Clinical Guideline for Management of Down Syndrome in Singapore

Kavitha Sothirasan¹, Amudha Jayanthi Anand¹,²,³,⁴, Melvin Peng Wei Chua⁵,⁶, Poh Choo Khoo¹,²,³,⁴, and Mei Chien Chua¹,²,³,⁴

Abstract
Physicians play a pivotal role in the management of children and adults with Down Syndrome. Achieving full developmental potential in a child with Down Syndrome depends on prompt treatment of medical complications, family support and early establishment of intervention programmes. The presence of evidence-based guidelines support the physician both in the community and in restructured hospitals to provide timely and appropriate management recommendations. It will also aid in counselling parents and caregivers. Although most co-morbidity characteristics are common for the syndrome, the prevalence of different morbidities can be region specific, hence it is useful to have recommendations tailored to suit local population. Here we share the clinical guideline for children and adults with Down Syndrome in Singapore.

Keywords
clinical guideline, down syndrome, early intervention, intellectual disability, transition of care

Background
Down syndrome (DS) is the most prevalent genetic condition worldwide with increasing survival into adulthood.¹ Survival has improved with many living into the sixth decade because of advances in intensive care and cardiac surgical facilities.² This trend is also observed locally.

Adults with DS have multiple medical concerns that originate earlier than the general population due to accelerated ageing that affects most organs systems.³ In addition, disorders such as Alzheimer’s dementia, epilepsy, mood and behavioural disorders as well as autoimmune conditions are also more prevalent, affecting 40% of those in their fifties. However, coordinated care for these patients are sadly lacking with a recent survey done in Massachusetts revealing that specialty clinics for DS adults met the needs of only 3–5% of this population.⁴

The aim of this guide is to provide community physicians, as well as parents and caregivers, information and medical recommendations for the management of children and adults with Down syndrome. Availability of a readily accessible reference in the primary care setting may be helpful for community physicians to provide uniform and consistent guidance to address each individual’s specific requirement not only in infancy and childhood but also in adulthood.

KK Women’s and Children’s Hospital Down Syndrome Programme
KK Women’s and Children’s Hospital (KKH) started a dedicated Down syndrome clinic in 1997 that offers specialized services for children with DS. There are currently 400 children in this programme. They receive comprehensive care by a multidisciplinary team, based on a standardised care pathway that starts from the antenatal period and continues through infancy until early adulthood.

Our robust multidisciplinary care includes, and is not limited to, services from Ophthalmology, Otorhinolaryngology (ENT), Cardiology, Neurology, Nephrology, Haematology, Paediatric Surgery, Adolescent Gynaecology,

¹KK Women’s and Children’s Hospital, Singapore
²Duke-NUS Medical School, Singapore
³Yong Loo Lin School of Medicine, Singapore
⁴Lee Kong Chian School of Medicine, Singapore
⁵Sengkang General Hospital, Singapore
⁶Singhealth Residency Program, Singapore

Corresponding author:
Kavitha Sothirasan, Department of Neonatology, KK Women’s and Children’s Hospital, 100 Bukit Timah Road, Singapore 229899, Singapore, Email: kavitha.sothirasan@kkh.com.sg

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Table 1. Health Supervision for Down Syndrome Children.

