A SET-CHC Framework for Addressing Non-Medical Challenges in Children with Kabuki Syndrome Type 2

ABSTRACT

The integration of science, engineering, and technology (SET) as a joint framework within the context of the Cattell-Horn-Carroll (CHC) theory offers a new lens to examine, understand and address the complex issues of managing children diagnosed with Kabuki Syndrome Type 2 (KS2). This integrated SET-CHC framework, which delineates both broad and narrow cognitive abilities identified in the CHC Theory, provides a systematic method for identifying specific learning needs and developing targeted strategies to address the KS2 challenges within the context of educational therapy. By integrating advancements in the SET-CHC framework, such as the application of assistive technologies and use of data-driven interventions, educational therapists and other allied professionals can develop and implement individualized strategies to support children diagnosed with KS2, particularly to address its coexisting or concurrent conditions, which include intellectual and developmental delays or disabilities (IDD/D), syndromic autism (SAu), and learning disabilities (LD), among others. The combination of CHC-based cognitive profiling and SET-supported innovative therapeutic tools fosters an adaptive learning environment, promoting holistic development and improving educational outcomes for those children with KS2.

Keywords: Cattell-Horn-Carroll Theory, Co-morbidities, Educational Therapy, Integrative Approach, SET-CHC Framework

ABBREVIATIONS

Term:	*Explanation:*
CHC	*: Cattell-Horn-Carroll*
IDD/D	*: Intellectual and Developmental Delays/Disabilities*
KS1	*: Kabuki Syndrome Type 1*
KS2	*: Kabuki Syndrome Type 2*
LD	*: Learning Disabilities*
SAu	*: Syndromic Autism*
SET	*: Science, Engineering, and Technology*

1. INTRODUCTION

According to Neumann and Karnik (2024) in their recently published treatise, Kabuki Syndrome (KS for short) - also known as Kabuki make-up syndrome and/or Niikawa-Kuroki Syndrome - is a rare inherited genetic syndrome first identified and diagnosed by Norio Niikawa and Yoshikazu Kuroki in Japan in 1981 (cited in Kuroki et al., 1981; Niikawa et al., 1988) and is the result of mutations in an H3 lysine 4 methylase (KMT2D) or an X-linked histone H3 lysine 27 demethylase (KDM6A) gene (Wang et al., 2019). The syndrome has a heterogeneous phenotype and it can affect multiple organ systems (Theodore-Oklota et al., 2020). The cardinal features of KS encompass the following phenotype: facial features

(including long palpebral fissures, eversion of the lateral one-third of the lower eyelid, arched eyebrows with lateral sparseness or notching, short nasal columella, large prominent or cupped ears, and cleft lip/palate), skeletal anomalies, dermatoglyphic anomalies, mild to moderate intellectual disability, and postnatal developmental delays as well as growth failure (Barry et al., 2022). Currently, there is no fundamental cure or treatment other than symptomatic management and prevention of complications (Miyake, 2024). KS is so rare that it is largely unknown to many physicians, clinicians and diagnosticians (Theodoe-Oklota et al., 2020).

Primarily speaking, KS is associated with mutations in the KMT2D gene (OMIM: #147920), which is located on chromosome 12, and it is considered as KS Type 1 (or KS1 for short). In some other cases, the mutations in the KDM6A gene (OMIM: #300867) found on the X chromosome result in what is referred to as the condition of KS Type 2 (or KS2 for short). This condition should not be mistaken or confused with the microdeletion in Xp11.3 gene in the Chromosome Xp11.3 Deletion Syndrome (OMIM: #300578), which accounts for co-segregation of Retinitis Pigmentosa (OMIM: #268020) and mental retardation (Zhang et al., 2006). Instead, these genetic mutations in the KDM6A gene can lead to the characteristic features and developmental challenges seen in typical cases of KS. While genetic variations can vary widely among children with the syndrome, the two genes mentioned here are the most commonly implicated (Adam, Hudgins, & Hannibal, 2021). Hence, for a definitive diagnosis or more detailed genetic information, caregivers and/or clients are strongly recommended to go for genetic counseling and testing from a healthcare professional.

