Numerical Computation

Owen's T/Q ??????????????????

1. ????????????

□□□□□ □□□□□□ "□□□□□□□□□□□□□□□□□□□□□ □□□□ □□□□ □□□ □ " □□□□ "□□□□ "□□□□□□□□□□□□□□ Owen's T/Q □□□□□□□□□□□ power □□□□□□

□□□□□□□□□□□□□□ □□□□□□□□ **bioequivalence, BE**□□□ □

- □□□□ generic drug□□□□□□□□□□□□□□□ reference□□□□□□□□□□ □□ □□□□□□□□□□□ AUC□ C_max □□□□□□□□ 0.80–1.25 □□□□
- □□□□□□□ □□□□□□ **TOST**□ □□□□ "□□ "□□□□□□□□□ □□□□□□□□□ □□□□□

□□□□□□□□□□□□ □□ "□□□□ "□□□□□ "□□□□□□□□□□□□□ " □□□□□□□□□□□□ 1□□ "□□□□ "□□□□ "□□□□□□□□□□□□□□□□□□□□□□□ $[0.80,1.25]$ □□□ "□□□ □□□□□□□□□□□□□□ **t** □□□ □□□□□□□ □□□□ □□□□□□□□ t □□□□□□□□□□□□□ **Owen □ Q** □□ □□□□□□□ Owen □ T □□□□□□□□□

> **Owen's T □ Owen's Q □□□ □**
>
> - **Owen's T**□ Owen 1956□□□□□ □□□□ □□□□□□□□
> - **Owen's Q**□ Owen 1965□□□□□□□□□□ □□□□□ **t** □□ ——□ TOST □□□□□ "□□□□□ -1 □□□□□□ t"□□□□□□□□□□ Owen □□□□□□□□□ *A Special Case of a Bivariate Non-Central t-Distribution*□□

□□□□□□□□□□□□□□□□ □ TOST □□□□□

$$ 1-\beta ;=; F_\nu!\left(-t_{1-\alpha,\nu};\delta_2\right) - F_\nu!\left(t_{1-\alpha,\nu};\delta_1\right) - \big[Q\text{-□□□ }\big], $$

□□ $F_\nu(\cdot;\delta)$ □□□□ t □ CDF□□□□□□ Q_ν □□□□□□ 0 □□□□□□□□□□□ Owen's Q □□□□□ $R>0$ □□□□□□ □□□ □□□□□□□□□□□ " □□□□□□□□□□□□ "□□□□□□□□□□□□□□ ——□□□□□□ Owen □ Q

2. ????

2.1 ??? t ??

t " " t $\delta\neq 0$

$Z\sim N(0,1)$ $V\sim\chi^2_\nu$

$$ T ;=; \frac{Z+\delta}{\sqrt{V/\nu}} ;\sim; t_\nu(\delta), $$

$\delta\in\mathbb R$ **noncentrality parameter, NCP** ν $\delta=0$ t

CDF Owen's Q $W=\sqrt{V/\nu}$

$$ F_\nu(t;\delta)=\Pr(T\le t)=\int_0^\infty \Phi(t w-\delta),f_W(w),dw, \qquad f_W(w)=\frac{2(\nu/2)^{\nu/2}}{\Gamma(\nu/2)},w^{\nu-1}e^{-\nu w^2/2},\quad w>0. $$

$W=w$ T $N(\delta/w,,1/w^2)$ $\Pr(T\le t\mid w)=\Phi(tw-\delta)$ w

$\nu>1$ $\nu>2$

$$ \mathbb E[T]=\delta\sqrt{\frac{\nu}{2}},\frac{\Gamma!\big(\frac{\nu-1}{2}\big)}{\Gamma!\big(\frac{\nu}{2}\big)}, \qquad \operatorname{Var}(T)=\frac{\nu}{\nu-2}(1+\delta^2)-\big(\mathbb E[T]\big)^2. $$

$\mathbb E[T]\approx\delta$ ν NCP δ " "

2.2 Owen's T ?????????

" X,Y " Owen's T " "

Owen 1956

$$ T(h,a)=\frac{1}{2\pi}\int_0^{a}\frac{\exp!\big[-\tfrac{h^2}{2}(1+x^2)\big]}{1+x^2},dx, \qquad -\infty<h<\infty,\ -\infty<a<\infty. $$

$$ T(h,0)=0,\qquad T(0,a)=\frac{1}{2\pi}\arctan a,\qquad T(-h,a)=T(h,a),\qquad T(h,-a)=-T(h,a),\qquad T(h,\infty)=\tfrac12,\Phi(-|h|). $$

