SUPPLEMENTARY INFORMATION

Table S1. Published progression-free survival (PFS) analyses, selected PFS cohorts, available risk tables, and published doubling times for each cancer type. The published PFS were used for data fitting and simulations, and the simulated output was compared to the published doubling times.

Published PFS data				Published DBT	
Cancer	Cohort	Risk Table (Y/N)	Reference	DBT (months)[1]	Reference
Pancreatic	Gemcitabine	Y	(1)	5.30 (3.84, 6.76) [42]	(2)
Melanoma	BRAF-mutant	Y	(3)	4.80 (2.1 – 8.5)[3]	(4)
				2.67 (1.3 – 13.33)[3]	(5)
				1.64 (1.31, 1.96) [112]	(6)
				6.84 (4.37, 9.31) [76]	(7)
				1.43 (0.99, 1.86) [87]	(8)
				4.80 (2.1 – 8.5)[3]	(4)
HCC	Placebo	Y	(9)	5.26(3.78, 6.74) [103]	(10)
RCC	Placebo	Y	(11)	2.37 (1 – 4.9)[4]	(12)
TN Breast	Tivantinib	Y	(13)	15.6 (13.34, 17.86) [18][5]	(14)

NSCLC	Placebo	Y	(15)	1.53 (0.85, 2.21) [96]	(16)
				Women: 22.93 (7.18, 38.69) [192]	(17)
				Men: 7.80 (0.92, 14.68) [191]	(17)
				15.07 (11.88, 18.25) [84]	(18)
				36.90 (0.13, 11.73) [36]	(19)
				2.07 (1.60, 2.93) [67]	(20)
HR+ Breast	Exemestane+Placebo	Y	(21)	8.03 (6.25, 9.82) [69]	(22)
HER-2+ Breast	Anastrazole	Y	(23)	5.40 (4.27, 6.53) [37]	(22)
Gastric	UFTM	N	(24)	10.08 (6.48, 13.67) [63]	(25)
GBM	Procarbazine	N	(26)	1.65[7]	(27)
CRC	BSC	Y	(28)	3.17 (0.05 – 10.63)[8]	(29)
Prostate	Mitoxantrone	Y	(30)	13.91 (4.75, 23.08) [82]	(31)

Note: references for all PFS curves included in the literature search can be found in (1,3,9,11,13,21,23,24,26,28,30,32-67).

Abbreviations: BSC = best supportive care; UFTM = uracil + fluorouracil + tegafur + mitomycin. CRC = colorectal cancer; GBM = glioblastoma multiforme; HER-2^{+} = human epidermal growth factor receptor-2 positive, HR^{+} = hormone receptor positive, TN = triple negative; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; HCC = hepatocellular carcinoma

