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Attributable and unattributable risks and fractions and other scenario comparisons

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Abstract. Scenarios are alternative versions of the same dataset with the same variables but different observations or values. Applied scientists frequently want to predict how much good an intervention will do by comparing outcomes from the same model between different scenarios. Alternatively, they may want to compare outcomes between different models applied to the same scenario, for instance, when standardizing statistics from different subpopulations to a common gender and age distribution. Standard Stata tools for scenario means and comparisons are margins and pwcompare. A suite of packages is presented for estimating scenario means and comparisons by using margins, together with normalizing and variance-stabilizing transformations implemented by using nlcom. margprev estimates marginal prevalences; marglmean estimates marginal arithmetic means; regpar estimates the difference between two marginal prevalences (the population attributable risk); punaf estimates the ratio between two marginal arithmetic means (the population unattributable fraction); and punafcc estimates a marginal mean between-scenario risk or hazard ratio for case–control or survival data (also known as a population unattributable fraction). The population unattributable fraction and its confidence limits are subtracted from 1 to estimate the population attributable fraction. Formulas and examples are presented, including an example from the Global Allergy and Asthma European Network.

Keywords: st0314, margprev, marglmean, regpar, punaf, punafcc, margins, nlcom, population, unattributable, attributable, risk, fraction, PAR, PAF, PUF, scenario, comparison, standardization

1 Introduction

Applied scientists, especially in the public health sector, usually want to know how much good they can do. In particular, they might want to estimate, from the available data, how much reduction they would see in a disease rate if everybody stopped smoking or if all children received a proposed vaccine. Alternatively, they might compare disease rates between different subpopulations, discover heterogeneity, and wonder whether that heterogeneity is caused by confounding factors, such as differences in the age distribution between different subpopulations. After all, if subpopulation $A$ has a higher rate of a particular cancer than subpopulation $B$, then this might be due to something in the environment of subpopulation $A$, to which subpopulation $B$ is not exposed, or it might be due to subpopulation $A$ being mostly older than subpopulation $B$. If we could
eliminate the second possibility by standardizing the disease rates to a standard age distribution, then we might have evidence for the first possibility. In both cases, we are comparing scenarios. In the first case, we are comparing two different scenarios, using data from the same sample. In the second case, we are comparing the same scenario, using data from two different samples, one from subpopulation A and one from subpopulation B.

In statistics, scenarios are alternative versions of the same data matrix, with equivalent columns (variables) but with different rows (observations). Different scenarios have a one-to-one correspondence between the columns, so equivalent columns have the same variable names. However, different scenarios may or may not have a one-to-one correspondence between equivalent rows. If we use regression methods, then we might want to estimate the scenario means of an outcome variable $Y$ under different scenarios defined by specifying values for particular $X$ variables. The $X$ variables that vary between scenarios are known as exposures, and the other $X$ variables, which are invariant between scenarios, are known as concomitant variables.

A seminal reference for scenario means and comparisons in generalized linear models is Lane and Nelder (1982). However, an important case is the estimation of population attributable fractions after fitting a logistic regression model, which is given with different formulas for cohort studies and for case–control studies by Greenland and Drescher (1993). These formulas were implemented in Stata by Brady (1998), who introduced the Stata 5 `aflogit` command. This command is still downloadable by using the command `findit aflogit`. However, it does not support factor variable lists, and the Stata 5 code sometimes has problems with the long variable names used in subsequent Stata versions. Another special case of a scenario comparison is the population attributable risk (PAR), which is defined in Gordis (2000).

In Stata 11, a new command, `margins`, was added (see [R] margins). `margins` inputs a set of estimation results and a set of $X$ variables and outputs scenario means for expressions involving predicted $Y$ values under one or more scenarios. These scenario means are estimated with covariance matrices, so the user can calculate confidence intervals for them. In Stata 12, the commands `contrast` and `pwcompare` were added (see [R] contrast and [R] pwcompare), along with the `pwcompare` and `pwcompare()` options for `margins` (see [R] margins, pwcompare). These commands can be used to calculate confidence intervals for differences between scenario means. However, users frequently want to estimate scenario means and their differences and ratios by using normalizing and variance-stabilizing transformations to generate confidence limits in which the user can have confidence. This can be done by using `nlcom` (see [R] nlcom).

