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## 1 (Poisson) Model for (Sampling)Variability of Count in a given amount of "experience"

## The Poisson Distribution: what it is, and some of its features

- The (infinite number of) probabilities $P_{0}, P_{1}, \ldots, P_{y}, \ldots$, of observing $Y=$ $0,1,2, \ldots, y, \ldots$ "events" in a given amount of "experience."
- These probabilities, $\operatorname{Prob}[Y=y]$, or $P_{Y}[y]$ 's, or $P_{y}$ 's for short, are governed by a single parameter, the mean $E[Y]=\mu$.
- $P[y]=\exp [-\mu] \mu^{y} / y!\quad\left\{\right.$ note recurrence relation: $\left.P_{y}=P_{y-1} \times(\mu / y).\right\}$
- Shorthand: $Y \sim \operatorname{Poisson}(\mu)$.
- $\operatorname{Var}[Y]=\mu ; \quad$ i.e., $\quad \sigma_{Y}^{2}=\mu_{Y}$.
- Approximated by $N\left(\mu, \sigma_{Y}=\mu^{1 / 2}\right)$ when $\mu \gg 10$.
- Open-ended (unlike Binomial), but in practice, has finite range.
- Poisson data sometimes called "numerator only": (unlike Binomial) may not "see" or count "non-events": but there is (an invisible) denominator "behind' the no. of incoming "wrong number" phone calls you receive.


## How it arises / derivations

- Count of events (items) that occur randomly, with low homogeneous intensity, in time, space, or 'item'-time (e.g. person-time).
- $\operatorname{Binomial}(n, \pi)$ when $n \rightarrow \infty$ and $\pi \rightarrow 0$, but $n \times \pi=\mu$ is finite. ${ }^{1}$
- $Y \sim \operatorname{Poisson}\left(\mu_{Y}\right) \Leftrightarrow T$ time $\mathrm{b} / \mathrm{w}$ events $\sim \operatorname{Exponential}\left(\mu_{T}=1 / \mu_{Y}\right) .{ }^{2}$
- As sum of $\geq 2$ independent Poisson rv's, with same or different $\mu$ 's: $Y_{1} \sim \operatorname{Poisson}\left(\mu_{1}\right) Y_{2} \sim \operatorname{Poisson}\left(\mu_{2}\right) \Rightarrow Y=Y_{1}+Y_{2} \sim \operatorname{Poisson}\left(\mu_{1}+\mu_{2}\right)$.
- Examples: numbers of asbestos fibres, deaths from horse kicks*, needlestick or other percutaneous injuries, bus-driver accidents*, twin-pairs*, radioactive disintegrations*, flying-bomb hits*, white blood cells, typographical errors, "wrong numbers", cancers; chocolate chips, radioactive emissions in nuclear medicine, cell occupants - in a given volume, area, line-length, population-time, time, etc. [*e.g. on website]

[^0]

Figure 1: Events in Population-Time.. randomly generated from intensities that are constant within ( 2 squares high by 2 squares wide) 'panels', but vary between such panels. In Epidemiology, each square might represent a number of units of Population-time, and each dot an event.

### 1.1 Does the Poisson Distribution apply to.. ?

- Yearly variations in no.s of persons killed in plane crashes? ${ }^{3}$
- Daily variations in numbers of births? ${ }^{4}$
- Daily variations in no.s of deaths [variation over the seasons]
- Daily variations in numbers of traffic accidents [variation over the seasons, and days of week, and with weather etc.]
- Daily variations in numbers of deaths in France in summer 2002 \& $2003^{5}$

[^1]

Figure 2: Events in Time: 10 examples, randomly generated from constant over time intensities. Simulated with 1000 Bernoulli(small $\pi$ )'s per time unit.

- Variations across cookies/pizzas in no. of chocolate chips/olives.
- Variations across days of year in no. of deaths from sudden infant death syndrome.


### 1.2 Calculating Poisson probabilities:

### 1.2.1 Exactly

- pdf: formula for $P_{y}$ (can use recursion).
- cdf:
- Summation of terms in pdf
- Using link between this sum and the cdf of $\chi^{2}$ Distribution ${ }^{6}$.
- Spreadsheet - Excel function $\operatorname{POISSON}(y, \mu$, cumulative)
- Statistical Packages: SAS function POISSON; see www.ats.ucla.edu/ stat/stata/faq/pprob.htm for 'how to' in Stata; R functions dpois(), ppois(), qpois() probability, distribution, and quantile functions.

[^2]
### 1.2.2 Using Gaussian Approximations to distribution of $y$ or transforms of it

Described below, under Inference.

## 2 Inference re $\mu$, based on observed count $y$

## 2.1 "First Principles" Confidence Interval

By first-principles $100(1-\alpha) \%$ CI, we mean "not usual point-estimate $\pm$ some multiple of standard error," but rather the pair ( $\left.\mu_{L O W E R}, \mu_{U P P E R}\right)$ such that

$$
P\left(Y \geq y \mid \mu_{L O W E R}\right)=\alpha / 2 \& P\left(Y \leq y \mid \mu_{U P P E R}\right)=\alpha / 2 .
$$

### 2.1.1 Exact - see Figure 3 for example, based on $y=6$

Tables: For a given $\alpha$, there is just one CI for each value of $y$; these exact CI's have been extensively tabulated and made available in several texts and Tables, e.g., the Documenta Geigy, and Biometrika Tables for Statisticians. ${ }^{7}$

## If don't have tables.. Can find exact lower and upper limits

 $\mu_{L O W E R / U P P E R}$ that yield the target $\alpha / 2$ 's either by trial \& error (rapidly with software that evaluates Poisson tail areas) or directly using the Link between the tail areas of the Poisson and tail areas of Chi- Square distributions (full details in article by Fisher, 1935, under Resources on webpage), $\mu_{L O W E R}=\frac{1}{2} \chi_{2 y, \alpha / 2}^{2}, \quad \mu_{U P P E R}=\frac{1}{2} \chi_{2 y+2,1-\alpha / 2}^{2}$. Some specialized software packages (eg in $R$ ) also have functions that provide them directly. ${ }^{8}$
### 2.1.2 Quite accurate approximation to exact tail area

Using Wilson-Hilferty approximation to Chi-square quantiles ${ }^{9}$ This has high accuracy for $y>10$; it uses $z$, the normal standardized variate

[^3]

Figure 3: Example of Exact 95\% CI of $\{2.2,13.06\}$ for $\mu$, based on $y=6$.
corresponding to $\alpha / 2$, e.g., $\alpha=0.10 \rightarrow z=1.645 ; \alpha=0.05 \rightarrow z=1.96$, etc.

$$
\begin{gathered}
\mu_{L O W E R}=y \times\left\{1-[9 y]^{-1}-z \times[9 y]^{-1 / 2}\right\}^{3} \\
\mu_{U P P E R}=(y+1) \times\left\{1-[9(y+1)]^{-1}+z \times[9(y+1)]^{-1 / 2}\right\}^{3}
\end{gathered}
$$

### 2.1.3 Not quite as accurate an approximation, but 1st principles

Using $Y \simeq N\left(\mu, \sigma=\mu^{1 / 2}\right)$ :
reference to an unpublished source, rather than the 1931 publication of Wilson and Hilferty. The Full Wilson and Hilferty citation, and evaluation of the above equation, can be found in Liddell's article "Simple exact analysis of the standardized mortality ratio" in J Epi and Comm. Health 37 85-88, 1984, available on website.