ρ

$$ \Pr(X\le h,\ Y\le k)=\Phi(h)\Phi(k)+\frac{1}{2\pi}\int_0^{\rho}\frac{1}{\sqrt{1-r^2}}\exp!\left[-\frac{h^2-2rhk+k^2}{2(1-r^2)}\right]dr, $$

Owen (1956) T

$$ \Pr(X\le h,Y\le k)=\tfrac12\Phi(h)+\tfrac12\Phi(k)-T!\left(h,\frac{k-\rho h}{h\sqrt{1-\rho^2}}\right)-T!\left(k,\frac{h-\rho k}{k\sqrt{1-\rho^2}}\right)-c, \qquad c=\begin{cases}0,&hk\ge0\ \tfrac12,&hk<0.\end{cases} $$

h $k=0$

2.3 Owen's Q ???????? t / ??? t CDF?

2.2 " " " t" ± 1 Owen's Q

Owen 1965 " A" tx/ν

$$ Q_\nu(t,\delta;0,R)=\frac{\sqrt{2\pi}}{\Gamma!\big(\tfrac\nu2\big),2^{(\nu-2)/2}}\int_R^{\infty}\Phi!\left(\frac{t x}{\nu}-\delta\right)x^{\nu-1}\phi(x),dx, \qquad \phi(x)=\frac{e^{-x^2/2}}{\sqrt{2\pi}}. $$

$tx/\sqrt\nu$ $x\mapsto x\sqrt\nu$

$x=w\sqrt\nu$ Q_ν 2.1 t CDF

$$ F_\nu(t;\delta)=Q_\nu!\big(t\sqrt\nu,\ \delta;\ 0,\ 0\big). $$

t CDF Owen's Q $R=0$ $R>0$ Q_ν " " TOST

2.4 ???????????TOST?

$$ \mu=\ln!\left(\frac{\text{test}}{\text{reference}}\right)=\ln(\text{ }), $$

$[\theta_1,\theta_2]$ log $[\ln 0.80,\ \ln 1.25]=[-0.2231,\ 0.2231]$

□□□□□□ **TOST, Schuirmann 1987□** □□ "□□ "□□□□□□□□

$$ H_{01}:\ \mu\le\theta_1 \quad \text{vs.}\quad H_{11}:\ \mu>\theta_1, \qquad H_{02}:\ \mu\ge\theta_2 \quad \text{vs.}\quad H_{12}:\ \mu<\theta_2. $$

□□□□□□□□□ **α** □□□□ □□□□□□□□□□□□□□ Westlake / Schuirmann □□□□□□□□□

$$ (1-2\alpha)\times100\%\ \text{□□□□}\ \subseteq\ [\theta_1,\theta_2] \iff \text{□□□□}. $$

> □□ BE □□ **90%** □□□□ □□□ $\alpha=0.05$ □ TOST□□□□□□□□ 95%□

□□□□□□□ **I** □□□ □□□□□□□□□□□ TOST □□ "□□ "□□□□□□ α□

2.5 BE ??????????

□□□□□ □□□□□□ μ□□□ (θ_1,θ_2) □□□□ TOST □□□□□□□□□□

$$ 1-\beta=\Pr!\big(T_1>t_{1-\alpha,\nu}\ \text{□}\ T_2<-t_{1-\alpha,\nu}\big). $$

□□□□□□□□□ □□□□□□□□□ □□□□□□□□ □□□ 2×2 □□□□□□□□ $[-\theta,\theta]$□□□□□□ μ□

$$ 1-\beta ;\approx; \Phi!\left(\frac{\sqrt{N},(\theta-|\mu|)}{\sigma_w\sqrt2}-t_{1-\alpha,N-2}\right), $$

□□□□□□□□□□□□

$$ N ;\approx; \frac{2,\sigma_w^2,(z_{1-\alpha}+z_{1-\beta})^2}{(\theta-|\mu|)^2}. $$

□□□□□□□ □□□□□□□□ □□ □□□□□□□□□□□□□□□□□□ "□□□□ "□□□□□ TOST □□□□□□□□□□□□□□□ □□□□ □□□□□□□□□□□ N=12 □□□□□ 64% □□□□□□ 83%□□□□□□□□□□□□□□□□ □□□□ **——Owen's Q□**

---

3. Owen's T/Q ?????????

3.1 ?????????? 2×2 ???????

