The co-occurrence of mental disorders in children and adolescents with intellectual disability/intellectual developmental disorder

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Purpose of review
The study summarizes supportive epidemiological data regarding the true co-occurrence (comorbidity) and course of mental disorders in children with intellectual disability/intellectual developmental disorders (ID/IDD) across the lifespan.

Recent findings
Published studies involving representative populations of children and adolescents with ID/IDD have demonstrated a three to four-fold increase in prevalence of co-occurring mental disorders. The effect of age, sex, and severity (mild, moderate, severe, and profound) and socioeconomic status on prevalence is currently not clearly understood. To date there are no prevalence estimates of co-occurring mental disorders in youth identified using the new DSM-5 (and proposed ICD-11) definition of ID/IDD using measures of intellectual functions and deficits in adaptive functioning with various severity levels defined on the basis of adaptive functioning, and not intellectual quotient scores.

Summary
The true relationship between two forms of morbidity remains complex and causal relationships that may be true for one disorder may not apply to another. The new conceptualization of ID/IDD offers a developmentally better informed psychobiological approach that can help distinguish co-occurrence of mental disorders within the neurodevelopmental section with onset during the developmental period as well as the later onset of other mental disorders.

Keywords
comorbidity, co-occurring mental disorders, intellectual disability/intellectual developmental disorders

INTRODUCTION
The new terminology introduced by the American Psychiatric Association Diagnostic and Statistical Manual, 5th Edition (DSM-5), defines intellectual disability/intellectual developmental disorder (ID/IDD) under the neurodevelopmental disorders section characterized by deficits in intellectual and adaptive functioning in terms of conceptual, social, and practical domains originating in the developmental period [1]. The conceptualization of ID/IDD as an ‘intellectual development disorder’ is the culmination of an extensive international effort undertaken to reach agreement on a new name, positioning, definition, and diagnostic principles for mental retardation [2]. The effort was led by the WHO working group (WHO-WG) for the revision of mental retardation in the International Classification of Diseases and Related Health Problems, 11th Revision (ICD-11) [2,3,4]. The DSM-5 has maintained the same severity levels by name, that is, mild, moderate, severe, and profound, but defines them on the basis of adaptive functioning, and not intellectual quotient (IQ) scores, ‘as it is adaptive functioning that determines the level of supports required, and IQ measures tend to be less valid in the lower end of the IQ range’ ([1], p. 33).

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Neurodevelopmental disorders

KEY POINTS

- The global burden of disease relative to the contribution of ID/IDD now ranks within the top 20 sources and among top 20 most costly disorders.
- Co-occurring mental disorder in children and adolescents with ID/IDD are common and persistent across the lifespan.
- Co-occurring mental disorders in children and adolescents with ID/IDD is substantive with multiple co-occurring mental disorders existing in a high proportion of study participants.
- Only 1 in 10 children and adolescents with co-occurring mental disorders receive specialized mental health services.
- Co-occurring mental disorders in children and adolescents with ID/IDD are more predictive of major restrictions in educational and vocational participation and social inclusion than the severity of the ID/IDD.
- Mental well-being of parents of young people with ID/IDD is more strongly influenced by the severity of their children’s co-occurring mental disorder than by the severity of the children’s ID/IDD.

For the purposes of this study, the acronym ID/IDD will be used to refer to mental retardation and ID across prior classifications. The terms mental disorder, mental ill-health, or psychopathology will also be used interchangeably and refers to occurrence in children and adolescents (youth). Given the prevalence figures for ID/IDD in the general population between 1 and 3% [5], and the co-occurrence rate of mental problems among youth with ID/IDD as high as three to four times greater than the rate among typically developing youth [6–9], it is estimated that the burden of mental ill-health among youth with ID/IDD is analogous to that experienced by individuals with schizophrenia and persists across the lifespan [10].

To date, there are no prevalence studies of mental ill-health among youth with ID/IDD identified using measures of adaptive functioning. It is likely that the burden of mental ill-health will be more inclusive – this is evidenced by reported psychiatric comorbidity patterns among youth with borderline intellectual functioning (BIF) (currently listed as a V Code on the DSM-5) bearing similarity to those reported among youth with mild ID/IDD [11,12].

