Medical Concerns & New Adult Medical Guidelines for Adults with Down Syndrome

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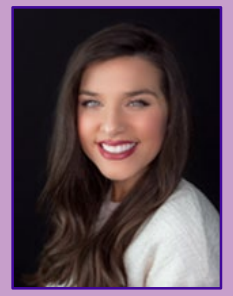

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How many adult Down Syndrome centers are there? 25!

- Population of adults with DS (age ≥ 18 years) in the United States =125,461.
- Total number of patients seen at the 25 specialty clinics for adults with DS = 6517
- Percentage of the population whose medical care needs could be met at a specialty clinic was **5%**!

Santoro, SL, Campbell, A, Balasubramanian, A, Haugen, K, Schafer, K, Mobley, W. Specialty clinics for adults with Down syndrome: A clinic survey. *Am J Med Genet Part A*. 2021; 185A: 1767– 1775. https://doi.org/10.1002/ajmg.a.62169

Outline

- Discuss common conditions in Adults with Down syndrome
- Describe ways to promote wellness throughout the lifespan of individuals with DS
- Discuss dementia the current and future Alzheimer's treatments, both supportive and pharmacologic
- Review the clinical aspects of the adult guidelines through the lifespan

Case #1: ‘That’s just the Down Syndrome’

- 30-year-old female
- Doesn’t want to leave the house
- Loose stools for years
- Chronically underweight

Question: Is this "just the Down Syndrome?"

- 1. Yes - no need to investigate this further
- 2. No – There are several medical problems that can present this way

Common behaviors and lab findings (don't panic)

- Self Talk
- High pain threshold – not complaining
- Complete blood count findings
- Low pulse, Low blood pressure

Red Flags

- Loss of skills
- Loss of Groove
- Loss of Focus
- Loss of Empathy
- Unintentional weight loss

Medical Issue Key Points

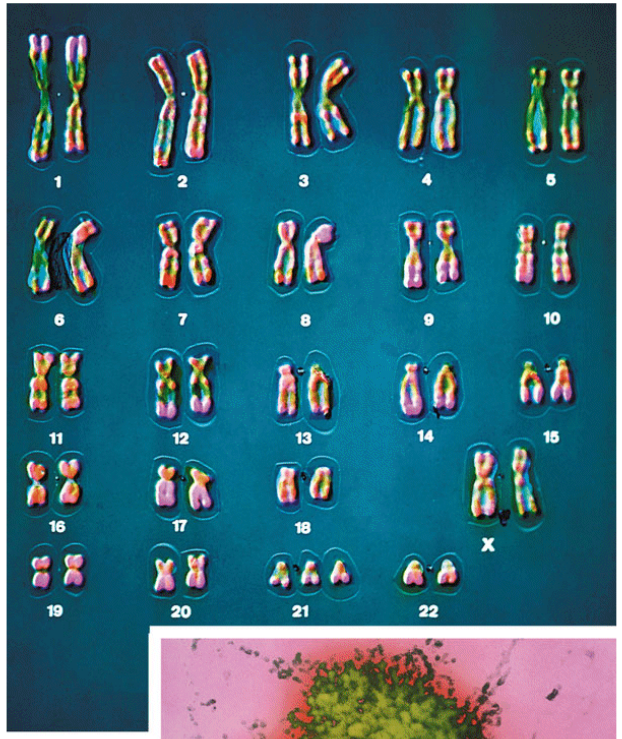
- Look for behavior as clue to diagnosis
- Encourage patient to actively participate in process of achieving good health
  - Speech therapy if needed to help discuss concerns and participate in treatment!
- Patients with Down Syndrome get many of the same medical issues as others, but some illnesses and issues are more common in patients with DS and may present differently
- Prevention!
  - Exercise, diet, a few blood tests…