- □□□□□ N□□□□ $n=N/2$□□□□□□□□

- [illegible] μ[illegible] [illegible] σ_w[illegible] CV [illegible]
  $\sigma_w=\sqrt{\ln(1+\text{CV}^2)}$[illegible]
- [illegible] $\hat\mu=\bar X_T-\bar X_R$[illegible]

$$ \operatorname{Var}(\hat\mu)=\sigma_w^2\cdot\frac{2}{N}, \qquad \hat\sigma_w^2:\ \frac{\nu\hat\sigma_w^2}{\sigma_w^2}\sim\chi^2_\nu,\ \ \nu=N-2. $$

> [illegible] [illegible] 2×2 [illegible]
> $\mathrm{SE}=\sigma_w\sqrt{2/N}$[illegible] N [illegible] [illegible] [illegible]
> $\sigma_w\sqrt{2/n}$[illegible] n [illegible] σ_w [illegible] "
> [illegible] "[illegible] $\sqrt2$——
> [illegible]
> $\mathrm{SE}=\sigma_w\sqrt{2/N}$[illegible]

[illegible]

$$ T_1=\frac{\hat\mu-\theta_1}{\hat\sigma_w\sqrt{2/N}},\qquad T_2=\frac{\hat\mu-\theta_2}{\hat\sigma_w\sqrt{2/N}}. $$

[illegible] [illegible] $Z=\dfrac{\hat\mu-\mu}{\sigma_w\sqrt{2/N}}\sim N(0,1)$[illegible] $W=\sqrt{V/\nu}$[illegible]
$V\sim\chi^2_\nu$[illegible]

$$ T_1=\frac{Z+\delta_1}{W},\quad T_2=\frac{Z+\delta_2}{W}, \qquad \delta_1=\frac{\mu-\theta_1}{\sigma_w\sqrt{2/N}},\quad \delta_2=\frac{\mu-\theta_2}{\sigma_w\sqrt{2/N}}. $$

[illegible] [illegible] **Z** [illegible] **W**——[illegible] "[illegible] -1 [illegible] t"[illegible] Owen (1965) [illegible]

3.2 ??????????????

TOST [illegible] α [illegible]

$$ T_1>t_{1-\alpha,\nu}\ \ \text{[illegible] }\ \ T_2<-t_{1-\alpha,\nu} \iff t_{\alpha}W-\delta_1 < Z < -t_{\alpha}W-\delta_2, \qquad t_\alpha:=t_{1-\alpha,\nu}. $$

[illegible] Z [illegible] [illegible] [illegible]

$$ t_\alpha W-\delta_1 < -t_\alpha W-\delta_2 \iff W < w^*:=\frac{\delta_1-\delta_2}{2t_\alpha} =\frac{\theta_2-\theta_1}{2,t_\alpha,\sigma_w\sqrt{2/N}}. $$

[illegible] W [illegible] [illegible] [illegible]

$$ 1-\beta=\int_0^{w^*}\Big[\Phi\big(-t_\alpha w-\delta_2\big)-\Phi\big(t_\alpha w-\delta_1\big)\Big],f_W(w),dw $$

□□ $f_W(w)=\dfrac{2(\nu/2)^{\nu/2}}{\Gamma(\nu/2)}w^{\nu-1}e^{-\nu w^2/2}$□

□□□□ □ $\mu=0$□□ $\pm\theta$□□ $\delta_1=\delta=-\delta_2$□□□□□

$$ 1-\beta=\int_0^{\theta/(t_\alpha\sigma_w\sqrt{2/N})}\big[2\Phi(\delta-t_\alpha w)-1\big],f_W(w),dw, $$

□□ $2\Phi(x)-1$ □□ "□□□□ $[-x,x]$"□□□ ——□□□□ □□□□□□□□□

3.3 ? Owen's Q ??????????

