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## Normative visual acuity in Chinese preschoolers aged 36 to < 48 months as measured with the linear HOTV chart

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1 Title page2 Normative visual acuity in Chinese preschoolers aged 36 to < 48  
3 months as measured with the linear HOTV chart4  
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20 **Synopsis**

21       The 5th percentile of the normative uncorrected visual acuity distribution in  
22 Chinese children aged 36 to < 48 months were 20/40, which could be used as a  
23 referral cutoff to detect amblyopia cases.

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24 **ABSTRACT**

25 **Objectives** To document population-based normative data for uncorrected visual  
26 acuity (UCVA) in Chinese preschoolers aged 36 to < 48 months without any  
27 sight-affecting abnormalities and to evaluate its effectiveness for vision referral.

28 **Methods** In a population-based cohort of children in the Yuhuatai Pediatric Eye  
29 Disease Study (YPEDS), UCVA was measured by using the linear HOTV chart,  
30 followed by other ocular examinations. Reference population was defined as children  
31 without ophthalmic abnormalities or refractive error. Normative UCVA was obtained  
32 from the reference population. The UCVA referral cutoff was defined as the lowest  
33 5th percentile of the normative distribution of UCVA.

34 **Results** The analysis cohort consisted of 1606 Chinese preschoolers aged 36 to < 48  
35 months. Among them, a total of 791 children were included in the reference  
36 population. The 5th, 50th, and 95th percentiles of the UCVA distribution in the  
37 reference population were 20/40, 20/32, and 20/25, respectively. UCVA improved  
38 with increasing age ( $p < 0.0001$ ), but worsen if prematurity was presented ( $p = 0.041$ ).  
39 Using the 5th percentile UCVA cutoff from the reference population generated referral  
40 rates of 26.9% in the general population, and detected more than 86% of amblyopia  
41 cases.

42 **Conclusions** We propose that UCVA no better than 20/40 measured by linear HOTV  
43 chart should be a referral cutoff for Chinese preschoolers aged 36 to < 48 months.  
44 Most amblyopia cases can be identified with this age-specific and chart-specific  
45 UCVA cutoff.

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46 **Strengths and limitations of this study**

- 47 • This is a population-based study, comprising 1606 preschoolers aged 36 to < 48  
48 months.
- 49 • Normative uncorrected visual acuity was obtained from 791 children without any  
50 sight-affecting abnormalities among the population-based cohort.
- 51 • The linear HOTV chart, which was recommended when measuring visual acuity  
52 in 3- and 4-year-old children, was used in the study.
- 53 • Only children with suspected abnormalities underwent cycloplegic refraction,  
54 which may impact the detection of sight-affecting refractive errors.
- 55 • 11.1% children were not testable when doing the HOTV test and were excluded  
56 from the analysis.
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## 58 INTRODUCTION

59 Accurate and timely determination of visual acuity (VA) is the basis of clinical  
60 management of many ocular conditions in children.<sup>1</sup> The American Academy of  
61 Pediatrics (AAP) recommended that objective evaluation of VA be initiated by 3 years  
62 of age.<sup>2</sup> Unfortunately, because of the different charts used in different countries and  
63 the developing visual and cognitive systems, normative VA levels in children of  
64 preschool age are not uniform internationally.<sup>3-5</sup> This makes it difficult to accurately  
65 set referral criteria for vision screening and to effectively monitor and manage eye  
66 conditions, requiring the development of age-specific and chart-specific normative  
67 VA.

68 For ensuring measures accurately reflect what could be expected in healthy eyes,  
69 VA norms need to be established on the basis of normative data, obtained by studying  
70 reference populations of children who do not have sight-affecting ocular conditions.  
71 Normative data of this kind have been reported in the Multi-Ethnic Pediatric Eye  
72 Disease Study (MEPEDS),<sup>6</sup> and the Sydney Pediatric Eye Disease Study (SPEDS).<sup>7</sup>  
73 The samples of preschool children were African American and Hispanic in MEPEDS,  
74 and predominantly European Caucasian in SPEDS. Given that ethnicity and  
75 socio-economic status have potential effects on the level of VA measured,  
76 population-specific norms still need to be established for Chinese preschoolers.<sup>6, 8-9</sup>

77 In China, only the Shenzhen Kindergarten Eye Study (SKES) provided  
78 population-based normative data for VA in children 3 to 6 years old.<sup>10</sup> However, in  
79 SKES, VA was measured by the Early Treatment Diabetic Retinopathy Study  
80 (ETDRS) Tumbling E chart, which is commonly used in children aged 5<sup>1</sup>/<sub>2</sub> years  
81 and older but too difficult for younger children to complete.<sup>11</sup> The HOTV or Lea  
82 Symbols chart tests were recommended by AAP when measuring VA in 3- and  
83 4-year-old children.<sup>12</sup>

84 This report aims to provide the population-based normative distribution of  
85 monocular uncorrected VA (UCVA) and interocular differences (IOD) in UCVA in  
86 Chinese children aged 36 to < 48 months by using the linear HOTV chart, and explore

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4 87 appropriate UCVA criteria for referral of cases of suspected amblyopia and refractive  
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6 88 error. This analysis is part of the Yuhuatai Pediatric Eye Disease Study (YPEDS).  
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89 **METHODS**

90 **Study population**

91 YPEDS is an ongoing prospective population-based vision screening study, with  
92 the specific aims of establishing a systematic database on refraction, visual acuity,  
93 ocular biometric parameters, ocular position and other ophthalmic measures,  
94 exploring the development rule of vision, and estimating the burden of common  
95 pediatric ocular disorders of preschool children.<sup>13</sup> All of the children, who resided in  
96 Yuhuatai District, were born between September 2011 and August 2012, and were  
97 about to enter a kindergarten in Yuhuatai District, were invited to participate in  
98 YPEDS and to undergo a further vision examination in addition to a compulsory  
99 health examination. The data presented in this paper were obtained from July 2015 to  
100 August 2015, when these children were 36 to < 48 months old.

101 This study was approved by the Ethics Committee of Nanjing Medical University  
102 and followed the tenets of the Declaration of Helsinki. Written informed consent was  
103 obtained from the parents or legal representatives of all the participating children.

104 **Ocular examinations**

105 A detailed parental interview was conducted, including questions regarding  
106 parental education level, monthly family income, employment of parent, history of  
107 pregnancy and delivery, parental history of smoking and drinking during pregnancy,  
108 and so on. Comprehensive eye examinations included distance VA, ocular alignment  
109 and motility, non-cycloplegic refractive error measurement, anterior segment  
110 examination, fundus evaluation and ocular biometric parameters.

