Received: 3 September 2024 | Revised: 11 December 2024 | Accepted: 13 December 2024

DOI: 10.1002/alz.14525

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE

Prevalence of idiopathic normal pressure hydrocephalus in older adult population in Shanghai, China: A population-based observational study

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Funding information
Foundation of Shanghai Municipal Health Commission, Grant/Award Numbers: 201740003, 20184Y0098, 202340152; Beijing Natural Science Foundation, Grant/Award Number: 7202237; National Natural Science Foundation of China, Grant/Award Number: 81771816; Investigator Initiated Research Projects, Grant/Award Number: H2022003; Key

Abstract

INTRODUCTION: Idiopathic normal pressure hydrocephalus (iNPH), a condition that primarily affects the elderly, has an unclear prevalence rate in China.

METHODS: A cross-sectional survey involving 1491 seniors aged 60 and above in Shanghai was conducted. Clinical symptoms and brain imaging data were collected for the diagnosis of suboptimal probable iNPH (s-probable iNPH). The crude prevalence was calculated and the estimated prevalence was inferred.

RESULTS: The crude prevalence of s-probable iNPH was 3.09% and 2.62% respectively, using DESH score ≥6 and Radscale score ≥7 as the primary imaging diagnostic criteria. The estimated prevalence of Shanghai was 2.59% among people over 60 years old and it rose to 7.99% among people aged over 90, and it was estimated that 134,152 and 11,708, respectively, had s-probable iNPH among the corresponding age group.

DISCUSSION: The prevalence of s-probable iNPH fluctuates based on the radiological scoring systems and the defined thresholds employed, and it tends to rise with advancing age.

KEYWORDS
Idiopathic normal pressure hydrocephalus, prevalence, s-probable iNPH

Xuhao Fang and Xinxin Xu contributed equally.

Discipline and Special Disease Construction Project of Huadong Hospital, Grant/Award Number: ZDZB2220

Highlights

- **Significant Prevalence**: The study identified a substantial prevalence of iNPH in older adults, with rates increasing significantly with age, particularly among those aged 90–99 years and centenarians.
- **Diagnostic Approach**: The research utilized novel diagnostic methodologies by integrating the DESH score or Radscale score with stringent clinical symptoms, providing a closer approximation to the true prevalence of iNPH.
- **Gender Disparity**: A marked gender difference was observed, with the prevalence of iNPH being significantly higher in males compared to females across all age groups.
- **Clinical Implications**: The findings underscore the importance of considering iNPH in the differential diagnosis of dementia, particularly among older male patients presenting with cognitive impairment and gait disturbances.
- **Public Health Impact**: The estimated number of s-probable iNPH patients in Shanghai highlights the need for increased awareness and better management strategies for this underdiagnosed condition in the aging population.

1 | BACKGROUD

Idiopathic normal pressure hydrocephalus (iNPH) refers to hydrocephalus with imaging findings of cerebral ventricle enlargement, clinical symptoms of the Hakim triad (gait disturbance, cognitive dysfunction, and urinary incontinence), and normal cerebrospinal fluid (CSF) pressure as measured by lumbar puncture, which is more common in the older adult population.[1–5] The symptoms caused by iNPH could largely be reversed by CSF shunting surgery[6,7] and the timely and adequate iNPH treatment had been proved to be cost-effective.[8] However, this disease has been ignored by both lay people and medical staffs for a long time, and the true prevalence of iNPH is intriguing as the published data varies widely. For example, it ranged from 21.9/100,000 in a Norwegian study[9] to 8.9% in a Swedish study[10] because of the inconsistency of the iNPH definitions, the differences between the populations sampled, and the differences in the methodological approach toward the populations in question.[11]

The different iNPH definitions of "confirmed/definite iNPH", "probable iNPH", and "possible iNPH" had been adopted previously. The diagnosis of confirmed/definite iNPH was directly based on favored results after the CSF shunting operation and the diagnosis of probable iNPH was based on favored results of a Tap Test according to either 2005 International[3] or 2012 Japanese iNPH guidelines.[4] Therefore, the prevalence of confirmed/definite iNPH[12–14] or probable iNPH[9] was easily underestimated in large population-based epidemiological research, because it was almost impossible to get every participant shunted or punctured. It was also unfortunate that the possible iNPH adopted in many studies[15–18] was prone to overestimate the true prevalence.

To obtain the prevalence closer to probable iNPH in the absence of lumbar puncture, the Japanese iNPH guideline identified that disproportionately enlarged subarachnoid space hydrocephalus (DESH) was the characteristic morphological sign of iNPH and thus recommended the definition of "possible iNPH with MRI support" in the population-based epidemiological study.[4] However, it may underestimate probable iNPH, because only about 64% of the surgically treated iNPH patients were DESH positive,[19] or overestimate probable iNPH, because people with DESH may not have any clinical symptoms.[20,21]

Recently, a combination of imaging indicators, including ventricular enlargement, cerebral convex tightening, Sylvian fissure widening, callosal angle, focal sulcus enlargement, periventricular edema, and temporal horn enlargement, has been used to evaluate ventricular enlargement of iNPH. These indicators have been synthesized into two image scoring methods: the DESH score and Radscale score. The DESH score has proven useful for the prediction of neurological improvement and prognosis after surgery for iNPH;[22] while the Radscale score has been suggested to be a valuable diagnostic screening tool.[23] Meanwhile, Andersson et al. utilized the term "modified probable iNPH (m-probable iNPH)" in accordance with the 2005 International guidelines, except for the criterion related to CSF opening pressure for probable iNPH, due to the invasive nature of lumbar puncture.[10] Based on these previous works, we propose the use of the term "suboptimal probable iNPH (s-probable iNPH)," which is defined as a diagnosis of iNPH made by applying a higher Radscale score or DESH score in conjunction with typical clinical symptoms. This diagnosis represents a case of iNPH that is closer to the probable iNPH category but lacks confirmation from a positive Tap test. In this study, we would like to take this new method integrating the typical clinical symptoms and either of the criteria Radscale score ≥ 7 or DESH score ≥ 6, as "s-probable iNPH" to estimate the prevalence of probable iNPH.

