performed as part of an annual history that clinicians obtain from all adults with Down syndrome, their families, and caregivers. |
| 2. | Statement of Good Practice 2: When concern for a mental health disorder in adults with Down syndrome is present, medical professionals should evaluate for medical conditions that may present with psychiatric and behavioral symptoms. |
| Obesity | |
| 3. | Statement of Good Practice 3: Healthy diet, regular exercise, and calorie management should be followed by all adults with Down syndrome as part of a comprehensive approach to weight management, appetite control, and enhancement of quality of life. |
| Celiac Disease | |
| 4. | Statement of Good Practice 4: Adults with Down syndrome should receive an annual assessment for gastrointestinal and non-gastrointestinal signs and symptoms of celiac disease using targeted history, physical examination, and clinical judgement of good practice. |

GLOBAL Guideline Checklist

GLOBAL MEDICAL CARE GUIDELINES

for Adults with Down Syndrome Checklist



GLOBAL
DOWN SYNDROME FOUNDATION*

This checklist is intended to support the health of adults with Down syndrome directly or through their caregivers. We encourage this checklist to be shared with your medical professionals. Statements in blue represent our recommended, periodic health screenings/assessments that should begin at a specific age. Below each blue screening/assessment recommendation, there are blank boxes. Caregivers or individuals with Down syndrome can check off, date, or initial each blank box when the screening/assessment is completed. For screening/assessment recommendations with a time range (e.g. 1-2 years), the box size represents the longer possible time frame, such as 2 years versus 1. Statements in gray represent advisory recommendations that individuals with Down syndrome and caregivers should follow throughout adulthood.

☐ Screening/Assessment ☐ Advisory ☐ Checkbox ☒ No Recommendations

| | 21-29 Years | 30-39 Years | 40-49 Years | 50-59 Years | 60+ Years |
|--------------------------|---|-------------|-------------|-------------|-----------|
| Behavior | A review of behavioral, functional, adaptive, and psychosocial factors should be performed as part of an annual history that clinicians obtain from all adults with Down syndrome, their families, and caregivers. (Boxes below represent 1 year increments) | | | | |
| | | | | | |
| | When concern for a mental health disorder in adults with Down syndrome is present, medical professionals should: a) Evaluate for medical conditions that may present with psychiatric and behavioral symptoms and b) Refer to a clinician knowledgeable about the medical, mental health disorders, and common behavioral characteristics of adults with Down syndrome. | | | | |
| Dementia | When concern for a mental health disorder in adults with Down syndrome is present, medical professionals should follow guidelines for diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (DSM 5). The Diagnostic Manual-Intellectual Disability 2 (DM-ID-2) also may be used to adapt diagnostic criteria from the DSM-5. | | | | |
| | Medical professionals should assess adults with Down syndrome and interview their primary caregivers about changes from baseline function annually beginning at age 40. Decline in the six domains as per the National Task Group - Early Detection Screen for Dementia (NTG-EDSD) should be used to identify early-stage age-related Alzheimer's-type dementia and/or a potentially reversible medical condition. (Boxes below represent 1 year increments) | | | | |
| | Caution is needed when diagnosing age-related, Alzheimer's-type Dementia in adults with Down syndrome less than age 40. | | | | |
| Diabetes | For asymptomatic adults with Down syndrome, screening for type 2 diabetes using HbA1c or fasting plasma glucose should be performed every 3 years beginning at age 30. (Boxes below represent 3 year increments) | | | | |
| | | | | | |
| | For any adult with Down syndrome and comorbid obesity, screening for type 2 diabetes using HbA1c or fasting plasma glucose should be performed every 2-3 years beginning at age 21. (Boxes below represent 3 year increments) | | | | |
| Cardiac | | | | | |
| | For adults with Down syndrome without a history of atherosclerotic cardiovascular disease, the appropriateness of statin therapy should be assessed every 5 years starting at age 40 and using a 10-year risk calculator as recommended for adults without Down syndrome by the U.S. Preventive Services Task Force. (Boxes below represent 5 year increments) | | | | |
| | For adults with Down syndrome, risk factors for stroke should be managed as specified by the American Heart Association/American Stroke Association's Guidelines for the Primary Prevention of Stroke. | | | | |
| Obesity | In adults with Down syndrome with a history of congenital heart disease, given the elevated risk of cardioembolic stroke, a periodic cardiac evaluation and a corresponding monitoring plan should be reviewed by a cardiologist. | | | | |
| | Healthy diet, regular exercise, and calorie management should be followed by all adults with Down syndrome as part of a comprehensive approach to weight management, appetite control, and enhancement of quality of life. | | | | |
| | Monitoring for weight change and obesity should be performed annually by calculating Body Mass Index in adults with Down syndrome. The U.S. Preventive Services Task Force Behavioral Weight Loss Interventions to Prevent Obesity-Related Morbidity and Mortality in Adults should be followed. (Boxes below represent 1 year increments) | | | | |
| Atlantoaxial Instability | | | | | |
| | In adults with Down syndrome, routine cervical spine x-rays should not be used to screen for risk of spinal cord injury in asymptomatic individuals. | | | | |
| | Annual screening for adults with Down syndrome should be based on a review of signs and symptoms of cervical myelopathy using targeted history and physical exam. (Boxes below represent 1 year increments) | | | | |
| Osteoporosis | | | | | |
| | For primary prevention of osteoporotic fractures in adults with Down syndrome, there is insufficient evidence to recommend for or against applying established osteoporosis screening guidelines, including fracture risk estimation; thus, good clinical practice would support a shared decision-making approach to this issue which would support a shared decision-making approach to this issue. | | | | |
| | All adults with Down syndrome who sustain a fragility fracture should be evaluated for secondary causes of osteoporosis, including screening for hyperthyroidism, celiac disease, vitamin D deficiency, hypoparathyroidism and medications associated with adverse effects on bone health. | | | | |
| Thyroid | Screening adults with Down syndrome for hypothyroidism should be performed every 1-2 years using a serum thyroid-stimulating hormone (TSH) test beginning at age 21. (Boxes below represent 2 year increments) | | | | |
| | | | | | |
| | | | | | |
| Celiac Disease | Adults with Down syndrome should receive an annual assessment for gastrointestinal and non-gastrointestinal signs and symptoms of celiac disease using targeted history, physical examination and clinical judgement of good practice. (Boxes below represent 1 year increments) | | | | |
| | | | | | |
| | | | | | |