COMORBIDITY

The DSM-5 recognizes that boundaries between disorder categories are more fluid over the life course than once believed and symptoms once assigned to a single disorder may also occur at varying levels of severity in other disorders. Comorbidity is defined as independent co-occurrence of one or more disorders (not symptoms) that truly reflects an increased relative risk of one or more disorders occurring in the presence of the index condition [13]. The concept accommodates dimensional and categorical measures of mental disorder and serious psychopathology.

The Epidemiological Catchment Area studies in the United States were the first DSM-based studies to note that although 87% of the population had no disorder, of the 13% that had at least one disorder, a fifth had two or more disorders. In the group with co-occurrence of disorders, there were more people with three or more disorders than one would expect if the disorders were independently distributed [14]. There may be elevated frequency of co-occurring disorders at a measure point in time (‘cross-sectional’ comorbidity), measured over a specified duration (‘period’ comorbidity), or across the life course (‘lifetime’ comorbidity) [15]. Three other notions of comorbidity are [16]: ‘pathogenic’ in which an index condition leads to another disorder that co-occurs and that is considered to be etiologically related to it [e.g., ID/IDD and autism spectrum disorder (ASD), or ID/IDD and stereotyped movement disorder]; ‘diagnostic’ in which diagnostic criteria are based on symptoms that are not specific to a single disorder but frequently overlap (leading to misclassification in assignment of symptoms across disorders) – this is especially relevant when one or more other mental disorders may co-occur with ID/IDD, as in attention deficit hyperactivity disorder (ADHD) and bipolar and related disorders and ID/IDD; and ‘prognostic’, in which the index condition predisposes (or is predictive) of the individual to develop other disorders (e.g., ID/IDD and emergence of high rates of depressive disorders, or trauma and stressor-related disorders). For example, a recent study examined the relationship of IQ scores in more than 2000 simplex cases of ASD, with behavior and language assessments, and rate of de novo loss of function mutations and family history of depressive disorders, bipolar disorder, and schizophrenia [17*]. Proband IQ scores were positively associated with family history of psychiatric disease. Low frequencies of family history of psychiatric illness were seen in individuals who were unable to complete a traditional IQ test, signifying the severe group of ID/IDD with the greatest degree of language and behavioral impairment. These analyses predict that among higher functioning individuals with ASD (with mild ID/IDD and higher IQ scores) there was stronger evidence for familial risk for neuropsychiatric disease.
The US National Comorbidity Survey studies, among individuals aged 15–54 years, also showed that comorbidity among mental disorders was common. In fact, as many as one-half of all lifetime mental disorders in the general population were shown to occur among people with a prior history of some other index mental disorder [18]. Therefore, the correlates, outcomes, and genetic characteristics reported for an index disorder may be attributable to another; and that the meaning of an index disorder with and without comorbidity may differ fundamentally [19]. A recent meta-analysis presented evidence on comorbidity between ID/IDD and ASD for the decade 2000–2010 for 6.2 million youth enrolled in special education services in the United States, ages 3–21 years, per year [20]. The 331% increase in the prevalence of ASD diagnosis observed during this period was noted to be potentially because of the diagnostic recategorization of ID/IDD to ASD. In fact, the decrease in ID/IDD prevalence equaled an average of 64.2% of the increase of ASD prevalence for youth ages 3–18 years. The proportion of ID/IDD youth undergoing recategorization from ID/IDD to ASD was significantly higher for older (75%) than for younger youth (48%). Some of the states showed negative correlations between the prevalence of ASD compared with that of ID/IDD, suggesting variations in health policies across states as a major factor in recategorization of the youth as ASD. In conclusion, the ascertainment practices were noted to be uniquely focused on ASD-specific standardized measures and did not necessarily consider associated comorbidity with ID/IDD that may confound ASD diagnosis.