111 Monocular distance UCVA measurements were attempted, first in the right eye,  
112 and then in the left, at 3 m by using a linear HOTV logMAR chart (GOOD-LITE,  
113 USA). A similar, standardized approach to the Amblyopia Treatment Study (ATS)  
114 HOTV VA testing protocol was adapted.<sup>14</sup> An initial screening phase determined an  
115 approximate threshold acuity, and then was followed by a first threshold  
116 determination phase, a reinforcement phase, and a second threshold determination  
117 phase. The best VA obtained from each of the two threshold phases was recorded as



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3 118 the final VA. VA scores were measured in 0.1 logMAR increments from 20/125 to  
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5 119 20/8.  
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7 120 Non-cycloplegic refraction was performed with the table-mounted autorefractor  
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9 121 (R-F10, Cannon, Tokyo, Japan), photorefractor (PlusoptiX GmbH, Nuremberg,  
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11 122 Germany) and retinoscopy. Cycloplegic refraction was performed in any of the  
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13 123 following conditions: (1) spherical equivalent refraction (SER) obtained from any of  
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15 124 the non-cycloplegic refraction measurements was  $\leq -0.50$  D in either eye,  $\geq +1.25$  D  
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17 125 in either eye, or showed a difference  $\geq 0.75$  D interocularly; (2) cylindrical diopter  
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19 126 obtained from any of the non-cycloplegic refraction measurements was  $\geq 0.75$  D in  
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21 127 either eye; (3) UCVA was  $< 20/40$  (logMAR 0.3) in either eye, or  $\geq 2$ -line IOD; (3)  
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23 128 abnormal results in the examinations of ocular alignment and motility, anterior  
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25 129 segment examination or fundus evaluation were found. Two drops of 1.0%  
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27 130 cyclopentolate (Cyclogyl, Alcon, Belgium) were instilled five minutes apart, with a  
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29 131 third drop administered 20 minutes later. Cycloplegia was then evaluated after an  
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31 132 additional 15 minutes. Cycloplegia was considered complete if a pupillary light reflex  
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33 133 was absent. If a light reflex was still detected, another drop of cyclopentolate was  
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35 134 administered, and the light reflex was evaluated again after 15 minutes. Cycloplegic  
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37 135 refraction was performed with the table-mounted autorefractor (R-F10, Cannon,  
38  
39 136 Tokyo, Japan). Subjective refraction was then assessed monocularly according to the  
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41 137 cycloplegic refraction values. The best-corrected VA (BCVA) was recorded based on  
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43 138 monocular subjective refraction, using the same protocol and VA chart as the UCVA  
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45 139 measurements.

#### 46 140 **Definitions**

47 141 The criteria of refractive errors were based on the cycloplegic refraction values:  
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49 142 myopia was defined as SER  $\leq -0.50$  D in either eye; hyperopia was defined as SER  $\geq$   
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51 143  $+2.00$  D in either eye; astigmatism was defined as a cylindrical refractive error  $\geq 0.75$   
52  
53 144 D; anisometropia was defined as an SER difference  $\geq 2.00$  D interocularly.

54 145 To be comparable with SKES, two definitions of amblyopia were also adopted in  
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56 146 the present report (Table 1): (1) the American Academy of Ophthalmology (AAO)

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3 147 amblyopia Preferred Practice Pattern (PPP),<sup>15</sup> (2) the Chinese Ophthalmology Society  
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5 148 (COS) guidelines.<sup>16</sup>  
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8  
9 **Table 1. The two definitions of amblyopia in preschoolers aged 36 to < 48 months\***

AAO Definition		COS Definition
Unilateral amblyopia	Bilateral amblyopia	Amblyopia
BCVA $\geq$ 2-line IOD	BCVA < 20/50 in either eye	BCVA $\geq$ 2-line IOD or < 20/40 in either eye

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19 \*Amblyopia risk factors should be identified when diagnosing amblyopia.

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22 151 **Inclusion and exclusion criteria**

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24 152 Only Chinese children aged 36 to < 48 months able to complete monocular  
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26 153 UCVA testing in both eyes were included in the analysis and considered as the general  
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28 154 study population. The reference population was defined as the children without  
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30 155 sight-affecting ocular conditions, including myopia, hyperopia, astigmatism,  
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32 156 anisometropia, amblyopia, strabismus, nystagmus, visual axis occlusion, or other  
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34 157 anterior segment or fundus abnormalities capable of causing visual impairment.

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36 158 **Statistical analysis**

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38 159 UCVA outcomes were recorded continuously as mean logMAR UCVA or mean  
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40 160 logMAR IOD in UCVA and dichotomously as the proportion of children achieving a  
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42 161 particular level of UCVA or IOD. The UCVA for right and left eyes in the reference  
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44 162 population were highly correlated (Pearson's correlation = 0.721,  $p < 0.01$ ), thus right  
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46 163 eye UCVA was used to report the distribution of UCVA. The UCVA cutoff for referral  
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48 164 was defined as the lowest 5th percentile of the normative distribution of UCVA.  
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50 165 Effectiveness in referral for amblyopia or refractive error using the estimated UCVA  
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52 166 cutoff was than calculated. Multiple linear regression was used to assess associations  
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54 167 of logMAR UCVA with age, gender, and other potential risk factors. All analyses  
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56 168 were performed by using SPSS 22.0 (IBM, China) and a 0.05 significance level.

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169 **RESULTS**

170 **Study population**

171 A total of 2,300 preschoolers were enrolled in this study, and 1,806 participated in  
172 the UCVA test (78.5% responses rate), among which 1,606 (88.9%) were testable in  
173 both eyes and considered as the general population. According to the definition  
174 outlined in the methods, 791 (49.3%) children were classified as the reference  
175 population. Table 2 shows the demographic characteristics of the reference and  
176 general population. Boys constituted 53.5% of the reference population and 52.5% of  
177 the general population. There was no statistically significant sex difference in the  
178 mean age of the reference population ( $P = 0.277$ ) and the general population ( $P =$   
179  $0.607$ ).

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**Table 2. Demographic and UCVA distribution of the reference and general population**

	The reference population (n=791)	The general population (N=1606)
<b>Gender, n</b>		
Male	423	843
Female	368	763
<b>Age in months, mean <math>\pm</math> SD</b>		
All	41.1 $\pm$ 3.4	41.0 $\pm$ 3.4
Male	41.2 $\pm$ 3.4	41.0 $\pm$ 3.4
Female	41.0 $\pm$ 3.3	40.9 $\pm$ 3.3

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182 **UCVA outcomes**

183 Table 3 presents the distributions of UCVA in the reference population. About 60%  
184 of the measured monocular UCVA's fell in the category of 20/32. The 5th, 50th, and  
185 95th percentiles fell in the UCVA categories of 20/40, 20/32, and 20/25, respectively.

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**Table 3. Distribution of UCVA and IOD in the reference population**

	n (%)
<b>LogMAR UCVA (Snellen equiv.)</b>	
0.6 (20/80)	1 (0.1)
0.5 (20/63)	2 (0.3)
0.4 (20/50)	6 (0.8)
0.3 (20/40)	106 (13.4)*
0.2 (20/32)	478 (60.4)*
0.1 (20/25)	170 (21.5)*
0 (20/20)	27 (3.4)
-0.1 (20/16)	1 (0.1)
<b>UCVA IOD, lines (LogMAR equiv.)</b>	
0 (0.0)	595 (75.2)
1 (0.1)	181 (22.9)
2 (0.2)	14 (1.8)
3 (0.3)	1 (0.1)

\*The 5th, 50th, and 95th percentiles fell in the UCVA categories of 20/40, 20/32, and 20/25, respectively.

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188 Age-specific and gender-specific mean logMAR UCVA levels for the right eye in  
 189 the reference population are shown in Table 4. A multivariate linear regression model  
 190 including age and gender showed that UCVA improved with increasing age ( $p <$   
 191  $0.0001$ ), but had no association with gender ( $p = 0.892$ ). Risk factors adjusted for age  
 192 and adjusted for age and gender for UCVA in the reference population are shown in  
 193 Table 5. Only prematurity was significantly associated with poorer UCVA after  
 194 adjustment for age ( $p = 0.040$ ), or adjusted for age and gender ( $p = 0.041$ ).