KS2, being associated with mutations in the KDM6A (Lysine Demethylase 6A) gene, is often connected to pathogenic variants - known to contribute to the development of a disease-causing mutations - in that gene located on the X chromosome at position Xp11.3 (Mansoor et al., 2023). Specifically, KDM6A genetic mutations can be point mutations, small deletions, or other types of alterations. However, these genetic mutations do not typically refer to a larger microdeletion impacting that region.

The KDM6A gene encodes a protein involved in the modulation of genetic expression by demethylating specific lysine residues on histone proteins (Boniel et al., 2021; Sterling et al., 2020; Tran, Broun, & Ge, 2020). This process is crucial for the control of various biological processes, which include development, differentiation, and response to environmental signals. Mutations in that specific gene (Fallah et al., 2021; Lavery et al., 2020) affects its role in several cellular functions leading to various disorders including certain types of cancers and genetic syndromes such as KS2 (Fallah et al., 2021; Tran, Broun, & Ge, 2020). Because of its locus on the X chromosome, it becomes subject to X-inactivation in females, and hence, impacts its expression in females compared to males (Arnold, 2022). Therefore, genetic testing is essential to establish a definitive diagnosis in order to understand the specific genetic mechanisms involved in KS2.

2. DIAGNOSTIC CODE FOR KABUKI SYNDROME TYPE 2 (KS2)

Educational therapists use the Educator Diagnostic Manual (EDM) (Pierangelo& Giuliani, 2007) as their nosological tool to identify different disabilities and disorders. Unfortunately, there is no latest updated version of EDM. As there is no diagnostic code specifically for the rare condition of KS2 in the field of educational therapy, which has been officially recognized and classified under the Procedure Code 93.82 in the International Classification of Diseases-9th Edition-Clinical Modification-Volume 3 (ICD-9-CM, Vol. 3; World Health Organization, 1986; also see Chua & Chia, 2023a, 2023b) since 1986, the abnormal chromosomal syndrome (based on its varied symptoms) has to be inferred from the following diagnostic codes found in the EDM:

- MR: Mental Retardation (EDM, pp.107-152)
- MR1.00: Mental Retardation due to Chromosomal Abnormalities (EDM, pp.115-116)
- MR1.09: Other Types of Mental Retardation due to Chromosomal Abnormalities (EDM, pp.123)
- MR1.09.a.ii: Mental Retardation due *to Kabuki Syndrome Type 2* (mutation in KDM6A gene on the X chromosome at position Xp11.3). Words in italic indicate an extension for this category of MR.

KS2 is associated with several co-morbid disorders, many of which are also shared with Kabuki Syndrome Type 1 (KS1). This list of the common co-morbidities can be classified under non-medical and medical issues of concern as follows:

- Non-medical issues of concern:
  1) Developmental delays (DD) (Boniel et al., 2021): These delays are often observed in motor skills, speech, and cognitive development.
  2) Intellectual disability (ID) (Adam, Hudgins, & Hannibal, 2021): Ranging from mild to moderate in terms of severity, it often co-exists or comes together with DD as a compound disorder, i.e., intellectual and developmental delays/disability (IDD/D).
  3) Syndromic autism (SAu) or with autistic traits (Akin Sari et al., 2008; Barry et al., 2022): Such traits associated with autism, especially difficulties in communication and social interaction, are frequently noted.
- Medical issues of concern:
  1) Congenital heart defects (Digilio et al., 2017; Lee et al., 2024; Yuan, 2013): Structural heart abnormalities (e.g., atrial or ventricular septal defects) may occur in children with KS2.
  2) Hypotonia (Boniel et al., 2021): Reduced muscle tone is often noted and it causes developmental delay in motor milestones (e.g., crawling, walking and sitting).
  3) Skeletal abnormalities (Adam, Hudgins, & Hannibal, 2021; Cheon&Ko, 2015): Noted in those with KS2, these problems may include scoliosis, joint laxity, or short stature.
  4) Sensorineural or conductive hearing loss (Barozzi et al., 2009; Digilioetal., 2017; Neumann &Karnik, 2024): This auditory impairment is common in children with KS2.
  5) Vision problems (Cheon&Ko, 2015; Merdler-Rabinowicz et al., 2021): Vision-related issues include strabismus and ptosis are often noted in those with KS2.
  6) Immune deficiencies (Comel et al., 2024; Margot et al., 2020): Children with KS2 are prone to infections due to their weakened immune system.
  7) Gastrointestinal issues (Barry et al., 2022; Boniel et al., 2021): Children with KS2 also experience feeding difficulties, reflux, and constipation.
  8) Seizures or epilepsy (Barry et al., 2022; Kurahashi et al., 2017; Zhitomirskaya et al., 2022): Some children with KS2 may experience or suffer seizures.
  9) Nephrological abnormalities (Adam, Hudgins, & Hannibal, 2021; Barry et al., 2022; Merdler-Rabinowicz et al., 2021): These problems include structural abnormalities or impaired function of kidneys.
  10) Endocrine problems (Barry et al., 2022; Boniel et al., 2021): Some of those with KS2 may experience growth hormone deficiencies or other endocrine-related concerns.

Generally, educational therapists working with children with KS2 focus on the first three co-morbidities under the non-medical issues of concern, and based on cross-battery assessment (X-BA) (Flanagan & McGrew, 1997; Flanagan, Ortiz, &Alfoso, 2007) results, they are able to identify among the several broad, intermediate and narrow cognitive, sensorimotor and affective abilities according to both the CHC (G-code) framework and the

non-CHC (Q-code) framework (Liu &Xie, 2024) that have been impacted. The educational therapists and the caregivers work collaboratively to enhance the quality of life for children with KS2.

2.1 The CHC-Based Diagnostic Analysis of Broad and Narrow Abilities

The Cattell-Horn-Carroll (CHC)-based analysis of broad and narrow (as well as intermediate) abilities is done for the purpose of diagnostic assessment as well as designing an overall individualized therapy program (ITP) from which specific Individualized Education Plans (IEPs) are derived (Flanagan et al., 2022; McGrew, 2023; Schneider & McGrew, 2018). The identification of broad and narrow abilities that are implicated by KS2 depends on the results collected from both formal, non-formal and informal assessment protocol for the condition.

For children with KS2, they often experience a range of cognitive, developmental, and learning challenges. Hence, educational therapists use both CHC (Schneider & McGrew, 2018; McGrew 2023) and non-CHC frameworks (Liu &Xie, 2024) to provide them a useful structure to analyze these impacts across broad and narrow abilities (Chua & Singh, 2022; Liu &Xie, 2024) in their design of a customized intervention program. This has to be broken down according to the three non-medical conditions that educational therapists will focus on - i.e., intellectual and developmental delay/disabilities (IDD/D), syndromic autism (SAu), and learning disabilities (LD), while also keeping in mind the unique traits of KS2.

The narrow abilities that are implicated by KS2 are dependent on the results obtained from the administration of formal, non-formal and/or informal assessment protocols according to the hierarchy of abilities and skills (Chia, 2008). Without the relevant assessment results, it is difficult to identify the target abilities that have been affected and how these issues can be best addressed in the context of educational therapy (Chua & Chia, 2023a, 2023b).

2.1.1 Intellectual & Developmental Delays or Disabilities (IDD/D)

Children with IDD/D may exhibit broad deficits in general intellectual ability (Gf) and specific cognitive and adaptive functioning. Figure 1 shows the CHC-based broad and narrow abilities (Schneider & McGrew, 2018) affected in KS2 related to IDD/D.

