This overview reviews the evolution of the definition and diagnostic criteria of autism spectrum disorder (ASD). The author starts to introduce the work on early infantile autism by Leo Kanner and the work on autistic psychopathy by Hans Asperger. Then, he describes how infantile autism is defined in ICD-9-CM, and pervasive developmental disorders in DSM-III and DSM-III-R, how autistic disorder and Asperger’s disorder as subtypes of pervasive developmental disorders in DSM-IV, as well as how ASD as a single category is listed in DSM-5. With all those background information, the author warns the impacts of DSM-5 ASD on future studies of ASD epidemiology and genetics in Taiwan. Overall, it seems that the implementation of DSM-5 ASD may cause more negative results than provides positive influences. Investigators of ASD in Taiwan must be mindful of the potentially negative impacts caused by the DSM-5 ASD.

Key words: DSM-IV, ICD-10, autism spectrum disorder, Asperger’s disorder


Introduction

To facilitate validation of psychiatric disorders, Robins and Guze [1] proposed a process which included the following phases: clinical descriptions, laboratory studies, follow-up studies, and family studies. The evolution of the American Psychiatric Association’s (APA) Diagnostic and Statistical Manual of Mental Disorder (DSM) has closely followed such process. Initially the DSM was developed for psychiatrists who were interested in describing and understanding the frequency with which mental illnesses developed in our society. In 1980, the DSM-III [2] moved from a descriptive or conceptual approach to an operationalized, criteria-defining approach to enable clinicians to make diagnoses based on whether a patient’s symptoms matched the diagnostic criteria. The DSM-III also intended to establish a higher degree of diagnostic consistency or reliability within the psychiatric community. The expectation of DSM-III and subsequent DSM-III-R [3], DSM-IV [4], and DSM-IV-TR [5] was that DSM-based research would identify the underlying etiologies of the disorders included in the manuals, which would allow greater refinement of the criteria and ultimately their validation by the biologi-
cal measures and etiologies which in turn can lead to specific treatments and even prevention or cures. But from *DSM-III* to *DSM-IV-TR*, the progress of research has not led to the definitive identification of etiologies or the validation of proven biological measures to define the mental disorders. Now *DSM-5* has been developed and officially launched in May 2014 [6]. This overview focuses only on how and what impact the new *DSM-5* would have on the autism spectrum disorder (ASD).

### Evolution of Definition and Diagnostic Criteria of Autism Spectrum Disorder

Before discussing the impact on the ASD by the newly published *DSM*, it is necessary to review the history of the changes of the definition and diagnostic criteria of ASD over the years.

**Leo Kanner’s early infantile autism**

In 1943, Leo Kanner [7], published his now classic paper, “Autistic Disturbance of Affect Contact,” which described a group of 11 physically normal children with a previously unrecognized disorder. He noted many characteristic features in these children, such as an inability to develop relationships with people, extreme aloofness, a delay in speech development, and non-communicative use of speech. Other features included repeated simple patterns of play activities and islets of ability. He described these children as having “come into the world with innate inability to form the usual, biologically provided affective contact with people” [7, p. 250].

Despite the variety of individual differences that appeared in the case descriptions, Kanner believed that only two features were of diagnostic significance: autisticaloneness and obsessive insistence on sameness. He adopted the term early infantile autism to describe this disorder and called attention to the fact that its symptoms were already evident in infancy.

**Hans Asperger’s autistic psychopathy**

Hans Asperger was also born and educated in Austria. He was trained as a pediatrician but was later appointed as the director of the Unit for Special Education at the Children’s Hospital. In 1944, after more than a decade of working at the hospital, he described four boys, aged 6 to 11 years, in his German postgraduate thesis, “Die Autistischen Psychopathen im Kindesalter” (Autistic Psychopathy in Childhood) [8].

He noted that all his cases exhibited autistic withdrawal, a symptom usually seen in schizophrenic patients. Asperger was not aware of Kanner’s work and the paper published in 1943. Both Kanner [7] and Asperger [8] independently used Bleuler’s [9] earlier term “autism” to describe the core clinical feature of their disorders. But Asperger did not consider his newly discovered disorder a form of psychosis. In fact, he appears to have used the term “psychopathy” to describe a personality disorder, consistent with the meaning of the word in German, since, while discussing the paper, he stated that those patients suffered “with the type of personality disorder presented here.”