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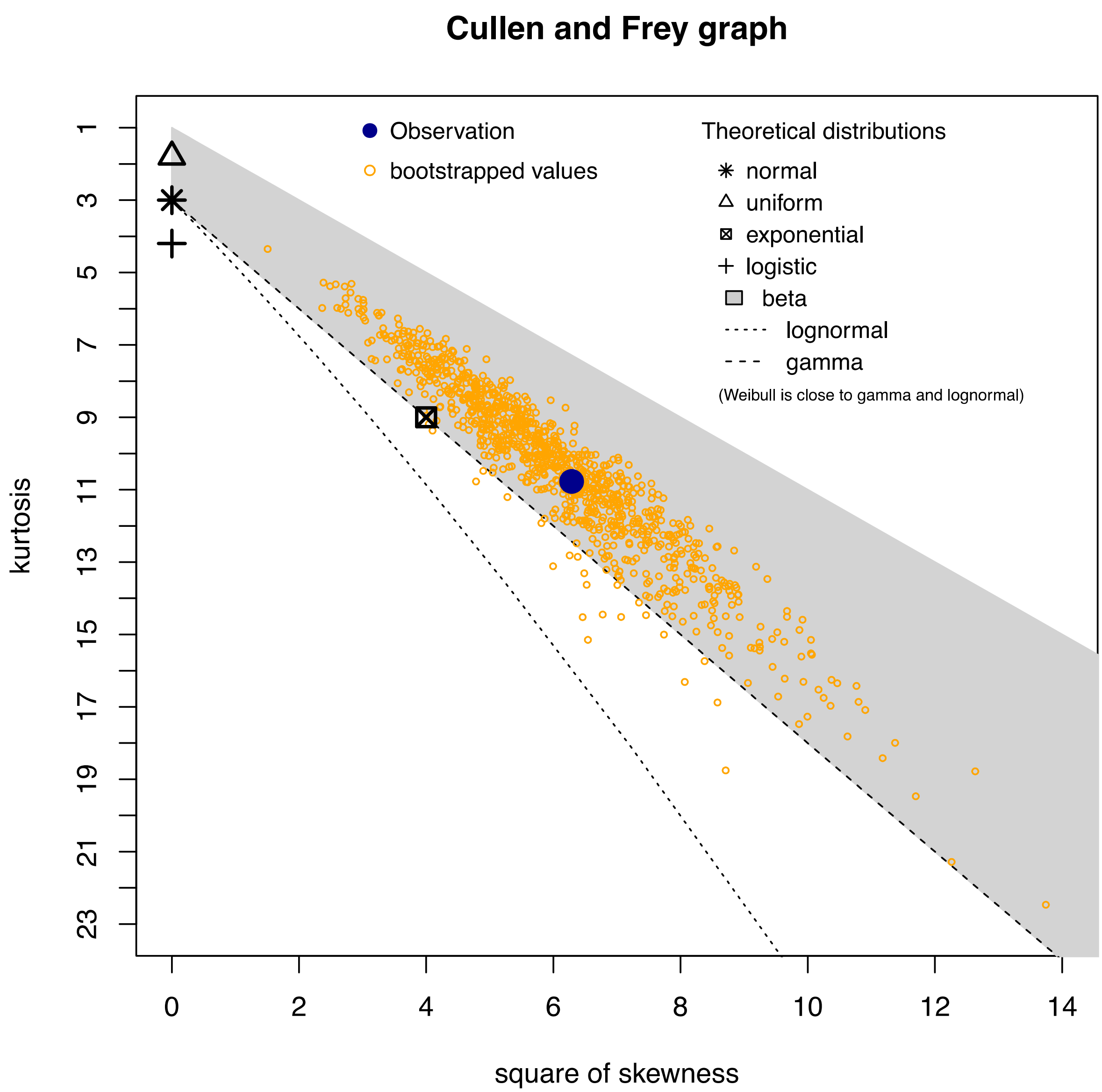
Figure S1. Distribution fitting and simulation workflow for pancreatic cancer. Panel A: Cullen and Frey plot with bootstrapped values. Panel B: Statistical fitting of calculated growth rates using the following distribution models: normal, uniform, lognormal, gamma, and weibull. For each distribution, the empirical and theoretical distribution (upper left), quantile-quantile (QQ: upper right), probability-probability (PP: lower right) and theoretical and empirical cumulative distribution function (CDF: lower left) plots are shown.

A.



B.