Figure 4: Poisson Distributions, over range $y=0$ to 40 , corresponding to $\mu=4,9,16$, and 25 .

Obtained by solving the two equations:

$$
y=\mu_{L O W E R}+z \times\left\{\mu_{L O W E R}\right\}^{1 / 2} ; y=\mu_{U P P E R}-z \times\left\{\mu_{U P P E R}\right\}^{1 / 2}
$$

to give

$$
\mu_{L O W E R, U P P E R}=\left(\left[y+z^{2} / 4\right]^{1 / 2} \mp z / 2\right)^{2} .
$$

### 2.1.4 Variance-stabilizing transformation, so first principles

With $\mu$ large enough, $Y^{1 / 2} \sim($ approx $) N\left(\mu^{1 / 2}, \sigma=1 / 2\right)$, i.e., the SD is independent of $\mu^{1 / 2}$, thus providing for a first-principles interval:

$$
\mu_{L O W E R, U P P E R}=y \mp z \times c^{1 / 2}+(z / 2)^{2} .
$$

## 2.2 "Not First Principles" Confidence Intervals, based on SE calculated at point estimate

2.2.1 Based on $Y \simeq N\left(\mu, \hat{\sigma}=y^{1 / 2}\right)$.

If lazy, or don't care about principles /accuracy, or if $y$ is large, can solve

$$
y=\mu_{L O W E R}+z \times y^{1 / 2} ; y=\mu_{U P P E R}-z \times y^{1 / 2}
$$

to give

$$
\mu_{L O W E R, U P P E R}=y \mp z \times y^{1 / 2}
$$

"Large- $n$ ": How Large is large?: The same rule of thumb: when expected no. of events, $\mu=E[Y]>5$. or the same JH rule: when the tables don't go as high as your value of $y$. It works well if the distribution is not 'crowded' into the left corner (cf. Figure 3), i.e., if, with the symmetric Gaussian approximation, the lower tail of the distribution does not spill over the 0 boundary.
The above model is used if one fits a generalized linear model, with Poisson error but IDENTITY link. Example with $y=4$ :
e.g. In SAS:

PROC GENMOD; model y = / dist = POISSON link = IDENTITY WALFCI;
e.g. In Stata
input y
1 * glm doesn't like file with 1 'observation'
3 *so ........... split across 2 'observations' end
glm y , family (poisson) link (identity)
e.g. In R: $y=4$; summary (glm(y $\sim 1, f a m i l y=p o i s s o n(l i n k=i d e n t i t y) ~)) ~$

### 2.2.2 Based on $\log Y \simeq N\left(\log [\mu], \hat{\sigma}=\{1 / \hat{\mu}\}^{1 / 2}\right)$

## - Derivation:

Use the "Delta Method" to derive the approximate variance for the random variable $\log Y$, assuming that $\operatorname{Prob}[Y=0]$ is negligible.
$\operatorname{Var}[\log Y] \approx \operatorname{Var}[Y] \times\left\{\left.(d \log Y / d Y)\right|_{Y=\mu_{Y}}\right\}^{2}=\mu \times\left(1 / \mu_{Y}\right)^{2}=1 / \mu_{Y}$.
We will make a lot of use of this result, especially for the variance of the $\log$ of a rate, and for the variance of the $\log$ of a rate ratio (i.e., the variance of the difference of two $\log$ rates).
(Empirical) rate ratio(rr) or $i d^{10}$ ratio (idr): $\hat{\lambda}_{2} \div \hat{\lambda}_{2}=\frac{y_{2}}{P T_{2}} \div \frac{y_{1}}{P T_{1}}$

$$
\begin{aligned}
\operatorname{Var}[\log (r r)] & =\operatorname{Var}\left[\log y_{2}-\log y_{1}\right] \\
& =\operatorname{Var}\left[\log y_{2}\right]+\operatorname{Var}\left[\log y_{1}\right] \\
& =1 / \mu_{2}+1 / \mu_{1} . \\
& =2 \div\left\{\text { Harmonic Mean of } \mu_{2} \text { and } \mu_{1}\right\}
\end{aligned}
$$

[^4]- CI:

CI: $\exp \left[\log (y) \mp z \times(1 / y)^{1 / 2}\right]$.
e.g., ...

In SAS: MODEL y $=/$ dist $=$ POISSON link $=$ LOG WALFCI;
In Stata: glm y , family (poisson) link (log)


## 3 Applications, and Notes

### 3.1 How large a count so that margin of error $<15 \%$ ?

An estimate of WBC concentration can be made by manually counting enough fields $(n)$ until say a total of $y=200$ cells have been observed. This is not quite a Poisson distribution since $y=200$ is fixed ahead of time and $n$ is the random variable - but the variability in the estimate $200 / n$ is close to Poisson-based, so as a first approximation we will treat the $y$ as the variable and the denominator $n$ as fixed. The estimate has margins of error (ME) of $13 \%$ and $15 \%$ - since [as one can derive from trial and error] a total count of 200 (marked by $\uparrow$ below) could be a high reading from a concentration which produces a $\mu$ of 173 (for the same $n$ ), or a low reading from a concentration which produces an average of $\mu=230$, i.e.
$y$ per $n$ : 160..170..180..190..200..210..220..230..240...

$\ldots . . . . . . . . . . . . . . .200=173+1.96 \times\{173\}^{1 / 2}$
. . . . . . . . . . . . . . . . . . . $200=230-1.96 \times\{230\}^{1 / 2}$

### 3.2 Leukemia Rate Triples near Nuke Plant: Study

OTTAWA (CP) ${ }^{11}$ - Children born near a nuclear power station on Lake Huron have 3.5 times the normal rate of leukemia, according to figures made public yesterday. The study conducted for the Atomic Energy Control Board, found the higher rate among children born near the Bruce generating station at Douglas Point. But the scientist who headed the research team cautioned that the sample size was so small that that actual result could be much lower - or nearly four times higher.

[^5]Dr. Aileen Clarke said that while the Douglas Point results showed 3.5 cases of leukemia where one would have been normal ${ }^{12}$, a larger sample size could place the true figure somewhere in the range from 0.4 cases to 12.6 cases. ${ }^{13}$
Clarke will do a second study to look at leukemia rates among children aged five to 14 . The first study was on children under age 5 . Clarke was asked whether parents should worry about the possibility that childhood leukemia rates could be over 12 times higher than normal around Douglas point. "My personal opinion is, not at this time," she said. She suggested that parents worried by the results should put them in context with other causes of death in children.
"Accidents are by far and away the chief cause of death in children, and what we're talking about is a very much smaller risk than that of death due to accidents," she said.

The results were detailed in a report on a year-long study into leukemia rates among children born within a 25 -kilometre radius of five Ontario nuclear facilities. The study was ordered after British scientists reported leukemia rates among children born near nuclear processing plants were nine times higher than was normal. The Ontario study was based on 795 children who died of leukemia between 1950 and 1986 and 951 children who were diagnosed with cancer between 1964 and 1985

It showed a lower-than-normal rate among children born near the Chalk River research station and only slightly higher than expected rates at Elliot Lake and Port Hope, uranium mining and conversion facilities
At the Pickering generating station, the ratio was slightly higher still, at 1.4 - meaning there were 1.4 cases for every expected case. But the confidence interval - the range of reliability - for that figure set the possible range between 0.8 cases and 2.2 cases. ${ }^{14}$

Comment: It is interesting that it is the more extreme, but much less precise, SIR of 3.5, based on $O=2, E=0.57$ that made the headline, while the less extreme, but much more precise, $S I R$ of 1.4, based on $O=18, E=12.8$, was relegated to the last paragraph.