Shanghai is a city experiencing a high level of aging population, with 36.8% of the total permanent resident population aged over 60 years old at the end of 2022.[24] In addition, Shanghai has the highest average life expectancy in China, reaching 83.18 years, with a considerable

proportion of the oldest old, which facilitating the prevalence analysis of the elderly at all ages. Therefore, we calculated the prevalence of s-probable iNPH among the population aged from 60 years to centenarians in Shanghai. This information might be of great significance and representativeness for understanding the burden of iNPH in China and even in Asia.

RESEARCH IN CONTEXT

1. **Systematic review**: We conducted a comprehensive search of existing literature on the prevalence of idiopathic normal pressure hydrocephalus (iNPH) in older adults, particularly focusing on population-based studies that employed clinical and imaging diagnostic criteria. Studies were evaluated for consistency in diagnostic methods, demographic sampling, and reported prevalence rates. We identified significant variability in prevalence estimates, ranging from 0.5% to 8.9%, often due to differences in diagnostic criteria and study populations.
2. **Interpretation**: Our study presents one of the first large-scale, population-based assessments of iNPH prevalence in Shanghai, China. We found that the prevalence of s-probable iNPH, based on stringent imaging criteria, is notably higher than previously reported in other populations. These findings underscore the need for heightened clinical awareness and diagnosis of iNPH in aging populations, particularly in urbanized regions experiencing significant demographic shifts.
3. **Future directions**: Future research should focus on refining diagnostic criteria for iNPH to reduce variability in prevalence estimates. Longitudinal studies are also necessary to assess the progression of s-probable iNPH and its response to treatment over time. Additionally, studies exploring the genetic and environmental factors contributing to iNPH in different populations could provide valuable insights into the pathogenesis and prevention of this condition.

2 | METHODS

2.1 | Study design and participants

This was an observational, cross-sectional study conducted from January 2018 to July 2022. The cluster sampling method was used to select all the retired older adults aged 60 years or older from three institutions including one vocational school, one healthcare provider company, and one state-owned enterprise in Shanghai as the participants regardless of whether they had attended hospital or not. A total of 1838 people should be included, but 347 people were unwilling to undergo brain imaging examinations, so they were excluded from this study. Considering the possible bias caused by excluding these individuals, we analyzed their basic characteristics, including comparing them with the included subjects and s-probable iNPH patients. Additionally, we also included them all as unlikely iNPH for sensitivity analysis to understand a minimum prevalence rate.

This study was approved by the Ethics Committee of Huadong Hospital Affiliated to Fudan University (2018K067).

2.2 | Data collection

The participants were provided with healthcare services in Huadong hospital, including physical examinations, laboratory tests, and radiological examinations, and the participants' healthcare data and medical recordings were stored in and obtained from the electronical systems of the hospital. The brain imaging data (computed tomography [CT] or magnetic resonance imaging [MRI]) were retrieved via Picture Archiving and Communication System of the hospital; the demographic information and health conditions were obtained from the Electronic Heathcare Management System, and medical data were retrieved from the Electronic Medical Case Management System (if any). In addition, we interviewed the participants with an Evans index (EI) score greater than 0.3 face to face or via phone, and/or consulted with their family members, caregivers, healthcare service providers, and medical practitioners for their clinical symptoms especially focused on the gait disturbance/balance dysfunction, dementia/memory loss, urinary dysfunction or incontinence. [3,4]

2.3 | Outcomes

1. Crude prevalence of s-probable iNPH in the sampled population: It was calculated by dividing the number of s-probable iNPH by the number of people being observed.
2. Estimated prevalence of s-probable iNPH in Shanghai: It was calculated with reference to the crude prevalence of each age and gender group in the sampled population and the population constitutions of Shanghai. We first estimated the number of iNPH patients in each age and gender group among all elderly people in Shanghai, then summed up the number to calculate a total number of patients, and divided the total number of patients by the total number of elderly people in Shanghai.