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**Table 4. Mean logMAR UCVA and IOD in reference generation, by age and by gender**

n	Mean UCVA (SD)	Mean absolute UCVA IOD (SD)
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<b>All</b>	791	0.19 (0.07)	0.03 (0.05)
<b>Age in months</b>			
36 to <42	438	0.19 (0.08)	0.03 (0.05)
42 to <48	353	0.18 (0.07)	0.02 (0.04)
<b>Gender</b>			
Male	423	0.19 (0.08)	0.03 (0.05)
Female	368	0.19 (0.07)	0.02 (0.05)

**Table 5. Risk factors adjusted for age and adjusted for age and gender for UCVA in the reference population**

Associated factors	Adjusted for age	Adjusted for age and gender		
	p value	$\beta$ coefficient	$r^2$	p value
Prematurity <37 weeks	<b>0.040</b>	0.082	0.032	<b>0.041</b>
Low birth weight <2500 g	0.163	0.054	0.028	0.163
Maternal smoking during pregnancy	0.770	0.012	0.023	0.758
Maternal drinking during pregnancy	0.264	-0.042	0.024	0.270
Parental tertiary education (University or College)	0.755	-0.012	0.024	0.754
Monthly family income	0.685	-0.019	0.016	0.689
Employment of one parent	0.501	-0.028	0.030	0.506
Employment of both parents	0.791	0.011	0.029	0.798

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198 75.2% children in the reference population achieved equal vision in both eyes and  
 199 only 1.9% had an IOD of two or more lines ( $\geq 0.2$  logMAR) (Table 3). Table 4 shows  
 200 mean absolute logMAR UCVA IOD in the reference population, by age and by gender.  
 201 A multivariate linear regression model including age and gender showed that absolute  
 202 UCVA IOD decreased with increasing age ( $p = 0.014$ ), but had no association with  
 203 gender ( $p = 0.227$ ).

204 The mean non-absolute logMAR UCVA IOD (right eye minus left eye logMAR  
 205 VA) in the reference population was 0.0023, with no significantly difference from  
 206 zero ( $p = 0.251$ ), indicating no influence of the order in which the eyes were tested on  
 207 UCVA.

### 208 Effectiveness of the UCVA and UCVA IOD referral cutoffs

209 Using the 5th percentile UCVA cutoff from the reference population (defined as  
 210  $UCVA \leq 20/40$ ) would generate referral rates of 26.9% (432 cases) in the general  
 211 population. Table 6 shows the effectiveness in terms of sensitivity, specificity, positive  
 212 predictive value (PPV) and negative predictive value (NPV) in referral for refractive  
 213 errors or amblyopia using the current UCVA cutoff. A total of 39.5% (301/762) of  
 214 cases with any refractive error were detected, with a specificity of 84.5%. For  
 215 amblyopia using the AAO definition, the sensitivity and specificity were 86.2%  
 216 (25/29) and 74.2% (1170/1577), respectively, which are similar to the findings when  
 217 using the COS amblyopia definition (86.7% and 74.2%).

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**Table 6. Effectiveness in Referral for Refractive Errors or Amblyopia Using the lowest 5th Percentile UCVA**

#### Cutoff Criteria

	Sensitivity, n/N (%)	Specificity, n/N (%)	PPV, n/N (%)	NPV, n/N (%)
<b>Refractive Errors</b>				
Myopia	112/319 (35.1)	967/1287 (75.1)	112/432 (25.9)	967/1174 (82.4)
Hyperopia	43/84 (51.2)	1133/1522 (74.4)	43/432 (10.0)	1133/1174 (96.5)
Astigmatism	252/518 (48.6)	908/1088 (83.5)	252/432 (58.3)	908/1174 (77.3)
Anisometropia	26/59 (44.1)	1141/1547 (73.8)	26/432 (6.0)	1141/1174 (97.2)
<b>Amblyopia</b>				
AAO Definition				
Unilateral Amblyopia	11/14 (78.6)	1171/1601 (73.1)	11/432 (2.5)	1171/1174 (99.7)
Bilateral Amblyopia	14/15 (93.3)	1173/1591 (73.7)	14/432 (3.2)	1173/1174 (99.9)
COS Definition	26/30 (86.7)	1170/1576 (74.2)	26/432 (6.0)	1170/1174 (99.7)

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4 220 When using the UCVA IOD of two or more lines as the criterion, only 4.3% (69  
5 221 cases) of the general population would be referred. According to the AAO definition,  
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7 222 this criterion detected 20.7% (6/29) of cases with any amblyopia, and 28.6% (4/14) of  
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9 223 cases with unilateral amblyopia. For amblyopia using the COS definition, 26.7%  
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11 224 (8/30) of cases with amblyopia were detected using such criterion.  
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3 225 **DISCUSSION**  
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5 226 In China, SKES was the only population-based investigation of UCVA normative  
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7 227 distribution in Chinese preschoolers before our study.<sup>10</sup> In order to be comparable  
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9 228 with SKES and also to ensure that children with sight-affecting ocular conditions  
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11 229 were excluded, we used the same stringent definition of the “reference population” as  
12  
13 230 SKES. However, the lowest 5th percentile in our reference population, falling in the  
14  
15 231 UCVA category of 20/40, was two lines better than this found in the 3-year-old  
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17 232 reference population in SKES (20/63). In addition, the 50th percentile in our reference  
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19 233 population was one line better than this in SKES (20/32 vs. 20/40). Two reasons  
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21 234 might contribute to the differences between our study and SKES. First, we measured  
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23 235 the UCVA using the HOTV chart, which is recommended and commonly used in  
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25 236 Western countries for young children,<sup>6-7, 12</sup> while SKES used the ETDRS Tumbling E  
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27 237 chart which is harder for young children.<sup>17-19</sup> Second, smaller sample size of the  
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29 238 3-year-old children (51 cases) in the reference population of SKES might have a  
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31 239 significant influence on the results of UCVA normative distribution.

32 240 We are unable to compare the mean logMAR UCVA in our study with that in  
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34 241 SKES as SKES didn't calculate this. When our mean logMAR UCVA is compared to  
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36 242 this obtained from the African American and Hispanic children without sight-affecting  
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38 243 abnormalities in MEPEDS, the mean logMAR UCVA in our reference population is  
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40 244 very close to this established in the MEPEDS 36- to 47-month-old children using the  
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42 245 ATS HOTV (0.19 vs. 0.17 logMAR).<sup>6</sup> If compared to the results obtained from the  
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44 246 European Caucasian and Asian children without sight-affecting abnormalities in  
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46 247 SPEDS, the mean logMAR UCVA in our reference population is close to one line  
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48 248 worse than this tested with the ATS HOTV in SPEDS (0.19 vs. 0.09 logMAR for  
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50 249 children aged 36 to <42 months; 0.18 vs. 0.07 for 42 to <48 months), and similar to  
51  
52 250 this tested with the linear ETDRS or HOTV logMAR chart (0.19 vs. 0.22 logMAR for  
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54 251 children aged 36 to <42 months; 0.18 vs. 0.16 for 42 to <48 months).<sup>7</sup> However, the  
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56 252 significances of such comparisons are not very clear, because that the ATS HOTV VA  
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58 253 test is quite different from the linear HOTV logMAR chart that we used, and SPEDS



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3 254 didn't specify the mean logMAR UCVA when only using linear HOTV logMAR  
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5 255 chart.