[^6]
### 3.3 Self-reported Percutaneous Injuries in Interns

Table 1. Rates of Percutaneous Injuries by Residency Program. ${ }^{15}$

|  | No. of | No. of | Rate (95\% CI*) |
| :---: | :---: | :---: | :---: |
| Type of | Intern- | Percutaneous | per |
| Residency | Months | Injuries | Intern-Month |
| All | 17003 | 498 | 0.0293 (0.0268-0.0318) |
| Internal medicine | 3995 | 57 | 0.0143 (0.0106-0.0179) |
| Surgery | 1730 | 124 | 0.0717 (0.0595-0.0838) |
| Family medicine | 2008 | 51 | 0.0254 (0.0185-0.0323) |
| Emergency medicine | 1007 | 40 | 0.0397 (0.0277-0.0518) |
| Pediatrics | 2159 | 24 | 0.0111 (0.0067-0.0155) |
| Psychiatry | 658 | 1 | 0.0015 (0.0000-0.0045) |
| Pathology | 283 | 15 | 0.0530 (0.0269-0.0791) |
| Obstetrics/gynecology | 964 | 94 | 0.0975 (0.0788-0.1160) |
| Other specialties | 4199 | 92 | 0.0219 (0.0175-0.0263) |
| Method not specified, b | \{498 干 | $\left.8^{1 / 2}\right\} \div 17003$ | $=\{0.0267,0.0318\}$. |

### 3.4 Cell Occupancy, Lotto 6/49, the Extremal Quotient, and Geographical Variation in Surgery Rates

What do these have in common? The answer may be easier to understand after seeing a few runs of the Excel Macro for visits to cells (in Resources).

### 3.5 Note: How is it that one can form a CI for $\mu$ from a single observation $y$ ?

If we had a single realization $y$ of a $N\left(\mu, \sigma_{Y}\right)$ random variable, we could not, from this single $y$, estimate both $\mu$ and $\sigma_{Y}$ : one would have to rely on outside information concerning $\sigma_{Y}$. However, the $\operatorname{Poisson}(\mu)$ distribution is different in that $\sigma_{Y}=\mu^{1 / 2}$, so we can calculate a "model-based" SE (or SE's if use a first principles CI) from this relationship between the mean and the variance.
Another way to understand why a SE is possible without going "outside" is to take advantage of the "divisibility" of a Poisson denominator, and its corresponding numerator.
We can split up the overall sample or slice of experience into ( $n$ ) small enough sub samples so that the subcount $y_{i}$ in each sub sample will be either a 0 or

[^7]a 1 The (unit) variance of the observed sub counts should be $p(1-p)$ where $p$ is the proportion of sub counts that are 1 . Thus the estimated variance of the total count $y=\sum_{i} y_{i}$ should be $n$ times the unit variance, or $n \times p(1-p)$. But if $p$ is small, so that $1-p$ is near unity, then the variance of the sub count is approximately $n \times p$, which is simply the observed overall count $y$. i.e. the variance of a Poisson variable is equal to its mean. see more under Resources.

The sum of independent Poisson r.v.'s with different expectations is still a random variable with a Poisson distribution. The same is not true of a sum of independent Bernoulli (or Binomial) r.v.'s with different expectations.

If you were told that $Y_{1} \sim \operatorname{Bernoulli}\left(\pi_{1}=0.1\right)$ and $Y_{2} \sim \operatorname{Bernoulli}\left(\pi_{2}=0.7\right)$, you would not argue that the distribution of $Y=Y_{1}+Y_{2}$ is $\operatorname{Binomial}(n=$ $2, \pi=0.4)$. You can check that yes, $\mathrm{E}(Y)=0.8$, but that $P_{0}=0.27, P_{1}=$ $0.66, P_{2}=0.07$, much more concentrated than the $\operatorname{Binomial}(2,0.4)$ probabilities $P_{0}=0.36, P_{1}=0.48, P_{2}=0.16$.

BUT, what if you were told that $Y_{1} \sim \operatorname{Poisson}\left(\mu_{1}=0.1\right)$ and $Y_{2} \sim$ Poisson $\left(\mu_{2}=0.7\right)$. Would you argue that the distribution of $Y=Y_{1}+Y_{2}$ is Poisson $(\mu=0.8)$ ? You can check that in fact it is.

In epidemiology, prevalence and other proportion-type statistics have denominators made up of (indivisible) individuals; the person is the statistical atom. However, when dealing with incidence density statistics, the denominators are made up of an infinite number of person-moments.

### 3.6 CI for Rate or Incidence Density parameter, ID ( $\lambda$ )

So far, we have focused on inference regarding $\mu$, the expected number on events in the amount of experience actually studied. However, for comparison purposes, the frequency is more often expressed as a rate, or intensity. e.g., we convert $y=211$ deaths from lung cancer in 232978 women-years (WY) in the age-group 55-60 in Quebec in 2002 into a rate of incidence density of $211 /(232,978 \mathrm{WY})=0.00091 / \mathrm{WY}$ or 91 per $100,000 \mathrm{WY}$. This makes it easier to compare the frequency with the rate in the same age group in 1971, namely 33 lung cancer deaths in 131200 WY , or $0.00025 / \mathrm{WY}$ $=\mathbf{2 5}$ per $100,000 \mathrm{WY}$.

The statistic, the empirical rate or empirical incidence density, is

$$
\text { rate }=i d=\hat{I} D=\hat{\lambda}=y / \mathrm{PT} .
$$

where $y$ is the observed number of events and PT is the amount of PopulationTime in which these events were observed. We think of $i d$ or $I D$ or $\lambda$ as a point estimate of the (theoretical) Incidence Density parameter, ID or $\lambda$.

To calculate a CI for the ID parameter, we treat the PT denominator as a constant, and the numerator, $y$, as a Poisson random variable, with expectation $E[y]=\mu=\lambda \times P T$, so that

$$
\begin{gathered}
\lambda=\mu \div \mathrm{PT} \\
\hat{\lambda}=\hat{\mu} \div \mathrm{PT}=y \div \mathrm{PT} \\
\mathrm{CI} \text { for } \lambda=\{\mathrm{CI} \text { for } \mu\} \div \mathrm{PT} .
\end{gathered}
$$

The $y=211$ leads to a (large-sample, SE-based)

$$
95 \% \text { CI for } \mu: 211 \mp 1.96 \times 211^{1 / 2} \Rightarrow 211 \mp 28.5 \Rightarrow\{182.5,239.5\}
$$

$95 \%$ CI for $\lambda:\{182.5,239.5\} \div 232,978 \mathrm{WY} \Rightarrow\{\mathbf{7 8 . 3}, \mathbf{1 0 2}\}$ per $100,000 \mathrm{WY}$
Whereas it matters little which method - exact or approximate - to use for the $95 \%$ CI from the 2002 data, the number of deaths in 1971 is a much smaller $y=33$. Thus we will use the exact first principles CI for $\mu$. The available tables stop at $y=30$, so we will use the Excel spreadsheet, in the Resources, with a count of 33. It yields lower and upper limits of 22.7 and 46.3. Thus, to accompany the point estimate of 25 per $100,000 \mathrm{WY}$, we have
$95 \%$ CI for $\lambda:\{22.7,46.3\} \div 131,200 \mathrm{WY} \Rightarrow\{\mathbf{1 7 . 3}, \mathbf{3 5 . 3}\}$ per $100,000 \mathrm{WY}$

## 4 Test of $H_{0}: \mu=\mu_{0}$, i.e. $\lambda=\lambda_{0}$.

Evidence: P-Value $=\operatorname{Prob}\left[y\right.$ or more extreme | $\left.H_{0}\right]$, with 'more extreme' determined by whether $H_{\text {alt }}$ is 1-sided or 2-sided.
For formal test, at level $\alpha$, compare this P -value with $\alpha$.

