Supplementary Materials

2 A. The qVA Method

3	In the qVA method (Patent: US 2019/0038125; Lesmes LA. IOVS 2018; 59: ARVO E-
4	Abstract 1073) ⁴¹ , a single-optotype d' psychometric function (Figure S1a) is described as:
5	$d' = \log_{10}(6) + \frac{\omega}{2\Delta}(x - \tau) - \frac{1}{2}\log_{10}(8 + 10^{\frac{\omega}{\Delta}(x - \tau)}),$ (S1)
6	where τ is the VA threshold, corresponding to the optotype size at d'=2, and a VA range of the
7	psychometric function Δ , that is, the range of optotype sizes that covers d' = 1 to d' = 4
8	performance levels, and $\omega = \log_{10} 35 - \log_{10} 1.25$. The smaller the range is, the steeper the
9	slope of the psychometric function. From this single-optotype d' psychometric function, qVA
10	derives the probability of observing the correct identification of different numbers of optotypes
11	(Figure S1c) via the single-optotype psychometric function of percent correct (Figure S1b),
12	taking into account the particular chart design. In this paper, a 10 alternative forced choice task
13	was implemented in the qVA methods.
14	PLEASE INSERT FIGURE S1 HERE
15	In the qVA simulations, the two-dimensional parameter space included 700 linearly
16	spaced threshold (τ) values between -0.5 and 1.3 logMAR, and 699 log-linearly spaced range
17	(Δ) values between 0.1 and 1.5 logMAR. The stimulus space consisted of 91 linearly spaced
18	optotype size values from -0.5 to 1.3 logMAR, with a sampling density of 0.02 logMAR.
19	Based on a pilot experiment, the prior (Figure S2, top left) was set to have highest
20	probabilities in the two-dimensional parameter space within a square of VA thresholds between -
21	0.1 and 0.9 logMAR and ranges between 0.2 and 0.6 logMAR. The prior distribution $p_0(\vec{\theta})$ was
22	constructed in the following steps, where $\vec{\theta} = (\tau, \Delta)$, p refers to probability density across

23 parameter space $\vec{\theta}$ and subscript 0 represents prior. First, marginal distributions for both

24 parameters were defined as hyperbolic secant functions:

25
$$p_{01}(\tau) = \operatorname{sech}\left(\tau_{\operatorname{confidence}}\left(\log 10(\tau) - \log 10(\tau_{\operatorname{mode}})\right)\right), \quad (S 2.1)$$

26
$$p_{01}(\Delta) = \operatorname{sech} \left(\Delta_{\operatorname{confidence}} \left(\log 10(\Delta) - \log 10(\Delta_{\operatorname{mode}}) \right), \right)$$
 (S 2.2)

27 where sech(x) = $\frac{2}{e^{x}+e^{-x}}$; ($\tau_{\text{mode}}, \Delta_{\text{mode}}$) = (0.2, 0.4) were the modes of the respective secant

functions; ($\tau_{\text{confidence}}$, $\Delta_{\text{confidence}}$) = (4, 4) were the spreads of the respective secant functions.

29 Then $p_{01}(\tau)$ was transformed into $p_{02}(\tau)$:

30
$$\begin{cases} p_{02}(\tau) = p_{01}(\tau), \tau \in (0.9, 1.3], \\ p_{02}(\tau) = p_{01}(0.9), \tau \in [-0.1, 0.9], \\ p_{02}(\tau) = \frac{(\tau + 0.5)[p_{01}(0.9) - p_{01}(1.3)]}{0.4}, \tau \in [-0.5, -0.1). \end{cases}$$
(S 3)

31 The prior distribution was then constructed as:

32
$$p_0(\vec{\theta}) = p_{02}(\tau)p_{01}(\Delta) / \sum_{\vec{\theta}} p_{02}(\tau)p_{01}(\Delta),$$
 (S 4)

33 where $\sum_{\vec{\theta}} p_{02}(\tau) p_{01}(\Delta)$ normalized the sum of the prior probability to 1.

Figure S2 shows the evolution of the joint posterior distribution in one simulated qVA run for simulated Observer 1. The procedure started with a broad prior distribution of the two parameters of the acuity psychometric function. As the test proceeded, the posterior distribution became narrower (decrease in 68.3% HWCI and SD) and converged on the true parameter values (decrease in bias).