This article introduces a suite of programs that call `margins` and `nlcom` to calculate scenario prevalences and means, their differences, their ratios, and other comparison statistics. These statistics are known as marginal means, marginal prevalences, and attributable and unattributable risks and fractions. Section 2 describes the commands. Section 3 describes the methods and formulas used. Finally, section 4 gives practical examples of the use of these commands.
2 The margprev, marglmean, regpar, punaf, and punafcc commands

2.1 Syntax

{\texttt{margprev}} [\textit{if}] [\textit{in}] [\textit{weight}] [\textit{, atspec(atspec)} subpop(subspecc) predict(pred\_opt) vce(vcespec) noesample force iterate(\#) eform level(\#) post]

{\texttt{marglmean}} [\textit{if}] [\textit{in}] [\textit{weight}] [\textit{, atspec(atspec)} subpop(subspecc) predict(pred\_opt) vce(vcespec) noesample force iterate(\#) eform level(\#) post]

{\texttt{regpar}} [\textit{if}] [\textit{in}] [\textit{weight}] [\textit{, atspec(atspec) atzero(atspec0)} subpop(subspecc) predict(pred\_opt) vce(vcespec) noesample force iterate(\#) level(\#) post]

{\texttt{punaf}} [\textit{if}] [\textit{in}] [\textit{weight}] [\textit{, atspec(atspec) atzero(atspec0)} subpop(subspecc) predict(pred\_opt) vce(vcespec) noesample force iterate(\#) eform level(\#) post]

{\texttt{punafcc}} [\textit{if}] [\textit{in}] [\textit{weight}] [\textit{, atspec(atspec)} subpop(subspecc) vce(vcespec) noesample force iterate(\#) eform level(\#) post]

where \textit{atspec} and \textit{atspec0} are specifications recognized by the \texttt{at()} option of \texttt{margins}, \textit{subspec} is a subpopulation specification of the form recognized by the \texttt{subpop()} option of \texttt{margins}, and \textit{vcespec} is a variance–covariance specification of the form recognized by \texttt{margins} and must have one of the values

\texttt{delta|unconditional}

\texttt{pweights, aweights, fweights, and iweights} are allowed and handled as \texttt{margins}.

2.2 Description

The \texttt{margprev}, \texttt{marglmean}, \texttt{regpar}, \texttt{punaf}, and \texttt{punafcc} commands are for use after the parameters of a regression model have been fit by using an estimation command. They estimate a range of scenario prevalences, means and mean risk ratios, and their between-scenario comparisons (differences and ratios). These are estimated with con-
confidence limits derived by using normalizing and variance-stabilizing transformations to estimate the transformed parameters and their dispersion matrix. A difference between two scenario prevalences is known as a PAR, and a ratio between two scenario arithmetic means, or a mean between-scenario risk ratio or hazard ratio, is known as a population unattributable fraction (PUF). When a PUF is estimated, a confidence interval is also calculated, using end-point transformation, for the population attributable fraction (PAF), which is derived by subtracting the PUF from 1. Table 1 lists the five commands, the estimated parameters, and the transformations used.