## Examples:

## 1. Cancers at Douglas Point:

Denote by $\left\{C Y_{1}, C Y_{2}, \ldots\right\}$ the numbers of Douglas Point child-years of experience in the various age categories that were pooled over. Denote by $\left\{\lambda_{1}^{O n t}, \lambda_{2}^{O n t}, \ldots\right\}$ the age-specific leukemia incidence rates during the period studied. If the underlying incidence rates in Douglas Point were the same as those in the rest of Ontario, the $\boldsymbol{E}$ xpected total number of cases of leukemia for Douglas Point would be

$$
E=\mu_{0}=\sum_{\text {ages }} C Y_{1} \times \lambda_{i}^{O n t}=0.57
$$

The actual total number of cases of leukemia $\boldsymbol{O}$ bserved in Douglas Point was

$$
O=y=\sum_{\text {ages }} O_{i}=2
$$

So, (age-) Standardized Incidence Ratio (SIR) $=O / E=2 / 0.57=3.5$.
Q: Is the $y=2$ cases of leukemia observed in the Douglas Point experience statistically significantly higher than the $E=0.57$ cases "expected" for this many child-years of observation if in fact the rates in Douglas Point and the rest of Ontario were the same? Or, is the $y=2$ observed in this community compatible with $H_{0}: y \sim \operatorname{Poisson}(\mu=0.57)$ ?
A: Since, under $H_{0}$, the age-specific numbers of leukemias $\left\{y_{1}=O_{1}, y_{2}=\right.$ $\left.O_{2}, \ldots\right\}$ in Douglas Point can be regared as independent Poisson random variables, their sum $y$ can be regarded as a Poisson random variable with $\mu=0.57$. Thus we can calculate $P=\operatorname{Prob}[Y \geq y \mid \mu=0.57]=$ $P[2]+P[3]+\ldots$, i.e.
$P_{\text {uppertail }}=1-\{P[0]+P[1]\}=1-\{\exp [-0.57] \times(1+0.57 / 1!)\}=0.11$.
At the Pickering generating station, the Observed number was 18, versus an Expected of 12.8, for an $S I R$ of 1.4. These larger numbers give us a chance to compare the uppertail P -values obtained by the exact method, i..e. $P=\sum_{y \geq 18}$ PoissonProb $\left[y \mid \mu_{0}=12.8\right]$ with those obtained from various approximations to the Poisson ( $\mu_{0}=12.8$ ) distribution:-

- Exactly $\quad P=$ Poisson $\operatorname{Prob}[18 \mid 12.8]+P[19 \mid 12.8]+\cdots=0.099$
- No (dis)-continuity correction: $\quad P=\operatorname{Prob}\left[Z \geq \frac{18-12.8}{12.8^{1 / 2}}\right]=0.073$
- No (dis)-continuity correction: $P=\frac{1}{2} \operatorname{Prob}\left[\chi^{2} \geq \frac{(18-12.8)^{2}}{12.8}\right]=0.073$
- No correction: ${ }^{16} P=\operatorname{Prob}\left[Z \geq \log (18 / 12.8) /\{1 / 12.8\}^{1 / 2}\right]=0.111$
- No correction: ${ }^{17} \quad P=\operatorname{Prob}\left[Z \geq\left(18^{1 / 2}-12.8^{1 / 2}\right) / 0.5\right]=0.092$
- With the correction: $\quad P=\operatorname{Prob}\left[Z \geq \frac{|18-12.8|-0.5}{12.8^{1 / 2}}\right]=0.094$
- With the correction:

$$
P=\frac{1}{2} \operatorname{Prob}\left[Z \geq \frac{(|18-12.8|-0.5)^{2}}{12.8}\right]=0.094
$$

[^8]
## 2. "Cluster of Events" Story in Montreal Gazette in May $1989{ }^{18}$

## Double Trouble in Moose Jaw School

(caption to a photograph showing 6 sets of twins)
Every morning, teachers at Prince Arthur school in Moose Jaw, Saskatchewan see double - and its not because of what they were up to the night before. Six pairs of identical twins attend the school, which has an enrollment of 375 . Identical births occur once in 270 births.

What is the probability $P$ of having 6 or more sets of twins in a school of size $n=375$, when the twinning probability is $\pi=1 / 270$ ?
This can be obtained with the $\operatorname{Binomial}(n, \pi)$ distribution; because $n$ is large and $\pi$ is small, the distribution can be approximated by the Poisson $(\mu)$ distribution, where $\mu=n \times \pi=1.3$.

$$
P=P[Y \geq 6]=1-P[Y \leq 5]
$$

i.e., as
$1-\exp [-1.3] \times\left\{1+1.3 / 1!+1.3^{2} / 2!+1.3^{3} / 3!+1.3^{4} / 4!+1.3^{5} / 5!\right\}=0.0022$.

Thus, the probability is low that this particular school would have six or more sets. BUT, on average, in 1000 schools of this size, there will be 2.2 with this many or more. Thus, if we scan over a large number of such schools, finding some school somewhere with this extreme a number is not didfficult. If the newswires scanned a large number of schhols in 2007, there is a good chance the Montreal Gazette could re-use the headline but they would have to change "Moose Jaw" to "Town X", with "X" to be filled in

Moral: The Law of Large Numbers at play here is the same as the one in the video display terminals and miscarriages" story. Natural "clusters" do occur by chance alone, and distinguishing ones caused simply by chance from ones caused by some environmental or other such factor is not an easy task.
3. (Large-sample) Example Where does the $O=78$ cases of cancer in the "Sour Gas" community of Alberta fall relative to $E=85.9$ "expected" for "non-sour-gas" communities with the same person years of experience and at Alberta cancer rates?

[^9]
## 5 Modelling Incidence Densities, or Rates, ( $\lambda$ 's) via regression

Figure 5 is a simple mathematical reversal of the fundamental epidemiologic definition of an empirical rate or incidence density (id)
rate $=i d=\frac{\text { number of cases }}{\text { amount of population-time that generated these cases }}$,
i.e.,
number of cases $=$ rate $\times$ amount of population-time.
There is a corresponding equation for the expected number of cases, in terms of the theoretical rate, $\lambda$

E [number of cases] $=$ theoretical rate $\times$ amount of population-time.