- CHC-based broad abilities affected are as follows:
  a) Gf (Fluid Reasoning): It refers to the difficulty in problem-solving and reasoning, especially novel situations.
  b) Gc (Comprehension-Knowledge): It refers to the word knowledge (i.e., both receptive and expressive vocabularies) and acquired knowledge might be below age level.
  c) Gq (Quantitative Knowledge): It concerns about challenges encountered in acquiring mathematical concepts as well as number processing.
  d) Gs (Processing Speed): It points to slower mental processing can be evident, impacting both learning and adaptive functioning.
  e) Gwm (Short-Term Working Memory): It refers to reduced capacity to hold and manipulate information in the short-term memory (STM).
- CHC-based narrow abilities affected are as follows:
  a) Induction or Deduction (Gf-I): This refers to the difficulty in drawing conclusions based on information and/or understanding patterns.
  b) Lexical Knowledge (Gc-VL): It refers to limited vocabulary for that age of an individual concerned.
  c) Attentional Control (Gwm-AC): It refers to the challenges in focusing and maintaining task-directed behavior.

Broad	Narrow

[Gf]	**I**	RG	**RQ**	RE	RP	
[Gwm]	**Wa**	**Wv**	**AC**	**Wc**		
[Gc]	**LD**	**VL**	**K0**	LS	**CM**	**MY**
[Gq]	**KM**	**KM**	**A3**			
[Gs]	**P*$^{+}$**	**Ps^{+}**	**Pc^{+}**	**N**	RS	WS

Key:

= Intelligence as Process
= Intelligence as Knowledge
= Intelligence as Process: Speed/Fluency
[ ] = CHC-based broad abilities
= CHC-based narrow abilities without [ ] designated as secondary loadings
Bold font = Major ability
Regular font = Minor ability
Italic font = Tentative abilities
* = Intermediate stratum abilities
$^{+}$ = The three narrow abilities P, PS, Pc within Gs (Processing Speed) that are likely to be further differentiated by content facets: such as reading-writing, figural-visual, auditory, quantitative-numeric, verbal.

Fig. 1. CHC Chart of Broad and Narrow Abilities for IDD/D

2.1.2 Syndromic Autism (SAu)

Many children with KS2 display autistic traits (Akin Sari et al., 2008; Barry et al., 2022), which typically affect socio-emotional, and sensorimotor domains. This co-morbidity is known as syndromic autism, which occurs with other identifiable genetic conditions. Figure 2 shows the CHC-based broad and narrow abilities (Schneider & McGrew, 2018) that are affected in KS2 related in SAu.

- CHC-based broad abilities affected are as follows:
  a) Gf (Fluid Reasoning): Problems with flexible thinking and abstract reasoning.
  b) Gwm (Short-Term Working Memory): Problems in recalling short-term information, such as socially-relevant details.
  c) Gq (Quantitative Knowledge): Challenges in mathematical reasoning.
  d) Ga (Auditory Processing): Difficulty in processing speech and/or sound patterns due to sensory sensitivities to sound.
  e) Gv (Visual Processing): Though sometimes visual processing strengths are preserved, spatial understanding is still impacted.
- CHC-based narrow abilities affected are as follows:
  a) Social Cognition (includes Gf-I, Gf-RG and Gf-RE): Problems in understanding social cues, recognizing emotions in others, and perspective-taking, with the following narrow abilities involved: I=Induction, RG=General Sequential Reasoning, and RE=Reasoning Speed within the broad ability of Gf.
  b) Phonetic Coding (Ga-PC): Difficulty in distinguishing/interpreting letter sounds that impacts language development.
  c) Perceptual Speed (Gs-P): Slower response to processing information in social contexts or sensory inputs.
  d) Nonverbal Sensory Integration (includes Gv-Vz, Gv-IM, Gv-CF, Gv-MV and Gv-P): Sensory sensitivities complicate interactions with the environment, involving the following narrow abilities: Vz=Visualization, IM=Imagery, CF=Flexibility of Closure, MV=Visual Memory, and P=Perceptual Speed within the broad ability of Gv.