Table 1. List of commands with estimated parameters and transformations used

<table>
<thead>
<tr>
<th>Package</th>
<th>Estimated parameters</th>
<th>Transformations</th>
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<tbody>
<tr>
<td>margprev</td>
<td>1 marginal prevalence</td>
<td>Logit</td>
</tr>
<tr>
<td>marglmean</td>
<td>1 marginal arithmetic mean</td>
<td>Log</td>
</tr>
<tr>
<td>regpar</td>
<td>2 marginal prevalences and their difference (PAR)</td>
<td>Log, Fisher’s z</td>
</tr>
<tr>
<td>punaf</td>
<td>2 marginal arithmetic means and their ratio (PUF)</td>
<td>Log</td>
</tr>
<tr>
<td>punafcc</td>
<td>1 mean between-scenario risk or hazard ratio (PUF)</td>
<td>Log</td>
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</table>

2.3 Options

atspec(atspec) is a specification allowed as a value of the at() option of margins (see [R] margins). This specification must identify a single scenario (denoted “Scenario 1” in the output), defined as a fantasy world in which a subset of the predictor variables in the model is set to values that may be different from their values in the real world. In the case of punafcc, which is intended for use with case–control or survival data, the specification is restricted and may set variables only to values (not to statistics). If atspec() is not specified, then its default value is atspec(asobserved all), implying that scenario 1 is the baseline scenario, represented by the predictor values actually present in the dataset currently in memory.

atzero(atspec0) is available for regpar and punaf only. It specifies a specification allowed as a value of the at() option of margins. This specification must identify a single baseline scenario (denoted “Scenario 0” in the output), defined as an alternative fantasy world in which a subset of predictors in the model is set to the values specified by atspec0. Scenario 0 will then be compared with the scenario specified by the atspec() option, scenario 1. If atzero() is not specified, then its default value is atzero(asobserved all), implying that scenario 0 is the baseline scenario, represented by the predictor values actually present in the dataset currently in memory.
Attributable and unattributable risks and fractions

\texttt{subpop(subspec), predict(pred_opt), vce(vcespec), noesample, and force} function as the options of the same names for \texttt{margins}. \texttt{subpop()} specifies a subpopulation; \texttt{predict()} specifies a predict option; \texttt{vce()} specifies the formula used for calculating the dispersion matrix of the estimated parameters; \texttt{noesample} specifies that the estimated statistics will not be restricted to the current estimation sample; and \texttt{force} specifies that the scenario means will still be estimated even if there are potential problems detected by \texttt{margins}. The \texttt{predict()} option is not currently available for \texttt{punafcc}, but it enables the use of the other four commands after a multiple-equation command. For instance, after \texttt{mlogit}, the option \texttt{predict(outcome(2))} allows scenario prevalences to be estimated and compared for the second value of a multinomial outcome. (See [R] \texttt{mlogit}.)

\texttt{iterate(\#)} has the same form and function as the option of the same name for \texttt{nlcom} (see [R] \texttt{nlcom}). \texttt{iterate()} specifies the number of iterations used by \texttt{nlcom} to find the optimal step size to calculate the numerical derivatives of the transformed scenario means and comparisons, with respect to the original scenario means calculated by \texttt{margins}.

\texttt{eform} specifies that the command will display an estimate, \textit{p}-value, and confidence limits instead of the log estimate; see the help files for \texttt{margprev}, \texttt{marglmean}, \texttt{punaf}, and \texttt{punafcc} for complete descriptions.

\texttt{level(\#)} specifies the percentage confidence level to be used in calculating the confidence intervals. If not specified, then \texttt{level()} is taken from the current value of the \texttt{c-class value c(level)}, which is usually \texttt{level(95)}.

\texttt{post} specifies that the command will post in \texttt{e()} the estimation results for estimating the transformed scenario means and any comparisons (differences or ratios). If \texttt{post} is not specified, then any existing estimation results are left in \texttt{e()}. Note that the estimation results posted are for the transformed parameters and not for the parameters themselves. This is done because the estimation results are intended to define symmetric confidence intervals for the transformed parameters, which can be back transformed to define asymmetric confidence intervals for the untransformed parameters and for the PAR in the case of \texttt{punaf} and \texttt{punafcc}.
2.4 Stored results

`margprev`, `marglmean`, `regpar`, `punaf`, and `punafcc` store the following results in `r()`:

Scalars

- `r(N)` number of observations
- `r(rank)` rank of `r(V)`
- `r(N_sub)` subpopulation observations
- `r(N_clust)` number of clusters
- `r(N_spu)` number of samples, primary sampling units, survey data only
- `r(N_strata)` number of strata, survey data only
- `r(df_r)` variance degrees of freedom, survey data only
- `r(N_poststrata)` number of post strata, survey data only
- `r(kMargins)` number of terms in `marginlist`
- `r(k_by)` number of subpopulations
- `r(k_at)` number of `at()` options
- `r(level)` confidence level

Macros

- `r(atzero)` `atzero()` option (`regpar` and `punaf` only)
- `r(atspec)` `atspec()` option

Matrices

- `r(cimat)` matrix of asymmetric confidence intervals (not stored by `marglmean`)
- `r(b)` vector of estimated transformed parameters
- `r(V)` dispersion matrix for transformed estimated parameters

The matrix `r(cimat)` is not stored by `marglmean`. It contains asymmetric confidence intervals (one per row) for the untransformed marginal prevalence in the case of `margprev`, for the untransformed marginal prevalences and their untransformed difference (the PAR) in the case of `regpar`, and for the PAF (equal to $1 - 	ext{PUF}$) in the case of `punaf` and `punafcc`. The matrices `r(b)` and `r(V)` contain the estimate and dispersion matrix, respectively, for the transformed parameters, as indicated in table 1.
Attributable and unattributable risks and fractions

If post is specified, then margprev, marglmean, regpar, punaf, and punafcc also store the following results in e():

Scalars
- e(N): number of observations
- e(rank): rank of e(V)
- e(Nsub): subpopulation observations
- e(Nclust): number of clusters
- e(Npsu): number of samples, primary sampling units, survey data only
- e(Nstrata): number of strata, survey data only
- e(df_r): variance degrees of freedom, survey data only
- e(Npoststrata): number of post strata, survey data only
- e(k_margins): number of terms in marginlist
- e(k_by): number of subpopulations
- e(k_at): number of at() options

Macros
- e(cmd): command name
- e(predict): program used to implement predict
- e(atzero): atzero() option (regpar and punaf only)
- e(atspec): atspec() option
- e(properties): b V

Matrices
- r(cimat): matrix of asymmetric confidence intervals (not stored by marglmean)
- e(b): vector of estimated transformed parameters
- e(V): dispersion matrix for transformed estimated parameters
- e(V_srs): simple-random-sampling-without-replacement (co)variance,  \( \hat{V}_{srswor} \), if svy
- e(V_srswr): simple-random-sampling-with-replacement (co)variance,  \( \hat{V}_{srswr} \), if svy and fpc()
- e(V_msp): misspecification (co)variance,  \( \hat{V}_{msp} \), if svy and available

Functions
- e(sample): marks estimation sample

3 Methods and formulas

This section is highly technical. The casual reader might like to skip it and proceed to section 4 and possibly return to this section for reference later.

The methods used are a combination of those in margins and in nlcom. We denote by  \( \theta \)  the vector of parameters estimated by the most recent model fit and denote by  \( f(z, \theta) \)  the function of the covariate row vector  \( z \)  and the parameter vector  \( \theta \)  whose mean we want to estimate. In general, we aim to estimate a population parameter of the form

\[
p(\theta) = \frac{1}{MR} \sum_{j=1}^{M} R_j f(Z_j, \theta)
\]  

(1)
where \( Z_j \) is the value of the covariate vector in the \( j \)th member of the population of \( M \) observations, \( R_j \) is a binary variable identifying membership of the \( j \)th observation in a subpopulation (0 for nonmembers and 1 for members), and \( M_R \) is the size of the subpopulation identified by the \( R_j \), equal to

\[
M_R = \sum_{j=1}^{M} R_j
\]

(This population of \( M \) observations may or may not be the population from which our data are sampled.)