□□ $\int_0^{w^}=\int_0^{\infty}-\int_{w^}^{\infty}$□□□□ 2.3 □ Q_ν □ F_ν □□□□□

$$ 1-\beta=F_\nu(-t_\alpha;\delta_2)-F_\nu(t_\alpha;\delta_1)-Q_\nu!\big(-t_\alpha\sqrt\nu,\delta_2;0,R\big)+Q_\nu!\big(t_\alpha\sqrt\nu,\delta_1;0,R\big) $$

□□

$$ R=w^*\sqrt\nu=\frac{\sqrt\nu,(\theta_2-\theta_1)}{2,t_\alpha,\sigma_w\sqrt{2/N}}. $$

□□□□ □

1. $F_\nu(-t_\alpha;\delta_2)-F_\nu(t_\alpha;\delta_1)$□□□□□□ t CDF □□ ——□ "□□ W □□□□□ "□□□□□□ $Q_\nu(\cdot;\cdot;0,0)$ □□□□□□
2. $-Q_\nu(-t_\alpha\sqrt\nu,\delta_2;0,R)+Q_\nu(t_\alpha\sqrt\nu,\delta_1;0,R)$□ $R>0$ □□ □□□□ □

□□□□□□□□□□□□□□□□□□□□□ "□□□□□ t CDF □□ "□□□□□□□□□□□□ □□□□□ □□□□□□□□□□□□□□□□□□□□□

> □□□□ Diletti et al. (1991) □ Phillips (1990) □ BE □□□□□□ Owen-Q □□□□□□□□□□□

3.4 ???????????

1. □ 2.5 □□□□□□□□□ N_0□
2. □□□ N □□□□□□□ 3.2 □ 3.3 □□□
3. □□□ $<1-\beta$ □□□ N□□□□□□□□□□□□
4. □ □□ N□□□□□□□□□□□□□□□□ 10–20% □□□□

3.5 ??????????

2×2 $\mathrm{CV}=20\%$ $\sigma_w=\sqrt{\ln 1.04}=0.19804$ 1.0 $\mu=0$ 0.80–1.25 $\alpha=0.05$ 80%

$N=16$ $\nu=14$ $t_{0.95,14}=1.7613$
$\mathrm{SE}=0.19804\sqrt{2/16}=0.07002$ $\delta_1=0.22314/0.07002=3.1869$
$\delta_2=-3.1869$ $=0.8332\ge 0.8$ $N=14$ 0.7549
$N=16$

vs

N	Owen Q		"t CDF "
12	0.6445	0.8283	0.6432
14	0.7549	0.8847	0.7548
16	0.8332	0.9230	0.8332
20	0.9249	0.9663	0.9249

$N=12$ 83% 64%
" t CDF " ——
Owen's Q

		N
CV=20% =1.0	80%	16
CV=20% =0.95 $\mu=-0.0513$	80%	19
CV=20% =0.95	90%	25
CV=30% =1.0	80%	32

> / a vs b σ_w c 80% vs 90% d $\sqrt2$ $\mathrm{SE}=\sigma_w\sqrt{2/N}$ Owen-Q

---

4. Owen's T/Q ??????????

4.1 Owen's T ???

- $[0,a]$ a $T(h,\infty)=\tfrac12\Phi(-|h|)$
- / **Patefield & Tandy 2000** $T(h,a)$ 14–15
- Young & Minder (1974) **AS 76** Boys (1989) **AS R80**
- CDF Genz 2004 T

4.2 ??? t CDF ???

- / **beta** Cooper (1968) **AS 5** Lenth (1989) **AS 243** beta R `pt(q, df, ncp)`
- Benton & Krishnamoorthy (2003) t t ν $|\delta|$
-
- Gil Segura Temme

4.3 Owen's Q ? TOST ???????

- **$R=0$** t CDF
- **$R>0$** $Q_\nu(t,\delta;0,R)=\int_{R/\sqrt\nu}^{\infty}\Phi!\big(\tfrac{tw}{\sqrt\nu}-\delta\big)f_W(w),dw$
- 3.3 TOST F_ν Q_ν
- R `OwenQ` Stéphane Laurent Rcpp Q_ν t

4.4 ???????

1. $2\Phi(x)-1$ x erfc
2. **t** $|\delta|$ /
3. $w^{\nu-1}e^{-\nu w^2/2}$
4. $|\delta|$ ν

---

5. ??????C/Fortran ?????