**EARLY EPIDEMIOLOGICAL FINDINGS ON INTELLECTUAL DISABILITY/INTELLECTUAL DEVELOPMENTAL DISORDER**

Using the Wechsler intelligence scale for children the Isle of Wight studies ascertained IQ scores for all 10 to 12-year-old children [21], noting that 2.5% scored two standard deviations or more below the mean, and that multiple disabilities and disorders were more common especially among children with severe ID/IDD. Two of the most common disabilities reported included epilepsy and cerebral palsy [21–23]. The Isle of Wight studies linked variations in levels of IQ with co-occurrence of mental disorders: teacher ratings showed an inverse relationship between the frequency of behavioral problems and IQ levels in children [21]. This inverse relationship between IQ scores and problem behavioral disturbance was also supported by other epidemiological studies [24]. A large scale study involving 175 000 residents in the Camberwell district of South East London, using two-stage total population assessments like in Isle of Wight, showed that study participants exhibited varying patterns of mental disorders across the IQ severity range [25].

The early studies examined the influence of a subject’s age, sex, family background, presence of biological factors, social, and environmental factors, as well as urban–rural differences [9]. The primary emphasis was on defining ID/DD by intellectual levels rather than examining co-occurring mental disorders. Nonetheless, the early studies painted a consistent picture: modestly higher rates of boys with severe/profound ID/IDD; consistently higher rates of boys with mild ID/IDD (excess particularly marked for IQ levels 70 and up, a similar sex pattern among youth with higher functioning ASD). With respect to family history of mental disorder, the prevalence of mental disorders was noted to be most marked among children with mild ID/IDD than with severe/profound ID/IDD. Higher rates of ID/IDD were reported in rural than urban areas, but the disparities were less pronounced when nationally uniform services were implemented with improved transportation and communication serving rural areas [9]. The early studies also established that co-occurring mental disorders exhibited a distinct pattern of higher co-occurrence with ASD, childhood psychosis, hyperkinetic disorder (ADHD) and stereotyped disorders among study participants with moderate ID/IDD with IQ scores 50, or lower. The rates were more than doubled in the presence of brain damage and epilepsy. The important confounders emerging that needed to be controlled included socioeconomic and family adversity factors and need for independent assessment of language from intellectual and adaptive impairments.

**EXCLUSION OF INTELLECTUAL DISABILITY/INTELLECTUAL DEVELOPMENTAL DISORDER IN EPIDEMIOLOGICAL STUDIES IN CHILD AND ADOLESCENT PSYCHIATRY**

Despite this early progress in research in epidemiology of ID/IDD and the resurgence of interest in psychiatric epidemiology in the post-DSM-III era, it is remarkable that these two streams did not converge. This may reflect the dichotomy in mental health and ID/IDD services during this period. It is therefore not surprising that ID/IDD, as well as ASD and pervasive developmental disorders not otherwise specified were excluded from studies citing challenges in ascertainment, difficulties in assessment by means of self-report or semi-structured or structured interviews, as well as ethical protections.
of vulnerable research study participants [26]. The omissions were not exclusive to developmental disorders in Axis II, but also included anorexia nervosa, posttraumatic stress disorder (PTSD), and specific learning disorders. Omission of preschool age children was also the norm. Children and adolescents with ID/IDD were also excluded from the National Comorbidity Surveys in the US [18], as well as the WHO Composite International Diagnostic Interview World Mental Health Surveys [27]. Similarly, many longitudinal epidemiological studies of prevalence, risk factors, and continuity/discontinuity of child and adolescent mental disorders omitted study participants with ID/IDD. Among these were the Dunedin study [28], the Dutch epidemiological studies [29], the New York longitudinal study [30], the Ontario child mental health study [31], and primary care study of US children [32].

GLOBAL BURDEN OF DISEASE AND INTELLECTUAL DISABILITY/ INTELLECTUAL DEVELOPMENTAL DISORDER

During the period 1990–2013 the global life expectancy at birth has increased by 6.2 years and healthier life expectancy at birth by 5.4 years [33,34]. The global burden of disease (GBD) relative to the contribution of ID/IDD now ranks within the top 20 sources and among top 20 most costly disorders [35]. In fact the improvements in infant mortality and childhood survival across the globe have enhanced the relevance of the GBD metric with respect to the entire neurodevelopmental group of disorders even in the sub Saharan African context [36,37]. The GBD resulting from the contribution of ID/IDD (because of IQ point decreases) has been estimated at a global scale in the context of specific environmental exposures such as lead [38].