We aim to estimate \( p(\theta) \) using the sample statistic

\[
\hat{p} = \frac{1}{w} \sum_{j=1}^{N} r_j w_j f\left(z_j, \hat{\theta}\right)
\]

where \( N \) is the number of observations in the sample, \( z_j \) is the vector of covariates in the \( j \)th observation in the sample, \( \hat{\theta} \) is the estimate of the parameter \( \theta \) derived from the sample, \( r_j \) is a binary variable identifying membership of the \( j \)th observation in a subsample corresponding to the subpopulation identified by the \( R_j \), \( w_j \) is the weight for the \( j \)th observation in the sample, and

\[
w = \sum_{j=1}^{N} r_j w_j
\]

is the sum of weights in the subsample. These weights are normally chosen so that \( \hat{p} \) is a consistent estimate of the population parameter \( p(\theta) \) in \( (1) \).

### 3.1 Scenario means estimated

The \texttt{margprev}, \texttt{marglmean}, \texttt{regpar}, \texttt{punaf}, and \texttt{punafcc} commands all start by estimating one or two population scenario means of the form \( (1) \) by using one or two corresponding sample scenario means of the form \( (2) \). Here scenarios are defined as alternative versions of the population and sample datasets, identified by alternative versions of the covariate vectors \( Z_j \) and \( z_j \), respectively. The scenarios are denoted scenario 1 (used by all five commands) and scenario 0 (currently used only by \texttt{regpar} and \texttt{punaf}). We will denote by \( Z_j^{(0)} \) and \( Z_j^{(1)} \) the values of the covariate vector for the \( j \)th population observation in scenarios 0 and 1, respectively, and denote by \( z_j^{(0)} \) and \( z_j^{(1)} \) the values of the covariate vector for the \( j \)th sample observation in scenarios 0 and 1, respectively. (We will continue to denote by \( Z_j \) and \( z_j \) the real-world values of the covariate vectors for the \( j \)th population observation and for the \( j \)th sample observation, respectively. Furthermore, we will assume that a mathematical function exists, deriving \( Z_j^{(i)} \) from \( Z_j \) and deriving \( z_j^{(i)} \) from \( z_j \), for \( i \in \{0, 1\} \).)
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Each of the commands estimates 1 or 2 scenario means $p^{(i)}(\theta)$ of functions $f^{(i)}(z, \theta)$, using estimators $\hat{p}^{(i)}$, for scenario indices $i \in \{0, 1\}$, over subpopulations defined by subpopulation indicators $R_j$ as in (1), using subsample indicators $r_j$ as in (2). The subpopulations and subsamples are the same for both scenarios. Therefore, for scenario $i$, the population scenario mean of (1) becomes

$$p^{(i)}(\theta) = \frac{1}{M_R} \sum_{j=1}^{M} R_j f^{(i)}(Z_j, \theta) \quad (3)$$

and the corresponding estimator of (2) becomes

$$\hat{p}^{(i)} = \frac{1}{w} \sum_{j=1}^{N} r_j w_j f^{(i)}(z_j, \hat{\theta}) \quad (4)$$

The commands vary in the specification of the functions to be averaged and of the subpopulations over which these functions are to be averaged. The subpopulation is governed by the subpop() option, which functions as the option of the same name for margins (see [R] margins). For a population index $j$ from 1 to $M$, we will denote by $S_j$ the binary variable indicating membership of the $j$th population observation in the subpopulation specified by the subpop() option. Similarly, for a sample index $j$ from 1 to $N$, we will denote by $s_j$ the binary variable indicating membership of the $j$th sample observation in the subsample specified by the subpop() option.

In the case of the commands margprev, marglmean, regpar, and punaf, the right-hand sides of (3) and (4) are specified by

$$R_j = S_j, \quad r_j = s_j, \quad f^{(i)}(Z_j, \theta) = \mu(Z_j^{(i)}, \theta), \quad f^{(i)}(z_j, \hat{\theta}) = \mu(z_j^{(i)}, \hat{\theta})$$

where $\mu(z, \theta)$ specifies the conditional arithmetic mean calculated by predict for the covariate vector $z$ and the parameter vector $\theta$.