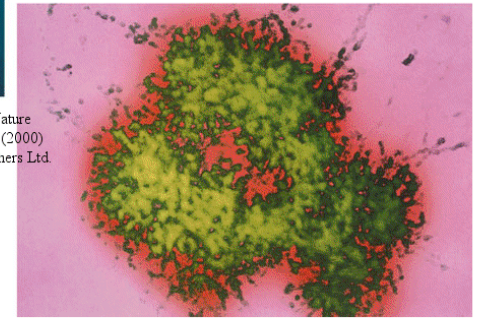
Down Syndrome – Reported Associations

- CARDIAC congen malformations
  - cor pulmonale
  - acqired valvular dysfunction
  - acquired conduction disorder
- ENT wax
  - Glue ear
  - Sensineural hearing loss
  - Upper airway obstruction, sleep apnoea
  - Conductive hearing loss
- IMMUNOLOGICAL
  - immunodeficiency states
  - autoimmune dis eg vitiligo, -ve arthropathies
- G-U Teratoma testis
- G-I congen abnormal esp duodenal atresia, imperforate anus
  - Gastro-oesoph reflux
  - Feeding diff
  - Coeliac disease
  - Hirschprung's disease
- DERMATOLOGICAL
  - Dry skin/eczema/folliculitis
  - alopecia
- PSYCHIATRIC
  - Depression
- RESPIRATORY- Large airways hypotonia
  - Small airways hypotonia
  - Lung hypoplasia
  - Subpleural cysts
  - Vascular compression
- OPHTHALMIC blepharitis
  - Nasolacrimal obstruction
  - Refractive errors
  - Keratoconus
  - Cataract
  - Squint
  - glaucoma
- ENDOCRINE obesity
  - Growth retardation
  - Hypo- and hyper- thyroidism
  - DM
- HAEMATOLOGICAL Neonatal myeloproliferative states, polycythaemia, thrombocytopaenia
  - leukaemia
- NEUROLOGICAL infantile spasms
  - Epilepsy
  - dementia
- ORTHOPAEDIC cervical spine instability
  - Hip instability
  - Patellar instability
  - Scoliosis
  - Pes planus
  - Metatarsus varus

The "Health Benefits" of DS

- **Decreased Risk of:**
  - Coronary Artery Disease
  - Hypertension
  - Solid tumors
- **Visual Memory**





Case: "Intractable Seizures"

- 35 YO with new-onset seizures consisting of arching his back and shaking
- On 4 anti-epileptic drugs that aren't helping
- EEG not able to be obtained

Gastrointestinal (GI) Issues

- Celiac
  - Check celiac panel for GI issues and/or behavior changes
  - Can be asymptomatic!

- Difficulty swallowing/aspiration: 30-50%
  - Coughing or choking?
  - Low threshold for swallow study

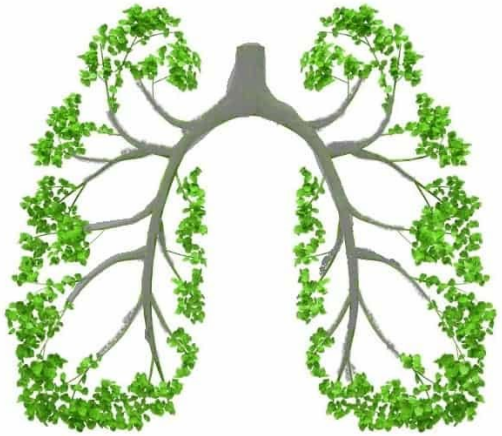
- Reflux/Gastritis: Try PPI for person with weight loss

Hematology

- Leukemia and transient myeloproliferative disorder more common in **children** with Down Syndrome; >90% present before age 20.
- High frequency of the following, often without underlying disease:
  - Mildly low white blood count (1/3)
  - Large red blood cells (2/3)
  - Mildly high red blood count

Pulmonology

- Pneumonia, influenza, aspiration pneumonia = 25% of hospital admissions among adults with DS
- Pneumonia leading cause of admission and second leading cause of death in adults with DS



Case: Depression?