| 4–6 weeks (first outpatient clinic visit) | Evaluate                                                                 | Action                                                                 | Anticipatory guidance |
|------------------------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------|-----------------------|
|                                          | • Family history and understanding of diagnosis                         | • Plot growth on DS specific growth chart                              | • Vaccinations - encouraged to follow National schedule               |
|                                          | • Pre or postnatal karyotype confirmatory test                          | • Blood tests — TFT, FBC                                                | • Offer resources e.g., Down Syndrome Association                     |
|                                          | • Feeding difficulties, nutritional intake                              | • Follow up on deranged laboratory results as needed                   | • Discuss overview of medical surveillance in the outpatient clinic   |
|                                          | • New born screening tests (hearing, inborn error of metabolism and cord | • Referral to medical social worker                                     | • Discussion with parents regarding diagnosis and long-term health    |
|                                          |   blood glucose-6-phosphate-dehydrogenase deficiency (G6PD) and          | • Referral to other specialties as required (Hematology, Cardiology,   | outcomes                                                            |
|                                          |   thyroid stimulating hormone                                           |   Pediatric Surgery, Renal, Neurology & Complex care)                 | • Importance of community EIPIC and early commencement of intervention|
|                                          |                                                                      | • Referral to Dietitian and feeding clinic if poor postnatal growth    |                                                                     |
|                                          |                                                                      | • Introduce and refer for EIPIC/therapy                                |                                                                     |
|                                          |                                                                      | • Blood tests — TFT, FBC                                                |                                                                     |
|                                          |                                                                      | • Referral to ophthalmology and otolaryngology specialist for long term|                                                                     |
|                                          |                                                                      |   follow up                                                            |                                                                     |
|                                          |                                                                      | • Anticipatory guidance                                                 |                                                                     |
|                                          |                                                                      | • Review vaccinations & offer influenza vaccine                         |                                                                     |
|                                          |                                                                      | • Will require 4–6 monthly follow up in clinic                         |                                                                     |
|                                          |                                                                      | • Plot growth on DS specific growth chart                              |                                                                     |
|                                          |                                                                      | • Blood tests — TFT, FBC                                                |                                                                     |
|                                          |                                                                      | • Screen for behavioural disorder and assess need for referral to CAMWS |                                                                     |
|                                          |                                                                      | • Screen for sleep disorders. Early referral to Sleep clinic to rule out|                                                                     |
|                                          |                                                                      |   obstructive sleep apnoea                                             |                                                                     |
|                                          |                                                                      | • Review for atlanto-axial instability and spine (any torticollis or    |                                                                     |
|                                          |                                                                      |   head tilt requires referral to neurosurgical service).               |                                                                     |
|                                          |                                                                      | • Asses dental hygiene & refer pediatric Dental special needs          |                                                                     |
|                                          |                                                                      | • Referral to Psychologist for IQ assessment at 5.5 years for school    |                                                                     |
|                                          |                                                                      |   placement                                                            |                                                                     |
|                                          |                                                                      | • Anticipatory guidance                                                 |                                                                     |
|                                          |                                                                      | • Parent to look out for change in gait, bowel and bladder function and|                                                                     |
|                                          |                                                                      |   new onset weakness                                                   |                                                                     |
|                                          |                                                                      | • Avoid contact sports and trampoline play                             |                                                                     |
|                                          |                                                                      | • Cervical spine X ray mandatory for contact sports and horse riding   |                                                                     |
|                                          |                                                                      | • Offer influenza vaccine yearly                                        |                                                                     |

(continued)
Dermatology, Anaesthesiology, Psychiatry, Orthopaedics, Sports Medicine and Allied health services.

Children receive comprehensive medical health surveillance from birth until transitioned to adult care at 18 years of age (Table 1). The discussion and preparation to transition care to adult services should begin early to allow families to adjust to the new multidisciplinary team and the different environment and location.5

Historically, transition of care to adult services were sporadic and ad-hoc for our patients. In March 2020, a pilot project, which follows a standardised workflow, was implemented in collaboration with Sengkang General Hospital. This framework has proved to be successful and gained acceptance over time with 60 patients successfully transferred to adult care thus far. The number of general hospitals accepting these patients for follow up have also increased. Currently, conversations are initiated early with the family, in preparation for transition to a suitable adult care facility of the family’s preference. Table 2 depicts the transition checklist that is used. The aim is to complete transition by 18–20 years of age.

Table 1. (continued)

| 6–18 years | Evaluate |
| --- | --- |
| | • Pubertal growth |
| | • Review vision & hearing every visit |
| | • Asses dental hygiene and refer pediatric Dental special needs |
| | • Growth and activity of daily living |
| | • School performance |
| | • Current medications and compliance |
| | • Review spinal, joint and orthopedic disorders (knock knee, flat feet, scoliosis, ligament laxity, atlanto axial stability) |
| | • Review for dermatological conditions folliculitis, Alopecia areata, seborrheic dermatitis, furunculosis and Impetigo |
| | • Review ophthalmology and audiology needs 1–2 yearly |
|  | Action |
| | • Plot growth on DS specific growth chart |
| | • Blood tests — TFT, FBC |
| | • Screen for Behavioural disorders and assess need for referral to CAMWS 11 |
| | • Screen for sleep disorders. Early referral to Sleep clinic to rule out obstructive sleep apnoea |
| | • May need referral to orthotics and, or orthopedics |
|  | Anticipatory guidance |
| | • Discuss sexual development and behaviours (relationship with opposite sex and gynecological care) |
| | • Offer influenza vaccine yearly |
| | • Encourage physical exercise, healthy diet discuss obesity and referral to weight management clinic if BMI >25 |
| | • Discuss transition to adult health care at 16 years of age |
| | • Discuss financial planning |
| | • Guardianship and lasting power of attorney |
| | • Future home/residential planning |