According to Asperger, individuals with autistic psychopathy usually began to speak at approximately the same time as children without this disorder. A full command of grammar was acquired sooner or later although some children showed difficulty in using pronouns correctly. But the content of speech was usually abnormal and pedantic and consisted of lengthy disquisitions on favorite subjects. Often a word or phrase was repeated over and over in a stereotyped fashion.
Other features he described were impaired two-way social interaction, totally ignoring demands of the environment, repetitive and stereotyped play, and isolated areas of interests. Asperger observed these children talking back at teachers, sometimes verbally abusing and hitting other children, and lashing out at objects. Some of them seemed to gain pleasure from their actions with no regard for the feelings of others or the consequences of their actions. Asperger believed that the condition was never recognized in infancy and early childhood and that those with the syndrome had excellent, logical abstract thinking and were capable of originality and creativity in chosen fields. The case histories also indicated the presence of developmental delay and/or social and behavioral difficulties from an early age.

Asperger subtly changed his descriptions of his syndrome over the years, perhaps affected by the opinions of other authors. In his later paper [10], he emphasized the high intelligence and special abilities in areas of logic and abstraction, whereas, in 1944, he had specified that his syndrome could be found in people of all levels of intelligence, including those with mental retardation. Asperger’s work remained relatively unknown in English-speaking countries until 1981 when Lorna Wing, a British psychiatrist, published an influential review of the topic and added a series of her own [11].

Infantile Autism in ICD-9-CM and Pervasive Developmental Disorders in DSM-III and DSM-III-R

Despite Kanner’s [7] and Asperger’s [8] clear elucidation of apparently new disorders, both early infantile autism and autistic psychopathy were not included in the Diagnostic and Statistical Manual of Mental Disorders (DSM), 2nd Edition [12]. Although in DSM-II diagnostic information for childhood schizophrenia, there were a number of symptoms similar to that being described as features of Kanner’s syndrome and Asperger’s disorder (e.g., autistic, atypical and withdrawn behavior” (p. 35), they were not equivalent to the diagnostic features of Kanner’s syndrome and Asperger’s disorder.

Infantile autism first appeared in DSM-III and ICD-9-CM [13]. Both the diagnostic systems had similar definitions and diagnostic criteria for infantile autism. But they differed in the way they conceptualized the disorder. In ICD-9-CM, infantile autism was classified as a subtype of “psychoses with origin specific to childhood,” whereas in DSM-III, infantile autism was viewed as a type of pervasive developmental disorders (PDDs) (defined as a group of severe, early developmental disorders characterized by delays and distortions in the development of social skills, cognition, and communication).

In DSM-III, the diagnosis of infantile autism required that the features associated with infantile autism (i.e., social problems, communication difficulties, and bizarre behavior) be present within the first 30 months of life. A childhood-onset PDD subtype was also included where symptoms appeared after 30 months but before 12 years of age, and did not meet all the symptoms for infantile autism. Thus, DSM-III covered the major areas of developmental concern first described by Kanner [7], but allowed for later development and for a residual state.

When DSM-III was published in 1980, Asperger’s disorder was unknown in the English literature. Hence, DSM-III did not include Asperger’s disorder as a subtype of PDD. However, when DSM-III-Revised appeared in 1987, Asperger’s work was fairly well-known to
professionals in the field of PDD in European countries, but not in the United States. Wing [11] suggested that Asperger’s disorder be considered as a part of the “autistic continuum.” She believed that Asperger’s disorder could be a mild variant of autism. DSM-III-R adopted Wing’s [11] view of Asperger’s disorder and did not offer any specific definition and diagnostic criteria for it.