39

PLEASE INSERT FIGURE S2 HERE

40 To assess VA, the qVA method uses an active learning algorithm to estimate two

- 41 parameters, the acuity and range, of the acuity psychometric function in four steps (Figure S3):
- 42 (1) The joint prior distribution of the two parameters of the acuity psychometric function, $p_0(\vec{\theta})$,
- 43 is defined in the two-dimension parameter space of $\vec{\theta}$. (2) The optotype size of the test stimulus

on the next row is selected to optimize the expected information gain on the parameters of the psychometric function. (3) The posterior distribution of $\vec{\theta}$, $p_n(\vec{\theta})$, is updated by Bayes' rule based on the observer's response after each trial that consists of multiple optotypes of the same size. (4) Steps (2) and (3) are repeated until the stop criterion is met (e.g., a pre-determined number of rows or precision).

49

PLEASE INSERT FIGURE S3 HERE

50 B. The E-ETDRS Method

The E-ETDRS method¹⁷ uses a heuristic procedure to measure VA (Figure S4). Test 51 52 stimuli consist of 10 optotypes at 20 sizes, equally spaced between -0.3 and 1.6 logMAR (20/10 and 20/800 Snellen equivalent) with a step size of 0.10 logMAR. The test has a screening phase 53 54 and a threshold phase. The screening phase provides a coarse estimate of the observer's VA and 55 the initial level(s) of optotype size to be tested in the threshold phase. In the threshold phase, the 56 test starts with the optotype size(s) determined in the screening phase. More levels are added 57 until the upper and lower bounds of the size range are found. The upper bound of the size range 58 is defined by the smallest optotype size at which all five letters are correctly identified or the 59 largest optotype size achievable, whichever is smaller. The lower bound of the size range is 60 defined by the largest optotype size at which none of the five letters is correctly identified or the smallest optotype size achievable, whichever is larger. In this manner, the E-ETDRS samples 61 the full size range of the acuity psychometric function. The E-ETDRS procedure samples a pool 62 63 of five letters (without replacement), presented one at a time at each of the optotype sizes within the size range, and counts the number of correctly identified letters as the final acuity estimate. 64 Visual acuity score (VAS) is the number of letters correctly identified in the threshold phase, 65 plus 5 letters for each size between the largest achievable test size in the E-ETDRS method, 66

3

which is 1.6 logMAR in our implementation, and the upper bound tested in the threshold phase.

68 Visual acuity in logMAR is computed as:

69
$$VA(logMAR) = 1.7 - 0.02 \times VAS.$$
 (S 5)

70

<u>PLEASE INSERT FIGURE S4 HERE</u>

71 C. The FrACT Method

The FrACT method is an adaptive procedure for measuring VA^{26,30}. It assumes that the acuity psychometric function has an unknown threshold v_0 but a fixed slope s = 2:

74
$$P(\nu) = p_{chance} + (1 - p_{chance})/(1 + (\nu/\nu_0)^s),$$
(S 6)

75 where $p_{chance} = 0.1$ is the guessing rate in a 10-AFC task, and the acuity threshold v_0

corresponds to the optotype size at which correct identification rate is 55% (Figure S5). ν and ν_0

in FrACT method is in decimal unit, equivalent to $-\log_{10}(v_0) \log$ MAR. Using the best PEST

algorithm, FrACT samples the optimal (maximum likelihood) test optotype from -0.76 to 1.11

79 logMAR in each trial and provides an estimated threshold acuity after each trial. In the

simulations, we found our MATLAB maximum likelihood implementation of the FrACT method

81 generated VA estimates that were 0.0145 logMAR higher than the original FrACT method in

82 each trial. This was corrected by adding a constant to the estimates from the MATLAB

- 83 implementation.
- 84

PLEASE INSERT FIGURE S5 HERE

85 D. Evaluations of accuracy and precision of the estimates from the qVA method.

The qVA provided a joint posterior distribution of the two parameters of the acuity psychometric function, acuity and range, on each row. The expected parameter value after the nth row in the mth simulation was computed from the corresponding marginal posterior distribution:

89
$$\theta_{anm} = \sum_{\theta_a} \theta_a \cdot p_{nm}(\theta_a | r_{nm}, x_{nm}), \qquad (S 7)$$

90 where $\theta_a = \tau$ and Δ , for a = 1 and 2, respectively; θ_{anm} , r_{nm} , x_{nm} , and $p_{nm}(\theta_a | r_{nm}, x_{nm})$ are 91 the estimated θ_a , observer's response, optotype size and marginal distribution after the n^{th} row 92 in the m^{th} simulation. The marginal distributions were computed from the joint posterior 93 distribution $p_{nm}(\vec{\theta} | r_{nm}, x_{nm})$:

$$p_{nm}(\tau | r_{nm}, x_{nm}) = \sum_{\Delta} p_{nm}(\vec{\theta} | r_{nm}, x_{nm}), \qquad (S 8)$$

95
$$p_{nm}(\Delta | r_{nm}, x_{nm}) = \sum_{\tau} p_{nm}(\vec{\theta} | r_{nm}, x_{nm}).$$
(S 9)

96 The bias of an estimated parameter after the
$$n^{\text{th}}$$
 row is defined as:

97
$$Bias_n = \sum_m (\theta_{anm} - \theta_{a,observer})/M, \qquad (S10)$$

98 where $\theta_{a,observer}$ is the parameter value of the simulated observer, and M (= 1000) is the total 99 number of simulated runs.

100 The cross-run variability of the estimated parameters was quantified by the standard 101 deviation across independent simulation runs. The standard deviation (SD) of the estimates of the 102 parameter θ_a after the *n*th row across *M* runs is defined as:

103
$$SD_n = \sqrt{\frac{\sum_m (\theta_{anm} - \overline{\theta}_{an})^2}{M}},$$
 (S 11)

104 where $\bar{\theta}_{an}$ is the average estimate of parameter θ_a after the *n*th row across M runs:

105
$$\bar{\theta}_{an} = \sum_m \theta_{anm} / M$$
. (S 12)

106 E. Between-block variability

94

107 Assume the following generative model for a subject:

108
$$\mathbf{x}_{ij} = \boldsymbol{\mu}_i + \boldsymbol{\varepsilon}_j + \boldsymbol{\varepsilon}_{ij}, \qquad (S13.1)$$

109
$$x_{kj} = \mu_k + \varepsilon_j + \varepsilon_{kj}, \qquad (S13.2)$$

110

$$\mathbf{x}_{lj} = \boldsymbol{\mu}_l + \boldsymbol{\varepsilon}_j + \boldsymbol{\varepsilon}_{lj}, \tag{S13.3}$$

where *i*, *k*, and *l* represent the qVA, E-ETDRS, and FrACT methods, respectively; *j* represents 111 the block number; x_{ij}, x_{kj}, and x_{lj} are the estimated VA from the qVA, E-ETDRS, and FrACT 112 methods, respectively, in j^{th} block; μ_{ij} , μ_{kj} , and μ_{lj} are the true acuity from the qVA, E-ETDRS, 113 and FrACT methods, respectively, in j^{th} block; ε_i , a normal random variable of N(0, $\sigma_{foil,block}$) 114 that only varies across blocks, is the noise introduced by the uneven transparency on the surface 115 of the foil; ε_{ij} , ε_{kj} , and ε_{lj} , normal random variables of $N(b_i, \sigma_i)$, $N(b_k, \sigma_k)$, and $N(b_l, \sigma_l)$ that 116 vary trial by trial, are the intrinsic measurement errors of the qVA, E-ETDRS and FrACT 117 118 methods, respectively. The mean estimated VA from each method approximates: 119 $\overline{\mathbf{x}}_{\mathbf{i}} = \mathbf{\mu}_{\mathbf{i}},$ (S14.1) 120 $\overline{x}_k = \mu_k,$ (S14.2)121 122 $\overline{x}_l = \mu_l.$ (S14.3) 123 We define: 124 $\overline{x}_{i-k}=\mu_i-\mu_k,$ (S15.1) 125 $\overline{\mathbf{x}}_{i-1} = \mu_i - \mu_i$. (S15.2) 126 The total variances of the estimated VA differences between the qVA and E-ETDRS 127 128 methods, and between the qVA and FrACT methods are: $Var_{i-k} = \frac{1}{I-1} \sum_{j} (x_{ij} - x_{kj} - \bar{x}_{i-k})^2 = \frac{1}{I-1} (\sum_{j} \varepsilon_{ij}^2 + \sum_{j} \varepsilon_{kj}^2),$ 129 (S16.1)