2.4 | Diagnostic procedures

The diagnostic criteria of s-probable iNPH were mainly based on 2005 international guideline[3] and the new definition of s-probable iNPH proposed in this study. Specifically, the diagnosis must meet all the following three requirements: (1) Brain imaging data (MRI and/or CT) indicated ventriculomegaly (EI > 0.3) without secondary factors; (2) Brain imaging data indicated the Radscale score or DESH score exceeding a certain threshold (different thresholds corresponded to different diagnostic outcomes respectively); (3) With necessary symptoms:

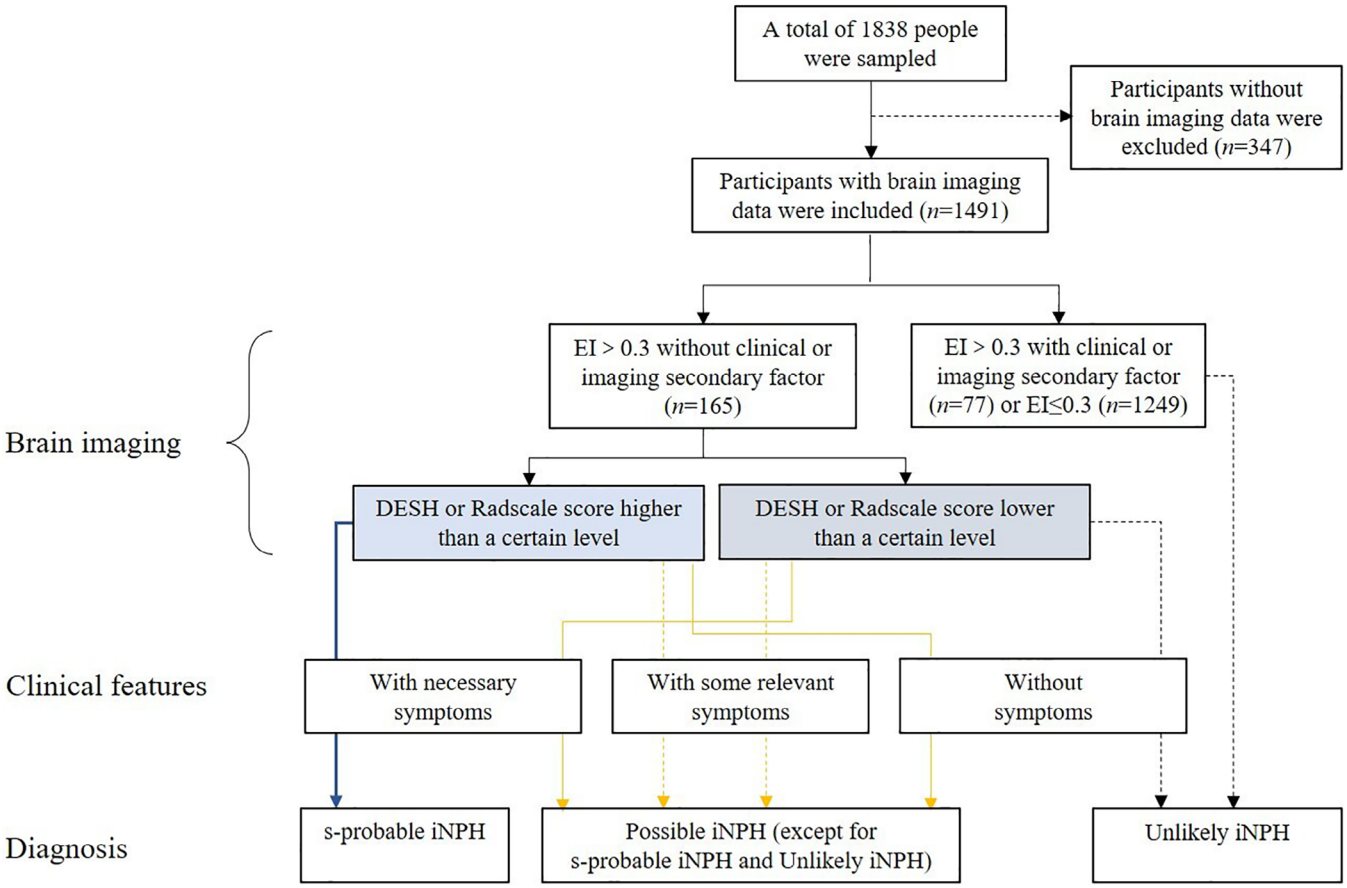

FIGURE 1 Diagnostic procedure of s-probable iNPH. The 1,491 eligible participants of retired older adults aged 60 years or older from three institutions were selected as our study object. iNPH, idiopathic normal pressure hydrocephalus.

presence of the typical Hakim triad or at least gait/balance disturbance with one of the other two symptoms of cognitive impairment or urinary incontinence/urgency. The definition of each requirement is as follows and the specific diagnostic procedure of this study is shown in Figure 1.

a) Measurement of EI

EI refers to the ratio of the maximum width of the frontal horns of the lateral ventricles to the maximal internal diameter of the skull at the same level employed in axial CT or MRI images. An EI > 0.3 indicates a pathological ventricular enlargement,[25] and the ventricular system almost never attains pathological values of EI in normal aging[26]. People with congenital hydrocephalus or obvious brain atrophy that can fully explain the enlargement of the ventricles by imaging data were excluded and those with clinical secondary factors including cerebral hemorrhage, cerebral tumor, meningitis, traumatic brain injury, or brain surgery that may introduce the formation of normal pressure hydrocephalus were further excluded after extensive medical history consultant[3,4]. EI measurements were conducted by two physicians (F.T. and Y.D.) under the supervision of a senior investigator (S.L.), and the intraclass correlation coefficient (ICC) was 0.979 ($p < 0.001$), indicating their high consistency.

b) DESH score and Radscale score

The DESH score includes five items: EI, cerebral convex tightening, Sylvian fissure widening, callosal angle, and focal sulcus enlargement. Two points for each item and 10 points in total.[22]

The Radscale score includes seven items: EI, cerebral convex tightening, Sylvian fissure widening, callosal angle, focal sulcus enlargement, periventricular edema, and temporal horn enlargement.[23] The score of each item is 1 or 2 points, and the total score is 12 points.