In the case of the punafcc command, used for case–control and survival data, the definitions are slightly more complicated and depend on whether the most recent estimation command is stcox or some other estimation command. We will define the truth value $T(x)$ of a numeric value $x$ to be 1 if $x$ is nonzero, 0 if $x$ is 0, and missing if $x$ is missing. For a population index $j$ from 1 to $M$, we will define $Y_j$ to be the failure indicator variable _d, generated by the command stset, if the most recent estimation command is stcox and to be the dependent variable given by the estimation result e(depvar) if the most recent estimation command is another estimation command. Similarly, for a sample index $j$ from 1 to $N$, we will define $y_j$ to be the failure indicator variable _d, generated by the command stset, if the most recent estimation command is stcox and to be the dependent variable given by the estimation result e(depvar) if the most recent estimation command is another estimation command. (See [ST] stcox for documentation of stcox and [ST] stset for documentation of stset.) We will also denote by $\beta$ the column vector containing the subvector of the parameter vector $\theta$ containing the coefficients corresponding to the covariates of the $z$ vector and denote by
\( \hat{\beta} \) the column vector containing the corresponding subvector of the parameter-estimate vector \( \hat{\theta} \). The right-hand sides of (3) and (4) are then specified by

\[
R_j = S_j T(Y_j) \\
r_j = s_j T(y_j) \\

f^{(i)}(Z_j, \theta) = \exp \left\{ \left( Z_j^{(i)} - Z_j \right) \beta \right\} \\
f^{(i)}(z_j, \hat{\theta}) = \exp \left\{ \left( z_j^{(i)} - z_j \right) \hat{\beta} \right\}
\]

This implies that (3) is the population mean risk ratio (or hazard ratio) between scenario \( i \) and the real world for the “subsubpopulation” of cases (or failures) of the subpopulation specified by the `subpop()` option and that (4) is a corresponding sample mean risk ratio (or hazard ratio) for the “subsubsample” of cases (or failures) of the subsample specified by the `subpop()` option. A mean between-scenario ratio is a subtly different quantity from a ratio between scenario means; however, both of these quantities are known as population unattributable fractions and can be subtracted from 1 to give population attributable fractions.

In all the above equations, the `margprev`, `marglmean`, `regpar`, and `punaf` commands assume that `predict` specifies a conditional arithmetic mean and that the `punafcc` command assumes that the parameters of the model are log odds or hazard ratios, while the truth values of the dependent or failure variable indicate case status or failure. It is the user’s responsibility to ensure that these assumptions are true.

Dispersion-matrix estimates for the estimated scenario means (4) are calculated by using methods depending on the `vce()` option as discussed in [R] `margins`.

### 3.2 Symmetric confidence intervals for transformed parameters

Having estimated the scenario means and their sampling dispersion matrix by using `margins`, we then estimate the transformed parameters by using the normalizing and variance-stabilizing transformations specified in table 1. This is done by using `nlcom`, so we will use similar notation to `nlcom` (see [R] `nlcom`). We will denote by \( H \) the number of transformed parameters that we want to estimate and denote the vector of transformed parameters by \( g(\theta) = \{g_1(\theta), \ldots, g_H(\theta)\} \).
The $g_h(\theta)$ are functions of the originally estimated parameter vector $\theta$ that are estimated by using the corresponding $g_h(\hat{\theta})$. However, we will define them in terms of the scenario means estimated by the margins. Table 2 lists the transformed parameters estimated by each command and identified by their formulas and their commonly used parameter names. The logit and log transformations are standard normalizing and variance-stabilizing transformations for the prevalences of binary variables and for the arithmetic means of nonnegative-valued variables and their ratios, respectively. The hyperbolic arctangent $\text{arctanh}(\cdot)$, also known as Fisher’s $z$ transform, was recommended by [Edwards (1995)] for the general Somers’ $D$ parameter, which is discussed extensively in [Newson (2006)] and includes as a special case the difference between two proportions, exemplified in the scenario-comparison case by the PAR.