On the other hand, empirical data published after 1980 could not find any significant differences (except age at onset) between individuals with infantile autism and those with childhood-onset PDD. In DSM-III-R, the category childhood-onset PDD was eliminated. In addition, it was found to be difficult to differentiate between atypical PDD and residual infantile autism. The DSM-III-R Pervasive Developmental Disorders Work Group therefore decided to take a combining (lumping) approach and to include only two subcategories under PDDs: autistic disorder (roughly corresponding to infantile autism) and PDD not otherwise specified (PDDNOS). Under such a system, many cases with features of Asperger’s disorder or cases with disintegrative forms were diagnosed as having either an autistic disorder or a PDDNOS.

Although the concept of PDDs was retained in DSM-III-R, the diagnostic criteria for autistic disorder were revised considerably. The DSM-III criteria were descriptive, whereas the menu like scheme of DSM-III-R criteria required the presence of a minimum number of criteria in each of the three cardinal areas of deficits. The revised criteria were much more concrete, observable, and operational than those in DSM-III. The revised criteria did not require raters to determine subjectively whether a “pervasive impairment” or a “gross deficit” was present; hence, clinicians no longer hesitated to use the diagnosis of autistic disorder in older and higher-functioning autistic individuals. DSM-III-R broadened the diagnostic concept of autism from DSM-III, allowing for the gradation of behavior seen in autistic individuals.

**Autistic disorder and Asperger’s disorder as subtypes of DSM-IV PDDs**

After the publication of DSM-III, reports suggested that other developmental disorders such as Asperger’s disorder [11], Rett’s disorder [14], and disintegrative psychosis [15] should also be considered as separate subgroups of PDDs. But the DSM-III-R Work Group on Pervasive Developmental Disorders did not believe that there was sufficient evidence for the taxonomic validity of the additional subgroups of PDDs to justify the establishment of separate diagnostic categories, preferring instead pervasive developmental disorder not otherwise specified (PDDNOS). This decision generated the concern that further research on the validity of the subtypes of PDDs would become virtually impossible if these disorders were grouped together [16].

DSM-IV [4] and ICD-10 [17] diagnostic schemes continue to adopt the term pervasive developmental disorders and include five subcategories: (A) autistic disorder (AD), (B) Asperger’s disorder (AspD), (C) Rett’s disorder, (D) childhood disintegrative disorder, and (E) PDDNOS (including atypical autism). DSM-IV and ICD-10 also offer operational diagnostic criteria for all the subtypes of PDDs except PDDNOS. The DSM-IV diagnostic criteria for autistic disorder resemble those of DSM-III-R, but the total number of diagnostic criteria has been reduced from 16 to 12, and the required minimum number for a diagnosis of autistic disorder also has been reduced from 8 to 6. These changes were made to facilitate the use of the criteria by clinicians while the diagnostic validity and reliability are maintained at a high level.
The concept of PDDs in *DSM-IV* adopts a “splitters” approach. It supports the taxonomic validity of each subtype and aims to facilitate research in the sub-classification of these disorders. Although the *DSM-IV* diagnostic criteria for PDDs are based on a well-designed multisite field trial study in which 977 patients participated [18], it is expected that these criteria will not satisfy everyone and they will be revised when improved understanding and further knowledge are gained to support the taxonomic validity of each subtype of the newer edition of *DSM*.

During the two decades since the publication of the ICD-10 [17] and the *DSM IV* [4], both clinicians and researchers, in various settings, have used the subtypes of PDD to describe children and adults with a range of social and other deficits. More than 500 studies of Asperger’s disorder alone (including about 150 comparative studies of AspD and high function autism (HFA)) have been published. However, the debate has continued between the “splitters” and the “lumpers,” with the latter maintaining that AD and AspD lie on a “continuum” with AspD at the less impaired end.

### DSM-5 autism spectrum disorder as a single category

In 2007, the American Psychiatric Association formed a Work Group on Neurodevelopmental Disorders to review *DSM-IV* PDDs and to develop a new definition and diagnostic criteria or to replace the PDDs in *DSM-5*. The Work Group concluded that there was sufficient evidence to replace the term “PDDs” with “autism spectrum disorder (ASD)” and to subsume Asperger’s disorder, childhood disintegrative disorder (CDD), and PDDNOS into the overarching category of ASD. The proposal asserted that symptoms of these three disorders represented a continuum from mild to severe of autism, rather than a simple yes or no diagnosis of a specific disorder. The Work Group also proposed to remove Rett’s disorder from *DSM-5’s* ASD category. The APA *DSM-5* Committee accepted the proposed change, the discrete disorders that formerly included in PDDs (e.g. autism, Asperger’s disorder, PDDNOS, and CDD) were eliminated and all were absorbed into a single category: autism spectrum disorder [6].