The raw measured data of the above items were achieved via reconstructing and analyzing the participants' DICOM data of brain imaging retrieved from PACS and reconstructed at RadiAnt DICOM Viewer (downloadable at http://www.radiantviewer.com/). Each participant's raw DICOM data were reconstructed by one neurosurgeon (X.F.) and calibrated by one radiologist (S.L.) as methods shown in Figures S1–S4, then the points were assigned to each item according to the corresponding rules.[22,23] Both the neurosurgeon and the radiologists were blinded to the assessment of the participants' clinical symptoms.

c) Clinical symptoms

The clinical symptoms were evaluated by the neurologist (L.Z.) using iNPH Grading Scales (iNPHGS),[4,27] which included three domains of

gait disturbance, cognitive dysfunction, and urinary incontinence. The grades of the three domains were scored separately and the clinical symptoms were divided into three situations on this basis: (1) With necessary symptoms: the necessary condition for s-probable iNPH, referring to the presence of the gait disturbance (grade 1–4) and at least one of the cognitive dysfunction (grade 1–4) and urinary incontinence (grade 1–4). (2) Without symptoms: the necessary condition for unlikely iNPH, referring to the absence of all three domains. (3) With some relevant symptoms: referring to symptoms other than the above two situations. The neurologist who conducted the evaluation was blinded to the participants' DESH score or Radscale score to ensure the objectivity of the evaluation.

2.5 | Statistical analysis

SPSS 22.0 software was used for the statistical analysis. Normality test was conducted for all continuous variables, and they were expressed as the mean and standard deviation ($X \mp SD$) for normal distribution data and median and interquartile range (IQR) for non-normal distribution data respectively; the categorical variables were presented as *n* (%). For the continuous variables, the *t*-test was used for the statistical analysis of normal distribution data and Wilcoxon nonparametric test for non-normal distribution data; for the categorical variables, the χ^2 test or Fisher's exact test was used for the statistical analysis of unordered categorical data and Wilcoxon nonparametric test was used for two groups of ordinal categorical data. A two-tailed *p*-value < 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Basic characteristics and brain imaging information

A total of 1491 participants were included in the study, ranging from 60 to 103 years old (median = 79, IQR = 88–69), and the proportion of male was 64.4%.

Among the research subjects, 242(16.23%) had ventricular enlargement (EI > 0.3), but 77 of them were identified with clinical or imaging secondary factors through further brain imaging analysis and interviews, including 20 cases with cerebral vascular diseases (2 cases of cerebral lobe hemorrhage, 2 cases of basal ganglia hemorrhage, 1 case of arteriovenous malformation hemorrhage, 1 case of aneurysmal subarachnoid hemorrhage, 2 cases of traumatic cerebral hemorrhage, 7 cases of cerebral lobe infarction, 2 cases of cerebellar infarction, 2 cases of basal ganglia infarction, and 1 case of brainstem infarction).

The proportion of EI > 0.3 in male was higher than that in female (20.31% vs. 8.85%, $p < 0.001$), and it increased with age (1.56% in 60–69 age group vs. 54.55% in 100–104 age group). Furthermore, for the proportion of EI > 0.3 without secondary factors, it was also higher in male than that in female (13.96% vs. 5.84, $P = 0.003$) and increased with age (1.30% in 60–69 age group and 36.36% in 100–104 age group). The DESH score and Radscale score of patients without secondary factors were higher than those with secondary factors ($p < 0.05$) (Table 1).

3.2 | Clinical symptoms

The 165 participants having ventricular enlargement (EI > 0.3) without any clinical or imaging secondary factors were comprehensively evaluated for clinical symptoms. As a result, 124 (75.15%) participants exhibited relevant symptoms that met the clinical requirement of s-probable iNPH, while 17 (10.3%) did not have any of the three symptoms and, thus, met the unlikely iNPH diagnostic criteria. (Table 2).

Further combining with the imaging score of these 124 participants, we finally got the number of s-probable iNPH was 81, 66, and 46 under the standard of DESH score ≥ 4, DESH score ≥ 5, DESH score ≥ 6, respectively. Similarly, it was 84, 59, 39, and 23 under the standard of Radscale score ≥ 5, Radscale score ≥ 6, Radscale score ≥ 7, Radscale score ≥ 8, respectively.

3.3 | Prevalence and distribution of s-probable iNPH

The overall prevalence of s-probable iNPH based on different DESH scoring rules was 5.43% (81/1491), 4.43% (66/1491), and 3.09% (46/1491), respectively, and it was 5.63% (84/1491), 3.96% (59/1491), and 2.62% (39/1491), respectively, when based on different Radscale scoring rules.

From the age perspective, the prevalence of s-probable iNPH increased with age, and it was 4.15%, 8.36%, and 9.09% in 80–89, 90–99, 100–104 age groups, respectively, while it was 0.26% and 0.75% in the 60–69 and 70–79 age groups, respectively, taking the diagnostic criteria of DESH score ≥ 6 as an example ($p < 0.001$).

From the gender perspective, the prevalence of men was much higher than that of women regardless of the diagnostic criteria. The prevalence was 4.17% and 1.13% in men and women, respectively, taking the diagnostic criteria of DESH score ≥ 6 as an example ($p < 0.001$), and it was 3.65% and 0.75% in men and women, respectively, taking the diagnostic criteria of Radscale score ≥ 7 as an example ($p < 0.001$) (Table 3).

