University of Texas, MD Anderson Cancer Center

Numerical Evaluation of Gamma Inequalities

John D. Cook*

*M. D. Anderson Cancer Center, cook@mdanderson.org

Numerical Evaluation of Gamma Inequalities

John D. Cook

Abstract

This paper addresses the problem of numerically evaluating the probabilities P(X>Y), P(X>max(Y,Z)), and P(X

Numerical Evaluation of Gamma Inequalities

John Cook

Department of Biostatistics, Box 447
The University of Texas, M. D. Anderson Cancer Center
1515 Holcombe Blvd., Houston, Texas 77030, USA
`cook@mdanderson.org`

January 1, 2006

Abstract

This paper addresses the problem of numerically evaluating the probabilities $P(X > Y)$, $P\left(X > \max(Y, Z)\right)$, and $P\left(X < \min(Y, Z)\right)$ where X, Y, and Z are independent gamma or inverse gamma random variables.

Keywords: gamma distribution, stochastic inequalities, Appell F2 function, generalized order statistics

1 Introduction

In adaptively randomized clinical trials, the probability of assigning a treatment increases as evidence accumulates in favor of that treatment being better than its competitors. Such a design will, on average, assign more patients to more effective treatments while retaining the benefits of randomization.

When the primary endpoint of the trial is survival time, a common method of conducting adaptively randomized trials requires calculating

$$P(X_1 > X_2)$$

or

$$P\left(X_1 > \max(X_2, X_3)\right)$$

1

for independent inverse gamma random variables X_i. When the primary end point is time to a desirable event, say transplant engraftment, one needs to calculate

$$P(X_1 < X_2)$$

or

$$P\left(X_1 < \min(X_2, X_3)\right).$$

One may also consider trials with binary end points. These commonly require evaluating similar stochastic inequalities, but for beta random variables. See [2] and [3] for more on calculating beta inequalities. In this note we focus on (inverse) gamma random variables.

See [4] and [8] for more on the application of stochastic inequalities to clinical trials. See [9] for clinical trial simulation software that employs the algorithms given in this paper.

Note that these inequality probabilities are of interest outside of medical applications. For example, in reliability engineering one may be interested in survival times of mechanical devices rather than survival times of cancer patients.

2 Preliminaries

2.1 Distribution parameterizations

There are two common parameterizations for both the gamma and inverse gamma distribution. To avoid confusion, we state our parametrization conventions as follows. A gamma random variable with shape parameter $a > 0$ and scale $b > 0$, abbreviated G(a, b), has PDF

$$\frac{1}{\Gamma(a)b^a}x^{a-1}e^{-x/b}.$$

And inverse gamma random variable with shape $a > 0$ and scale $b > 0$, abbreviated IG(a, b), has PDF

$$\left(\frac{b^a}{x^{a+1}\Gamma(a)}\right)e^{-b/x}.$$

With these parameterizations, $X \sim$ G(a, b) iff $1/X \sim$ IG$(a, 1/b)$.

2

2.2 Reductions

Since

$$P(X_1 > X_2) = 1 - P(X_2 > X_1)$$

and

$$P\left(X_1 < \min(X_2, X_3)\right) = 1 - P(X_1 > X_2) - P(X_1 > X_3) + P\left(X_1 > \max(X_2, X_3)\right)$$

we need only consider how to compute inequality probabilities of one random variable being greater than another or the maximum of others.

Also, if $X_i \sim \text{IG}(a_i, b_i)$ and $Y_i = 1/X_i$,

$$P(X_1 > X_2) = P(Y_1 < Y_2)$$

and

$$P\left(X_1 > \max(X_2, X_3)\right) = P\left(Y_1 < \min(Y_2, Y_3)\right).$$

Therefore we may restrict our attention to gamma random variables.

3 Two variables

In a two-arm trial, we need to evaluate $g_2(a_1, b_1, a_2, b_2)$ defined as the probability $P(X_1 > X_2)$ where $X_i \sim \text{G}(a_i, b_i)$.

In [2] we show that

$$g_2(a_1, b_1, a_2, b_2) = I_{b_1/(b_1+b_2)}(a_2, a_1)$$

where $I_x(a, b)$ is the incomplete beta function.

4 Three variables

In a three-arm trial, we need to evaluate $g_3(a_1, b_1, a_2, b_2, a_3, b_3)$ defined as $P\left(X_1 > \max(X_2, X_3)\right)$ where $X_i \sim \text{G}(a_i, b_i)$.