This simple re-statement has two important implications (i) in epidemiology, we are students of rates and (ii) Generalized Linear Models (GLMs) allow us to fit equations of this very type. Even though we put the numbers of cases on the left hand side of the regression equation, these GLMs allow us to express the theoretical rates (the focus of our investigations) as functions of the determinants of interest (e.g. age, smoking, diet, calendar time, treatment, ... etc) while treating the amounts of population time as constants that are of no intrinsic interest. In the lung cancer mortality dataset, we could have a (no. deaths, PT) 'data point' for every 'covariate pattern' or $x$-vector
The two most common theoretical rate models are the additive and multiplicative forms:-

$$
\boldsymbol{r a t e}[x]=\beta_{0}+\beta_{1} x \quad \& \quad \text { rate }[x]=\exp \left(\beta_{0}+\beta_{1} x\right) .
$$

More later...

## 6 Planning: Sample Size for CIs and Tests

### 6.1 Precision

Even though it is tempting to specify the 'sample size' in terms of the Amount of Experience that needs to be studied to achieve this precision, ultimately the precision is governed by the number of events. So it is safer to specify sample size in these terms.


Figure 5: Depiction of empirical lung cancer mortality rate in age-group 55-60 in Quebec in 2002 as the slope of the line joining the point ( $Y=0$ cases, $P T=$ $0 W Y)$ and the point $(Y=33, P T=121300 W Y)$. Also shown are the Poisson Distributions, with $\mu_{U P P E R}=46.3$ and $\mu_{L O W E R}=22.7$ respectively, such that $\operatorname{Prob}[Y \geq 33 \mid \mu=22.7=\operatorname{Prob}[Y \leq 33 \mid \mu=46.3=0.025$.


Figure 6: Using exact Poisson Probabilities

### 6.2 Amount of experience required to achieve a specified Coefficient of Variation (CV) for an estimated rate

See the example of the number of cells needed to count: approx. 200 so that have a margin or error of $15 \%$.

### 6.3 Power - to detect Rate Ratio $R R=E_{\text {alt }} / E_{0}$

Exactly, using a spreadsheet or R:
Approximately, using a Gaussian approximations to $\operatorname{Poisson}\left(\mu=E_{0}\right)$ and $\operatorname{Poisson}\left(\mu=E_{\text {alt }}=R R \times E_{0}\right)$ : solve

$$
Z_{\alpha / 2} \times\left\{E_{0}\right\}^{1 / 2}+Z_{\beta} \times\left\{E_{\text {alt }}\right\}^{1 / 2}=E_{\text {alt }}-E_{0}
$$

## 7 References

*Clayton D and Hill M. Statistical Models for Epidemiology Chs 4, 5, 12.2
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Miettinen O Theoretical Epidemiology p 295.
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Rothman K, Greenland S [1998] Modern Epidemiology pp 234- pp404-5 (overdispersion) 570-571 (Poisson regression).
Rothman K, Boice J Epidemiologic Analysis on a Programmable Calculator.
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Rothman K [2002] Introduction to Epidemiology pp 133-4 \& 137-139

| $1-2 \alpha$ |  |  | 0.9 |  | 0.8 |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\alpha$ | 0.025 |  | 0.05 |  | 0.1 |  |
| count | Lower | Upper | Lower | Upper | Lower | Upper |
| 0 | 0.00 | 3.69 | 0.00 | 3.00 | 0.00 | 2.30 |
| 1 | 0.03 | 5.57 | 0.05 | 4.74 | 0.11 | 3.89 |
| 2 | 0.24 | 7.22 | 0.36 | 6.30 | 0.53 | 5.32 |
| 3 | 0.62 | 8.77 | 0.82 | 7.75 | 1.10 | 6.68 |
| 4 | 1.09 | 10.24 | 1.37 | 9.15 | 1.74 | 7.99 |
| 5 | 1.62 | 11.67 | 1.97 | 10.51 | 2.43 | 9.27 |
| 6 | 2.20 | 13.06 | 2.61 | 11.84 | 3.15 | 10.53 |
| 7 | 2.81 | 14.42 | 3.29 | 13.15 | 3.89 | 11.77 |
| 8 | 3.45 | 15.76 | 3.98 | 14.43 | 4.66 | 12.99 |
| 9 | 4.12 | 17.08 | 4.70 | 15.71 | 5.43 | 14.21 |
| 10 | 4.80 | 18.39 | 5.43 | 16.96 | 6.22 | 15.41 |
| 11 | 5.49 | 19.68 | 6.17 | 18.21 | 7.02 | 16.60 |
| 12 | 6.20 | 20.96 | 6.92 | 19.44 | 7.83 | 17.78 |
| 13 | 6.92 | 22.23 | 7.69 | 20.67 | 8.65 | 18.96 |
| 14 | 7.65 | 23.49 | 8.46 | 21.89 | 9.47 | 20.13 |
| 15 | 8.40 | 24.74 | 9.25 | 23.10 | 10.30 | 21.29 |
| 16 | 9.15 | 25.98 | 10.04 | 24.30 | 11.14 | 22.45 |
| 17 | 9.90 | 27.22 | 10.83 | 25.50 | 11.98 | 23.61 |
| 18 | 10.67 | 28.45 | 11.63 | 26.69 | 12.82 | 24.76 |
| 19 | 11.44 | 29.67 | 12.44 | 27.88 | 13.67 | 25.90 |
| 20 | 12.22 | 30.89 | 13.25 | 29.06 | 14.53 | 27.05 |
| 21 | 13.00 | 32.10 | 14.07 | 30.24 | 15.38 | 28.18 |
| 22 | 13.79 | 33.31 | 14.89 | 31.41 | 16.24 | 29.32 |
| 23 | 14.58 | 34.51 | 15.72 | 32.59 | 17.11 | 30.45 |
| 24 | 15.38 | 35.71 | 16.55 | 33.75 | 17.97 | 31.58 |
| 25 | 16.18 | 36.90 | 17.38 | 34.92 | 18.84 | 32.71 |
| 26 | 16.98 | 38.10 | 18.22 | 36.08 | 19.72 | 33.84 |
| 27 | 17.79 | 39.28 | 19.06 | 37.23 | 20.59 | 34.96 |
| 28 | 18.61 | 40.47 | 19.90 | 38.39 | 21.47 | 36.08 |
| 29 | 19.42 | 41.65 | 20.75 | 39.54 | 22.35 | 37.20 |
| 30 | 20.24 | 42.83 | 21.59 | 40.69 | 23.23 | 38.32 |

Figure 7: (Exact) Confidence limits for the expectation [i.e. the $\mu$ parameter] of a Poisson random variable E.g. if observe 6 events in a certain amount of experience, then $95 \%$ CI for the mean count for this same amount of experience is $(2.20,13.06)$


POISSON, Siméon Denis 1781-1840
from...
http://www.york.ac.uk/depts/maths/histstat/people/sources.htm
See also...
http://www.encyclopedia.com/topic/Simeon_Denis_Poisson.aspx
http://en.wikipedia.org/wiki/Poisson_distribution

## 0 Exercises

## 0.1 (m-s) Working with logs of counts and logs of rates

In order to have a sampling distribution that is closer to Gaussian - sample counts, and ratios of them tend to have nasty sampling distributions -we often transform from the $(0, \infty)$ scale for a count $y$ and its expectation, $\mu$, to the $(-\infty, 0) \log [y]$ and $\log [\mu]$ scale.