DS: Down syndrome; IQ: Intelligent Quotient; EIPIC: Early Intervention Programme for Infants and Children; TFT: thyroid function test; FBC: full blood count; CAMWS: child and adolescent mental wellness service; LPA: Lasting Power of Attorney.  
*www.cdc.gov/ncbddd/birthdefects/downsyndrome/growth-charts.html*

Table 2. KK Women’s and Children’s Hospital Down Syndrome Adult Transition Checklist.

| Pre - Transfer | Discussion on transfer with patient and caregiver (youth aged 14–16) |
| --- | --- |
|  | Summarize medical concerns |
|  | Social worker and sub-specialties informed |
|  | Discuss guardianship with caregivers |
|  | Offer resources on community services (insurance/adult workshop/subsidies) |
|  | Confirm date and hospital of transfer |
| Transfer | Patient and caregiver agree for transfer |
|  | Appointment fixed - date, time and location conveyed to caregiver |
|  | Transition summary completed |
|  | Caregiver and patient agreeable to be contacted via email or via a phone call post transfer |
| Post - Transfer | Contact caregiver or patient 3–6 months to confirm attendance to transfer hospital |
|  | Elicit feedback questionnaire and experiences of transition process |

Dermatology, Anaesthesiology, Psychiatry, Orthopaedics, Sports Medicine and Allied health services.
Table 3. Health Supervision for Down Syndrome Adults.

| No. | Topic                                      | Details                                                                 |
|-----|--------------------------------------------|-------------------------------------------------------------------------|
| 1   | Diabetes screen                            | Screening for Type 2 Diabetes Mellitus using Hb A1C or fasting plasma glucose every 2–3 years from age 30 years |
| 2   | Thyroid disorders                          | Occurs in 20% of persons with DS. Two yearly TFTs if not on thyroxine or bi-annually if already on thyroxine replacement therapy or anti thyroid medications |
|     |                                            | Explore role of autoimmune thyroid disease and clustering of autoimmune disorders |
| 3   | Obesity                                    | Monitoring for weight change and obesity performed annually by calculating the BMI |
|     |                                            | Healthy diet, regular exercise and calorie management recommended to all adults/care givers for enhanced life quality. Referral to sports medicine if indicated |
| 4   | Osteoporosis                               | Any fracture should be evaluated for secondary causes including hypothyroidism, Vitamin D deficiency, hyperparathyroidism and medications associated with adverse effects on bone health |
| 5   | Cardiovascular disease                     | Need for statin therapy assessed every 5 years from age 40. Lipid profile and 10-year risk calculator as recommended for adults without DS |
| 6   | Stroke                                     | In adults with history of congenital heart disease, a periodic cardiac evaluation. For adults with DS, risk factors for stroke is managed as specified for general population |
| 7   | Atlanta-axial instability                  | Screening for signs and symptoms of cervical myelopathy. |
|     |                                            | Signs-gait disturbances, spasticity, weakness, increased deep tendon reflexes, Babinski responses & clan us |
|     |                                            | Symptoms: Neck pain, torticollis, change in gait, loss of upper or lower body strength, change in bowel or bladder function. Routine cervical spine X-ray is not needed |
| 8   | Behaviour                                  | When concern for a mental health disorder is present, refer to a psychiatrist familiar with dealing with these disorders in adults with DS |
| 9   | Dementia                                   | Medical professionals should assess adults with DS and interview their primary care givers about changes from baseline function annually beginning age 40 |
|     |                                            | Decline in the following six domains should be used to identify early age-related Alzheimer’s dementia and/or potentially reversible medical condition |
|     |                                            | ▪ Cognition, memory and executive function |
|     |                                            | ▪ Behaviour and personal |
|     |                                            | ▪ Communication |
|     |                                            | ▪ Adaptive functioning |
|     |                                            | ▪ Ambulation and motor skills |
|     |                                            | ▪ General decline in established skills |
| 10  | Ophthalmology                              | Recommended 2 yearly for risk of developing cataracts, keratoconus and refractive error |
| 11  | Respiratory                                | Obstructive sleep apnea is seen in 50–60% of adults. This can be due to hypotonia and structural abnormalities associated with DS and complicated by obesity. Sleep questions (apnea, snoring, daytime somnolence, obesity and patulous uvula) at every visit and early referral to the respiratory specialist |
|     |                                            | Can also present with irritability, depression paranoia and behavior changes |
| 12  | Dental disease                             | Gingivitis and periodontal disease are more common in DS and can cause tooth loss. Orthodontic problems like bruxism are more common. Recommend 6 monthly dental visit |
| 13  | Dermatological disorders                   | Review for dermatological conditions- folliculitis, alopecia areata, vitiligo and hidradenitis suppurativa |
| 14  | Coeliac disease                            | Targeted history and physical examination for gastrointestinal (GI) and non-GI signs and symptoms of celiac disease. |
| 15  | Reproductive health                        | Testicular examination for males |
|     |                                            | Mammography and Pap smears as per standard guidelines. Cancer screening as per national guidelines |
|     |                                            | Discuss recurrence risk if planning for family |
| 16  | Estate planning                            | Future independent (supervised) or group living should be planned |
|     |                                            | Parents should be encouraged to plan for the future of DS adult and encourage |
| 17  | Guardianship                               | Important for legal matters (Deputyship/LPA) [https://www.msfgov.sg/policies/mental-capacity-matters](https://www.msfgov.sg/policies/mental-capacity-matters) |
| 1   | Adult vaccines                             | Influenza (INF) |
|     |                                            | Pneumococcal vaccines (PCV13, PPSV23) |
|     |                                            | Tetanus, Diphtheria & Pertussis (Tdap) |
|     |                                            | Human Papilloma Virus (HPV) |
|     |                                            | Hepatitis B (Hep B) |
|     |                                            | Measles, Mumps, Rubella (MMR) |
|     |                                            | Varicella (VAR) |