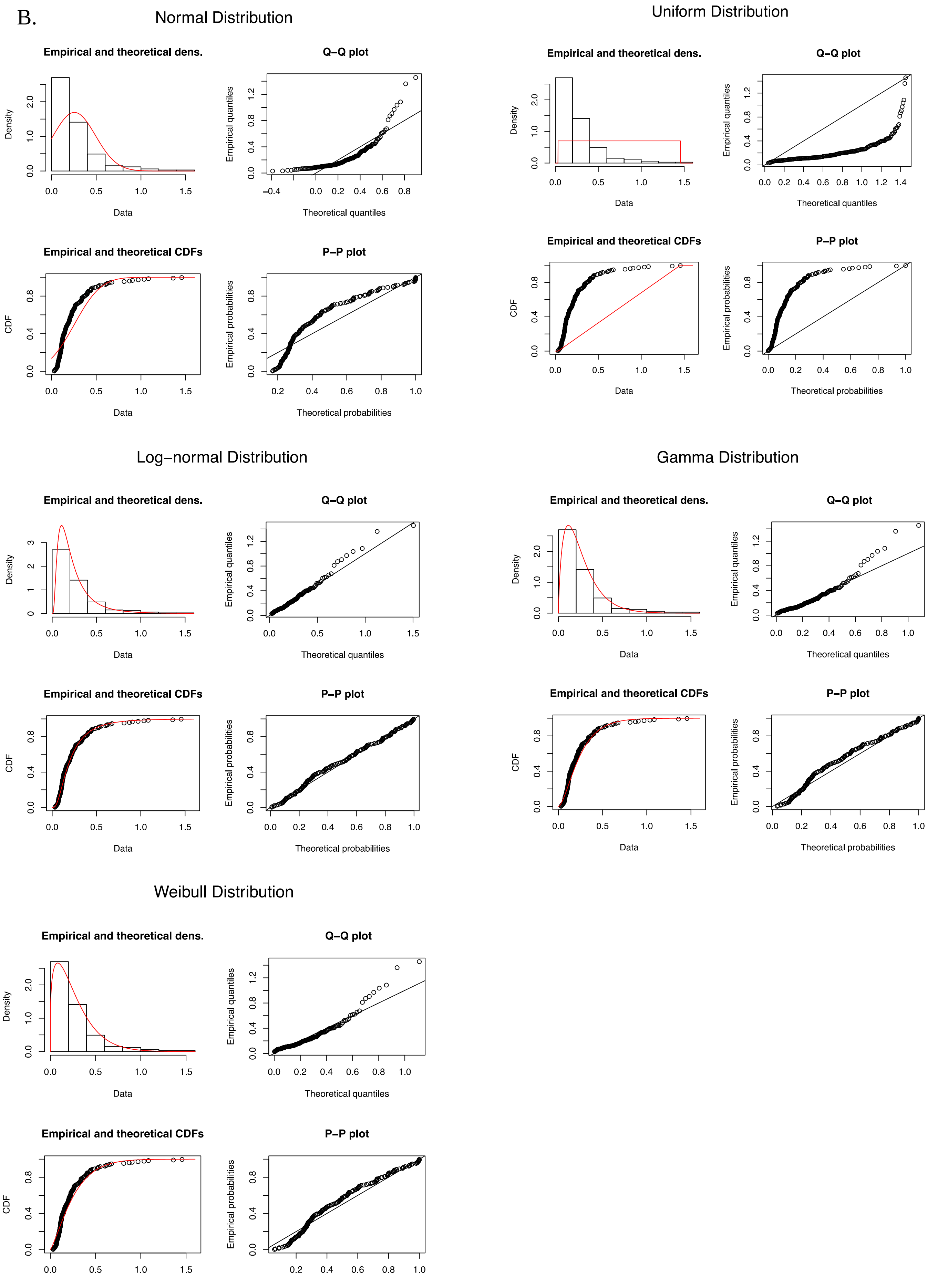

Normal Distribution
Uniform Distribution
Log–normal Distribution
Gamma Distribution
Weibull Distribution
Empirical and theoretical dens.
Q–Q plot
Empirical and theoretical CDFs
P–P plot
Density
Data
CDF
Empirical quantiles
Theoretical quantiles
Empirical probabilities
Theoretical probabilities

Figure S2. The progression free survival (PFS) curves for melanoma.(3) (A) Kaplan-Meier plot generated using the numbers at risk provided by *Kim et al.*(3) (B) Kaplan Meier plot generated using the growth rate values extracted using the first approach.