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7 256 We found improvement in UCVA with increasing age, as has been reported in  
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9 257 several studies despite different charts used.<sup>6-7, 10, 18, 20</sup> Gender was not associated with  
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11 258 UCVA both in our sample and SPEDS, opposite to that reported in MEPEDS.<sup>6-7</sup> As  
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13 259 for risk factors of UCVA, prematurity was related with worse UCVA in our reference  
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15 260 population, which was consistent with the finding in SPEDS. However, socio  
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17 261 economic status (SES) factors, such as the employment status of parents and family  
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19 262 income, which were significantly associated with UCVA in MEPEDS and SPEDS,  
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21 263 showed no associations with UCVA in our study. In addition, maternal smoking  
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23 264 during pregnancy, which was related with slightly better UCVA in SPEDS, had no  
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25 265 relationship with UCVA in our study.

26  
27 266 As the penalty for missing one amblyopia case is a lifetime disability and  
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29 267 treatment exists, the UCVA referral cutoff for amblyopia should target high sensitivity,  
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31 268 while the specificity should be high enough not to put immense load on  
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33 269 ophthalmologists.<sup>21-22</sup> The sensitivity of detecting amblyopia by using the UCVA  
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35 270 referral cutoff in our study ( $UCVA \leq 20/40$  at age 36 to < 48 months), was as high as  
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37 271 86%, and at the same time, the specificity was high enough (74.2%). On the other  
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39 272 hand, this cutoff only identified a total of 39.5% refractive errors, even though the  
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41 273 overall specificity was high (84.5%). The sensitivity in detecting myopia was not  
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43 274 good in our study (35.1%), lower than hyperopia (51.2), astigmatism (48.6%), and  
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45 275 anisometropia (44.1%). In SKES, even though a high sensitivity (83.3%) in detecting  
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47 276 myopia was observed in all 3- to 6-year-old preschoolers, it's not available to  
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49 277 calculate the sensitivity in detecting myopia in 3-year-old children because of no  
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51 278 presence of myopia in this age group. And for all refractive errors in 3-year-old  
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53 279 children in SKES, the overall sensitivity was only 8.6%. Therefore, only using the  
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55 280 UCVA cutoff as referral criterion might be difficult to detect refractive errors in  
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57 281 3-year-old children, and additional refraction examination might be necessary for  
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59 282 vision screening.

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3 283 The normative distribution of UCVA IOD in our study was consistent with that in  
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5 284 SKES, with most children achieving equal vision in both eyes. No effect of gender or  
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7 285 testing order on IOD was observed in our study, which was consistent with MEPED.  
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9 286 However, we found that absolute UCVA IOD decreased with increasing age of month  
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11 287 in our sample, which was not consistent with the findings in 30- to 72-month-old  
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13 288 children in MEPED. The reason of this difference might be that, in MEPED, equal  
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15 289 vision in both eyes in older children hid the effect of age on UCVA IOD in younger  
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17 290 children.

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19 291 When using UCVA IOD of two or more lines as the criterion, approximately 4%  
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21 292 in the general population would be referred in both of SKES and our study. The  
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23 293 sensitivity of using this criterion alone for detecting amblyopia, including unilateral  
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25 294 amblyopia, was very low in our study, similar to the results in SKES.

26  
27 295 To our knowledge, the present study is the first to provide population-based  
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29 296 HOTV-specific normative UCVA data in Chinese preschoolers aged 36 to < 48  
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31 297 months without significant refractive error or other ophthalmic abnormalities.  
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33 298 However, there are several limitations in the present study. Because that young  
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35 299 children are very afraid of using eye drops, which makes cycloplegia difficult and  
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37 300 unacceptable for parents, only children with suspected abnormalities underwent  
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39 301 cycloplegic refraction in our study. Even though not all children had refraction results  
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41 302 under cycloplegia, we adopted stringent criteria to identify children who needed  
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43 303 cycloplegic refraction, which could effectively detect sight-affecting refractive errors.  
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45 304 11.1% children were not testable when doing the HOTV test and were excluded from  
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47 305 the analysis, which may influence the normative UCVA distribution. However, the  
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49 306 testability in our study was at an average level of published reports,<sup>6, 10</sup> and difficulty  
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51 307 to increase further in young children.

52  
53 308 In conclusion, our study suggests that Chinese preschoolers aged 36 to < 48  
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55 309 months with UCVA no better than 20/40 measured by linear HOTV chart should be  
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57 310 referred for further ophthalmic examinations. Most amblyopia cases can be identified  
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59 311 with this age-specific and chart-specific UCVA cutoff.  
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5  
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9 315 **Contributors** Conceived and designed the experiments: HL, HZ, DH and QS.  
10  
11 316 Performed the experiments: HZ, DH, QS, HD, JB, JC, YW, XZ, JW and XL.  
12  
13 317 Analyzed the data: HZ, DH, QS and XC. Contributed reagents/materials/analysis  
14  
15 318 tools: HL, HZ, DH, HD, JB, JC, and XC. Wrote the paper: HL, HZ, DH, QS, XC, HD,  
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29  
30 326 **Patient consent** Obtained.

31  
32 327 **Ethics approval** The Institutional Review Board of Jiangsu Province Hospital.

33  
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36 329 **Data sharing statement** No additional data are available.  
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# BMJ Open

## Normative visual acuity in Chinese preschoolers aged 36 to < 48 months as measured with the linear HOTV chart: the Yuhuatai Pediatric Eye Disease Study

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1 Title page2 Normative visual acuity in Chinese preschoolers aged 36 to < 48  
3 months as measured with the linear HOTV chart: the Yuhuatai  
4 Pediatric Eye Disease Study5  
6 Hui Zhu<sup>1†</sup>, Dan Huang<sup>1†</sup>, Qigang Sun<sup>1†</sup>, Hui Ding<sup>2</sup>, Jing Bai<sup>2</sup>, Ji Chen<sup>2</sup>, Xuejuan  
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18 83275171.19  
20 Word count: 3700.



21 **ABSTRACT**

22 **Objectives** To document population-based normative data for uncorrected visual  
23 acuity (UCVA) in Chinese preschoolers aged 36 to < 48 months without any  
24 sight-affecting abnormalities and to evaluate its effectiveness for vision referral.

25 **Methods** In a population-based cohort of children in the Yuhuatai Pediatric Eye  
26 Disease Study (YPEDS), UCVA was measured by using the linear HOTV chart,  
27 followed by other ocular examinations. Reference population was defined as children  
28 without ophthalmic abnormalities or refractive error. Normative UCVA was obtained  
29 from the reference population. The UCVA referral cutoff was defined as the lowest  
30 5th percentile of the normative distribution of UCVA.

31 **Results** The analysis cohort consisted of 1606 Chinese preschoolers aged 36 to < 48  
32 months. Among them, a total of 791 children were included in the reference  
33 population. The 5th, 50th, and 95th percentiles of the UCVA distribution in the  
34 reference population were 20/40, 20/32, and 20/25, respectively. UCVA improved  
35 with increasing age ( $p < 0.0001$ ), but worsen if prematurity was presented ( $p = 0.041$ ).  
36 Using the 5th percentile UCVA cutoff from the reference population generated referral  
37 rates of 26.9% in the general population, and detected more than 86% of amblyopia  
38 cases.