Thus, we do all our inference (SE calculations, CI's, tests) on the log scale, then transform back to the count or rate (or if comparative, rate ratio) scale.

1. Suppose $Y \sim \operatorname{Poisson}(\mu)$ with associated rate estimate $\hat{\lambda}=Y / P T^{19}$. Derive the variances for the random variables $\log [Y]$ and $\log [\hat{\lambda}]$. Ignore the possibility of obtaining $\hat{\mu}=0$ i.e., $\hat{\lambda}=0 / P T=0$.
2. What is the variance for the $\log$ of a rate ratio, i.e., $\log \left[\hat{\lambda}_{2} \div \hat{\lambda}_{1}\right]$ ?

## 0.2 (m-s) The Poisson Family as a 'Closed under Addition' Family

Show that if $Y_{1} \sim \operatorname{Poisson}\left(\mu_{1}\right)$ and $Y_{2} \sim \operatorname{Poisson}\left(\mu_{2}\right)$ are independent random variables, then $Y=Y_{1}+Y_{2} \sim \operatorname{Poisson}\left(\mu_{1}+\mu_{2}\right)$.

## 0.3 (m-s) Link between Poisson and Exponential Distributions

Show that if the random times $T_{1}, T_{2}, \ldots$ between successive events can be regarded as i.i.d observations from an exponential distribution with mean $\mu_{T}$, then the number $Y$ of events in a fixed time-window of length $W$ has a Poisson Distribution with mean or expectation $\mu_{Y}=W \times \lambda=W \times\left(1 / \mu_{T}\right)$.

## 0.4 (m-s) Link between tail areas of Poisson and $\chi^{2}$ Distributions

In section 5 of Fisher 1935, he states that 'it will be noticed' (from section 4) that, when its number of degrees $n$ is even, the probability of the variate $\frac{1}{2} \chi^{2}$

[^10]exceeding any specified value $\mu$ is
$$
e^{-\mu}\left\{1+\mu+\mu^{2} / 2!+\cdots+\mu^{(n-2) / 2} /[(n-2) / 2]!\right\} .
$$

From this, with $Y \sim \operatorname{Poisson}[\mu]$, and $n=2 y$, derive a way to obtain $\operatorname{Prob}[Y \geq$ $y \mid \mu]$ from the cdf function of the $\chi^{2}$ Distribution. From this, derive a way to obtain, from a single Poisson count $y$, the exact lower $\alpha / 2$ and upper $\alpha / 2$ limits for the mean of the Poisson Distribution it arose from. The article in Accrom $\alpha$ th illustrates this link, using a diagram we adapted from the tireruptures example.

## 0.5 (m-s) The Fisher information that a Poisson random

 variable carries about its expectation and about the $\log$ of this expectation(Wikipedia) "The Fisher information is the amount of information that an observable random variable $Y$ carries about an unknown parameter $\theta$ upon which the likelihood function of $\theta, L(\mu)=f(Y ; \theta)$, depends." The Fisher Information is defined as

$$
I(\theta)=E\left\{\left.\left[\frac{d}{d \theta} \ln f(Y ; \theta)\right]^{2}\right|_{\theta}\right\}
$$

As per Casella and Berger, 2nd Ed. p338, in an exponential family we also have that

$$
E\left\{\left.\left[\frac{d}{d \theta} \ln f(Y ; \theta)\right]^{2}\right|_{\theta}\right\}=-E\left\{\left.\frac{d^{2}}{d \theta^{2}} \ln f(Y ; \theta)\right|_{\theta}\right\} .
$$

1. Calculate the Fisher Information about the parameter $\mu$ in the case of the random variable $Y \sim \operatorname{Poisson}(\mu)$, with

$$
L(\mu)=f(Y ; \mu)=\exp [-\mu] \times \mu^{Y} / Y!
$$

2. Calculate the Fisher Information about the parameter $\theta=\log (\mu)$.

## 0.6 (m-s) The Poisson distribution as an approximation to the binomial distribution

Stigler, in The American Statistician, February 2013 (see Resources), writes
"The Poisson distribution is often introduced as an approximation to the binomial distribution, an approximation that improves in accuracy as $n$, the number of binomial trials, increases, while $n p$, the expected value, does not:

$$
\frac{e^{-n p}(n p)^{k}}{k!} \cong\binom{n}{k} p^{k}(1-p)^{n-k}
$$

The presentation is usually accompanied by a proof that invokes some version of the approximation $(1-1 / n)^{-n} \cong e=2.71828 \ldots$. Poisson's own derivation proceeded in much the same manner (Poisson 1837, p. 206; Stigler 1982a), as did a bestselling textbook published in 1936 by Hyman Levy and Leonard Roth. Those authors were, respectively, professor of Mathematics and assistant lecturer in Mathematics at Imperial College London. Figure 1 reproduces the relevant passage from Levy and Roth (1936).
to $b$ is $1-1 / n$. If we now consider the sample $t$, containing $n t / T$ elements, the probability that none of them belongs to $b$ is

$$
\begin{aligned}
\left(1-\frac{1}{n}\right)\left(1-\frac{1}{n}\right) \ldots\left(1-\frac{1}{n}\right) \ldots \text { to } \frac{n t}{T} \text { factors } & =\left(1-\frac{1}{n}\right)^{n(T}, \\
& =\left(1-\frac{1}{n}\right)^{-n(-t \mid T)}
\end{aligned}
$$

If $n$ is sufficiently large, $\dagger\left(1-\frac{1}{n}\right)^{-n}$ is approximately $e$, where

$$
e=1+\frac{1}{1!}+\frac{1}{2!}+\ldots=2 \cdot 71828 \ldots
$$

Hence the required probability is approximately $e^{-l / T}$.
$\dagger$ For example, if $n=10$, the error in replacing $\left(1-\frac{1}{n}\right)^{-n}$ by $e$ does not affect the sixth decimal place.

Figure 1. Part of page 80 of Levy and Roth (1936), showing the approximation and the footnote.

For many years, I have been presenting my class with a copy of this page from Levy and Roth and asking them, as a homework exercise, to answer a simple question: Is the footnote correct?"

1. BIOS601 Exercise: Answer Stigler's question.

### 0.7 CI's for the incidence of percutaneous injuries in the various types of residencies

The authors of the NEJM paper did not say how they got the CIs for the Rates per Intern-Month, shown in their Table 1. The CI for the overall rate closely matches the large-sample one that JH has in his Notes. Apply the exact method to obtain CI's for the '3-P's', Pediatrics, Psychiatry and Pathology, where the observed numerators are all under 30 .

### 0.8 Comparison of various CI's for the expectation, $\mu$ of a Poisson random variable, on the basis of a single count $y$

Fill in the blanks in the table below, and compare the accuracy of different approximations to the exact $95 \%$ CI for $\mu$, based on a count of $y$.

| Observe $y=$ | $3^{*}$ | 6 | 15 | $33^{* *}$ | $78^{* * *}$ | 100 |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
| Exact CI: | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |
| Approximation |  |  |  |  |  |  |
| Wilson-Hilferty | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |
| 1st principles, $y$ | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |
| 1st principles, $y^{1 / 2}$ | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |
| SE-based, $y$ | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |
| SE-based, $\log (y)$ | $?$ | $?$ | $?$ | $?$ | $?$ | $?$ |

* Rothman 2002 p134: 3 cases in 2500 PY. ** No. of lung cancer deaths in women aged 55-60 in Quebec in 1971. ***Total number of cancers in concerned area in Alberta SourGas study.