3.4 | Estimation of the prevalence of s-probable iNPH in the elderly ≥ 60 in Shanghai

The number and the prevalence of s-probable iNPH in the older adults over 60 years old in Shanghai were calculated in different age and gender groups in the sample population (Table 4). On this basis, the number and the prevalence of s-probable iNPH in the older adults over 60 years old in Shanghai were estimated, and they were 134,152 and 2.59% when taking DESH score ≥ 6 as the diagnostic standard, and they were 110,961 and 2.14% when taking Radscale score ≥ 7 as the diagnostic standard (Table 5).

TABLE 1 The 1,491 participants with brain imaging data.

Paramter	EI ≤ 0.3	EI > 0.3			*p-value	**p-value	***p-value
		Total	Without secondary factors	With secondary factors			
Total, *n* (%)	1,249 (83.77)	242 (16.23)	165 (11.07)	77 (5.16)			
Gender, *n* (%)					<0.001*	0.003**	/
Male, *n* = 960	765 (79.69)	195 (20.31)	134 (13.96)	61 (6.35)			
Female, *n* = 531	484 (91.15)	47 (8.85)	31 (5.84)	16 (3.01)			
Age (years), *n* (%)					<0.001*	<0.001**	/
60–69, *n* = 385	379 (98.44)	6 (1.56)	5 (1.30)	1 (0.26)			
70–79, *n* = 398	366 (91.96)	32 (8.04)	25 (6.28)	7 (1.76)			
80–89, *n* = 410	322 (78.54)	88 (21.46)	61 (14.88)	27 (6.59)			
90–99, *n* = 287	177 (61.67)	110 (38.33)	70 (24.39)	40 (13.94)			
100–104, *n* = 11	5 (45.45)	6 (54.55)	4 (36.36)	2 (18.18)			
DESH score, median (q1,q3)	/	4 (2,5)	4 (2,6)	3 (2,4)	/	/	0.002***
Radscale score, median (q1,q3)	/	5 (4,6)	5 (4,7)	4 (3,5)	/	/	<0.001***

Abbreviations: DESH, disproportionately enlarged subarachnoid space hydrocephalus; EI, Evans index.
**p*-Value: difference of proportion of EI > 0.3 between gender and age groups.
***p*-Value: difference of proportion of EI > 0.3 without secondary factors between gender and age groups.
****p*-Value: difference between participants with EI > 0.3 without secondary factors and participants with Note: EI > 0.3 with secondary factors.

3.5 | Sensitivity analysis

The baseline characteristics of 347 subjects excluded because of having not undergone imaging examinations were analyzed. It was found that there were statistically significant differences in age and gender distribution when compared with the 1,491 study subjects and compared with the s-probable iNPH patients previously diagnosed in this study. The 347 subjects had a much lower proportion of males and were much younger (Table S1,2).

Therefore, we further assumed that the 347 subjects were not excluded and they were included as unlikely iNPH patients to calculate the prevalence. Naturally, the prevalence was lower than that previously calculated. (Table S3,4). Similarly, we estimated the number and prevalence of s-probable iNPH in the older adults over 60 years old in Shanghai based on this result, and they were 110,931 (2.14%) when taking DESH score ≥ 6 as the diagnostic standards, while they were 134,152 (2.59%) in the 1,491 participants. Their prevalence gap was getting smaller in the older age group because these people were concentrated between the ages of 60 and 79 (Table S5).

4 | DISCUSSION

In previous studies on the prevalence of iNPH, populations with coexisting disease[16,28–31] or those recruited from hospital nursing and long-term care institutions[18] were often used as subjects. This might have led to either an overestimation or underestimation of the prevalence due to the lack of representativeness of the target population. Additionally, despite several studies conducted on community populations that were well-represented and showed varying prevalence rates of iNPH ranging from 0.51% to 3.7% among those over 65 years old,[10,15,17,32,33] with rates as high as 5.9%–8.9% among those over 80 years old,[10,33,34] a common issue that persisted was the low response rate among surveyed participants. For instance, one study[17] in the Tajiri region of Japan reported a 75% response rate, while another Japanese study[20] had a response rate of 69.2%. Even a more recent study in Sweden encountered difficulties retaining participants, particularly older individuals, contributing to a low response rate.[10] Notably, many of the nonresponders in these studies, particularly those who did not undergo head CT or MRI scanning, were over 85 years old and likely suffered from iNPH-related symptoms such as gait disturbance, cognitive impairment, or other neurological defects. The exclusion of these individuals would have inevitably led to an underestimation of the true prevalence of iNPH within the population. In this study, we have made considerable efforts to obtain a population sample that is both highly representative and boasts a high response rate.

In addition to the improved population sample and the high response rate, we utilized novel methodologies by integrating the DESH score or Radscale score with stringent and typical clinical symptoms. This enabled us to determine the varying prevalence of s-probable iNPH across various radiological intensities, based on distinct score thresholds. Our approach provided us with the opportunity to evaluate which result most accurately approximated the true prevalence of iNPH. In this study, the crude prevalence of s-probable iNPH

TABLE 2 Participants with EI > 0.3 without any clinical or imaging secondary factor.