39 **Conclusions** We propose that UCVA no better than 20/40 measured by linear HOTV  
40 chart should be a referral cutoff for Chinese preschoolers aged 36 to < 48 months.  
41 Most amblyopia cases can be identified with this age-specific and chart-specific  
42 UCVA cutoff.

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44 **Strengths and limitations of this study**

- 45 • This is a population-based study, comprising 1606 preschoolers aged 36 to < 48  
46 months.  
47 • Normative uncorrected visual acuity was obtained from 791 children without any  
48 sight-affecting abnormalities among the population-based cohort.  
49 • The linear HOTV chart, which was recommended when measuring visual acuity  
50 in 36- and 48-month-old children, was used in the study.  
51 • Only children with suspected abnormalities underwent cycloplegic refraction,  
52 which may impact the detection of sight-affecting refractive errors.  
53 • 11.1% children were not testable when doing the HOTV test and were excluded  
54 from the analysis.  
55

## 56 INTRODUCTION

57 Accurate and timely determination of visual acuity (VA) is the basis of clinical  
58 management of many ocular conditions in children.<sup>1</sup> The American Academy of  
59 Pediatrics (AAP) recommended that objective evaluation of VA be initiated by 36  
60 months of age.<sup>2</sup> Unfortunately, because of the different charts used in different  
61 countries and the developing visual and cognitive systems, normative VA levels in  
62 children of preschool age are not uniform internationally.<sup>3-5</sup> This makes it difficult to  
63 accurately set referral criteria for vision screening and to effectively monitor and  
64 manage eye conditions, requiring the development of age-specific and chart-specific  
65 normative VA.

66 For ensuring measures accurately reflect what could be expected in healthy eyes,  
67 VA norms need to be established on the basis of normative data, obtained by studying  
68 reference populations of children who do not have sight-affecting ocular conditions.  
69 Normative data of this kind have been reported in the Multi-Ethnic Pediatric Eye  
70 Disease Study (MEPEDS),<sup>6</sup> and the Sydney Pediatric Eye Disease Study (SPEDS).<sup>7</sup>  
71 The samples of preschool children were African American and Hispanic in MEPEDS,  
72 and predominantly European Caucasian in SPEDS. Given that ethnicity and  
73 socio-economic status have potential effects on the level of VA measured,  
74 population-specific norms still need to be established for Chinese preschoolers.<sup>6-9</sup>

75 In China, only the Shenzhen Kindergarten Eye Study (SKES) provided  
76 population-based normative data for VA in children 36 to 72 months old.<sup>10</sup> However,  
77 in SKES, VA was measured by the Early Treatment Diabetic Retinopathy Study  
78 (ETDRS) Tumbling E chart, which is commonly used in children aged 66 months and  
79 older but too difficult for younger children to complete.<sup>11</sup> The HOTV or Lea Symbols  
80 chart tests were recommended by AAP when measuring VA in 36- and 48-month-old  
81 children.<sup>12</sup>

82 This report aims to provide the population-based normative distribution of  
83 monocular uncorrected VA (UCVA) and interocular differences (IOD) in UCVA in  
84 Chinese children aged 36 to < 48 months by using the linear HOTV chart, and explore

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85 appropriate UCVA criteria for referral of cases of suspected amblyopia and refractive  
86 error. This analysis is part of the Yuhuatai Pediatric Eye Disease Study (YPEDS).

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87 **METHODS**

88 **Study population**

89 YPEDS is an ongoing prospective population-based vision screening study, with  
90 the specific aims of establishing a systematic database on refraction, visual acuity,  
91 ocular biometric parameters, ocular position and other ophthalmic measures,  
92 exploring the development role of vision, and estimating the burden of common  
93 pediatric ocular disorders of preschool children.<sup>13</sup> All of the children, who resided in  
94 Yuhuatai District, were born between September 2011 and August 2012, and were  
95 about to enter a kindergarten in Yuhuatai District, were invited to participate in  
96 YPEDS and to undergo a further vision examination in addition to a compulsory  
97 health examination. The data presented in this paper were obtained from July 2015 to  
98 August 2015, when these children were 36 to < 48 months old.

99 This study was approved by the Ethics Committee of Nanjing Medical University  
100 and followed the tenets of the Declaration of Helsinki. Written informed consent was  
101 obtained from the parents or legal representatives of all the participating children.

102 **Ocular examinations**

103 A detailed parental interview was conducted, including questions regarding  
104 parental education level, monthly family income, employment of parent/s, history of  
105 pregnancy and delivery, and parental history of smoking and drinking during  
106 pregnancy. Comprehensive eye examinations included distance VA, ocular alignment  
107 and motility, non-cycloplegic refractive error measurement, anterior segment  
108 examination, fundus evaluation by indirect ophthalmoscopy and ocular biometric  
109 parameters.

110 Monocular distance UCVA measurements were attempted, first in the right eye,  
111 and then in the left, at 3 m by using a retroilluminated (ESV1200 Illuminated Cabinet,  
112 GOOD-LITE, USA) linear HOTV logMAR chart (600017, GOOD-LITE, USA) with  
113 matching letter card. VA scores were measured in 0.1 logMAR increments from  
114 20/100 to 20/16. A similar, standardized approach to the Amblyopia Treatment Study  
115 (ATS) HOTV VA testing protocol was adapted:<sup>14</sup>

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3 116 **1) Screening**  
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5 117 Patch the eye not being tested. Project a 20/100 optotype. If correct, go down a  
6  
7 118 logMAR level and again show a single optotype. Continue through 20/20 with  
8  
9 119 1 letter per level until an incorrect response.

10  
11 120 **2) Phase 1**  
12

13 121 Move up 2 letter sizes from the letter size with the incorrect response in  
14  
15 122 screening up to maximum size of 20/100.

16  
17 123 • Present 4 new letters (if first 3 new letters are correct, then the fourth does not  
18  
19 124 need to be tested; as soon as 2 letters are missed, testing of a level stops).

20  
21 125 • If less than 3 letters are correct, proceed to the next largest size and so on until  
22  
23 126 3 of 4 are correct. When 3 of 4 are correct, proceed to “reinforcement”. If  
24  
25 127 20/100 is failed, stop testing.

26  
27 128 • If 3 letters are correct, repeat on next smallest optotype. Continue to move to  
28  
29 129 smaller optotypes as long as first 3 or 3 of 4 are correct. If 20/16 is passed,  
30  
31 130 test is over. When 2 letters on a level are missed, stop and move to  
32  
33 131 “reinforcement”.

34 132 **3) Reinforcement**  
35

36 133 Move up 3 level from the level missed in phase 1 and show 3 successively  
37  
38 134 smaller single letters. If the patient fails phase 1 at 20/63 or 20/80, show three  
39  
40 135 20/100 letters but still start phase 2 at the level failed in phase 1. Whether or  
41  
42 136 not all 3 are correct in reinforcement, proceed to phase 2.

43 137 **4) Phase 2**  
44

45 138 Retest the last level failed in phase 1. Continue the test by the same procedure  
46  
47 139 as described for phase 1, with the exception that if 2 letters are missed, testing  
48  
49 140 stops.

