Managing the care of adults with Down’s syndrome

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Down’s syndrome results from increased genetic material on all or a portion of chromosome 21 and is characterized by intellectual disability and risk for comorbidities involving multiple organ systems.1–3 The survival of people with Down’s syndrome has improved dramatically in the past few decades; the median age at death is now the mid-50s compared with less than 10 years of age in the 1970s.1–6,10 The aim of this clinical review is to assist healthcare professionals in caring for the growing population of adults with Down’s syndrome, highlighting areas for increased vigilance as this population ages and develops comorbidities.

How common is Down’s syndrome?

Down’s syndrome affects approximately 1 per 1000 live births worldwide,1,4 with increased incidence associated with advanced maternal age.1 With the introduction of commercially available first trimester fetal DNA testing in 2011,2 the proportion of prenatal diagnoses of Down’s syndrome in the United Kingdom has increased from 54% (2008) to 66% (2012) for women younger than 35 years but has remained relatively stable at 71% for women older than 35 years.13 Pregnancy termination rates after prenatal diagnosis of Down’s syndrome vary by country (67% in the United States, 90% in the United Kingdom) but seem to be unaffected by the new fetal DNA testing.11–13

Nevertheless, the prevalence of Down’s syndrome continues to increase worldwide, with dramatic gains in life expectancy in the past few decades.1–4 6–8 As such, care for affected adults is relatively new territory with little evidence to guide providers. To date, few clinical trials have involved adults with Down’s syndrome. Unless otherwise noted, the information contained in this review is collected from international literature resulting from observational studies and expert consensus.

How long do people with Down’s syndrome live?

The survival of people with Down’s syndrome has dramatically increased in the past few decades, largely as a result of improved surgical repair of congenital heart defects.1 4–6 8 Until the 1970s, the median age at death for children with Down’s syndrome was less than 10 years.1 4–5 Now, 80% of affected individuals survive into adolescence,15 with a median age at death in their mid-50s.6–10

The leading causes of death in adults with Down’s syndrome are diseases of the respiratory and circulatory systems. The percentage of adults who die of cardiac causes (including consequences of congenital heart disease) is 25–40%, with an additional 20–60% of deaths resulting from respiratory infections.8 16–17 The development of dementia becomes considerable after age 40, contributing to nearly one third of deaths.6 Aside from childhood leukemia, the incidence of neoplasms—hematologic or solid tumor—is low in all age groups with Down’s syndrome.8 The risk of cardiovascular atherosclerosis remains lower than in the general population without Down’s syndrome but increases to 13% in adults aged 50 or older.8

What are the most common comorbid conditions in Down’s syndrome?

The table details our recommendations for evaluation of comorbid conditions and their frequency.

Endocrinology

Hypothyroidism is present in 15–37% of people of all ages with Down’s syndrome.16 26 44 45 It presents with symptoms such as fatigue, weight gain, decreased interest in activities, or a decline in skills.2 27 81 Hyperthyroidism is slightly more common in people with Down’s syndrome (0.65%) than in the general population, presenting with weight loss, heat intolerance, and irritability.43 Currently accepted guidelines advocate annual thyroid function tests.1 35

SUMMARY POINTS

People with Down’s syndrome have experienced a dramatic increase in life expectancy, which is now in their mid-50s. The approach to primary care for adults with Down’s syndrome is similar to that for the general adult population, with the addition of screening for conditions specific to Down’s syndrome.

Practitioners must be vigilant for conditions that are more common in Down’s syndrome than in the general population, such as hypothyroidism, obstructive sleep apnea, and osteoporosis.

Adults with Down’s syndrome have a lower risk of hypertension, coronary artery disease, and solid tumors than the general population.

People with Down’s syndrome have an increased risk of Alzheimer’s dementia, but not all adults experience this; the onset of dementia is not typically seen before age 40. By age 60, 40–77% of adults will have Alzheimer’s dementia.

Respiratory infection is the leading cause of death in adults with Down’s syndrome.