### 0.9 Power Calculations

A researcher wishes to compare the numbers of new cases of a particular disease in the 'PT' Population-Time units exposed to a potentially noxious agent with the $E_{0}=\mu_{0}=15.6$ that would be expected in this amount of Population Time if rates (already observed) in a LARGE unexposed experience prevailed. The researcher will use a 1 -sided test with $\alpha=0.05$ to test $H_{0}$ : $\mu_{\text {in this amount of exposed PT }}=15.6$ vs. $H_{\text {alt }}: \mu_{\text {in this amount of exposed PT }}>15.6$.

The amount of PT is fixed. Thus there is no point in the researcher calculating what amount of PT would be required so that, if $\mu_{\text {exposed }}=$ (say) $2 \times \mu_{\text {un-exposed }}$, there would be an $80 \%$ chance of obtaining a statistically significant elevation (i.e., an experience large enough to have $80 \%$ power
to 'detect' a doubling of the incidence rate). Instead, the researcher decided to calculate the power, with the given fixed amount of PT that can be studied, to 'detect' a doubling or a tripling of the incidence rate.
Perform this power calculation. You may find it easier (and more transparent) to work with the exact Poisson probabilities (e.g. in a spreadsheet or in $R$ ).

### 0.10 Perfect Results?

The following excerpt is from the Vaccine Arm of Table 3 of an Article in the NEJM in $2002^{20}$. We will look at the comparison with the Placebo arm when we get to comparative studies.

Efficacy Analyses of a Human Papillomavirus Type 16 L1 Virus-like-particle Vaccine.

## End point

HPV-16 VACCINE GROUP
Efficacy

Analysis \begin{tabular}{llccr}
Type of <br>
HPV-16 <br>
Infection

$\quad$

No. of <br>
Women

$\quad$

Cases <br>
Of <br>
Infection

$\quad$

Woman-Yr <br>
At <br>
Risk

$\quad$

Rate per 100 <br>
Woman-Yr <br>
At Risk
\end{tabular}

(1) Primary per-protocol
(2) Including women with general protocol violations
(3) Secondary per-protocol
$\mathrm{P}=$ Persistent; $\mathrm{T}=$ transient
*The per-protocol population included women who received the full regimen of study vaccine and who were seronegative for HPV-16 and negative for HPV-16 DNA on day 0 and negative for HPV-16 DNA at month 7 and in any biopsy specimens obtained between day 0 and month 7 ; who did not engage in sexual intercourse within 48 hours before the day 0 or month 7 visit; who did not receive any nonstudy vaccine within specified time limits relative to vaccination; who did not receive courses of certain oral or parenteral immunosuppressive agents, immune globulin, or blood products; who were not enrolled in another study of an investigational agent; and who had a month

[^11]7 visit within the range considered acceptable for determining the month 7 HPV-16 status.
**The population includes women who received the full regimen of study vaccine and who were seronegative for HPV-16 and negative for HPV-16 DNA on day 0 and negative for HPV-16 DNA at month 7 and in any biopsy specimens obtained between day 0 and month 7 .
Questions

1. In their Statistical Methods, the authors state: "The study employed a fixed-number-of-events design. At least 31 cases of persistent HPV-16 infection were required for the study to show a statistically significant reduction in the primary end point (assuming that the true vaccine efficacy was at least 75 percent with a power of at least 90 percent). Accounting for dropouts and women who were HPV-16-positive at enrollment and assuming an event rate of approximately 2 percent per year, we estimated that approximately 2350 women had to be enrolled to yield at least 31 cases of HPV-16 infection. Although the study will continue until all women complete four years of follow-up, the primary analysis was initiated on August 31, 2001, as soon as at least 31 cases were known to have occurred. Thus, the primary analysis includes all safety and efficacy data from visits that occurred on or before that date."
Why did the authors use a 'fixed-number-of-events' rather than 'fixed number of subjects for a fixed amount of time' design?
2. Calculate $95 \%$ 2-sided CIs to accompany the 3 point estimates of infection rate.

### 0.11 With luck, will the Royal Mint have enough coins?

Refer to the story "Babies who share royal birthday will coin it" 21 and to the average of 1,983 births a day.

1. (From the information in the article) what is the probability that the Mint will have enough, if they mint 2,013 coins? State any assumptions made.
2. How many should they mint to be $99.99 \%$ sure of having enough?
3. The average number of births per day varies slightly by season, and substantially by day of the week - JH could not find day-of-week data for the UK ${ }^{22}$, but did find 2010 data from the USA. ${ }^{23}$ Rework questions 1 and 2 using a worst case scenario, and assuming the same day-of-week patterns seen in the USA apply in England and Wales [scale USA down to size of $\boldsymbol{U K}]$
4. For shorthand purposes, refer to the probability of having enough coins as the 'non-exceedance' probability. ${ }^{24}$ How close is the mean of the 7 nonexceedance probabilities to the non-exceedance probability calculated at the mean no. of births per day? How close is the median non-exceedance probability? What if we switched focus to the exceedance probability rather than the non-exceedance probability?
5. (Again, under your worst case scenario) how many pink and blue pouches would you recommend they have ready?

[^12]

CONTENTS
EDITION

Beyond 20／20 WDS－Table view－ME＿ROUT by DOB＿WK（2010 Birth Data－State Detail）

CDC Home｜NCHS Home｜Contact NCHS｜NVSS Home｜VitalStats Home｜Privacy Policy｜Accessibility


Trables $\backslash$ Table $\$ Chart $]$

## 

ME＿ROUT by DOB＿WK（2010 Birth Data－State Detail）

| Other： |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| DOB WK | Total | Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
| ME ROUT ${ }^{\text {（ }}$ | へひ | 勺 | 勺 | ヘヱु | ヘひ | ヘひ | ヘひ | ヘ®， |
| Total | 3，999，386 | 369，704 | 606，424 | 666，686 | 656，694 | 649，636 | 633，899 | 416，343 |
| Vaginal－Spontaneous | 1，931，624 | 203，437 | 280，188 | 310，516 | 309，225 | 306，652 | 295，023 | 226，583 |
| Vaginal－Forceps | 20，868 | 2，069 | 3，055 | 3，456 | 3，506 | 3，352 | 3，056 | 2，374 |
| Vaginal－Vacuum | 89，879 | 9，114 | 12，669 | 14，962 | 14，761 | 14，358 | 13，566 | 10，449 |
| Cesarean | 995，945 | 67，410 | 163，540 | 176，929 | 170，666 | 168，245 | 170，456 | 78，699 |
| Not stated | 17，568 | 1，574 | 2，682 | 3，022 | 2，964 | 2，793 | 2，730 | 1，803 |
| Not on certificate | 943，502 | 86，100 | 144，290 | 157，801 | 155，572 | 154，236 | 149，068 | 96，435 |