50  
51 141 **5) Recording Visual Acuity**  
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53 142 Acuity is the smallest letter size (level) passed in phase 1 or phase 2.

54  
55 143 Non-cycloplegic refraction was performed with the table-mounted autorefractor  
56  
57 144 (R-F10, Cannon, Tokyo, Japan), photorefractor (PlusoptiX GmbH, Nuremberg,

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3  
4 145 Germany) and retinoscopy. Cycloplegic refraction was performed in any of the  
5  
6 146 following conditions: (1) spherical equivalent refraction (SER) obtained from any of  
7  
8 147 the non-cycloplegic refraction measurements was  $\leq -0.50$  D in either eye,  $\geq +1.25$  D  
9  
10 148 in either eye, or showed a difference  $\geq 0.75$  D interocularly; (2) cylindrical diopter  
11  
12 149 obtained from any of the non-cycloplegic refraction measurements was  $\geq 0.75$  D in  
13  
14 150 either eye; (3) UCVA was  $< 20/40$  (logMAR 0.3) in either eye, or  $\geq 2$ -line IOD; (4)  
15  
16 151 abnormal results in the examinations of ocular alignment and motility, anterior  
17  
18 152 segment examination or fundus evaluation were found. Two drops of 1.0%  
19  
20 153 cyclopentolate (Cyclogyl, Alcon, Belgium) were instilled five minutes apart, with a  
21  
22 154 third drop administered 20 minutes later. Cycloplegia was then evaluated after an  
23  
24 155 additional 15 minutes. Cycloplegia was considered complete if a pupillary light reflex  
25  
26 156 was absent. If a light reflex was still detected, another drop of cyclopentolate was  
27  
28 157 administered, and the light reflex was evaluated again after 15 minutes. Cycloplegic  
29  
30 158 refraction was performed with the table-mounted autorefractor (R-F10, Cannon,  
31  
32 159 Tokyo, Japan). Subjective refraction was then assessed monocularly according to the  
33  
34 160 cycloplegic refraction values. The best-corrected VA (BCVA) was recorded based on  
35  
36 161 monocular subjective refraction, using the same protocol and VA chart as the UCVA  
37  
38 162 measurements.

### 37 163 **Definitions**

39 164 The criteria of refractive errors were based on the cycloplegic refraction values:  
40  
41 165 myopia was defined as  $SER \leq -0.50$  D in either eye; hyperopia was defined as  $SER \geq$   
42  
43 166  $+2.00$  D in either eye; astigmatism was defined as a cylindrical refractive error  $\geq 0.75$   
44  
45 167 D; anisometropia was defined as an SER difference  $\geq 2.00$  D interocularly.

46  
47 168 To be comparable with SKES, two definitions of amblyopia were adopted in the  
48  
49 169 present report. Amblyopia risk factors should be identified when diagnosing  
50  
51 170 amblyopia in each of the definitions: (1) the American Academy of Ophthalmology  
52  
53 171 (AAO) amblyopia Preferred Practice Pattern (PPP) guidelines define unilateral  
54  
55 172 amblyopia in preschoolers aged 36 to  $< 48$  months as an IOD of greater than or equal  
56  
57 173 to two lines of BCVA, and bilateral amblyopia as BCVA less than 20/50 in either

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3 174 eye;<sup>15</sup> (2) the Chinese Ophthalmology Society (COS) guidelines define amblyopia in  
4  
5 175 preschoolers aged 36 to < 48 months as an IOD of greater than or equal to two lines  
6  
7 176 of BCVA or BCVA less than 20/40 in either eye.<sup>16</sup>  
8

9 **177 Inclusion and exclusion criteria**

10  
11 178 Only Chinese children aged 36 to < 48 months able to complete monocular  
12  
13 179 UCVA testing in both eyes and without neurological problems were included in the  
14  
15 180 analysis and considered as the general study population. The reference population was  
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17 181 defined as the children without sight-affecting ocular conditions, including myopia,  
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19 182 hyperopia, astigmatism, anisometropia, amblyopia, strabismus, nystagmus, visual axis  
20  
21 183 occlusion, or other anterior segment or fundus abnormalities capable of causing visual  
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23 184 impairment.

24 **185 Statistical analysis**

25  
26 186 UCVA outcomes were recorded continuously as mean logMAR UCVA or mean  
27  
28 187 logMAR IOD in UCVA and dichotomously as the proportion of children achieving a  
29  
30 188 particular level of UCVA or IOD. The UCVA for right and left eyes in the reference  
31  
32 189 population were highly correlated (Pearson's correlation = 0.721,  $p < 0.01$ ), thus right  
33  
34 190 eye UCVA was used to report the distribution of UCVA. The UCVA cutoff for referral  
35  
36 191 was defined as the lowest 5th percentile of the normative distribution of UCVA.  
37  
38 192 Effectiveness in referral for amblyopia or refractive error using the estimated UCVA  
39  
40 193 cutoff was then calculated. Multiple linear regression was used to assess associations  
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42 194 of logMAR UCVA with age, gender, and other potential risk factors. All analyses  
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44 195 were performed by using SPSS 22.0 (IBM, China) and a 0.05 significance level.  
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3 196 **RESULTS**

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5 197 **Study population**

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7 198 A total of 2,300 preschoolers were enrolled in this study, and 1,806 participated in  
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9 199 the UCVA test (78.5% responses rate), among which 1,606 (88.9%) were testable in  
10  
11 200 both eyes and considered as the general population. According to the definition  
12  
13 201 outlined in the methods, 791 (49.3%) children were classified as the reference  
14  
15 202 population. Boys constituted 53.5% of the reference population and 52.5% of the  
16  
17 203 general population. There was no statistically significant sex difference in the mean  
18  
19 204 age of the reference population ( $P = 0.277$ ) and the general population ( $P = 0.607$ ).

20  
21 205 **UCVA outcomes**

22  
23 206 Table 1 presents the distributions of UCVA in the reference population. About 60%  
24  
25 207 (478 out of 791) of the measured monocular UCVA fell in the category of 20/32. The  
26  
27 208 5th, 50th, and 95th percentiles fell in the UCVA categories of 20/40, 20/32, and 20/25,  
28  
29 209 respectively.

30  
31 210

32 **Table 1. Distribution of UCVA and IOD in the reference population**

	n (%)
<b>LogMAR UCVA (Snellen equiv.)</b>	
0.6 (20/80)	1 (0.1)
0.5 (20/63)	2 (0.3)
0.4 (20/50)	6 (0.8)
0.3 (20/40)	106 (13.4)*
0.2 (20/32)	478 (60.4)*
0.1 (20/25)	170 (21.5)*
0 (20/20)	27 (3.4)
-0.1 (20/16)	1 (0.1)
<b>UCVA IOD, lines (LogMAR equiv.)</b>	
0 (0.0)	595 (75.2)
1 (0.1)	181 (22.9)

2 (0.2)	14 (1.8)
3 (0.3)	1 (0.1)

\*The 5th, 50th, and 95th percentiles fell in the UCVA categories of 20/40, 20/32, and 20/25, respectively.