REFERENCES

See the BMJ website for more information about this article. Links to other content are not included in the references section. The references are available as a PDF or in the online version of this article.
### Suggestions for periodic screening of various health domains

<table>
<thead>
<tr>
<th>Domain</th>
<th>Prevalence</th>
<th>Screening Tests</th>
<th>Frequency*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>40-50%</td>
<td>Per cardiologist</td>
<td>Per cardiologist</td>
</tr>
<tr>
<td>Acquired valve disease</td>
<td>8-46%</td>
<td>Echocardiography</td>
<td>Evaluation guided by symptoms</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>7-17%</td>
<td>IgA and IgG anti-gliadin antibodies; total IgA; IgA anti-tissue transglutaminase antibodies; endomyosal antibody</td>
<td>Evaluation guided by symptoms</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td></td>
<td>Cervical smear test</td>
<td>Every 3-5 years as dictated by history and risk factors</td>
</tr>
<tr>
<td>Cervical spine</td>
<td>40-60%</td>
<td>Atlantoaxial instability, 15%; cervical spondylosis; 36%; degenerative disease of the cervical spine, 64-70%</td>
<td>Confirm neutral position of cervical spine for all procedures involving anesthesia; evaluate neurologic function annually; evaluation is otherwise recommended based on symptoms and involvement in extracranial activities</td>
</tr>
<tr>
<td>Dementia screening/behavioral changes</td>
<td>15-45%</td>
<td>Alzheimer’s disease: age 40-49, 10-22%; age 50-59, 20-25%, age 60+, 40-77%</td>
<td>Adaptive behavior dementia questionnaire and Camex-R</td>
</tr>
<tr>
<td>Dental care</td>
<td>50-90%, or higher hearing loss</td>
<td>Per dentist</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Hearing</td>
<td></td>
<td>Auditory testing</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td>Complete blood count</td>
<td>Monitor as needed for anemia, myelodysplastic syndrome, leukemia, especially with symptoms of easy bruising, petechiae, onset of lethargy, or change in feeding patterns.</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>15-37%</td>
<td>Thyroid stimulating hormone, free thyroxine</td>
<td>Annually</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>0.65%</td>
<td>Thyroid stimulating hormone, free thyroxine</td>
<td>Annually</td>
</tr>
<tr>
<td>Immunizations (per adult guidelines)</td>
<td>0.65%</td>
<td>Influenza; tetanus; pneumonia</td>
<td>Annually; every 10 years, with 1 containing pertussis in adulthood; one dose at age 6-12, 1 or 2 doses at age ≥65 based on risk factors, with reimmunization again at age ≥65</td>
</tr>
<tr>
<td>Mental health</td>
<td>25-30%</td>
<td>Assess for behavioral changes and loss of function</td>
<td>Every visit</td>
</tr>
<tr>
<td>Obesity</td>
<td>89-95%</td>
<td>Body mass index</td>
<td>Every visit</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>30% or nearly 100%</td>
<td>Polysomnography, overnight pulse oxymetry may be useful</td>
<td>Guided by symptoms</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>25-50% (men and women)</td>
<td>Bone densometry</td>
<td>Start screening women no later than onset of menopause or age 50, whichever comes first; screen men and women earlier based on risk factors, such as poor mobility, anti-psychotic medications, anti-seizure medications, poor nutritional status, non-weight bearing status</td>
</tr>
<tr>
<td>Vision</td>
<td></td>
<td>Vision problems, 60-70%, cataracts, 15-22%, keratoconus, 5-15%</td>
<td>Every 1 or 2 years</td>
</tr>
</tbody>
</table>

*Cumulative results of studies cited led to suggested screening frequencies for each domain.

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Obesity is widespread in people with Down’s syndrome, likely due to lower activity levels and a lower metabolic rate, making exercise and energy restriction critical in maintaining a healthy weight. Although exercise does improve muscle strength and balance in this population, significant weight loss requires programs combining interventions in exercise, nutrition, and behavior. A comprehensive behavioral management program involving the patient’s family in conjunction with calorie limitations has been shown to be successful for weight loss in the Down’s syndrome population.

Down’s syndrome is an independent risk factor for osteoporosis. Incidence of fracture is reported to be as high as 15-25% in adults with Down’s syndrome over 50 years old. To prevent such fractures, we recommend screening adults for osteoporosis in their 40s based on these observational studies.

**Cardiology**

Congenital heart disease is present in 40-50% of people with Down’s syndrome, with up to 60% attributable to some type of atrioventricular canal defect. Common additional congenital heart disease pathology in this population includes atrial septal defect, ventricular septal defect, patent ductus arteriosus, tetralogy of fallot, and double outlet right ventricle. Using routine prenatal ultrasound screening, prenatal diagnosis rates for serious congenital heart disease varies from 15-75% within the medical literature, with significantly improved detection resulting from consistent documentation of both the four chamber view of the heart and the fetal cardiac outflow tracts. In the past, life expectancy was noticeably reduced due to heart defects and was the primary reason for early death in children with Down’s syndrome. Now, these lesions are routinely surgically corrected.