This checklist is not intended to be diagnostic. Presentation of medical and mental health conditions for people with Down syndrome may be atypical. Similar signs and symptoms may be a consequence of multiple reasons, including different disease processes. Thus, the patient evaluation should include considerations of additional causes for any detected sign or symptom. The development of new and/or changes in signs or symptoms should prompt a comprehensive evaluation with your clinician.

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How to Access the GLOBAL Guideline

- ❖ JAMA Abstract: <https://jamanetwork.com/journals/jama/article-abstract/2771907>
- ❖ JAMA Podcast: <https://edhub.ama-assn.org/jn-learning/audio-player/18553652>
- ❖ GLOBAL Guideline Website: <https://www.globaldownsyndrome.org/global-adult-guidelines/>
- ❖ Guideline Press Release: <https://www.globaldownsyndrome.org/medical-care-guidelines-press-release/>
- ❖ Crnic Institute: <https://medschool.cuanschutz.edu/linda-crnic-institute>
- ❖ Crnic Institute Human Trisome Project™: <http://www.trisome.org/>
- ❖ JAK inhibitor clinical trial: <https://medschool.cuanschutz.edu/linda-crnic-institute/research/immune-skin-clinical-trial>
- ❖ Sie Center: <https://www.childrenscolorado.org/doctors-and-departments/departments/down-syndrome/>
- ❖ Be Beautiful Be Yourself Fashion Show: <https://bebeautifulbeyourself.org/>

Global's Multi-year Plan for the Guidelines Translations

❖ Culturize and Translate the guidelines into several languages:

1. Chinese
2. Spanish
3. Hindi
4. Bengali
5. Arabic
6. Malay
7. Portuguese
8. Russian
9. Japanese
10. Turkish
11. Korean
12. French
13. German
14. Vietnamese
15. Italian
16. Albanian
17. Icelandic



Global's Multi-year Plan for the Guidelines

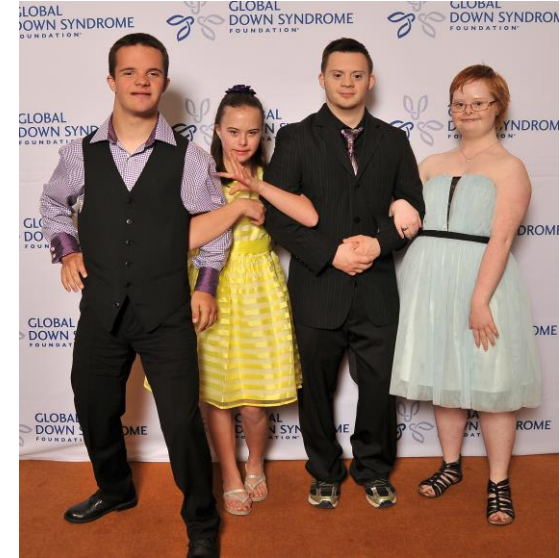
We are in this for the long haul - we hope you are too

❖ The Timeline

- Oct 2020 - Published in JAMA!
- 2021 Translate into 10 languages
- 2021-2025
 - Stimulate Research to Bolster Current Guidelines; Create Additional Toolkits; Add 2 medical focus areas
- 2026 Publish updated guidelines

❖ How You Can Help:

- Use the checklist
- Outreach to local medical professionals
- Participate in GLOBAL surveys
- Participate in GLOBAL advocacy for adults
- Help underwrite our work if you can



GLOBAL Medical Care Guidelines for Adults with DS©

THANKS TO OUR GENEROUS COMMUNITY SUPPORTERS!

KEY COLLABORATORS

The Ritter Family

BENEFACTORS

Down Syndrome Association of Greater Richmond
Down Syndrome Association of Minnesota
Down Syndrome Guild of Dallas
Rocky Mountain Down Syndrome Association

KEY SUPPORTERS

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Down Syndrome Association of Central Ohio
Down Syndrome Association of Jacksonville
Down Syndrome Association of Middle Tennessee
Down Syndrome Association of Orange County
Down Syndrome Connection of the Bay Area
Down Syndrome of Louisville, Inc
Linda Crnic Institute for Down Syndrome
National Down Syndrome Congress

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Down Syndrome Association of Acadiana

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Down Syndrome Family Connection

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International Mosaic Down Syndrome Association
Kern Down Syndrome Network
Red River Valley Down Syndrome Society
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Sampson Collaborative Law
S.M.I.L.E. on Down Syndrome
Southern Arizona Network for Down Syndrome
The UpSide of Downs of Northeast Ohio
Wisconsin Upside Down

GLOBAL Medical Care Guidelines for Adults with DS©

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