DS: Down syndrome; BMI: Body mass index.
*https://www.moh.gov.sg/resources-statistics/nationally-recommended-vaccines

Based on our experience, 30% of DS patients in the outpatient clinic are lost to follow up as they grow older (unpublished hospital data). This group of patients may approach community physicians for support, as shifts in healthcare environment have resulted in primary care physicians taking on a greater role. Hence, it is important that community physicians are comfortable managing this cohort of patients, and this includes supporting their emotional and physical needs as well as providing basic medical surveillance.

With this in mind, the adult DS medical surveillance guidelines are drafted (Table 3) based on the Global Down Syndrome Foundation guidelines, which was framed by the workgroup for adults with DS and published in 2020.6
Suggested guidance are also in accordance with the health supervision clinical report for Children with Down syndrome by the American Academy of Paediatrics, published in 2011. In addition to literature review, the development of this guideline also involved expertise consensus from the multidisciplinary team of specialists who are involved in the medical care and follow up of these children in KKH. Consideration was given to established local prevalence of comorbidities in this group of patients based on our cohort of 176 patients (unpublished data).

Professional expert opinions from physicians in Sengkang General Hospital, who care for adults with disability, were sought and incorporated into this set of local guidelines. The aim is to ensure uniformity in care delivery for these DS adult patients in the outpatient setting, whether in tertiary institutions or in the community.

**The KK Women’s and Children’s Hospital Down Syndrome Clinical Care Path**

Standard care plan for mothers early in the pregnancy include routine screening for Hepatitis B, HIV status and Syphilis as well as an early dating scan. All mothers are offered Down syndrome screening at 11–13 weeks of pregnancy. The first trimester screening involves an ultrasound alone or in combination with a blood test. The ultrasound alone (to look for nuchal translucency) has a detection rate of about 80% and a combined test (including a blood test) has a detection of well above 90%. The blood tests measures free beta human chorionic gonadotropin and placenta associated protein A. A more sensitive test, the Non Invasive Pregnancy Test is also offered at the first and second trimesters where fetal cells from maternal blood is extracted and analyzed for chromosomal defects. This has the highest detection rate of 99%. If screening tests reveal the baby has high risk for aneuploidy then a chorionic villus sampling or amniocentesis is offered for confirmatory diagnosis, after counseling by a genetic counselor.

A second trimester screening ultrasound scan is scheduled at 20 weeks. If there is suspicion of structural anomalies, the fetal medicine specialist verifies the findings and the relevant medical or surgical specialists will be involved in the family conference with the support of the medical social worker (MSW). At this stage, information about DS and any co-morbidities, treatment options, recurrence risk, short and long term prognosis and community support services are discussed with parents in detail. Comprehensive birth plans must be in place should parents decide to continue the pregnancy. In the event they choose to terminate the pregnancy, they should get the necessary support.