SUSTAINABLE DEVELOPMENT GOALS AND THE NONCOMMUNICABLE DISEASE FRAMEWORK

The United Nations now makes specific mention of disabilities under five of its sustainable development goals [33]: education; economic growth and employment; creation of inclusive, safe, resilient, and sustainable cities; reduction of inequalities; and data collection related to monitoring of the sustainable development goals. Mental and neurodevelopmental disorders are also increasingly considered under the noncommunicable disease framework [39] with increased multiple physical and mental health comorbidity in individuals with ID/IDD and noncommunicable diseases [40]. Links between ID/IDD subtypes and cause-specific mortality rates need to be further explored. There is evidence that for individuals with mild cognitive impairment as part of the Neurological Disorders in Central Spain study, adjusted by socio-demographic factors, the risk of death at 13 years was increased for all mild cognitive impairment subtypes [41]. These outcomes reflect poor detection rates of cardiovascular and cancer, as well as co-occurring mental disorders in ID/IDD populations. For example, the duration of untreated depression and duration of untreated psychosis in the general population have both been estimated to be about 8 and 2 years, respectively. Although the ‘duration of untreated co-occurring mental disorders in individuals with ID/IDD’, including depression and psychosis, has not been formally studied, it is likely to be even higher compared to typically developing individuals.

It is now well established that there are significant inequalities in the provision of cardiovascular screening to people with severe mental illnesses in primary care. The co-occurrence of mental disorders reduces the rate of screening, monitoring, and treatment of various medical conditions. In a study of a national sample of primary care patients in the United Kingdom comparing the screening for cardio-metabolic risk factors among patients with severe mental illness (SMI) and diabetes, the percentage of patients who received screening across four parameters (BMI, blood pressure, blood glucose, and cholesterol) in the previous 15 months was higher among patients with diabetes than among those with SMI (97.3% vs. 74.7%, P < 0.001) [42]. Unfortunately, metabolic syndrome and its complications are highly predictive of cardiovascular diseases, and individuals with co-occurring SMI and ID/IDD therefore stand to be at much higher risk of developing cardiovascular disease and die sooner than the general population [43]. Indeed, the detection of co-occurring mental disorders in individuals with ID/IDD is likely to be much lower than the 30% in the context of unmonitored primary care practices in the United Kingdom [44].

CURRENT STATUS OF COMORBIDITY OF MENTAL ILL-HEALTH AND INTELLECTUAL DISABILITY/ INTELLECTUAL DEVELOPMENTAL DISORDER AMONG YOUTH

The population-based estimates of co-occurring mental disorders in children and adolescents with ID/IDD vary considerably, ranging from 10 to 60% because of methodological limitations in terms of biased sampling, changes in diagnostic criteria, different IQ cut-offs, and approaches use to measure psychopathology [45]. A methodologically rigorous
review [46] excluded: unrepresentative samples; sample sizes less than 100; single mental disorders; unreliable diagnoses; diagnosis made by a single rater or with no indication of method used; and response rate less than two-thirds. Nine studies remained from a pool of 85 original identified. Only four of the nine studies included a comparison group. The rate of co-occurring mental disorders ranged from 30 to 50% in ID/IDD compared to 8 to 18% in the comparison group. The relative risk of co-occurrence of mental disorder associated with ID/IDD was 2.8–4.5. Among the remaining five of nine studies without a comparison group the reported prevalence estimates for co-occurring mental disorder ranged from 30 to 41%, comparable to rates for studies with a comparison group [47].

Three risk factors were examined with respect to their effect on co-occurrence of mental disorders: child’s age, sex, and severity of ID/IDD. A fourth included socioeconomic status that could be elicited in two studies. Reporting on positive findings: by age: there was higher level of co-occurring mental disorders in younger children (5–13 years) [46]; older children with ID/IDD (aged 11–16) were more likely to be identified as having emotional disorder, younger children (aged 5–10) were more likely to have hyperactivity [47]; Obsessive Compulsive Disorder was more common in older children (aged 13–20 years); by sex: higher prevalence of co-occurring mental disorder among men only; men were significantly more likely to be identified as having a conduct disorder/hyperactivity; significantly higher overall prevalence rates of co-occurring mental disorders among men reported; and by socioeconomic status: one study found an association between socioeconomic status and mental disorder with significantly greater risk of exposure to social disadvantage, and 3% of children with ID/IDD accounted for 14% of total child and adolescent psychiatric morbidity in Britain [48].