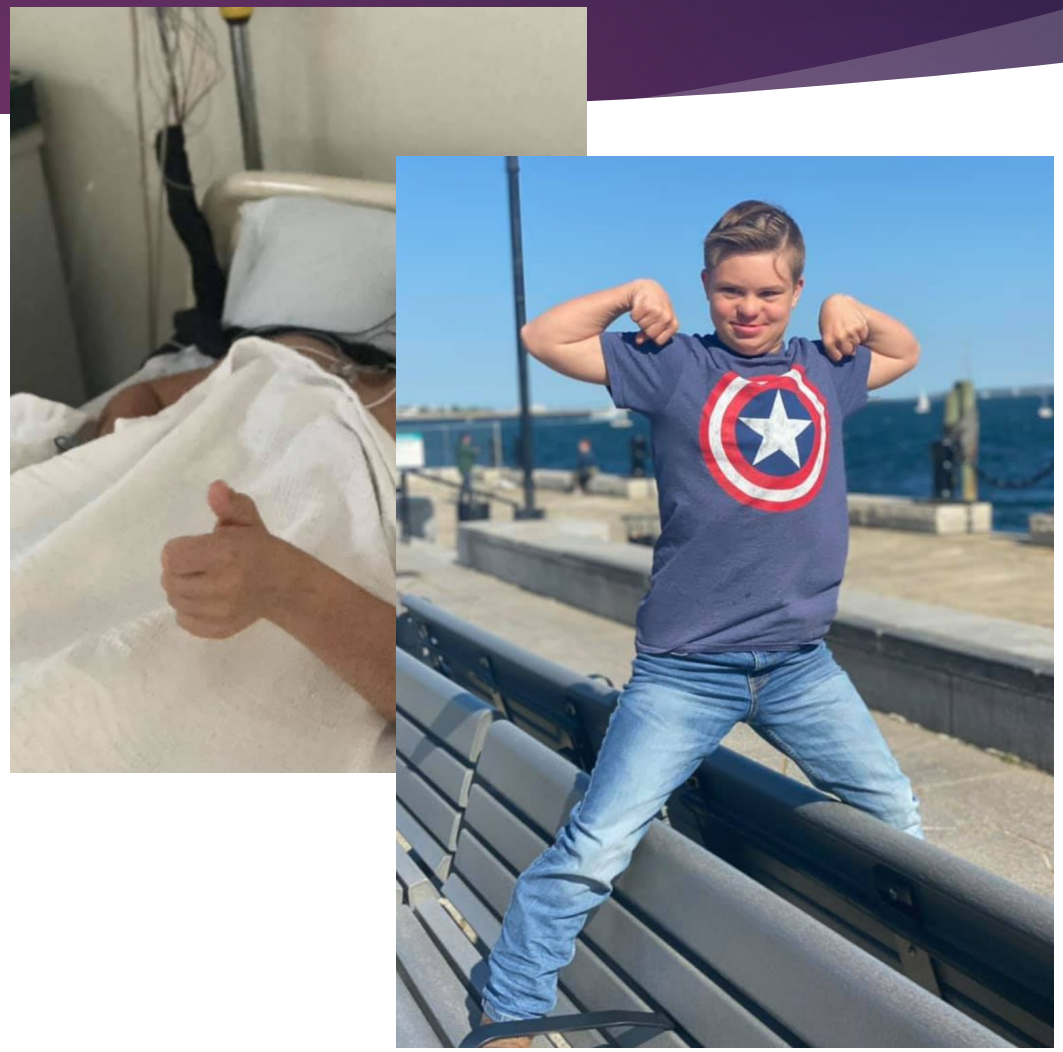
- 30 year old male with months of poor mood, weight gain, now having hallucinations
- Brought to Down Syndrome Center clinic
- Thyroid tests and celiac normal
- One test and treatment brought him back to himself!

Case: Depression?

- Patient had sleep study showing **severe sleep apnea**
- Sleep doctor recommended positive pressure (CPAP)
- With the help of his family and a behavioral therapist, patient able to wear CPAP!
- Vacation: Forgot CPAP! Patient required family to turn around! ("The groove!")
- Hallucinations and depression resolved. Weight improved!