Parameter	*n*	With necessary symptoms	With some relevant symptoms	Without symptoms
Total	**165**	124 (75.15)	24 (14.55)	17 (10.30)
With DESH				
Yes	36	35 (97.22)	1 (2.78)	0 (0.00)
No	129	89 (68.99)	23 (17.83)	17 (13.18)
DESH score standard-$_1$				
≥4	93	81 (87.10)	8 (8.60)	4 (4.30)
<4	72	43 (59.72)	16 (22.22)	13 (18.06)
DESH score standard-$_2$				
≥5	73	66 (90.41)	6 (8.22)	1 (1.37)
<5	92	58 (63.04)	18 (19.57)	16 (17.39)
DESH score standard-$_3$				
≥6	48	46 (95.83)	1 (2.08)	1 (2.08)
<6	117	78 (66.67)	23 (19.66)	16 (13.68)
Radscale score standard-$_1$				
≥5	94	84 (89.36)	7 (7.45)	3 (3.19)
<5	71	40 (56.34)	17 (23.94)	14 (19.72)
Radscale score standard-$_2$				
≥6	64	59 (92.19)	5 (7.81)	0 (0.00)
<6	101	65 (64.36)	19 (18.81)	17 (16.83)
Radscale score standard-$_3$				
≥7	42	39 (92.86)	3 (7.14)	0 (0.00)
<7	123	85 (69.11)	21 (17.07)	17 (13.82)
Radscale score standard-$_4$				
≥8	24	23 (95.83)	1 (4.17)	0 (0.00)
<8	141	101 (71.63)	23 (16.31)	17 (12.06)

Abbreviation: DESH, disproportionately enlarged subarachnoid space hydrocephalus; EI, Evans index.

was 4.43% (66/1,491) and 3.09% (46/1,491) when using the DESH score ≥ 5 or DESH score ≥ 6, respectively, as the key imaging diagnostic standard. Similarly, it was 3.96% (59/1,491) and 2.62% (39/1,491), respectively, based on the diagnostic criteria of Radscale score ≥ 6 or ≥ 7. Additionally, the crude prevalence of DESH-supported iNPH was found to be 2.35% (35/1,491) in this study. Based on these data and the estimated percentage of DESH-positive iNPH from previous studies, we can reasonably infer that the prevalence rates of 2.62% (using Radscale score ≥ 7) and 3.09% (using DESH score ≥ 6) are potentially the closest approximations to the true prevalence of iNPH. These findings suggest that both the Radscale and DESH scales when applied with their respective higher thresholds, provide valuable insights into the prevalence of this condition.

The prevalence of s-probable iNPH in this study exhibited a pronounced upward trend with increasing age, mirroring findings from previous studies. Specifically, utilizing a DESH score of ≥ 6 as a diagnostic criterion, the prevalence rose markedly from 0.26% in the youngest age group (60–69) and 0.75% in the middle age group (70–79) to 4.15% in the upper age group (80–89). Strikingly, among the super-aged (90–99) and centenarian cohorts (100–103), the prevalence soared to 8.36% and 9.09%, respectively. These remarkable discoveries have delicately filled a crucial gap in our understanding of the prevalence of this disease among the elderly. In doing so, they have imparted invaluable insights that not only gently illuminate the path for public health policies but also offer subtle guidance to clinical practices pertaining to this condition, thereby enhancing our ability to manage it more effectively.

From a gender perspective, our study consistently revealed that the prevalence of the disease was markedly higher among men compared to women, regardless of the diagnostic criteria applied. This finding concurs with previous population-based epidemiological studies,[10,12,14,33,35] albeit only one of them had specifically reported a statistically significant gender difference.[35] However, a recent, large cohort study, focusing on operated iNPH patients, has now definitively confirmed a statistically significant higher prevalence in men compared to women, thereby corroborating our research findings.[5] In contrast, Alzheimer's disease (AD), a condition that can be clinically confused with iNPH, has a clear female predilection.[36]

Our study exhibited selection bias in terms of gender and age, particularly an overrepresentation of elderly participants, similar to the trend seen in the Sweden study.[33] This potential bias may have resulted in an overestimated prevalence of s-probable iNPH. Consequently, we have made adjustments to derive a more accurate estimate of the prevalence of s-probable iNPH in the older adult population in Shanghai. Following these adjustments, the estimated prevalence of s-probable iNPH is 2.14% using a Radscale score of ≥ 7, or 2.59% using a DESH score of ≥ 6. Correspondingly, the estimated number of s-probable iNPH patients in Shanghai is 110,961 or 134,152, respectively. It is noteworthy that, while s-probable iNPH cases are prevalent across a wide age range, from individuals in their 70s to centenarians, only a small proportion of these cases are currently being diagnosed and treated in Shanghai, a major metropolis and one of the most developed cities in China. These statistics may not yet be shocking enough to alarm everyone in society, but they are sufficient to capture the attention of our medical practitioners. As a medical condition that can cause dementia with the potential for reversal in some patients, iNPH has been overlooked for a long time in epidemiological studies of dementia diseases.[37–39] However, with the development of diagnostic guidelines, specific treatment options, and the increasing recognition of its distinct clinical presentation, iNPH is increasingly being recognized as a disease. Given its unique ability to cause reversible dementia, we believe that iNPH deserves a proper position in the classification of dementia diseases and should be recognized and studied more extensively within the broader context of dementia research.