One of the most important longitudinal studies examining comorbidity in youth with ID/IDD was part of the Australian Child to Adult Development study in New South Wales and Victoria involving an epidemiological cohort of 578 children and adolescents aged 4–19.5 years at wave 1, recruited from health, education, and family agencies that provide services to children with ID/IDD of all levels. The developmental behavior checklist (DBC) was the key measure of psychopathology [10]. At wave 1, 41% of participants met criteria for major psychopathology or definite psychiatric disorder; by wave 4, this prevalence had decreased to 31%. Only 10% of those participants with definite psychiatric disorder had received specialist mental health interventions. The differences between initial total scores for ID/IDD groups were not significant; however, the scores for mild ID/IDD declined more rapidly than those with severe or profound ID/IDD. In fact, the more severe the ID/IDD, the less rapidly problem behaviors declined. All DBC subscale scores declined significantly over time, except social-relating disturbance, which increased. Age, severity of ID/IDD, and sex effects by DBC subscales were as follows: ‘Disruptive’: scores for mild ID/IDD youth were higher than those with severe or profound ID/IDD, but showed larger decreases over time; ‘Self-absorbed’: the severe or profound ID/IDD group had the highest scores, older individuals had lower self-absorbed scores but decreased at a slower rate; ‘Anxiety’: older individuals had lower anxiety scores that decreased at a slower rate; anxiety in girls decreased at less than half the rate for boys, and individuals with severe or profound ID/IDD similarly decreased less than those with mild ID/IDD. In fact, for girls with severe or profound ID/IDD, there was an increase in anxiety, particularly at older ages; ‘Communication disturbance’: symptoms were more prominent in the mild compared with the severe or profound ID/IDD group. More rapid decreases in scores were observed in the older individuals; ‘Social-relating disturbance’: the scores were higher for older individuals and those with severe or profound ID/IDD, and in contrast with the other scales, increased over time, although at a slower rate for older individuals. The persistence of the symptoms over time and the fact that only 10% of the participants with a confirmed mental disorder received specialist mental health services were remarkable, the overall prevalence of serious psychopathology decreased from 41% at wave 1 to 31% at wave 4. Co-occurring mental disorders in children and adolescents with ID/IDD are more predictive of major restrictions in educational and vocational participation and social inclusion than the severity of the ID/IDD. Mental well-being of parents of young people with ID/IDD is more strongly influenced by the severity of their children’s co-occurring mental disorder than by the severity of the children’s ID/IDD [49].

SEVERE AND PROFOUNDD INTELLECTUAL DISABILITY/INTELLECTUAL DEVELOPMENTAL DISORDER AND CO-OCCURRING MENTAL DISORDERS

In the Australian Child to Adult Development study 5–19 year children and adolescents with severe and profound ID/IDD were compared [50]; the youth with profound ID/IDD had additional physical disabilities and both groups were noted to have high mortality during follow-up. The profound ID/IDD group had significantly lower scores across all the
DBC subscales including disruptive behavior, except the social relating subscale. It was concluded that the fewer endorsed items on the disruptive behavior subscale may potentially reflect both positive and negative connotations – positive, requiring less interventions; negative, reflecting greater passivity. The authors caution in combining severe and profound ID groups into a single category in research.

**BORDERLINE INTELLECTUAL FUNCTIONING IN CHILDREN AND ADOLESCENTS**

BIF is defined as scoring between 1 and 2 SDs below the mean on standardized tests, equivalent to an IQ score 71–84. Obviously this definition will need to be revised on the basis of measures of adaptive functioning and not IQ scores. Secondary analysis of a population-based cohort of 4337 children, ages 4–5 years followed up at age 6–7 years as part of the Longitudinal Study of Australian Children [51] showed that the BIF group represented 15% of the total child population, but accounted for up to 40% of total child psychiatric morbidity within their age group.