130
$$\operatorname{Var}_{i-l} = \frac{1}{J-1} \sum_{j} (x_{ij} - x_{lj} - \overline{x}_{i-l})^2 = \frac{1}{J-1} (\sum_{j} \varepsilon_{ij}^2 + \sum_{j} \varepsilon_{lj}^2). \quad (S16.2)$$

131 where *J* is the total number of blocks. We define:

132
$$\bar{x}_G = \frac{\mu_i + \mu_k + \mu_l}{3},$$
 (S17.1)

133 then we have:

134
$$Var_{i,G} = \frac{1}{J-1} \sum_{j} (x_{ij} - \bar{x}_G)^2 = \frac{1}{J-1} \sum_{j} (\frac{2\mu_i - \mu_k - \mu_l}{3} + \varepsilon_j + \varepsilon_{ij})^2 = \frac{1}{J-1} (\sum_{j} (\frac{2\mu_i - \mu_k - \mu_l}{3})^2 + \sum_{j} \varepsilon_j^2 + \sum_{j} \varepsilon_{ij}^2), \quad (S17.2)$$

136
$$Var_{k,G} = \frac{1}{J-1} \sum_{j} (x_{kj} - \bar{x}_G)^2 = \frac{1}{J-1} \sum_{j} (\frac{2\mu_k - \mu_i - \mu_l}{3} + \varepsilon_j + \varepsilon_{kj})^2 = \frac{1}{J-1} (\sum_{j} (\frac{2\mu_k - \mu_i - \mu_l}{3})^2 + \sum_{j} \varepsilon_j^2 + \sum_{j} (\sum_{j} (\frac{2\mu_k - \mu_i - \mu_l}{3})^2 + \sum_{j} (\sum_{j} (\sum_{j} (\frac{2\mu_k - \mu_i - \mu_l}{3})^2 + \sum_{j} (\sum_{j} (\sum$$

138
$$Var_{l,G} = \frac{1}{J-1}\sum_{j} (x_{lj} - \bar{x}_G)^2 = \frac{1}{J-1}\sum_{j} (\frac{2\mu_l - \mu_i - \mu_k}{3} + \varepsilon_j + \varepsilon_{lj})^2 = \frac{1}{J-1} (\sum_{j} (\frac{2\mu_l - \mu_i - \mu_k}{3})^2 + \sum_{j} \varepsilon_j^2 + \sum_{j} \varepsilon_{lj}^2) + \sum_{j} (\sum_{j} (\frac{2\mu_l - \mu_i - \mu_k}{3})^2 + \sum_{j} (\sum_{j} (\sum_{j} (\frac{2\mu_l - \mu_i - \mu_k}{3})^2 + \sum_{j} (\sum_{j} (\sum_{j}$$

141
$$Var_i = (Var_{i,G} - Var_{k,G} + Var_{i-k})/2,$$
 (S18.1)

142
$$Var_k = (Var_{k,G} - Var_{i,G} + Var_{i-k})/2,$$
 (S18.2)

143
$$Var_{l} = (Var_{l,G} - Var_{i,G} + Var_{i-l})/2.$$
(S18.3)

The standard deviation of the estimated VA from each method for the subject in the foil 144 condition is 145

146
$$SD_i = \sqrt{(Var_{i,G} - Var_{k,G} + Var_{i-k})/2},$$
 (S19.1)

147
$$SD_k = \sqrt{(Var_{k,G} - Var_{i,G} + Var_{i-k})/2},$$
 (S19.2)

 $SD_l = \sqrt{(Var_{l,G} - Var_{i,G} + Var_{i-l})/2}.$ (S19.3) 148

F. Estimated VA and range in the psychophysical experiment 149

PLEASE INSERT FIGURE S6&S7 HERE 150