Postnatal karyotyping is necessary when there is clinical suspicion of DS or when a definitive antenatal diagnosis was not established through amniocentesis. The baby is admitted to a level 2 care facility for monitoring and comprehensive assessment, including haematological and radiological tests, for possible associated co-morbidities, in addition to a thorough physical examination. These include:

- Full blood count and peripheral blood film to screen for leukemoid reactions, transient myeloproliferative disorder, thrombocytopenia and polycythemia, which are relatively common in infancy and is seen in 10% of this population.

2. These infants have a 1% risk of congenital hypothyroidism and deranged thyroid levels are common in infancy. This is much higher than the reported incidence of 0.025–0.05% among the general population. Further evaluation with a thyroid function test (TFT) is often needed till adulthood.

3. Cardiac assessment with two-dimensional echocardiogram. 50% of infants may have an abnormal echocardiogram and hence require a review with the cardiologist. Commonly associated cardiac abnormalities identified within our cohort are Ventricular septal defect, Atrial septal defect, Tetralogy of Fallot.

4. Gastro-intestinal disorders include imperforate anus, duodenal and ileal stenosis/atriesia and meconium peritonitis. These abnormalities if missed may be life threatening hence imaging is required.

5. Renal evaluation is also important. Associated conditions include horse-shoe, dysplastic kidney and vesicoureteric reflux.

6. Common endocrine disorders noted in or cohort include hypothyroidism (28%) and hyperthyroidism (2.5%). Frequent TFT will be required.

7. Major intestinal and renal abnormalities may be missed if the infant did not have an early fetal screening scan.

8. Universal newborn hearing screening assessment is done on all infants before discharge home to identify congenital hearing loss.

9. Feeding assessment by the speech therapist is important if clinically indicated as a proportion may have feeding difficulties due to hypotonia.

10. Physiotherapy services should commence during the birth admission to equip caregivers with the skills in handling and stimulating the infant with marked hypotonia.

The MSW continues to support the family postnatally by providing support to the family with emotional support as well, and to assist with resources for financial support, if required. The MSW usually helps to facilitate enrolment into the Early Intervention Programme for Infants and Children (EIPIC) centres during infancy and coordinate school placement at 5–6 years of age. They play an important role in introducing families to various community services like the Down Syndrome Association of Singapore, Family Service Centre and Social Service Centre.

Once a diagnosis of DS is made, a family conference is held while the infant is still in-patient, and the overall care plan until adulthood is explained and discussed with the family, to provide clarity regarding long-term follow-up. In this meeting, the need for continued follow up with the primary team, ophthalmologist, otolaryngologist, subspecialty teams as required and therapists is emphasized. Our cohort showed over 60% of eye and ENT disorders each (unpublished data). Hence, long term surveillance for refractory errors, movement disorders of the eye, cataracts, otitis media, hearing loss & chronic ear infections are highlighted.
The first specialist clinic visit is within 4–6 weeks of hospital discharge during which results of investigations done in the ward are explained and questions from parents are answered. Feeding and growth assessments are performed and routine vaccinations can be administered. Referral to the community EIPIC program is made at this juncture as the waiting time may be up to a year for some centres. Some parents opt to enrol their child in private intervention centres, integrated child care programme or home based therapies (either from private therapists, or by the Down Syndrome Association). Either choice will be supported and the child’s progress monitored by the primary team of doctors. Once the child has secured a place for intervention, they are advised to continue therapies until school placement.

A psychological assessment is undertaken to evaluate the child’s cognitive functional level and understand the child’s weaknesses and strengths, in order to provide suitable recommendations for school placement. In addition, it is also to exclude underlying behavioural disorders, such as Autism. Special education placement requires an Intelligent Quotient (IQ) assessment to be done by a psychologist, by age 6, as school placements vary according to level of intellectual disability.

The child continues medical surveillance yearly at KKH until age 18. The process of transition to adult care is guided by the checklist given in Table 2.

Adults with DS have multiple medical issues that develop at an earlier age compared to their peers without DS. Table 3 gives an overview of the morbidities and the need for continuing surveillance by an adult physician.

Referral to the KKH Down syndrome clinic can be via a written referral from any polyclinic or private clinic in Singapore.

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Author Contributions
Dr Kavitha Sothirasan researched literature and conceived the study. Dr Kavitha Sothirasan and Dr Amudha Jayanthi wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Data Availability
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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ORCID iD
Kavitha Sothirasan https://orcid.org/0000-0002-6880-2195

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