BIF children were at significantly increased risk of possible mental health problems in early childhood when compared to their typically developing peers. Three groups of children with ID/IDD, BIF, and typical developing children were compared: higher rates of mental health problems for total difficulties on all five Strength and Difficulties Questionnaire subscales at age 6–7 years for children with ID/IDD or BIF were observed compared with typical developing children. Controlling for socioeconomic disadvantage reduced but did not prevent significance of group differences. The BIF children experienced more PTSD and V Codes (twice as high); they had the lowest rate of psychotic disorders among the three groups. There was no difference in ADHD, substance use and somatoform disorders among the three groups.

**PROFESSIONAL PRACTICE GAPS**

Children and adolescents with ID/IDD are highly heterogeneous across and within disease groups, with a broad range of cognitive abilities and behaviors that can vary across their life course, making measurements difficult. A major obstacle is the lack of agreed upon endpoints to assess function. The measures need to be sensitive, reliable, valid, able to detect change over time, and appropriate for use in specific populations [52]. There are limitations across patient assessments (self or interview), caregiver (observations), clinician (direct examination or interview) and combined assessments. There is a particular need to develop clinical scales for use in youth who are nonverbal. The targets need to include: Cognition (e.g., executive function, visuospatial skills, memory, learning, inhibition, attention); Behavior and emotion (e.g., anxiety, arousal, stress response, irritability, sociability); Physical/medical (e.g., motor symptoms, sleep disorders, sensory alterations such as ocular or auditory function, seizures, endocrine or immune regulation, respiratory or autonomic dysregulation); and Adaptive behavior (e.g., functional abilities in a variety of living situations, such as home, community or school settings).

ID/IDD services should be designed with the knowledge that a very high proportion of persons with ID/IDD will have substantial and persistent co-occurring mental disorders across the lifespan [53**]. Primary public health and secondary clinical interventions should aim at reducing the prevalence and severity of co-occurring mental disorder in ID/IDD populations. Mental health service development needs to identify and leverage supports and to enhance capacity in education and skills training among parents and families of persons with ID/IDD, with special relevance to the burden of care of co-occurring mental disorders.

**CONCLUSION**

The prevalence of ID/IDD is around 1–3%, and co-occurring mental ill-health is around 40%, with persistent mental ill-health around 30%. The burden of mental ill-health in ID/IDD is comparable with that of schizophrenia. Currently, only one in 10 youth with ID/IDD with comorbid mental disorder receive specialized mental health services. In reconciling neurodevelopmental and lifespan approaches in classification of psychopathology, both the DSM-5 and the ICD-11 emphasize adaptive functioning as measures of ID/IDD severity. With improved child survival and life expectancy, this approach will better identify at-risk youth and offer policies for support not only in high income but across low and middle-income country or resource poor settings.

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Conflicts of interest

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REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest


The chapter provides a comprehensive compendium summarizing changes from DSM-IV-TR to DSM-5, associated features, comorbidity, epidemiology, etiology, and pathophysiology of ID/IDD.


Among simplex ASD cases, the proband IQ was negatively associated with de novo loss of function mutation rate and positively associated with family history of neuropsychiatric disease.


The current estimates of ASD prevalence fail to take into account the impact of comorbidity with ID/IDD, and epilepsy, part of the 2000–2011 US special education enrollment data. 33.1% increase in ASD prevalence in special education was potentially because of recategorization from frequently comorbid ID/IDD.


The latest estimates from the GBD address both increase in life expectancy and additional life associated with good health. Among individuals with disability evidence such as there is suggests that years of life expectancy gained are not necessarily lived healthily.


The study highlights the improvement in childhood survival and low rate of competing mortality from infectious diseases in Sub-Saharan Africa and need to focus research priorities on neurodevelopmental disorders and ID/IDD.


The study highlights the need for equal consideration for neurodevelopmental and mental health disorders under the broader noncommunicable diseases framework that includes cardiovascular, cancer, respiratory, and diabetes.


Multiple physical and mental health burdens in individuals with ID/IDD are greater and occur at a much earlier age, increases with age and is highly prevalent at all ages.


The comparative study showed that radiologically isolated cognitive deficits versus clinical isolated syndrome were present regardless of the presence of risk factors for a latent demyelinating event.

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Individuals with ID/DD receive care for a distinct range of mental disorders and experience uncertainty regarding their diagnosis. Specific allocation of services and resources is needed.