Treatment options for sleep apnea

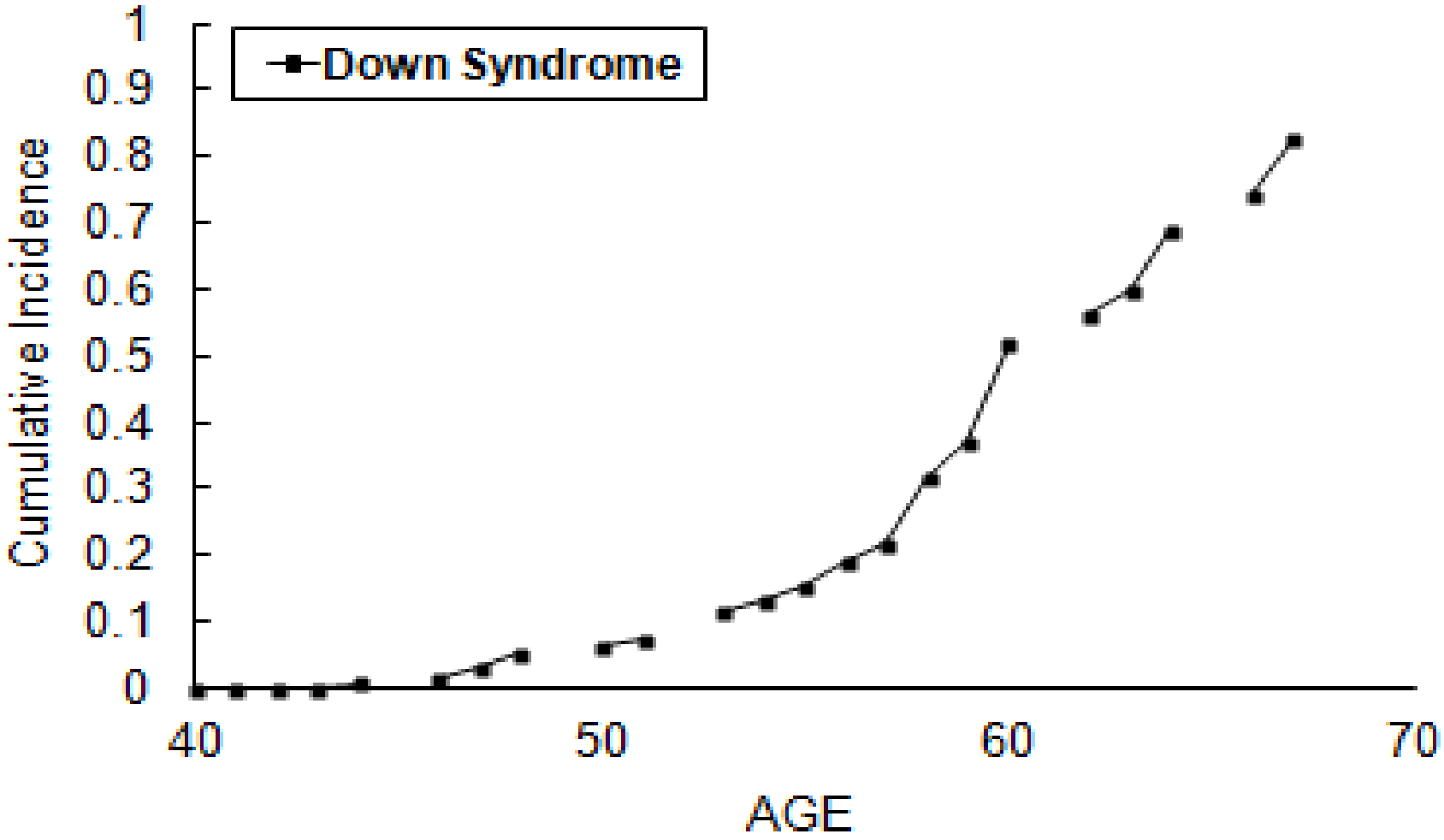
- Tennis ball/Positioning
- Positive pressure
  - CPAP
  - Bipap
  - APAP
- Surgeries
  - Hypoglossal nerve stimulator



What we now know about aging in older adults with Down Syndrome

- Life expectancy is far greater than before, but aging is 'atypical' in many respects
  - Premature graying and skin changes
  - Increased risk of aging associated:
    - Cataracts
    - Arthritis
    - Hearing loss
    - Alzheimer's