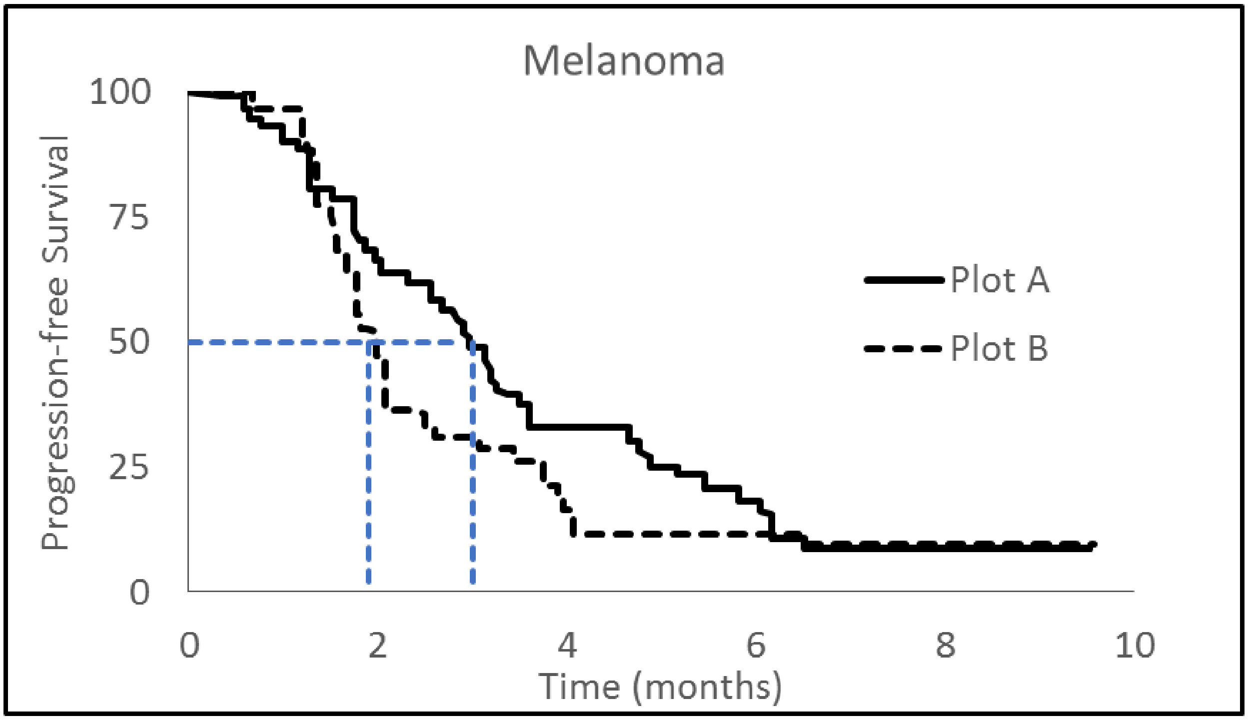
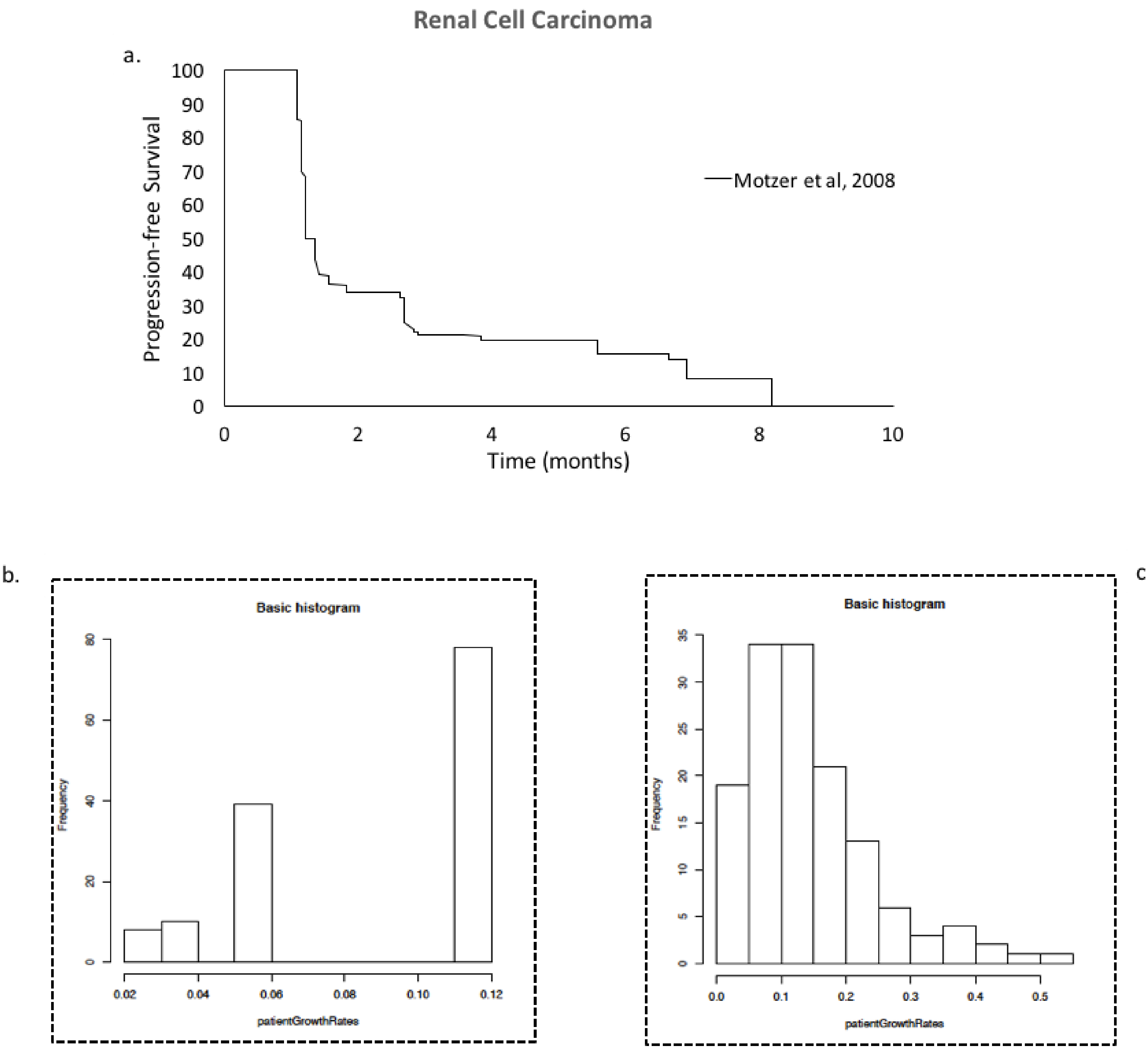