This study boasts several advantages. Firstly, we adopted a reasonable diagnostic approach for s-probable iNPH to estimate the prevalence of iNPH as accurately as possible. Secondly, we conducted a cross-sectional, population-based study using cluster sampling, which ensured better representation and achieved the response rate of 81.12% and conducted a thorough analysis to reduce potential bias caused by the excluded population. Thirdly, by adjusting for age and

TABLE 3 Prevalence of s-probable iNPH by gender and age groups based on DESH score and Radscale score (*n*, [%]).

Gender	Age (years)	*N*	s-probable iNPH based on DESH score			s-probable iNPH based on Radscale score		
			DESH score ≥ 4	DESH score ≥ 5	DESH score ≥ 6	Radscale score ≥ 5	Radscale score ≥ 6	Radscale score ≥ 7
Male	60–69	172	1(0.58)	1(0.58)	1(0.58)	1(0.58)	1(0.58)	1(0.58)
	70–79	248	6(2.42)	6(2.42)	3(1.21)	5(2.02)	5(2.02)	3(1.21)
	80–89	307	26(8.47)	22(7.17)	16(5.21)	26(8.47)	21(6.84)	17(5.54)
	90–99	222	34(15.32)	26(11.71)	19(8.56)	36(16.22)	25(11.26)	14(6.31)
	100–104	11	1(9.09)	1(9.09)	1(9.09)	3(27.27)	1(9.09)	0(0.00)
	Total	960	68(7.08)	56(5.83)	40(4.17)	71(7.4)	53(5.52)	35(3.65)
Female	60–69	213	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
	70–79	150	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
	80–89	103	3(2.91)	2(1.94)	1(0.97)	3(2.91)	1(0.97)	1(0.97)
	90–99	65	10(15.38)	8(12.31)	5(7.69)	10(15.38)	5(7.69)	3(4.62)
	100–104	0	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
	Total	531	13(2.45)	10(1.88)	6(1.13)	13(2.45)	6(1.13)	4(0.75)
Total	60–69	385	1(0.26)	1(0.26)	1(0.26)	1(0.26)	1(0.26)	1(0.26)
	70–79	398	6(1.51)	6(1.51)	3(0.75)	5(1.26)	5(1.26)	3(0.75)
	80–89	410	29(7.07)	24(5.85)	17(4.15)	29(7.07)	22(5.37)	18(4.39)
	90–99	287	44(15.33)	34(11.85)	24(8.36)	46(16.03)	30(10.45)	17(5.92)
	100–104	11	1(9.09)	1(9.09)	1(9.09)	3(27.27)	1(9.09)	0(0.00)
	Total	1,491	81(5.43)	66(4.43)	46(3.09)	84(5.63)	59(3.96)	39(2.62)
*p-value			<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
**p-value			<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Abbreviation: DESH, disproportionately enlarged subarachnoid space hydrocephalus; iNPH, idiopathic normal pressure hydrocephalus; s-probable iNPH, suboptimal probable iNPH.
**p*-Value: difference of prevalence of s-probable iNPH between gender.
***p*-Value: difference of prevalence of s-probable iNPH between age groups.

TABLE 4 Prevalence of s-probable iNPH in different age and gender groups of the sample (%).

Age (years)	Male			Female			Total		
	N	Based on DESH score ≥ 6 (p11*)	Based on Radscale score ≥ 7 (p12*)	*N*	Based on DESH score ≥ 6 (p21*)	Based on Radscale score ≥ 7 (p22*)	*N*	Based on DESH score ≥ 6 (crude p1*)	Based on Radscale score ≥ 7 (crude p2*)
≥60	960	4.17 (40/960)	3.65 (35/960)	531	1.13 (6/531)	0.75 (4/531)	1491	3.09 (46/1,491)	2.62 (39/1,491)
≥65	883	4.53 (40/883)	3.96 (35/883)	417	1.44 (6/417)	0.96 (4/417)	1300	3.54 (46/1,300)	3 (39/1,300)
≥70	788	4.95 (39/788)	4.31 (34/788)	318	1.89 (6/318)	1.26 (4/318)	1106	4.07 (45/1,106)	3.44 (38/1,106)
≥75	689	5.66 (39/689)	4.93 (34/689)	255	2.35 (6/255)	1.57 (4/255)	944	4.77 (45/944)	4.03 (38/944)
≥80	540	6.67 (36/540)	5.74 (31/540)	168	3.57 (6/168)	2.38 (4/168)	708	5.93 (42/708)	4.94 (35/708)
≥85	398	7.29 (29/398)	5.78 (23/398)	92	6.52 (6/92)	4.35 (4/92)	490	7.14 (35/490)	5.51 (27/490)
≥90	233	8.58 (20/233)	6.01 (14/233)	65	7.69 (5/65)	4.62 (3/65)	298	8.39 (25/298)	5.7 (17/298)

Abbreviation: DESH, disproportionately enlarged subarachnoid space hydrocephalus; iNPH, idiopathic normal pressure hydrocephalus; s-probable iNPH, suboptimal probable iNPH.
*p11, p12: prevalence of s-probable iNPH calculated based on DESH score ≥ 6 and Radscale score ≥ 7 respectively in male; p21, p22: prevalence of s-probable iNPH calculated based on DESH score ≥ 6 and Radscale score ≥ 7 respectively in female; Crude p1, Crude p2: prevalence of s-probable iNPH calculated based on DESH score ≥ 6 and Radscale score ≥ 7 respectively in total population.