Cumulative Incidence of Alzheimer's Disease in DS



Schupf et al, 2009

Alzheimer's Disease Survival

Survival After Diagnosis	General Population[1]	Down Syndrome[2,3]
	8 to 10 years	5-7 years

1 Statistics from AHCPR Clinical Practice Guideline, Recognition and Initial Assessment of Alzheimer's Disease and Related Dementias
2 Statistics from Van Dyke, Harper, Dyken, Alzheimer's Disease and Down Syndrome, Down Syndrome Quarterly, Sept 98
3 M. McCarron, P McCallion, E Reilly, N Mulryan,Journal of Intellectual Disability Research, A prospective 14-year longitudinal follow-up of dementia in persons with Down syndrome , Volume 58. Part 1, 2014, 61-70.

‘Triggers’ of Dementia

- Environmental stressors
- Life stage changes and transitions

Physical Findings

- Change in gait may be an early marker of cognitive decline
  - Gait dyspraxia: "diminished capacity to correctly use the legs for ambulation" not attributable to other factors
    - Difficulty initiating walking
    - Harder to make turns
    - Shuffling
    - Fear and avoidance of obstacles – including stairs!
- New onset seizures, Incontinence, Major behavior change
  - Anderson-Mooney 2016

Evaluation:

- NTG-EDSD
- Medical issues that can mimic dementia
- 1. Activities of Daily Living
- 2. Language & Communication
- 3. Sleep-Wake Change Patterns
- 4. Ambulation
- 5. Memory
- 6. Behavior and Affect

Conditions that can mimic dementia

- Depression
- Anxiety
- OCD
- Adjustment disorder
- Thyroid disease
- B12 deficiency
- Menopause
- Celiac Disease and other GI conditions
- Constipation
- Urinary Retention
- Hearing or Vision Loss-Sensory Impairment
- Sleep Apnea

Symptom Treatment

- Music
- Sensory input
- Picture books
- Small group of dedicated caregivers
- Predictability, Consistency, Schedule

Therapy for Dementia

Medication for treatment?

- No long term nor randomized controlled trials in adults with Down syndrome
- Donepezil (Aricept)
- Memantine (Namenda)
- Aducanumab (Aduhelm)
- Lecanemab-irmb (Leqembi)

Brain chemistry drugs

- Donepezil, Galantamine, Rivastigmine
  - Cholinesterase inhibitors
- Memantine
  - Glutamate blockade

Monoclonal antibodies: stimulate the immune system to eliminate Amyloid

Aducanumab (Aduhelm)

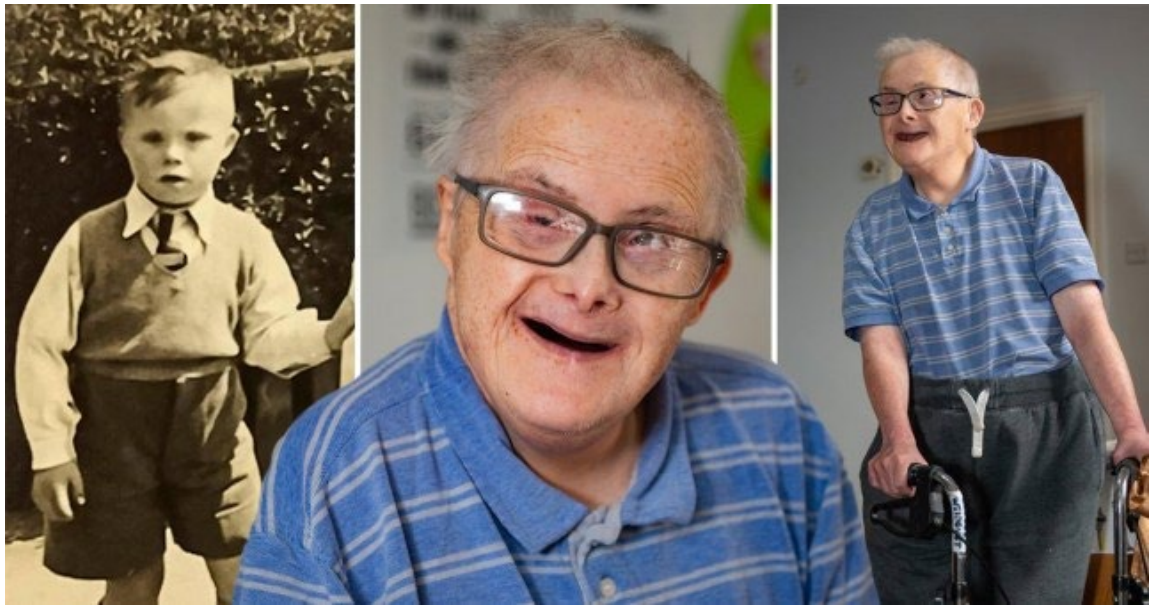
- Mixed results on benefit, better in early stages
- Significant brain swelling as an adverse affect (40%), bleeds
- $56,000 a year
- No studies in adults with Down syndrome
- IV Infusion every four weeks