—— Fortran Applied Statistics C/C++ R

[illegible] / [illegible]	[illegible]	[illegible]	[illegible]

AS 5 (Cooper 1968)	Fortran	t CDF	statlib `/apstat/5`
AS 76 (Young & Minder 1974)	Fortran	Owen's T	statlib `/apstat/76`
AS R80 (Boys 1989)	Fortran	AS 76	statlib `/apstat/R80`
AS 243 (Lenth 1989)	Fortran	t CDF	statlib `/apstat/243`
DCDFLIB (Brown, Lovato, Russell)	C + Fortran	`cdftnc` t `cdft` `cdffnc`	statlib
Boost.Math	C++	`owens_t` `non_central_t` `bivariate_normal`	boost.org
GSL	C	t `gsl_cdf_tdist`	t
R `stats::pt(q, df, ncp)`	C AS 243	t CDF	R
R `PowerTOST` (Labes & Schütz)	R/C	`power.TOST` `sampleN.TOST` Owen Q	CRAN
R `OwenQ` (Laurent)	R/Rcpp	`OwenQ1/Q2/Q3` t	CRAN / GitHub
R `sn` (Azzalini) `mnormt`	R	`T.Owen` `pst` `sadmvn` `biv.nt.prob`	CRAN
SciPy `scipy.stats.nct`	C/Python	t	SciPy

- **Fortran** AS " " DCDFLIB C Fortran t
- **C++** Boost.Math `owens_t(h, a)` Owen's T `non_central_t` t CDF/PDF/ `bivariate_normal`
- **BE** " " R **`PowerTOST`** Owen's Q Phillips 1990 / Diletti 1991
- / **`OwenQ`** Q_ν

---

6. ????

1. **Owen's T/Q** " / " —— **t** TOST
2. t CDF $\int_0^\infty\Phi(tw-\delta)f_W(w)dw$ Owen's Q 0 R $F_\nu(t;\delta)=Q_\nu(t\sqrt\nu,\delta;0,0)$ TOST = t CDF Q_ν 0 w^*
3. $N=12$ 83% vs 64% " t CDF "

4. Fortran AS 5/76/243 DCDFLIB C++ Boost.Math R `pt(..., ncp)` `PowerTOST` `OwenQ` `sn`/`mnormt` Patefield–Tandy (2000) Lenth (1989) Owen's T t Gil–Segura–Temme
5. 2×2 $\mathrm{SE}=\sigma_w\sqrt{2/N}$ $\nu=N-2$

$$1-\beta=\int_0^{w^*}\Big[\Phi\big(-t_\alpha w-\delta_2\big)-\Phi\big(t_\alpha w-\delta_1\big)\Big]\frac{2(\nu/2)^{\nu/2}}{\Gamma(\nu/2)}w^{\nu-1}e^{-\nu w^2/2}\,dw, \qquad w^*=\frac{\theta_2-\theta_1}{2\,t_\alpha\,\sigma_w\sqrt{2/N}}.$$

/

- Owen, D. B. (1956). Tables for computing bivariate normal probabilities. *Ann. Math. Statist.* 27, 1075–1090.
- Owen, D. B. (1965). A special case of a bivariate non-central t-distribution. *Biometrika* 52, 437–446.
- Owen, D. B. (1968). A survey of properties and applications of the non-central t-distribution. *Technometrics* 10, 445–478.
- Schuirmann, D. J. (1987). A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability. *J. Pharmacokinet. Biopharm.* 15, 657–680.
- Phillips, K. F. (1990). Power of the two one-sided tests procedure in bioequivalence. *J. Pharmacokinet. Biopharm.* 18, 137–144.
- Diletti, E., Hauschke, D., & Steinijans, V. W. (1991). Sample size determination for bioequivalence assessment by means of confidence intervals. *Int. J. Clin. Pharmacol. Ther. Toxicol.* 29, 1–8.
- Patefield, M., & Tandy, D. (2000). Fast and accurate computation of Owen's T function. *J. Stat. Softw.* 5(5), 1–25.
- Young, J. C., & Minder, C. E. (1974). Algorithm AS 76. *Appl. Statist.* 23, 455–457; Boys, R. J. (1989). AS R80. *Appl. Statist.* 38, 580–582.
- Lenth, R. V. (1989). Algorithm AS 243: Cumulative distribution function of the non-central t distribution. *Appl. Statist.* 38, 185–189.
- Benton, D., & Krishnamoorthy, K. (2003). Computing discrete mixtures of continuous distributions. *Comput. Statist. Data Anal.* 43, 249–267.
- Genz, A. (2004). Numerical computation of rectangular bivariate and trivariate normal and t probabilities. *Stat. Comput.* 14, 251–260.