Broad	Narrow							
[Gf]	**I**	RG	**RQ**	RE	RP			
[Gwm]	**Wa**	**Wv**	**AC**	**Wc**				
[Gv]	**Vz**	**SR**	**IM**	CF	CS	MV	SS	PI
	LE	IL	PN	P*				
[Ga]	**PC**	US	UR	**U8**	UM	U1/U9	UP	UL
[Gq]	**KM**	**A3**						

Fig. 2. The CHC Chart of Broad and Narrow Abilities for AS

2.1.3 Learning Disabilities (LD)

Many children with KS2 experience learning disabilities, particularly in reading and mathematics. Figure 3 shows the CHC-based broad and narrow abilities (Schneider & McGrew, 2018) affected in KS2 related in LD.

- CHC-based broad abilities affected as follows:
  a) Gc (Comprehension-Knowledge): An under-development in language and reading skills.
  b) Gwm (Short-Term Working Memory): Difficulty in retaining verbal or auditory information relevant to learning.
  c) Gq (Quantitative Knowledge): Delays in numerical operations and math problem-solving.
  d) Ga (Auditory Processing): Difficulty in phonological processing which is crucial for reading development.
  e) Grw (Reading & Writing Ability): Both reading and writing delays that often impact academic achievement.
- CHC-based narrow abilities affected are as follows:
  a) Reading Decoding (Grw-RD): Struggles with sound-letter correspondence, leading to challenges in reading.
  b) Mathematical Achievement (Gq-A3): Problems encountered in arithmetic operations and understanding mathematical principles.
  c) Phonetic Awareness (Ga-PC, Ga-US and Ga-UR): Challenges in breaking down and manipulating phonetic components of language, with the following narrow abilities involved: PC=Phonetic Coding, US=Speech Sound Discrimination, and UR=Resistance to Auditory Stimulus Distortion within the broad ability of Ga.
  d) Orthographic Processing (Gv-Vz, Gv-IM, Gv-MV and Gv-CS): Challenges in recognizing and processing written symbols, with the following narrow abilities involved: Vz=Visualization, IM=Imagery, MV=Visual memory, and CS=Closure speed within the broad ability of Gv.
  e) Emotional and Sensory Abilities: Generally, these are found in the CHC-based broad abilities of Gei (Emotional Intelligence), Gv (Visual Processing), Gs (Processing Speed), Go (Olfactory Abilities), Gh (Tactile Abilities), Gk (Kinesthetic Abilities) - across the three co-morbidities associated with KS2.
  f) Sensory Sensitivities (auditory, tactile, visual): These are referred to the CHC-based broad abilities of Ga (Auditory Processing), Gh (Tactile Abilities) and Gv (Visual Processing): These are common in both syndromic autism (SAu) or autism spectrum disorder (ASD) and learning disabilities (LD), impacting the ability of an individual with KS2 to engage in certain environments.
  g) Emotion Regulation, which is often impacted in SAu or ASD (Gei-Em and Gei-Eu): Difficulties in managing emotions, leading to heightened anxiety, meltdowns, or inappropriate responses in social contexts, where the following narrow abilities are:

Em=Emotion Management and Eu=Emotion Utilization within the broad ability of Gei (Emotional Intelligence).