Monoclonal antibodies: stimulate the immune system to eliminate Amyloid

- Lecanemab-irmb (Leqembi)
  - Better results in slowing decline in adults without Down syndrome (27%)
    - Five-month delay in getting worse
  - Still with risks of brain bleeds and swelling (12.5%)
  - Risk may be higher in adults with down syndrome who have a high degree of cerebral amyloid angiopathy
  - Plaques adhere to blood vessels
  - Still more on the way! Lumind

Take home points

- Dementia is the most significant issue facing adults with Down syndrome over the age of 40
- There are several conditions that mimic dementia that must be considered before making the diagnosis as treatment options are limited



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 Gelaro, MA, LSW; Terry Odell Harville, MD, PhD, D(ABMLI), D(ABHI); Barry A. Martin, MD; Dennis E. McGuire, PhD, LCSW; Kent D. McKelvey, MD; Moya 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

Diagnosis of Dementia

Recommendation 3

Caution is needed when diagnosing age-related, Alzheimer-type dementia in adults with Down syndrome younger than 40 years because of its low prevalence before this age.

Recommendation 4

Medical professionals should assess adults with Down syndrome and interview primary caregivers about changes from baseline function annually, beginning at age 40 years. Decline in 6 domains specified by the National Task Group–Early Detection Screen for Dementia (NTG-EDSD)[39] should be used to identify early-stage age-related Alzheimer-type dementia, a potentially reversible medical condition, or both.

GLOBAL DOWN SYNDROME FOUNDATION®

Dedicated to significantly improving the lives of people with Down syndrome through RESEARCH, MEDICAL CARE, EDUCATION AND ADVOCACY

- Recruited expert guideline creation group (ECRI)
- Recruited 11 expert DS clinicians as authors and co-authors
- Formed 9 separate committees organized by medical content area

Medical Care Guidelines for Adults with DS

Topics to be Covered

- **The initial update of the adult medical care guidelines will address the following 9 health areas as they pertain to adults with DS:**
  1. Cardiac Metabolism
  2. Muscular Skeletal
  3. Thyroid-Immunology
  4. Bone Density
  5. Metabolic Disorders
  6. Behavior/Mental Health
  7. Dementia
  8. GI-Immune-Special Diets
  9. Obesity-Lifestyle Activity-Special Diets

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- ECRI combed through thousands of studies to locate only the best possible evidence
- 11,000 Articles
- Evidence was given to committees
- Authors met in person and agreed upon final recommendation statements

21-year-old with Down syndrome

What issues are unique to Adults with Down Syndrome that we should address?

21 year old

- Thyroid?
- Diabetes?
- Celiac?
- Is a Cardiologist needed?
- Exercise?
- Screen for Atlanto-Axial Instability?

21 year old

Thyroid? Yes!

Diabetes? Only if BMI greater than 30

Celiac? Only if symptomatic

Is a Cardiologist needed? If history of congenital heart disease

Exercise? Yes!