The Work Group proposed to have diagnostic criteria that included: A. persistent deficits in social communication and social interaction across multiple contexts; and B. restricted, repetitive patterns of behavior, interests, or activities. There are three symptom groups under diagnostic criteria A (social-communication domain); and four symptom groups under diagnostic criteria B (restricted-repetitive domain). The proposed *DSM-5* ASD required that all three symptom criteria under social-communication domain and at least two symptom criteria under restricted-repetitive domain must be present to be endorsed as having an ASD.

For unknown reason, the officially published *DSM-5* ASD does not specifically require any minimal number of the symptom criteria under diagnostic criteria A (i.e., social-communication domain) must be present to qualify for a diagnosis of *DSM-5* ASD while it specifically requires “at least two” symptoms under diagnostic criteria B (i.e., restricted-repetitive domain) must be present to qualify for a diagnosis of *DSM-5* ASD [6, page 50]. Although many clinicians and investigators assume that all three symptoms are required, but some have argued that this is unclear [19]. Some professionals in the field of ASD even consider this as a “major” flaw of *DSM-5* ASD (www.huffingtonpost.com/allen-frances/two-fatal-technical-flaws_b_3337009.html?view=screen)
The other decision by DSM-5 ASD that also has been considered as a “major” flaw (www.huffingtonpost.com/allen-frances/two-fatal-technical-flaws_b_3337009.html?view=screen) is that at the end of the criteria set of ASD, a note is attached which states “individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger’s disorder, or pervasive developmental disorder not otherwise specified should be given the diagnosis of autism spectrum disorder” [6, page 51]. This statement may be interpreted by many clinicians/raters as “free to choose” how to define and diagnose ASD. Those cases with “mild” autism who would not qualify for DSM-5 ASD under “all three symptom criteria” rule would qualify for DSM-5 ASD under the “note” rule.

As Frances [20] has pointed out that “DSM-5 has essentially made it clinician’s choice how to define and diagnose autism spectrum disorder. Some will require one item from criterion A; others two; yet others three; and some will chuck DSM-5 altogether and use the very different definitions that are contained in DSM-IV.”

These are the reasons for expecting future inconsistent reports of prevalence rates of ASD by various groups of investigators “discretionally” using DSM-5 ASDs “loose” diagnostic criteria.

Impact on Epidemiological Study of Autism Spectrum Disorder in Taiwan

Impact on finding a true and consistent prevalence of ASD in Taiwan

A recent extensive and comprehensive review of the prevalence of ASD between 1966 and 2014 (unpublished manuscript of LY Tsai) shows that there are three epidemiological studies of ASD in Taiwan [20-22]. As shown in Table 1, one study [20] investigated AD and two studies [21, 22] studied ASD. The prevalences were determined based on DSM-IV, DSM-IV-TR, or ICD-10. Although there are only two studies of ASD prevalence in Taiwan, median values of ASD reported by the two Taiwanese studies are similar (Table 1).

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Cited reference</th>
<th>Diagnostic system</th>
<th>Studied population</th>
<th>Age (years)</th>
<th>Gender ratio M/F</th>
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M, male; F, female, AD, autistic disorder; ASD, autism spectrum disorder
§ Median value

Table 1. Published studies of Autism Spectrum Disorder in Taiwan
So far, there has no study of ASD prevalence in Taiwan based on DSM-5 ASD. As described above, the investigators plan to study the ASD prevalence in Taiwan need to make it clear which “diagnostic system/how many symptom groups are required under Criteria A” is being used to ascertain the prevalence of ASD in Taiwan. Such an approach would help readers of future published reports to appreciate the reported discrepancies.