Broad	Narrow							
[Gwm]	**Wa**	**Wv**	**AC**	**Wc**				
[Ga]	**PC**	US	UR	**U8**	UM	U1/U9	UP	UL
[Gc]	**LD***	**VL**	**K0**	LS	**CM**	**MY**		
[Grw]	**RC**	**RD**	RS	**WA**	**SG**	EU	WS	
[Gq]	**KM**	**A3**						

Fig. 3. The CHC Chart of Broad and Narrow Abilities for LD

In summary, the following key points are highlighted as follow:

1) Intellectual and Developmental Delays or Disabilities (IDD/D): Broad impairments occur across many cognitive abilities, especially in fluid reasoning, working memory, and processing speed.
2) Syndromic Autism (SAu): Significant impacts fall on social cognition, sensory processing, and specific memory and auditory/visual processing areas.
3) Learning Disabilities (LD): Specific impacts affect reading, writing, and mathematical abilities, as well as difficulties in phonological processing and working memory.

Understanding these CHC-based broad and narrow abilities affected in children with KS2 and the co-morbidities provides a basis for individualized intervention strategies that educational therapists can use to address cognitive, sensory, and emotional challenges.

In summary, the CHC framework offers a useful cognitive map to identify strengths and deficits, while science helps clarify the neurodevelopmental aspects of Kabuki Syndrome. Engineering provides the tools and environment modifications, and technology offers personalized interventions. Together, these domains can create a comprehensive educational therapy plan for children dealing with developmental delays, intellectual disabilities, and autism.

3. THE INTERACTION OF SCIENCE, ENGINEERING AND TECHNOLOGY (SET) WITH THE CHC FRAMEWORK

The interaction of science, engineering, and technology (SET) with the Cattell-Horn-Carroll (CHC) theory of broad and narrow abilities can be integrated to create the SET-CHC framework that can contribute to playing a significant role, especially in planning what the authors of this paper have termed it a “circumvention approach” to manage the complex condition of KS2, particularly in coping with co-morbidities like intellectual and developmental delays or disabilities (IDD/D), syndromic autism (SAu) and learning disabilities (LD) (see Figure 4).

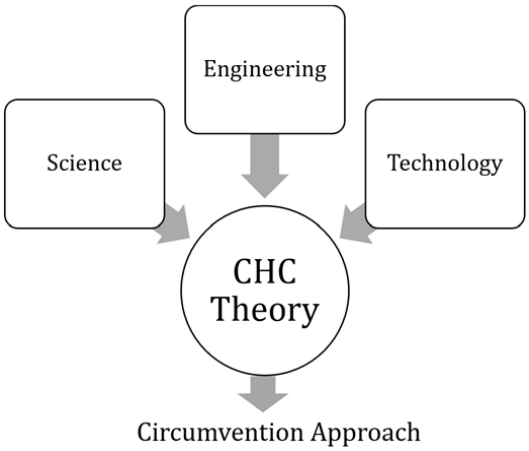

Fig. 4. The SET-CHC Framework

Each of these three domains in the SET framework can contribute to a more comprehensive and in-depth application of educational therapy in managing IDD/D, SAu and LD that coexist within the condition of KS2.

3.1. Science (Understanding the Cognitive Abilities and Co-morbidities)

3.1.1. Cognitive Models (CHC Framework)

The CHC framework categorizes cognitive abilities into broad and narrow abilities, such as fluid reasoning (Gf), comprehension-knowledge (Gc), processing speed (Gs), and working memory (Gwm). In the case of KS2, understanding the individual's cognitive profile through this framework can help identify specific strengths and weaknesses.

3.1.2. Neurodevelopmental Research

Current research on KS2 helps to pinpoint how cognitive abilities are affected, including potential impacts on attention, memory, problem-solving, and language abilities. SAu and IDD/D, which often accompany Kabuki Syndrome, may lead to specific deficits that can be framed within the CHC model.