3

4.1 Analytical representations

In [4] we show that

$$
\begin{aligned}
g_3 \;=\; & \frac{\Gamma(a_1 + a_2 + a_3)}{a_2 a_3 \Gamma(a_1)\Gamma(a_2)\Gamma(a_3)} \left(\frac{b_1}{b_2}\right)^{a_2} \left(\frac{b_1}{b_3}\right)^{a_3} \\
& \times F_2 \left(\begin{array}{c} a_1 + a_2 + a_3,\; a_2,\; a_3 \\ a_2 + 1,\; a_3 + 1 \end{array} \;\middle|\; -\frac{b_1}{b_2}, -\frac{b_1}{b_3} \right)
\end{aligned}
\qquad (1)
$$

where F_2 denotes the Appell function of the second kind. Note that a $G(a, b)$ random variable in the notation of this note corresponds to a $G(1/b, a)$ in the parameterization used in [4].

See [6] for numerically evaluating F_2 for general arguments. Here, however, we take advantage of the special form of the arguments of F_2 needed for our our application.

Note that equation (1) only depends on the ratios b_1/b_2 and b_1/b_3 and not on the b's individually. This is because if $X \sim G(a, b)$, $kX \sim G(a, kb)$ for any positive constant k. Thus we can multiply all the b's by a positive constant and not change the inequalities. We now simplify notation slightly by assuming without loss of generality that $b_1 = 1$.

Appell's F_2 function is defined in terms of a double series, though the series representation is only valid for arguments (x, y) satisfying $|x| + |y| < 1$. However, using results from section 206D of [7], one can express F_2 as a double integral obtaining

$$
g_3 = \frac{\Gamma(a_1 + a_2 + a_3)}{\Gamma(a_1)\Gamma(a_2)\Gamma(a_3) b_2^{a_2} b_3^{a_3}} \int_0^1 \int_0^1 \frac{u^{a_2-1} v^{a_3-1}}{(1 + u/b_2 + v/b_3)^{a_1+a_2+a_3}} \, du \, dv. \qquad (2)
$$

This integral representation gives an analytic continuation valid for all arguments we need.

5 Upper and lower bounds

For any independent random variables X_i,

$$
P(X_1 > X_2 \text{ and } X_1 > X_3) \leq P(X_1 > X_2).
$$

4

By symmetry one can reverse X_2 and X_3 and so

$$P(X_1 > X_2 \text{ and } X_1 > X_3) \leq \min\left(P(X_1 > X_2), P(X_1 > X_3)\right).$$

Also,

$$
\begin{aligned}
P(X_1 > X_2 \text{ and } X_1 > X_3) &= P(X_1 > X_2)P(X_1 > X_3 \mid X_1 > X_2) \\
&\geq P(X_1 > X_2)\, P(X_1 > X_3).
\end{aligned}
$$

Therefore if we let $p_j = P(X_1 > X_j)$ then

$$p_2\, p_3 \leq P\left(X_1 > \max(X_2, X_3)\right) \leq \min(p_2, p_3) \tag{3}$$

6   Numerical considerations

Routines for accurate and efficient evaluation of the incomplete beta function are readily available. See for example [1] and [5]. Therefore the evaluation of g_2 is a solved problem. However, I am not aware of software any other software to evaluate g_3.

The integral (2) is easy to evaluate numerically if a_2 and a_3 are larger than 1, but we only know that these parameters are positive. If either were less than 1, the integrand would be singular along an edge of its domain. To obtain a well-behaved integrand for all positive values of a_2 and a_3 we integrate by parts twice. Let $s = a_1 + a_2 + a_3$ and denote

$$I = \int_0^1 \int_0^1 \frac{u^{a_2-1} v^{a_3-1}}{(1 + u/b_2 + v/b_3)^s} \, du\, dv.$$

Then integration by parts show that

$$
\begin{aligned}
a_2 a_3 I \;=\; & \frac{s(s+1)}{b_2 b_3} \int_0^1 \int_0^1 \frac{u^{a_2} v^{a_3}}{(1 + u/b_2 + v/b_3)^{s+2}} \, du\, dv \\
& + \frac{s}{b_3} \int_0^1 \frac{v^{a_3}}{(1 + 1/b_2 + v/b_3)^s} \, dv \\
& + \frac{s}{b_2} \int_0^1 \frac{u^{a_2}}{(1 + u/b_2 + 1/b_3)^s} \, dv \\
& + \frac{1}{(1 + 1/b_2 + 1/b_3)^s}
\end{aligned}
\tag{4}
$$