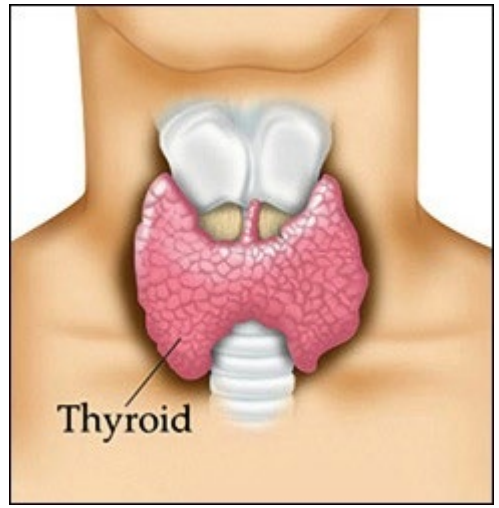
Screen for Atlanto-Axial Instability? Only if symptomatic

Screening for hypothyroidism

- Background:
  - Prevalence of hypothyroidism in adults with Down syndrome is extremely high
    - 40% ages 18-29 and approximately 50% in adults older than 30 years
  - Treatment may improve cognitive function and weight management

How often to screen for hypothyroidism?

- Screening adults with Down syndrome for hypothyroidism should be performed every 1 to 2 years using a serum thyrotropin test beginning at age 21 years.



Obesity

- Obesity
- Is there a healthy target BMI?
- Are there Safe and Effective Treatments?
  - Annual BMI
  - No interventions in the literature for weight loss

Review: Physical Exercise

Benefits of physical exercise intervention on fitness of individuals with Down syndrome: a systematic review of randomized-controlled trials

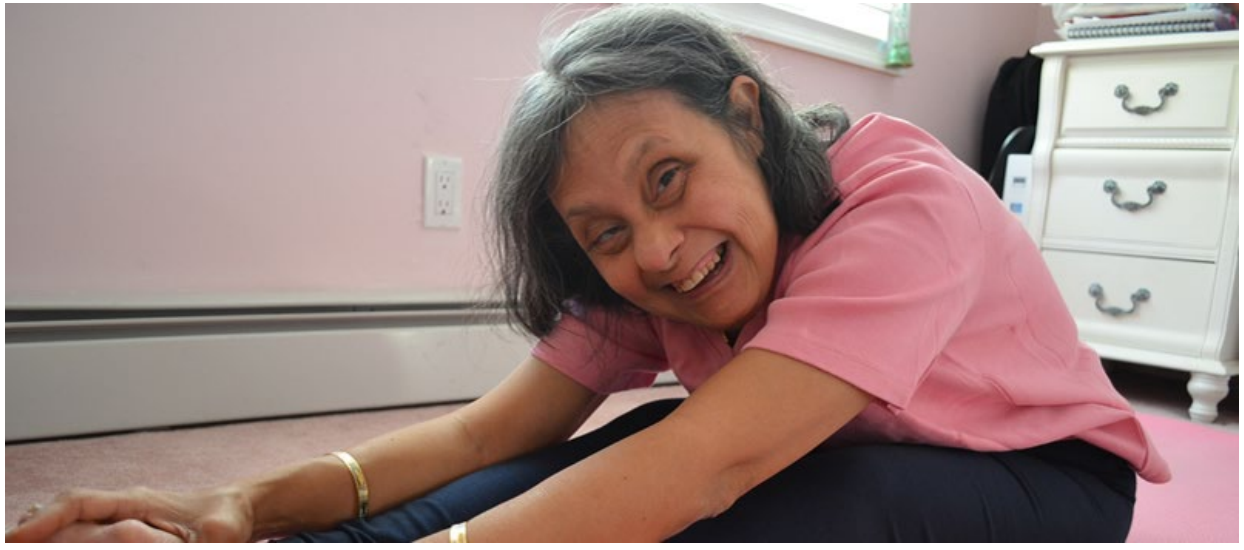
International Journal of Rehabilitation Research 2013 Sep;36(3):187-95

Li C, Chen S, Meng How Y, Zhang AL.

Physical Exercise Review

Exercise interventions led to moderate to high effects on improving muscular strength, endurance and balance

Other outcomes showed less conclusive or limited positive evidence.