3.2. Engineering (Development of Therapeutic Tools and Approaches)

3.2.1. Assistive Technology and Adaptive Tools

Engineering can provide customized solutions through assistive technologies (Pontikas, Tsoukalas, &Serdari, 2022; Rahlin, 2024; Rayar, 2024), e.g., augmentative and alternative communication (ACC) devices, sensory aids (e.g., hearing aid and glasses), or software applications that address specific deficits (e.g., language processing or working memory) in children with KS2. In other words, technological interventions have made a big difference in the lives of individuals with rare genetic diseases and neurodevelopment disorders by supporting them in learning and daily functioning (Ribas et al., 2023; Stasolla et al., 2024; van Karnebeek et al., 2024). There are also technological tools specially designed for cognitive training, such as NeuroLat Training Program (Chia & Ng, 2021; Rabi, May, &Lek, 2019) or sensory integration, such as STAR Treatment Program (Schoen et al., 2019), can enhance the learning experience.

3.2.2. Design of Educational Therapies

Using engineering principles (also with an incorporation of the seven principles of the Universal Design) (see Ramos Aguiar et al., 2022, for detail), the educational therapy can be structured to optimize the learning context. For instance, according to Dering and Camulli (2019/2020), incorporating sensory-friendly classroom designs or task-specific devices helps in creating an adaptive learning environment that accommodates the developmental challenges faced by children with this syndrome.

3.3. Technology (Implementation of Cognitive and Educational Interventions)

3.3.1. Technological Interventions

Advanced technology (He et al., 2024), e.g., the **T**echnological **P**ed**A**gogical**C**ontent **K**nowledge framework or TPACK for short (Koehler et al., 2013), can aid in the development of personalized educational intervention programs (also known as individualized education programs or IEP for short). It can also be incorporated into neuropsychological profiling of KS in the same way it has been done with KAT6A syndrome (Ng, Kalinousky, & Harris, 2024). Computerized cognitive training programs (Chia & Ng, 2021; Hallion, Hsu, &Schleider, 2024; Stasolla et al., 2024) that target narrow abilities (such as STM or attention) can be customized to cater to an individual's cognitive profile (Hall, based on the CHC framework. For example, apps that focus on executive function can help in strengthening working memory (Gwm) or fluid reasoning abilities (Gf).

3.3.2. Data-Driven Instructional Planning

Using technologies, such as artificial intelligence or machine learning, (Choon et al., 2024; He et al., 2024), educational therapists can gather data about the responses of an individual with KS2 to various intervention programs. This feedback loop allows an educational therapist to make adjustments according to evidence-based measurable progress in targeted abilities that have been identified earlier via the X-BA, supporting real-time refinements to the design of the therapy program.

4. CIRCUMVENTION STRATEGIES IN EDUCATIONAL THERAPY

As KS2 is such a complex genetic disorder caused by mutations in specific genes, particularly those involved in developmental processes, there is no cure for it (Miyake, 2024). The reason is fivefold: Firstly, the genetic mutations associated with KS2 are rather diverse. As a result, they can impact various biological pathways. The genetic complexity of KS2 also makes it more challenging to develop a one-size-fits-all intervention approach. Secondly, KS2 affects multiple systems in the body. For instance, there is a wide range of symptoms: developmental delays, intellectual disabilities, autistic-like traits, and physical abnormalities. Hence, managing the condition of KS2 with such varied symptoms requires a multi-disciplinary approach. Thisinvolves different allied professionals to collaborate with each other to address the issues of concern rather than working on a singular cure that might not exist at all. Besides, the treatment can be very costly for an individual with KS2. Thirdly, the current research on rare genetic disorders like KS1 or KS2 is still evolving. There is an insufficient understanding of the underlying mechanisms to develop targeted therapies for KS2 treatment. Fourthly, current interventions for KS2 focus on managing the symptoms and improving quality of life through conventional therapies (e.g., physical, occupational, and educational support) rather than finding a definitive cure. Lastly, application of genetic therapies and interventions can raise ethical and practical challenges, making them very difficult to implement across the world.

As research progresses, there may be advancements in gene therapies or development of other better treatments. However, for now, the focus remains on supportive care for children with KS2.