Providers must be alert for the development of acquired valve disease, specifically mitral valve prolapse and aortic regurgitation. Mitral valve prolapse can present in up to 45% of adults with Down’s syndrome, which is often associated with mitral regurgitation. In many of these cases a murmur is not detectable, so any signs of heart failure should be evaluated with an echocardiogram, such as dyspnea, orthopnea, raised jugular venous pressure, pulmonary rales, lower extremity edema, increased brain natriuretic peptide levels, or radiologic evidence of pulmonary edema.
Current expert opinion includes obtaining an echocardiogram for those who did not have one in childhood and a new echocardiogram for patients presenting with a new murmur or any clinical signs of heart failure. Electrocardiograms should be obtained for any concerns of arrhythmia.

Gastroenterology
Gastroesophageal reflux is common in people with Down’s syndrome, as is dysphagia. Both can present with weight loss, decline in skills, or behavioral changes. The prevalence of gastroesophageal reflux is not well documented in the medical literature for children or adults with Down’s syndrome, likely due to the fact that it is often treated empirically. Twenty five percent of adults with Down’s syndrome have major problems with swallowing, and dysphagia accompanies the aging process in this condition. In an observational study of adults with Down’s syndrome without known swallowing difficulties, more than 50% showed risks for aspiration. One should assess for swallowing difficulties in the presence of signs of aspiration, such as coughing, sighing, burping, or throat clearing during mealtimes. Evaluation consists of a modified barium swallow study in conjunction with a speech pathology consultation. Interventions for aspiration can range from dietary restrictions to avoidance of easily aspirated foods, as well as guidance during meals to normalize eating rate.

Celiac disease can develop throughout the lifespan of people with Down’s syndrome, with an overall prevalence of 7-17%. The condition can be asymptomatic or can present with non-specific symptoms such as changes in behavior or mood, as well as weight loss and diarrhea. Current recommendations suggest screening for symptomatic celiac disease in both children and adults. The only known effective treatment is a strict gluten-free diet.

Hematology-oncology
Though leukemia and transient myeloproliferative disorder are more common in children with Down’s syndrome, new presentations decrease with age; more than 90% of cases occur before age 20. A Danish study of more than 2800 people with Down’s syndrome found no cases of leukemia after age 29. It is notable that childhood leukemias in people with Down’s syndrome are unusually sensitive to chemotherapy, and outcomes can be excellent.

People with Down’s syndrome have a high frequency of leukopenia, idiopathic macrocytosis, and mild polycythemia, often without underlying disease. In one observational study, approximately two thirds of people with Down’s syndrome had an increased mean corpuscular volume and one third had mild leukopenia. Nonetheless, healthcare professionals must have a high index of suspicion for underlying disease, as adult onset leukemias do occur, albeit at a reduced rate. Providers should check a complete blood count in circumstances that would raise suspicion for hematologic processes, such as easy bruising, petechiae, onset of lethargy, or change in feeding patterns.

Pulmonology
Respiratory illnesses such as influenza, pneumonia, and aspiration pneumonia are common, accounting for 25% of hospital admissions among adults with Down’s syndrome in an Israeli study. Pneumonia is the leading cause of admission to hospital and the second leading cause of death in adults with Down’s syndrome after congenital heart disease. The number of deaths attributable to pneumonia in Down’s syndrome increases proportionately with age, as the rate of death from congenital heart disease decreases.

Obstructive sleep apnea is among the most common comorbidities in adults with Down’s syndrome. Many of the physical attributes associated with Down’s syndrome predispose affected people to sleep apnea, such as mid-face hypoplasia, small upper airway, small jaw, and relative macroGLOSSIA. Obstructive sleep apnea can occur at any age and can present with changes in mood and behavior, a decline in skills, fatigue, and daytime sleepiness, as well as nocturnal gasping or choking episodes.

Behavioral and mental health
Concurrent mental health problems are common in people with Down’s syndrome, with depression, anxiety, obsessive-compulsive tendencies, and behavioral issues making up most diagnoses. Mental illness can present with a decline in skills or urinary incontinence, which can be mislabeled as Alzheimer’s dementia. Depression can be triggered by a stressful life event, such as separation from a parent or a death in the family. As depression is often responsive to medical therapy in those with Down’s syndrome, differentiating it from dementia is vital. Discriminating depression from dementia can be difficult, as many symptoms overlap and depression can be an early sign of developing dementia. The more common presenting symptoms of depression in those with Down’s syndrome include withdrawal, decreased appetite, and decrease in speech.

Autism spectrum disorder is up to 10 times more common in children with Down’s syndrome than the general population. Concurrent Down’s syndrome and autism in adulthood can be extremely difficult to treat, often requiring a specialist who works with adults with special needs. Medical therapies, behavioral management, maintenance of a stable environment, and reduction of stressors are all accepted forms of therapy.