**Impact on Genetic Studies of Autism Spectrum Disorder in Taiwan**

**Impact on finding potential genes for ASD**

Bespalova and Buxbaum [23] suggested that family studies and several genome-wide linkage analyses supported the hypothesis of complex inheritance of ASD with involvement of as many as 10-100 genes of moderate effect. A decade later, Iossifov et al. [24] estimated between 350 and 400 autism susceptibility genes have been identified and the number is still counting. There are many genetic studies of ASD, concluding that ASD is a heterogeneous group of neurodevelopmental disorders with heterogeneous genetic etiologies [26].

So far, there has no published genetic study of ASD based on Taiwan population. The future challenges faced by ASD investigators include high possibility of having heterogeneous subjects in the studies due to the use of broad and loose selection criteria (i.e. DSM-5 ASD) and using a diagnostic system (i.e. DSM-5 ASD) that has many ‘flaws” allowing investigators “discretionally” use the DSM-5 ASD diagnostic criteria [6].

AS the new DSM-5 ASD will exclude many mild and borderline cases with severe language/speech deficits because these cases would be diagnosed as having “social communicative disorders.” The future genetic study of ASD may reduce the number of potential “ASD genes” that are also being identified as the “potential genes” for language disorders (e.g., CNTNAP2 gene).

The “miss the cut” cases may also include many cases with AspD and co-morbid mood disorders as described by Asperger [8] that many of his cases had “most severe tantrum,” “serious rows,” and “for days they may cry desperately.” The field of PDD/ASD has just begun to appreciate the mood problems/disorders in children and adolescents with Asperger syndrome. A recent review of the issue of Asperger syndrome and co-morbid psychiatric disorders [26] shows that as high as 70% of cases with AspD had experienced at least one episode of major depression. The “elimination” of AspD by DSM-5 ASD will impede the opportunity of further studying of such shared genes for both ASD and mood disorder.

Future investigators of ASD genetics in Taiwan should be mindful of these potential impacts caused by using DSM-5 ASD to select the subjects and should plan ahead more appropriate study methods that would minimize such impacts.

**Conclusion**

It is quite clear that whenever there is a major change of mental health diagnostic system, it will bring with enormous impacts on many areas relating to mental health. The present review addresses the impact of the newly launched DSM-5 ASD. With limited space, the present overview focuses only on two areas: ASD epidemiology and genetics of ASD.

All previous studies based on DSM-IV/DSM-IV-TR or ICD-10 PDD, or non-official term of ASD, used various definitions and inclusion criteria which result the broad range of prevalences of PDD/ASD (unpublished manuscript of L. Y. Tsai).
In the future, whatever prevalences obtain by various research groups using “DSM-5 ASD” not only cannot be used to compare with previously reported prevalence rates due to very different definitions of ASD were used, it most likely will produce inconsistent prevalences due to the reason described earlier.

On the other hand, the DSM-5 ASD Work Group members had argued that one of the strengths of the DSM-5 ASD would be its improved “utility” (i.e., more patients would be taken care) [28]. But the review by Tsai (unpublished manuscript) notes that several recent studies that compared the utility of DSM-IV/DSM-IV-TR ASD and the proposed DSM-5 ASD (i.e., all three symptom criteria under social-communicative domain must be present), and reported that about 9% to 54% with a median of 33%, of DSM-IV PDD/ASD cases did not qualify for DSM-5 ASD.

Overall, the mildly impaired (or the higher functioning) end of the autism spectrum has significantly “missed” cases [28]. If future clinicians and researchers in Taiwan require that all three symptom groups under diagnostic criteria A (i.e., social-communicative domain) must be present to qualify for a diagnosis of DSM-5 ASD, it is expected that about one third of individuals who would qualify for a PDD/ASD diagnosis based on DSM-IV/DSM-IV-TR or ICD-10 would be missed according to the DSM-5 ASD criteria.

Learning from last two decades’ research experiences, the field of ASD genetic study is now calling for a need to reduce the heterogeneity of the ASD population under study by subgrouping individuals according to clinical phenotypes, specific traits or even comorbidities, which has been demonstrated to improve logarithm of the odds (LOD) scores in genome-wide linkage analyses [25]. Such an approach may lead to identifying genes that are unique to subtypes of disorders.

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References