4.1 Conventional KS2 Intervention Approach

As it remains that there is no cure for KS2 (Miyake, 2024), the general intervention plan focuses on managing symptoms and improving quality of life. It typically involves a multi-disciplinary team of specialists like geneticists, pediatricians, neurologists, and allied therapists. The six main components in the conventional KS2 intervention approach consist of the following: (1) Early intervention and developmental support, e.g., speech-language therapy, occupational therapy, physiotherapy, and sensory integration therapy; (2) Educational support & services, e.g., educational therapy, counselling and psycho-educational program for family members to cope with loved ones born with KS2, behavioral therapy, and implementation of Universal Design (UD) to create a conducive environment for an individual with KS2; (3) Medical management, e.g., hearing (which may involve verbal-auditory therapy) & vision care, cardiological attention for congenital heart defects, feeding issues & gastrointestinal care; (4) Endocrinological and growth support, e.g., growth hormone therapy for those with short stature, pharmacological treatment for thyroid dysfunctions and hormonal imbalances, which can occur in KS2; (5) Neurological functioning skills and psychiatric care, e.g., seizure management, behavioral and mental wellness support, and training in neurological functioning skills; and (6) Genetic counseling for families to understand the inheritance patterns of KS2, especially in cases of future pregnancies, which is often linked to X-linked inheritance through the KDM6A gene.

Each intervention plan is highly personalized to the individual, depending on the specific symptoms and patterns of strengths and weaknesses or any other challenges they encounter daily. Regular follow-up with healthcare professionals is essential to ensure ongoing monitoring and adaptation of both medical treatments and non-medical interventions as the individual with KS2 grows.

4.2 The Novel KS2 Circumvention Approach

While it has yet to be proven feasible with enough scientific evidence, the SET-CHC framework could offer a new approach to manage KS2. Instead of directly intervening, the idea of ‘circumvening’ is worth serious consideration and further study.Generally speaking, to ‘circumvene’ means to find a way around a problem or obstacle, often by avoiding it or bypassing it in some clever or indirect manner. A good example is to investigate a viable alternative through neural pathways. It is somewhat like terraforming - the hypothetical process of modifying an alien environment, such as Mars (Fogg, 1998), to make it more habitable (Earth-like) and suitable for future human colonization. In other words, to circumvene is to imply an effort is made to provide alternative methods or strategies to address the challenges posed by KS2.It offers a different approach from direct intervention in traditional or conventional ways. This novel approach focuses on adapting and using creative solutions to navigate difficulties.

Therefore, the authors want to emphasize that managing a complex and rare syndrome like KS2 (or KS1) requires circumvention (instead of intervention) - like a preventive approach - not just treating symptoms as they appear. Hence, to apply the circumvention in managing KS2, there is a need to focus on three things: First, supportive measures;second, early screening; andthird, adaptive strategies. These would help reduce the impact of early symptoms before they fully appear in someone already diagnosed with KS2.

5. CONCLUSION

To circumvene the condition of KS2, there are two possible strategies in educational therapy to do so. The first strategy is to target narrow abilities to compensate for weaknesses. Using the SET-CHC framework, educational therapists can focus on a child's strengths in certain abilities, like comprehension or verbal skills (under Gc). This can also help them manage challenges in other areas, like processing speed (Gs).For example, if a child has difficulty with the working memory (Gwm), tasks that require extensive recall might be broken into smaller steps to accommodate cognitive limitations.

The second strategy is to take a holistic approach to cope with co-morbidities associated with KS2. By combining neuropsychological assessments, tools like robots that teach social skills, and technology-based interventions (e.g., ACC devices), educational therapy can better address the needs of children with KS2.For instance, educational therapists may use technology to build structured routines that reduce anxiety (common in syndromic autism) while simultaneously engaging cognitive training activities.

Finally, there is always room for more improvement in the treatment approach for children with KS2.

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COMPETING INTERESTS

The authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

The first author planned and wrote the first draft of the manuscript. The second author did the literature review and checked the references for citations. Both authors read and approved the final manuscript.