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# ON THE YAO–IYER INEQUALITY IN BIOEQUIVALENCE STUDIES

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*Abstract.* In this note, we present a simple proof of a probabilistic inequality by Yao-Iyer, which arises in bioequivalence studies.

Consider the ratio

$$r(z) := \frac{\mathsf{P}(|X| < z)}{\mathsf{P}(|Z| < z)}$$

of the distribution functions of random variables $|X|$ and $|Z|$, where $Z \sim N(0,1)$, $X \sim N(\mu, \sigma^2)$, $\mu \in \mathbb{R}$, $\sigma > 0$, and $(\mu, \sigma^2) \neq (0,1)$. We present a simple proof of the Yao-Iyer (1999) [1] inequality

$$r(z) > \min(r(\infty), r(0+)) \quad \forall z \in (0, \infty), \tag{1}$$

which arises in bioequivalence studies; here $r(\infty) := \lim_{z\to\infty} r(z) = 1$ and $r(0+) := \lim_{z\downarrow 0} r(z) = \frac{1}{\sigma}\varphi(\frac{\mu}{\sigma})/\varphi(0)$, $\varphi$ being the standard normal density.

Rewrite (1) as

$$D(z) := \mathsf{P}(|X| < z) - c\,\mathsf{P}(|Z| < z) > 0 \quad \forall z \in (0, \infty), \quad \text{with} \tag{2}$$

$$c := \min(r(\infty), r(0+)) = \min(1, \rho(0)), \quad \text{where} \tag{3}$$

$$\rho(z) := \frac{\frac{1}{\sigma}\varphi\left(\frac{z-\mu}{\sigma}\right) + \frac{1}{\sigma}\varphi\left(\frac{z+\mu}{\sigma}\right)}{2\varphi(z)}.$$

Note that

$$D'(z) = 2(\rho(z) - c)\varphi(z) \quad \forall z \in (0, \infty). \tag{4}$$

The proof of (2) is based on the following observation.

LEMMA 1. *For all $\mu \in \mathbf{R}$ and $\sigma > 0$, there exists some $b \in [0, \infty]$ such that $\rho$ is (strictly) increasing on $(0, b)$ and decreasing on $(b, \infty)$. (In particular, if it turns out that $b = 0$, then $\rho$ is decreasing on the entire interval $(0, \infty)$; if $b = \infty$, then $\rho$ is increasing on $(0, \infty)$.)*

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We shall prove Lemma 1 a little later. At this point, let us use it to prove (2).

Indeed, (3) implies that $\rho(0) \geqslant c$. Hence, by Lemma 1, $\exists z_* \in [0,\infty]$ such that $\rho > c$ on $(0,z_*)$ and $\rho < c$ on $(z_*,\infty)$. Thus, in view of (4), $D$ is increasing on $(0,z_*)$ and decreasing on $(z_*,\infty)$. It follows that $\forall z \in (0,\infty)$ $D(z) > \min(D(0),D(\infty)) \geqslant 0$, because $D(0) = 0$ and $D(\infty) = 1-c \geqslant 0$.

It remains to prove Lemma 1. In turn, it is based on

LEMMA 2. *Let*

$$\lambda(x) := \lambda_\mu(x) := \varphi(x-\mu) + \varphi(x+\mu).$$

*Then there exists some* $d \in [0,\infty]$ *such that* $\lambda$ *is increasing on* $(0,d)$ *and decreasing on* $(d,\infty)$.

*Proof.* One has

$$\lambda'(x) = \varphi(x+\mu)f(x), \text{ where } f(x) := -(x+\mu) - (x-\mu)e^{2\mu x}; \tag{5}$$

$$f'(x) = e^{2\mu x}g(x), \text{ where } g(x) := -e^{-2\mu x} - 1 - 2\mu x + 2\mu^2. \tag{6}$$

Note that $g'(x) = 2\mu(e^{-2\mu x} - 1) < 0$ $\forall x \in (0,\infty)$ if $\mu \neq 0$, and $g(x) = -2 < 0$ $\forall x$ if $\mu = 0$. Hence, $\exists a \in [0,\infty]$ such that $g > 0$ on $(0,a)$ and $g < 0$ on $(a,\infty)$; by (6), the same holds for $f'$ in place of $g$. Note next that $f(0) = 0$. Hence, $\exists d \in [0,\infty]$ such that $f > 0$ on $(0,d)$ and $f < 0$ on $(d,\infty)$; by (5), the same holds for $\lambda'$ in place of $f$. Therefore, $\lambda$ is increasing on $(0,d)$ and decreasing on $(d,\infty)$. □

Now we can finish the proof of Lemma 1. Observe that

$$\rho(z) = e^{Q(z)} + e^{Q(-z)}, \tag{7}$$

for some quadratic polynomial $Q(z) = Az^2 + Bz + C$, where $A$, $B$, and $C$ may depend only on $\mu$ and $\sigma$. Moreover, the condition $(\mu,\sigma^2) \neq (0,1)$ implies $A \neq 0$ or $B \neq 0$; namely, $\sigma^2 \neq 1$ implies $A \neq 0$, and $\mu \neq 0$ implies $B \neq 0$. Note that $\rho$ is an even function.

If $A \geqslant 0$, then $\rho$ is also convex on $\mathbf{R}$, and so, $\rho$ is non-decreasing on $(0,\infty)$; moreover, then the condition $(\mu,\sigma^2) \neq (0,1)$ implies that $\rho$ is strictly convex on $\mathbf{R}$, and so, increasing on $(0,\infty)$. Thus, if $A \geqslant 0$, then the statement of Lemma 1 is true, with $b = \infty$.

In the remaining case, $A < 0$, Lemma 1 follows from Lemma 2. Indeed, in this case, (7) can be rewritten as $\rho(z) = K\lambda_\nu(tz)$, where $K > 0$, $\nu$, and $t > 0$ are some constants, which may depend only on $\mu$ and $\sigma$.

## REFERENCES

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