Figure S3. Visual representation of how random uniform distribution affects calculated exponential growth rates of renal cell carcinoma. Panel a shows the published progression free survival (PFS) plot from which growth rates in Panels b and c were calculated.(11) The histograms in panels b and c represent the growth rates derived without and with the application of random uniform distribution to the event times.



Supplementary Equations 1: Deriving Kaplan Meier estimate for number of events

Defining Kaplan Meier (KM) estimate for the survival function

$$S(t) = \prod_{i=1}^{k} \left(1 - \frac{d_i}{n_i}\right) \qquad \text{Equation S1}$$

Survival estimate for the first time point of observation, $S(t)_1$

$$S(t)_1 = 1 - \frac{d_1}{n_1} \qquad \text{Equation S2}$$

Solving for number of deaths at 1st time point of observation

$$d_1 = (1 - S(t)_1) \bullet n_1 \qquad \text{Equation S3}$$

Survival estimate at 2nd time point of observation

$$S(t)_2 = \left(1 - \frac{d_1}{n_1}\right) \bullet \left(1 - \frac{d_2}{n_2}\right) \qquad \text{Equation S4}$$

Solving for number of deaths at 2nd time point of observation

$$d_2 = n_2 \left(1 - \frac{S(t)_2}{1 - \frac{d_1}{n_1}}\right) \qquad \text{Equation S5}$$

Using Equation S2 we know

$$d_2 = n_2 \bullet \left(1 - \frac{S(t)_2}{S(t)_1}\right) \qquad \text{Equation S6}$$

Generalizing the function for number of deaths

$$d_i = n_{i-1} \bullet \left(1 - \frac{S(t)_i}{S(t)_{i-1}}\right) \qquad \text{Equation S7}$$

where n_0 is the sample size and $S(t)_0 = 1$.

Supplementary Equations 2: Determining the growth rate of a tumor progression "event"

An event is defined as a 20 or 25% growth in sum of longest diameter (SLD) by RECIST and WHO respectively.

Here, the tumor is assumed to be spherical, and the standard equation is used to describe the volume of a sphere

$$Sphere\ volume = \frac{4}{3} \cdot \pi \cdot r^3$$

Equation S8

Where r is the radius of the circle or diameter/2, *D*.