Developmental regression (young adults with disintegrative syndrome) is a rare condition that occurs in adolescents with Down’s syndrome, involving rapid, atypical loss of previously acquired skills in cognition, socialization, and activities of daily living, with an increase in maladaptive behaviors. Clinical experience suggests this seems to occur in relation to transitions, hormonal or menstrual changes, or major life events. Given the rarity of this phenomenon, little evidence exists to recommend standard treatment modalities, and management may need to involve a specialist working with adults with special needs.

Neurology
Alzheimer’s dementia is a clinical diagnosis with increased incidence associated with aging in adults with Down’s
Practical tips for the care of adults with Down’s syndrome

- The differential diagnosis for a decline in skills includes:
  - depression
  - hypothyroidism
  - sleep apnea
  - hearing loss
  - vision loss
  - dementia
  - seizure disorder
  - developmental regression
- Optimal evaluation includes the involvement of specialists with expertise in these domains in people with developmental disabilities
- Sleep apnea can present with a decline in skills and new mood disorders without other typical symptoms of apnea
- Important causes of unexplained weight loss include celiac disease and gastroesophageal reflux or dyspepsia
- Skin problems are widespread in people with Down’s syndrome, such as
  - xerosis
  - hyperkeratosis
  - folliculitis
  - acne
  - psoriasis
  - atopic dermatitis
- Skin problems should be managed with traditional medical therapy as used in the general population
- People with Down’s syndrome generally do well with consistent schedules and can blossom in a setting of predictable routine

At this time, the treatments available for adults with Down’s syndrome and dementia are mainly supportive. While some providers will use traditional pharmacologic agents to slow the rate of decline, multiple Cochrane reviews of pharmacological treatment for dementia in adults with Down’s syndrome do not support this treatment owing to lack of evidence. The largest trial of pharmaceutical intervention in adults with Down’s syndrome and dementia used memantine, which showed no benefit and a trend toward worse behaviors in the treatment group. Consequently, current recommendations focus on interventions to minimize caregiver burden, including respite care and creating an environment in which the patient can maintain function.

Adult onset seizure disorder can occur as a precursor to the cognitive decline of Alzheimer’s dementia and can further impair cognitive function if uncontrolled.

Problems in the cervical spine are common in adults and children. While atlantoaxial instability is the most common problem in children, degenerative disease of the cervical spine is more prevalent in adults (64–70%), with an additional 36% demonstrating lower cervical spondylosis. Spinal imaging should be obtained to evaluate signs of spinal stenosis, such as hyperreflexia, clonus, and ataxia.

Are there any medical advantages in people with Down’s syndrome?

Several conditions are less common in people with Down’s syndrome than in the general population.

Hematology and oncology

Though the risk of leukemia is significantly increased in children with Down’s syndrome, this risk normalizes after age 20, with a cumulative risk of leukemia of 2.7% by age 30. Adults with Down’s syndrome are at lower risk for most solid tumors, such as cervical, breast, lung, and prostate cancers; however, they do seem to have a slight increased risk of ovarian and testicular germ cell tumors (standardized incidence ratios of 1.97 and 1.86, respectively).

Cardiology

While the risk of congenital heart disease is quite high, the incidence of coronary artery disease in adults with Down’s syndrome is decreased compared with the general population. Autopsy studies show decreased plaque deposition in all arteries of adults with Down’s syndrome compared with the general population.

Adults with Down’s syndrome have decreased risk of hypertension, with blood pressure measurements averaging approximately 10 points lower than their age matched peers.

What is the approach to social aspects of care?

People with Down’s syndrome benefit greatly from consistent schedules and can blossom in a setting of predictable routine.

This need for consistency of care is due in part to their intellectual disabilities and in part to their developmental disabilities. Though the risk of dementia is significantly increased in adults with Down’s syndrome compared with the general population, the majority of adults with Down’s syndrome do not develop dementia.

The diagnosis of Alzheimer’s dementia relies on the report of caregivers, which often focuses on behaviors that impact the caregivers themselves. This can lead to an overestimation of the diagnosis compared with direct assessment. Additionally, clinicians are predisposed to over-diagnose dementia in people with Down’s syndrome, as the clinical diagnosis of dementia is difficult to make and the inevitability of dementia is assumed. Traditional tools, such as the mini-mental status examination, are unreliable and unusable in nearly half of adults with Down’s syndrome.