30-year-old with Down syndrome

Mood seems changed from the last visit-

Less interested in friendships, activities

30 year old

- Thyroid?
- Diabetes?
- Behavior change?
- Screen for high cholesterol?
- Screen for Dementia?

30 year old

Thyroid? Yes! Every 1-2 years

Diabetes? Yes! Every 1-3 years

Behavior change? Screen for medical issues, treat any mental health issues

Screen for high cholesterol? Not routinely at age 30

Screen for Dementia? Not at age 30

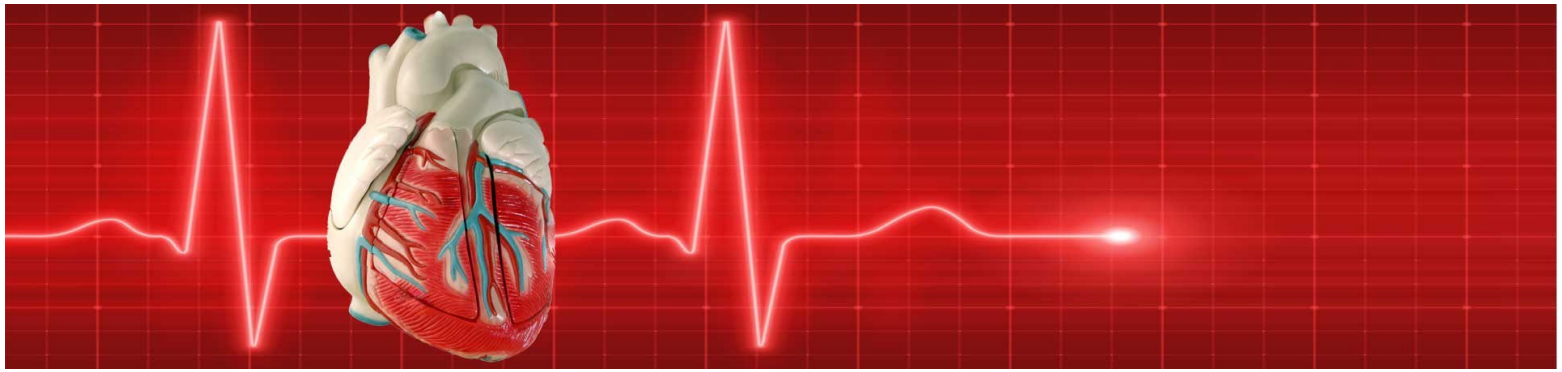
Diabetes Screening

- For asymptomatic adults with Down syndrome, screening for type 2 diabetes using glycated hemoglobin or fasting plasma glucose levels should be performed every 3 years beginning at age 30 years.

- For any adult with Down syndrome and comorbid obesity, screening for type 2 diabetes using glycated hemoglobin or fasting plasma glucose level should be performed every 2 to 3 years beginning at age 21 years.

Other Highlights from the Guidelines: Cardiology

- In those with congenital heart disease, periodic cardiology evaluation to assess stroke risk
- Does treating high cholesterol prevent heart attacks and strokes?
  - Statins and Aspirin – No evidence of impact



40-year-old with Down syndrome

With some new gastrointestinal issues

40 year old

Screen for high cholesterol?

Screen for dementia?

How about celiac testing now? Is it too late?

50-year-old with Down syndrome

What issues are unique to Adults with Down Syndrome that we should address?

He also has a new vertebral fracture

50 year old

Diabetes screening now? Thyroid?

What to do about the fracture?

More screening for dementia?

How do I remember all of this?

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.				
	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.				
Dementia	Caution is needed when diagnosing age-related, Alzheimer's Type Dementia in adults with Down syndrome less than age 40.		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)*		
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.				
	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.				
Obesity	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 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, hyperparathyroidism 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.

Coming soon…

- Sleep apnea
- Cancer screening
- Ophthalmology and more…

Take home points

- New guidelines regarding thyroid and diabetes screening, heart disease, obesity
- Dementia and Respiratory issues still most important in adult's medical care

Thank you!!

Mean and Median Life Expectancy