Assuming the initial tumor diameter D_0=1cm, the 20% increased diameter $D_{20\%}$=1.2cm indicates a progression event and the corresponding spherical volumes are

$$V_0 = \frac{4}{3} \cdot \pi \cdot \left(\frac{1}{2}\right)^3 = 0.5236cm^3$$

Equation S9

$$V_{20\%} = \frac{4}{3} \cdot \pi \cdot \left(\frac{1.2}{2}\right)^3 = 0.9048cm^3$$

Equation S10

Equation 2 of the main manuscript is

$$TV = TV_0 \cdot e^{k_g \cdot t}$$

Rearranging this equation to find the time of the event (t_{event}) and using the solution to Equations S9 and S10 allows us to find the growth rate

$$0.9048 = 0.5236 \cdot e^{k_g \cdot t_{event}}$$

$$k_g = \frac{ln(1.728)}{t_{event}}$$

Equation S11

If a tumor progression event were defined by a 25% increase in diameter, $D_{25\%}$=1.25cm

$$V_{25\%} = \frac{4}{3} \cdot \pi \cdot \left(\frac{1.25}{2}\right)^3 = 1.023cm^3$$

Equation S12

Rearranging Equation 2 of the main manuscript to find the growth rate

$$1.023 = 0.5236 \cdot e^{k_g \cdot t_{event}}$$

$$k_g = \frac{ln(1.954)}{t_{event}}$$

Equation S13

Equation S11 is equivalent to Equation 3 of the main text when an event is defined using the RECIST criteria of 20% increase in SLD and Equation S13 is equivalent to Equation 3 of the main text when an event is defined using the WHO criteria of 25% increase in SLD.

Supplementary Equations 3: Assuming tumors are oblong rather than spherical

This manuscript assumes that tumors are spherical and grow accordingly. If we instead assumed tumors were oblong shaped with equal short axes measurements, we find the eventual values of growth rates of a progression “event” are equal to those derived under the spherical assumption. In this supplementary document we show how that happens when an event is defined as 20% increase in the diameter (results are the same when the WHO 25% increase criteria is used).

The oblong volume can be determined using

$$Oblong\ volume = \frac{4}{3} \cdot \pi \cdot w^2 \cdot L$$

Equation S14

where *w* is the radius of the two short axes and *L* is the radius of the longest length. We have no information to inform the relationship between L and w, so we first assume *w*=0.5·L and then *w*=0.66·L

If the longest diameter of the initial tumor is D_0=1cm, the 20% increased diameter $D_{20\%}$=1.2cm indicates a progression event and *w*=0.5·L. The corresponding oblong volumes are

$$V_0 = \frac{4}{3} \cdot \pi \cdot \left(0.5 \cdot \frac{1}{2}\right)^2 * \frac{1}{2} = 0.131cm^3$$

Equation S15

$$V_{20\%} = \frac{4}{3} \cdot \pi \cdot \left(0.5 \cdot \frac{1.2}{2}\right)^2 * \frac{1.2}{2} = 0.226cm^3$$

Equation S16

Rearranging Equation 2 of the main manuscript to find the growth rate

$$0.226 = 0.131 \cdot e^{k_g \cdot t_{event}}$$

$$k_g = \frac{ln(1.728)}{t_{event}}$$

Equation S17

Note, this is the same equation we derived when assuming tumors are spherical (Equation S11). If we instead assume the oblong width is two thirds the longest length

$$V_0 = \frac{4}{3} \cdot \pi \cdot \left(0.66 \cdot \frac{1}{2}\right)^2 * \frac{1}{2} = 0.228cm^3$$

Equation S18

$$V_{20\%} = \frac{4}{3} \cdot \pi \cdot \left(0.66 \cdot \frac{1.2}{2}\right)^2 * \frac{1.2}{2} = 0.394cm^3$$

Equation S19

Rearranging Equation 2 of the main manuscript to find the growth rate

$$0.394 = 0.228 \cdot e^{k_g \cdot t_{event}}$$

$$k_g = \frac{ln(1.728)}{t_{event}}$$

Equation S20

Again, this is the same equation we derived when assuming tumors are spherical (Equation S11).