5

We obtain an accurate and efficient algorithm for evaluating the integrals given in the appendix using Gaussian (product) quadrature with 32 nodes. The integrals in equation (4) have no singularities and Gaussian quadrature works quite well. However, one must be careful about numerical overflow and underflow. In application, the shape parameters a_i can be large enough that the factor

$$\frac{\Gamma(a_1 + a_2 + a_3)}{\Gamma(a_1)\Gamma(a_2)\Gamma(a_3)} \tag{5}$$

will overflow or that the integrals in equation (4) underflow. The solution to this problem is to first evaluate the logarithm of expression (5) by using a routine for $\log \Gamma(x)$. Then in the routines for evaluating the integrands in equation (4) first evaluate the logarithm of the integrands, add the logarithm of expression (5), and then exponentiate.

This procedure becomes less accurate when one of the random variables X_i is very likely to be larger than one of the others. Fortunately, this is precisely when inequality (3) becomes tighter. For our application to clinical trial randomization, we are interested in controlling absolute error rather than relative error: we do not need to know small probabilities to many significant figures.

Define p_i as in (3). Furthermore, let $p_{\min} = \min(p_2, p_3)$ and $p_{\max} = \max(p_2, p_3)$. Then

$$p_{\min}\, p_{\max} \leq g_3 \leq p_{min}$$

and so if $p_{\min}(1 - p_{\max}) < 2\varepsilon$ then the error in the approximation

$$g_3 \approx \frac{p_{\min}(1 - p_{\max})}{2} \tag{6}$$

is less than ε.

7   Testing the algorithm

We implemented the algorithm in this report, using the approximation (6) whenever one of the probabilities on the right was either below $\varepsilon = 0.001$ or above $1 - \varepsilon$. We generated 100,000 vectors of the form $(u_1, \ldots, u_6)$ with each u_i being a uniform random sample from $(0.1, 90)$. For each such vector, we evaluated $g_3(u_1, u_2, u_3, u_4, u_5, u_6)$, $g_3(u_3, u_4, u_5, u_6, u_1, u_2)$, and $g_3(u_5, u_6, u_1, u_2, u_3, u_4)$. In theory, these values should sum to 1.

6

The average absolute error was 5.477×10^{-5} and the maximum error was 0.00343. The largest errors occur when one of the three probabilities is very small. If we throw out cases where one of the probabilities is less than 0.005, the average error drops to 1.016×10^{-6} and the maximum error to 0.00261.

References

[1] Barry W. Brown. CDFLIB. [Computer software]

Available at http://biostatistics.mdanderson.org/SoftwareDownload

[2] John D. Cook. Numerical Computation of Stochastic Inequality Probabilities. MDACC technical report UTMDABTR-008-03. (2003)

Available at http://www.mdanderson.org/pdf/biostats_utmdabtr00803.pdf.

[3] John D. Cook. Exact calculation of beta inequalities. MDACC technical report UTMDABTR-005-05. (2005)

Available at http://www.mdanderson.org/pdf/biostats_utmdabtr_005_05.pdf

[4] John D. Cook and Saralees Nadarajah. (2006) Stochastic Inequality Probabilities for Adaptively Randomized Clinical Trials. *Biometrical Journal*, to appear.

[5] Armido R. Didonato and Alfred E. Morris. Algorithm 708: Significant Digit Computations of the Incomplete Beta Function Ratios. *ACM Transactions on Mathematical Software*. Vol 18, No. 3, 360-373. (1992).

[6] G. Gasaneo and S. Otranto. Evaluación numérica de la función de Appell F_2. *Mecánica Computacional* Vol. XXII. M. B. Rosales, V. H. Cortínez, and D. V. Bambill editors. Bahía Blanca, Argentina (2003).

[7] Mathematical Society of Japan, Kiyosi Itô editor. *Encyclopedic Dictionary of Mathematics*, second edition. MIT Press (1996).

[8] Peter F. Thall, Leiko H. Wooten, and Nizar M. Tannir. Monitoring Event Times in Early Phase Clinical Trials: Some Practical Issues, *Clinical Trials* vol 2, 467-478. (2005)

[9] J. Kyle Wathen and Odis Wooten. Adaptive Randomization 3.1.1 [Computer software]. (2005)

Available at http://biostatistics.mdanderson.org/SoftwareDownload.

7