211

212 Age-specific and gender-specific mean logMAR UCVA levels for the right eye in  
 213 the reference population are shown in Table 2. A multivariate linear regression model  
 214 including age and gender showed that UCVA improved with increasing age ( $p <$   
 215  $0.0001$ ), but had no association with gender ( $p = 0.892$ ). Risk factors adjusted for age  
 216 and adjusted for age and gender for UCVA in the reference population are shown in  
 217 Table 3. Only prematurity was significantly associated with poorer UCVA after  
 218 adjustment for age ( $p = 0.040$ ), or adjusted for age and gender ( $p = 0.041$ ).

219

**Table 2. Mean logMAR UCVA and IOD in reference generation, by age and by gender**

	<b>n</b>	<b>Mean UCVA (SD)</b>	<b>Mean absolute UCVA IOD (SD)</b>
<b>All</b>	791	0.19 (0.07)	0.03 (0.05)
<b>Age in months</b>			
36 to <42	438	0.19 (0.08)	0.03 (0.05)
42 to <48	353	0.18 (0.07)	0.02 (0.04)
<b>Gender</b>			
Male	423	0.19 (0.08)	0.03 (0.05)
Female	368	0.19 (0.07)	0.02 (0.05)

220 75.2% (595 out of 791) children in the reference population achieved equal vision  
 221 in both eyes and only 1.9% had an IOD of two or more lines ( $\geq 0.2$  logMAR) (Table  
 222 1). Table 2 shows mean absolute logMAR UCVA IOD in the reference population, by  
 223 age and by gender. A multivariate linear regression model including age and gender  
 224 showed that absolute UCVA IOD decreased with increasing age ( $p = 0.014$ ), but had  
 225 no association with gender ( $p = 0.227$ ).  
 226 The mean non-absolute logMAR UCVA IOD (right eye minus left eye logMAR

**Table 3. Risk factors adjusted for age and adjusted for age and gender for UCVA in the reference population**

Associated factors	Adjusted for age	Adjusted for age and gender		
	p value	$\beta$ coefficient	$r^2$	p value
Prematurity <37 weeks	<b>0.040</b>	0.082	0.032	<b>0.041</b>
Low birth weight <2500 g	0.163	0.054	0.028	0.163
Maternal smoking during pregnancy	0.770	0.012	0.023	0.758
Maternal drinking during pregnancy	0.264	-0.042	0.024	0.270
Parental tertiary education (University or College)	0.755	-0.012	0.024	0.754
Monthly family income	0.685	-0.019	0.016	0.689
Employment of one parent	0.501	-0.028	0.030	0.506
Employment of both parents	0.791	0.011	0.029	0.798

227 VA) in the reference population was 0.0023, with no significantly difference from  
 228 zero ( $p = 0.251$ ), indicating no influence of the order in which the eyes were tested on  
 229 UCVA.

### 230 Effectiveness of the UCVA and UCVA IOD referral cutoffs

231 Using the 5th percentile UCVA cutoff from the reference population (defined as  
 232 UCVA  $\leq 20/40$ ) would generate referral rates of 26.9% (432 cases) in the general  
 233 population. Table 4 shows the effectiveness in terms of sensitivity, specificity, positive  
 234 predictive value (PPV) and negative predictive value (NPV) in referral for refractive

235 errors or amblyopia using the current UCVA cutoff. A total of 39.5% (301/762) of  
 236 cases with any refractive error were detected, with a specificity of 84.5% (713/844).  
 237 For amblyopia using the AAO definition, the sensitivity and specificity were 86.2%  
 238 (25/29) and 74.2% (1170/1577), respectively, which are similar to the findings when  
 239 using the COS amblyopia definition (86.7% and 74.2%).  
 240

**Table 4. Effectiveness in Referral for Refractive Errors or Amblyopia Using the lowest 5th Percentile UCVA**

**Cutoff Criteria**

	Sensitivity, n/N (%)	Specificity, n/N (%)	PPV, n/N (%)	NPV, n/N (%)
<b>Refractive Errors</b>				
Myopia	112/319 (35.1)	967/1287 (75.1)	112/432 (25.9)	967/1174 (82.4)
Hyperopia	43/84 (51.2)	1133/1522 (74.4)	43/432 (10.0)	1133/1174 (96.5)
Astigmatism	252/518 (48.6)	908/1088 (83.5)	252/432 (58.3)	908/1174 (77.3)
Anisometropia	26/59 (44.1)	1141/1547 (73.8)	26/432 (6.0)	1141/1174 (97.2)
All	301/762 (39.5)	713/844 (84.5)	301/432 (69.7)	713/1174 (60.73)
<b>Amblyopia</b>				
AAO Definition				
Unilateral Amblyopia	11/14 (78.6)	1171/1601 (73.1)	11/432 (2.5)	1171/1174 (99.7)
Bilateral Amblyopia	14/15 (93.3)	1173/1591 (73.7)	14/432 (3.2)	1173/1174 (99.9)
All	25/29 (86.2)	1170/1577 (74.2)	25/432 (5.8)	1170/1174 (99.7)
COS Definition				
	26/30 (86.7)	1170/1576 (74.2)	26/432 (6.0)	1170/1174 (99.7)

241

242 When using the UCVA IOD of two or more lines as the criterion, only 4.3% (69  
 243 cases) of the general population would be referred. According to the AAO definition,  
 244 this criterion detected 20.7% (6/29) of cases with any amblyopia, and 28.6% (4/14) of  
 245 cases with unilateral amblyopia. For amblyopia using the COS definition, 26.7%  
 246 (8/30) of cases with amblyopia were detected using such criterion.

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## 247 DISCUSSION

248 In China, SKES was the only population-based investigation of UCVA normative  
249 distribution in Chinese preschoolers before our study.<sup>10</sup> In order to be comparable  
250 with SKES and also to ensure that children with sight-affecting ocular conditions  
251 were excluded, we used the same stringent definition of the “reference population” as  
252 SKES. However, the lowest 5th percentile in our reference population, falling in the  
253 UCVA category of 20/40, was two lines better than this found in the 36-month-old  
254 reference population in SKES (20/63). In addition, the 50th percentile in our reference  
255 population was one line better than this in SKES (20/32 vs. 20/40). Two reasons  
256 might contribute to the differences between our study and SKES. First, we measured  
257 the UCVA using the HOTV chart, which is recommended and commonly used in  
258 Western countries for young children,<sup>6-7, 12</sup> while SKES used the ETDRS Tumbling E  
259 chart which is harder cognitively for the child to understand and thus affect the  
260 threshold acuity that can be achieved by the child.<sup>17-19</sup> Second, smaller sample size of  
261 the 36-month-old children (51 cases) in the reference population of SKES might have  
262 a significant influence on the results of UCVA normative distribution.