| DayOfWeek | Total | January | February | March | April | May | June | July | August | September | October | November | December |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total | 3999386 | 323249 | 301994 | 338613 | 325028 | 328273 | 334535 | 345199 | 349747 | 350745 | 336809 | 326220 | 338974 |
| Sunday | 369704 | 34516 | 27851 | 27331 | 27326 | 34675 | 28456 | 29104 | 36658 | 30460 | 36798 | 28536 | 27993 |
| Monday | 606424 | 45873 | 45899 | 57699 | 46839 | 54815 | 47351 | 44502 | 61073 | 45406 | 47795 | 60967 | 48205 |
| Tuesday | 666686 | 50373 | 49751 | 62979 | 50302 | 51071 | 63178 | 51325 | 65572 | 53189 | 51056 | 65209 | 52681 |
| Wednesday | 656694 | 49042 | 49277 | 62067 | 49237 | 50024 | 63541 | 52202 | 51530 | 67103 | 49698 | 49109 | 63864 |
| Thursday | 649636 | 49448 | 49230 | 48981 | 61017 | 49637 | 50787 | 64681 | 51511 | 67279 | 49963 | 45162 | 61940 |
| Friday | 633899 | 55630 | 48382 | 48155 | 59075 | 48472 | 48887 | 62232 | 49800 | 52728 | 61238 | 45280 | 54020 |
| Saturday | 416343 | 38367 | 31604 | 31401 | 31232 | 39579 | 32335 | 41153 | 33603 | 34580 | 40261 | 31957 | 30271 |


[^0]:    ${ }^{1}$ See also: derivation \& applications (counting yeast cells in beer) in Student's 1907 paper "On the Error of Counting with a Haemacytometer"; and Ch. from Armitage et al. ${ }^{2}$ cf. ${ }^{* * * * * ~ " R a n d o m n e s s ~ a t ~ t h e ~ r o o t ~ o f ~ t h i n g s: ~ P o i s s o n ~ s e q u e n c e s " ~-~ P h y s i c s ~ E d u c a t i o n . ~}$

[^1]:    ${ }^{3}$ Yearly variations in no.s of plane crashes may be closer to Poisson [apart from variation due to improvements in safety, fluctuations in no.s of flights etc].
    ${ }^{4}$ See e.g. Number of weekday and weekend births in New York in August 1966 on web page: the variations are closer to Poisson if use weekly count.
    ${ }^{5}$ c.f. Impact sanitaire de la vague de chaleur en France survenue en août 2003. Rapport d'étape 29 aot 2003 [on course webpage] and Vanhems P et al. Number of in-hospital deaths at Edouard Herriot Hospital , and Daily Maximal Temperatures during summers of 2002 and 2003, Lyon, France. New Eng J Med Nov 20, 2003, pp2077-2078. ibid. see Resources.

[^2]:    ${ }^{6}$ Fisher 1935: see Resources

[^3]:    ${ }^{7}$ (See (homemade) "Confidence limits for the expectation [i.e. the 'mean' parameter] of a Poisson random variable" on last page and (more fully) under Resources.
    ${ }^{8}$ Note that the above "First Principle" is a general and important one; it "just so happens" that in this particular discrete distribution, if one has access to the percentiles of the Chi-Square distribution, the link helps avoid the trial and error process involved.
    ${ }^{9}$ Rothman[2002], page 134, provides an adaptation from "D. Byar, unpublished" in which he makes a further approximation, using the average $(y+0.5)$ for both the lower an upper limits, rather than the more accurate $y$ for the lower and $y+1$ for the upper limit. JH is surprised at Rothman's eagerness to save a few keystrokes on his calculator, and at his

[^4]:    ${ }^{10}$ incidence density

[^5]:    ${ }^{11}$ Montreal Gazette, Friday May 12, 1989.

[^6]:    ${ }^{12}$ SIR $=3.5=$ No.Observed/No.Expected. It is not $O=3.5, E=1$, since one cannot observe a fractional number of cases): $\operatorname{SIR}=3.5$; she simply scaled the $O$ and the $E$ so that $E$ (reference "rate") is 1
    ${ }^{13} \mathrm{CI}=(\mathrm{CI}$ derived from $O) /$ Expected $=0.4$ to 12.6 (a 31-fold range). $O$ is an integer. By trial and error, starting with $O=1$, and "trying all the CI's on for size" until one gets a 31 -fold range, one comes to $O=2$. (CI 0.242 to 7.22 , range 31 fold). Dividing 2 by 3.5 gives an $E$ of 0.57 . Check: $95 \%$ CI for SIR $(0.242$ to 7.22$) / 0.57=0.4$ to 12.6 .
    ${ }^{14} S I R=1.4=O / E ; C I=(C I$ derived from $O) / E$ has 0.8 to 2.2. This $2 . / 0.8=2.75$-fold uncertainty comes from uncertainty generated by $O$. Examine range of $95 \%$ CI associated with each possible value of $O$, until come to 10.67 to 28.45 when $O=18$. Divide 18 by 1.4 to get $E=12.8$. Check $95 \%$ CI 10.67 to 28.45 ) $/ 12.8=0.8$ to 2.2 .

[^7]:    ${ }^{15}$ Ayas NT, et al. JAMA. 2006;296:1055-1062

[^8]:    ${ }^{16}$ Using $\log y \simeq N\left(\log \mu, \sigma=(1 / \mu)^{1 / 2}\right)$.
    ${ }^{17} \mathrm{U} \operatorname{sing} y^{1 / 2} \simeq N\left(\mu^{1 / 2}, \sigma=1 / 2\right)$.

[^9]:    ${ }^{18}$ See Hanley JA "Jumping to coincidences: defying odds in the realm of the preposterous". the American Statistician, 1992, 46(3) 197-202. - under Resources

[^10]:    ${ }^{19} P T=$ amount of Population Time

[^11]:    ${ }^{20}$ The New England Journal of Medicine Vol 347 Nov 21, 2002, p1645 A Controlled trail of a Human Papillomavirus Type 16 Vaccine. Laura A. Koutsky et al., for The Proof of Principle Study Investigators.

[^12]:    ${ }^{21}$ Seems that 'to coin it' means means 'to profit'
    ${ }^{22}$ http://www.statistics.gov.uk/hub/population/births-and-fertility /live-births-and-stillbirths
    ${ }^{23} \mathrm{http}: / / \mathrm{www} . c d c . g o v / \mathrm{nchs} /$ data_access/Vitalstatsonline.htm
    ${ }^{24}$ A New Zealand webpage entitled What does Annual Exceedance Probability or AEP mean? says 'This term is generally referred to in rules that regulate discharges of contaminants including stormwater, wastewater, greywater. It can also be referred to in rules that regulate the use of land that may result in a discharge including offal pits, storage facilities for animal effluent, stockpiling organic matter (including composting) and storage of hazardous substances.
    The Annual Exceedance Probability is the chance or probability of a natural hazard event (usually a rainfall or flooding event) occurring annually and is usually expressed as a percentage. Bigger rainfall events occur (are exceeded) less often and will therefore have a lesser annual probability.
    Example 1: $2 \%$ exceedance probability rainfall event: A $2 \%$ Annual Exceedance Probability rainfall event has a $2 \%$ chance of occurring in a year, so once in every 50 years.
    Example 2: $20 \%$ exceedance probability rainfall event: A $20 \%$ Annual Exceedance Probability rainfall event has a $20 \%$ chance of occurring in a year, so once in every 5 years.