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gender, we obtained a more precise estimation of the s-probable prevalence of iNPH in the older adult population in Shanghai. Furthermore, our survey encompassed a large sample size and the broadest age span (60–103 years), enabling us to determine the prevalence of iNPH in ultra-elderly individuals aged 90–103 years. This not only fills gaps in the existing literature but also provides a scientific foundation for health administrative departments to formulate policies that cater to the needs of an aging and super-aging society.

This study is subject to several limitations. First, the precise prevalence of probable iNPH remains elusive due to the challenges associated with the lumbar puncture Tap test. Similar to other large-scale epidemiological studies, only five patients with s-probable iNPH underwent this diagnostic procedure in our study. Secondly, the study's sampling scope was limited (sampled individuals were covered by commercial insurance, were mainly non-farmers, urban-living, and had a relatively higher level of education), representing only a fraction of the total older adult population in Shanghai. Thirdly, as a cross-sectional study with a broad time frame, the disease status of participants may have evolved during the study period, introducing potential biases. Lastly, our findings on the prevalence of s-probable iNPH in a single Chinese city may not be directly comparable to other regions due to variations in timing, population characteristics, and methodological approaches employed in different studies, highlighting the need for more standardized and comprehensive research.

TABLE 5 Estimated number and prevalence of s-probable iNPH in people ≥ 60 in Shanghai, China, adjusted by gender and age.

	Male			Female			Total		
Age (years)	N1	Based on DESH score ≥ 6 (n11 = N1*p11)	Based on Radscale score ≥ 7 (n12 = N1*p12)	N2	Based on DESH score ≥ 6 (n21 = N2*p21)	Based on Radscale score ≥ 7 (n22 = N2*p22)	N1 + N2	Based on DESH score ≥ 6 (adjusted p1)*	Based on Radscale score ≥ 7 (adjusted p2)*
≥60	2,484,715	103,613	90,692	2,702,539	30,539	20,269	5,187,254	2.59 (134,152/5,187,254)	2.14 (110,961/5,187,254)
≥65	1,741,634	78,896	68,969	1,946,439	28,029	18,686	3,688,073	2.90 (106,925/3,688,073)	2.38 (87,655/3,688,073)
≥70	1,035,120	51,238	44,614	1,215,177	22,967	15,311	2,250,297	3.30 (74,205/2,250,297)	2.66 (59,925/2,250,297)
≥75	573,083	32,436	28,253	747,521	17,567	11,736	1,320,604	3.79 (50,003/1,320,604)	3.03 (39,989/1,320,604)
≥80	324,488	21,643	18,626	480,106	17,140	11,427	804,594	4.82 (38,783/804,594)	3.74 (30,053/804,594)
≥85	166,057	12,106	9598	279,866	18,247	12,174	445,923	6.81 (30,353/445,923)	4.88 (21,772/445,923)
≥90	49,076	4211	2949	97,493	7497	4504	146,569	7.99 (11,708/146,569)	5.09 (7453/146,569)

Abbreviation: DESH, disproportionately enlarged subarachnoid space hydrocephalus; iNPH, idiopathic normal pressure hydrocephalus.

*Adjusted p1 = ([n11 + n21]/[N1 + N2])*100%; adjusted p2 = ([n12 + n22]/[N1 + N2])*100.

5 | CONCLUSION

The study has revealed a substantial prevalence of s-probable iNPH, which varies depending on the radiological scoring systems and thresholds used, and significantly increases with age. These discoveries provide invaluable insights for advancing the management and treatment of iNPH in the elderly, a particularly vulnerable group. Nevertheless, further standardized and comprehensive studies are imperative to fully understand the epidemiological characteristics of iNPH nationwide.

AUTHOR CONTRIBUTIONS

Xuhao Fang, Xinxin Xu, Renling Mao, Shihong Li, Li Zhang, Yan Xing, and Jin Hu made a substantial contribution to the concept and design, acquisition of data, and interpretation of data. Xuhao Fang, Xinxin Xu, Chunyan Liu, and Renling Mao drafted the manuscript. Xuhao Fang, Yao Deng, Feng Tang, and Shihong Li performed the radiological reconstruction and data analysis. Yao Deng, Feng Tang, and Li Zhang fulfilled the clinical assessment of participants. Xuhao Fang, Shihong Li, and Renling Mao were responsible for funding the acquisition. All authors revised the article critically and approved the submitted version.

ACKNOWLEDGMENTS

We thank the participants for allowing us to survey their imaging data and clinical data, we also thank the staffs and experts involved in the study. This work was supported by the Foundation of Shanghai Municipal Health Commission (201740003, 20184Y0098, 202340152); Beijing Natural Science Foundation (7202237); National Natural Sci-

ence Foundation of China (81771816); Investigator Initiated Research Projects (H2022003); Key Discipline and Special Disease Construction Project of Huadong Hospital (ZDZB2220). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

CONFLICT OF INTEREST STATEMENT

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript. Author disclosures are available in the Supporting Information.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, and further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Huadong Hospital Affiliated to Fudan University (2018K067) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CONSENT STATEMENT

For this study, consent was not necessary as the research involved the use of anonymized and publicly available data. The data were collected and shared in accordance with established ethical guidelines and regulations, and no identifiable personal information was used or disclosed.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Fang X, Xu X, Liu C, et al. Prevalence of idiopathic normal pressure hydrocephalus in older adult population in Shanghai, China: A population-based observational study. *Alzheimer's Dement*. 2025;21:e14525. https://doi.org/10.1002/alz.14525