263 We are unable to compare the mean logMAR UCVA in our study with that in  
264 SKES as SKES didn't calculate this. When our mean logMAR UCVA is compared to  
265 this obtained from the African American and Hispanic children without sight-affecting  
266 abnormalities in MEPEDS, the mean logMAR UCVA in our reference population is  
267 very close to this established in the MEPEDS 36- to 47-month-old children using the  
268 ATS HOTV (0.19 vs. 0.17 logMAR, respectively).<sup>6</sup> If compared to the results  
269 obtained from the European Caucasian and Asian children without sight-affecting  
270 abnormalities in SPEDS, the mean logMAR UCVA in our reference population is  
271 close to one line worse than this tested with the ATS HOTV in SPEDS (0.19 vs. 0.09  
272 logMAR for children aged 36 to <42 months; 0.18 vs. 0.07 for 42 to <48 months), and  
273 similar to this tested with the linear ETDRS or HOTV logMAR chart (0.19 vs. 0.22  
274 logMAR for children aged 36 to <42 months; 0.18 vs. 0.16 for 42 to <48 months).<sup>7</sup>  
275 However, the significances of such comparisons are not very clear, because the ATS

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3 276 HOTV VA test, which uses a single letter surrounded by bars optimally placed at half  
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5 277 the optotype height from the letter optotype, is quite different from the linear HOTV  
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7 278 logMAR chart that we used, and SPEDS didn't specify the mean logMAR UCVA  
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9 279 when only using linear HOTV logMAR chart. The better VA by approximately 1 line  
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11 280 (using the ATS HOTV test) found in SPEDS when compared to our study might be  
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13 281 due to the following reasons: (1) Non-cycloplegic refraction was performed on part of  
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15 282 children in our reference population, which may underdiagnose hyperopia due to  
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17 283 accommodative reserves<sup>20-21</sup> and then produce slightly reduced VA in the reference  
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19 284 population due to hyperopia; (2) The ATS HOTV is cognitively easier to perform by  
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21 285 preschoolers than the linear chart;<sup>22</sup> (3) Leone et al found that East Asian children had  
22  
23 286 significantly poorer VA than their European Caucasian counterparts,<sup>7</sup> which indicated  
24  
25 287 that ethnicity differences might have impacted our findings.

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27 288 We found improvement in UCVA with increasing age, as has been reported in  
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29 289 several studies despite different charts used.<sup>6-7, 10, 18, 23</sup> However, the difference  
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31 290 between UCVA in the 36- to <42-month-old children was only 0.01 logMAR worse  
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33 291 than the 42- to <48-month-old children (Table 2), which might have no clinical  
34  
35 292 significance. Gender was not associated with UCVA both in our sample and SPEDS,  
36  
37 293 opposite to that reported in MEPEDS.<sup>6-7</sup> As for risk factors of UCVA, prematurity was  
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39 294 related with worse UCVA in our reference population, which was consistent with the  
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41 295 finding in SPEDS. However, the  $r^2$  value was only 0.032, indicating that the  
42  
43 296 significance of prematurity to UCVA might not be very high. Socio economic status  
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45 297 (SES) factors, such as the employment status of parents and family income, which  
46  
47 298 were significantly associated with UCVA in MEPEDS and SPEDS, showed no  
48  
49 299 associations with UCVA in our study. In addition, maternal smoking during pregnancy,  
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51 300 which was related with slightly better UCVA in SPEDS, had no relationship with  
52  
53 301 UCVA in our study.

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55 302 As the penalty for missing one amblyopia case is a lifetime disability and  
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57 303 treatment exists, the UCVA referral cutoff for amblyopia should target high sensitivity,  
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59 304 while the specificity should be high enough not to put immense load on  
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3 305 ophthalmologists.<sup>24-25</sup> The sensitivity of detecting amblyopia by using the UCVA  
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5 306 referral cutoff in our study ( $UCVA \leq 20/40$  at age 36 to < 48 months), was as high as  
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7 307 86%, and at the same time, the specificity was high enough (74.2%). On the other  
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9 308 hand, this cutoff only identified a total of 39.5% refractive errors, even though the  
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11 309 overall specificity was high (84.5%). The sensitivity in detecting myopia was not  
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13 310 good in our study (35.1%), lower than hyperopia (51.2), astigmatism (48.6%), and  
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15 311 anisometropia (44.1%). In SKES, even though a high sensitivity (83.3%) in detecting  
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17 312 myopia was observed in all 36- to 72-month-old preschoolers, it's not available to  
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19 313 calculate the sensitivity in detecting myopia in 36-month-old children because of no  
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21 314 presence of myopia in this age group. And for all refractive errors in 36-month-old  
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23 315 children in SKES, the overall sensitivity was only 8.6%. Therefore, only using the  
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25 316 UCVA cutoff as referral criterion might be difficult to detect refractive errors in  
26  
27 317 36-month-old children, and additional refraction examination might be necessary for  
28  
29 318 vision screening.

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31 319 The normative distribution of UCVA IOD in our study was consistent with that in  
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33 320 SKES, with most children achieving equal vision in both eyes. No effect of gender or  
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35 321 testing order on IOD was observed in our study, which was consistent with MEPEDS.  
36  
37 322 However, we found that absolute UCVA IOD decreased with increasing age of month  
38  
39 323 in our sample, which was not consistent with the findings in 30- to 72-month-old  
40  
41 324 children in MEPEDS. The reason of this difference might be that, in MEPEDS, equal  
42  
43 325 vision in both eyes in older children concealed the effect of age on UCVA IOD in  
44  
45 326 younger children.

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47 327 When using UCVA IOD of two or more lines as the criterion, approximately 4%  
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49 328 in the general population would be referred in both of SKES and our study. The  
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51 329 sensitivity of using this criterion alone for detecting amblyopia, including unilateral  
52  
53 330 amblyopia, was very low in our study, similar to the results in SKES.

54  
55 331 To our knowledge, the present study is the first to provide population-based  
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57 332 HOTV-specific normative UCVA data in Chinese preschoolers aged 36 to < 48  
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59 333 months without significant refractive error or other ophthalmic abnormalities.  
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3 334 However, there are several limitations in the present study. Because young children  
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5 335 are very afraid of using eye drops, which makes cycloplegia difficult and  
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7 336 unacceptable for parents, only children with suspected abnormalities underwent  
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9 337 cycloplegic refraction in our study. Even though not all children had refraction  
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11 338 results under cycloplegia, we adopted stringent criteria to identify children who  
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13 339 needed cycloplegic refraction, which could effectively detect sight-affecting refractive  
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15 340 errors. However, Fotedar et al<sup>20</sup> and Leone et al<sup>21</sup> found that hyperopia and some  
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17 341 astigmatism might not be as detectable without cycloplegia, which might impact the  
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19 342 findings of our reference population at some degree. 11.1% children were not testable  
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21 343 when doing the HOTV test and were excluded from the analysis, which may influence  
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23 344 the normative UCVA distribution. However, the testability in our study was at an  
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25 345 average level of published reports,<sup>6, 10</sup> which tested VA using the HOTV single  
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27 346 surrounded letters, not linear, and difficult to increase further in young children.

28 347 In conclusion, our study suggests that Chinese preschoolers aged 36 to < 48  
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30 348 months with UCVA no better than 20/40 measured by linear HOTV chart should be  
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32 349 referred for further ophthalmic examinations. Most amblyopia cases can be identified  
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34 350 with this age-specific and chart-specific UCVA cutoff.



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10  
11 355 Performed the experiments: HZ, DH, QS, HD, JB, JC, YW, XZ, JW and XL.  
12  
13 356 Analyzed the data: HZ, DH, QS and XC. Contributed reagents/materials/analysis  
14  
15 357 tools: HL, HZ, DH, HD, JB, JC, and XC. Wrote the paper: HL, HZ, DH, QS, XC, HD,  
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27  
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29  
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31  
32 366 **Ethics approval** The Institutional Review Board of Jiangsu Province Hospital.

33  
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36 368 **Data sharing statement** No additional data are available.  
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