Despite multiple options, there is no evidence based consensus on the single best method for assessment of dementia in people with Down’s syndrome. Two of these tools that are often used and generally accepted include the adaptive behavior dementia questionnaire or the Camdex-R assessment of cognitive functioning. An assessment for dementia must include neuropsychiatric testing demonstrates that people with Down’s syndrome have much stronger
ADDITIONAL EDUCATIONAL RESOURCES

**Resource for healthcare professionals**
- United Kingdom Down Syndrome Medical Interest Group (www.dsmig.org.uk)
  — A review for healthcare professionals of “best practice” medical care for people with Down’s syndrome in the United Kingdom and Ireland

**Resources for patients**
- National Down Syndrome Congress (www.ndscenter.org)
  — Resources, advocacy, and support for persons with Down’s syndrome in the United States
- National Down Syndrome Society (www.ndss.org)
  — Advocacy information for persons with Down’s syndrome in the United States
- Canadian Down Syndrome Society (www.cdss.ca)
  — Resources for the care and support of persons with Down’s syndrome living in Canada
- Down Syndrome Australia (www.downsindrome.org.au)
  — A comprehensive site of resources for persons with Down’s syndrome living in Australia
- Alzheimer’s and Down Syndrome (http://alzheimers.gov/down_syndrome.html)
  — Resources regarding the diagnosis and treatment of Alzheimer’s dementia in persons with Down’s syndrome through the US Department of Health and Human Services

**Visual Immediate Memories**

Visual immediate memories are more effective than verbal immediate memories. As such, many persons with Down’s syndrome are able to remember people and events with excellent accuracy. While this is often an advantage, it can pose a problem with traumatic events, causing longer term impact than in the general population.

**Can people with Down’s syndrome have children?**

Women with Down’s syndrome have decreased fertility compared with women in the general population but can conceive and bear children. Approximately 50% of their children will have Down’s syndrome; they also have increased risks for other congenital malformations. It is therefore important to properly educate persons with Down’s syndrome about their reproductive capacity and to consider contraceptive methods to prevent undesired pregnancy. This should occur as conversations between the primary care provider, patient, and caregiver, in addition to what occurs within formal education settings.

Men with Down’s syndrome are typically considered sterile, but there have been case reports of children being fathered.

**What ethical issues should be considered in the care of adults with Down’s syndrome?**

Although people with mild to moderate intellectual disabilities can be trained in self advocacy skills, many people with Down’s syndrome require assistance in making medical and legal decisions for their lives. This often results in establishing formal guardianship, lasting power of attorney (United Kingdom), or durable power of attorney (United States). However, given the spectrum of intellectual ability and disability present in people with Down’s syndrome, patients, caregivers, and providers must weigh the delicate balance between preserving autonomy and medical capacity.

To demonstrate capacity, people should understand in simple language the purpose and nature of the proposed medical treatment, its benefits, risks, and alternatives, and the consequences of foregoing treatment. People must be able to retain this information long enough to make an effective decision that is free from pressure.

The UK Mental Capacity Act of 2005 requires that providers assume patients are competent to make decisions unless they are obviously unable to do so and that patients must be given a reasonable chance to demonstrate their capacity. The treatment of adults without capacity must be both necessary and in their best interests. As with the Adults with Incapacity Act 2000 (Scotland), proxy decision makers must ensure that all decisions confer benefits on the patient and are advocated to use substituted judgment (that is, “what would the patient want?”) in such decisions. Full guardianship, then, is intended for situations in which no other means are sufficient to safeguard or promote the best interest of adults without capacity.

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References are in the version on thebmj.com.

## ANATOMY QUIZ

**Axial T2 weighted magnetic resonance imaging of the male pelvis**

A: Central gland of the prostate  
B: Peripheral zone of the prostate  
C: Rectum  
D: Left periprostatic neurovascular bundle  
E: Left musculus obturator internus  
F: Anterior fibromuscular stroma

## STATISTICAL QUESTION

**Standardising outcome measures using z scores**

Statements a and d are true, whereas b and c are false.

## PICTURE QUIZ

**A cutaneous manifestation of intra-abdominal disease**

1. Epigastric pain radiating to the back along with vomiting and a raised amylase suggest a diagnosis of pancreatitis. The presence of right upper quadrant pain as well as signs and features of obstructive jaundice points to gallstones as the likely underlying cause.
2. In suitable patients, cholecystectomy is the treatment of choice; however, in those unfit for surgery, endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy may be appropriate.
3. The associated skin lesions are known as pancreatic panniculitis and are seen in 2–3% of patients diagnosed as having acute pancreatitis. Tender subcutaneous nodules usually occur on the distal lower limbs and often precede the onset of abdominal symptoms.
4. The exact mechanism is not fully understood, but they are thought to be secondary to pancreatic enzyme release (notably lipase) into the systemic circulation, which results in necrosis of subcutaneous fat.