The `nlcom` command inputs the estimates and dispersion matrix for the scenario means $p^{(i)}(\theta)$, generated by `margins`, and outputs the estimates and dispersion matrix for the $g_h(\theta)$ by using numerically estimated derivatives of the transformed parameters with respect to the scenario means. The output estimates vector and dispersion matrix are stored in $r(b)$ and $r(V)$, respectively. If the user specifies the `post` option, then these matrices are also stored in $e(b)$ and $e(V)$, respectively. In either case, the matrices can be used in the same way to compute symmetric confidence intervals for the transformed parameters.

<table>
<thead>
<tr>
<th>Package</th>
<th>Parameter formulas</th>
<th>Parameter names</th>
</tr>
</thead>
<tbody>
<tr>
<td>margprev</td>
<td>$g_1(\theta) = \logit{p^{(1)}(\theta)}$</td>
<td>Logit prevalence</td>
</tr>
<tr>
<td>marglmean</td>
<td>$g_1(\theta) = \log{p^{(1)}(\theta)}$</td>
<td>Log arithmetic mean</td>
</tr>
<tr>
<td>regpar</td>
<td>$g_1(\theta) = \logit{p^{(0)}(\theta)}$</td>
<td>Logit prevalence</td>
</tr>
<tr>
<td></td>
<td>$g_2(\theta) = \log{p^{(1)}(\theta)}$</td>
<td>Logit prevalence</td>
</tr>
<tr>
<td></td>
<td>$g_3(\theta) = \text{arctanh}{p^{(0)}(\theta) - p^{(1)}(\theta)}$</td>
<td>$z$ transformed PAR</td>
</tr>
<tr>
<td>punaf</td>
<td>$g_1(\theta) = \log{p^{(0)}(\theta)}$</td>
<td>Log arithmetic mean</td>
</tr>
<tr>
<td></td>
<td>$g_2(\theta) = \log{p^{(1)}(\theta)}$</td>
<td>Log arithmetic mean</td>
</tr>
<tr>
<td></td>
<td>$g_3(\theta) = \log{p^{(1)}(\theta)/p^{(0)}(\theta)}$</td>
<td>Log PUF</td>
</tr>
<tr>
<td>punafcc</td>
<td>$g_1(\theta) = \log{p^{(1)}(\theta)}$</td>
<td>Log PUF</td>
</tr>
</tbody>
</table>

### 3.3 Asymmetric confidence intervals for untransformed parameters

Generally, the user really wants to see confidence intervals for arithmetic means and their ratios or for prevalences and their differences instead of seeing confidence intervals for the transformed parameters of table 2. In the case of the logged parameters estimated by `marglmean`, `punaf`, and `punafcc`, the `eform` option allows the user to view the untransformed parameters and their confidence limits. However, in the case of `margprev`, the `eform` option displays the odds and not the prevalence, and the `eform`
option is not available for `regpar`. Moreover, even in the case of the logged parameters of `punaf` and `punafcc`, the user wants to estimate the PAF instead of the PUF. To cater for these cases, the commands of the `punaf` suite (except for `marglmean`) also output a matrix of confidence intervals for the untransformed parameters of interest. This confidence interval matrix is stored in `r(cimat)` and is also automatically listed in the output. For each command, it has one row for each of the $K$ parameters $c_k(\theta)$ for $k \in \{1 \ldots K\}$ and three columns containing the estimates, lower confidence limits, and upper confidence limits, respectively, of these parameters. The confidence intervals in this matrix are asymmetric.

Table 3 lists the parameters whose asymmetric confidence intervals are listed and saved in the confidence interval matrix by the four commands that produce such a matrix. In each case, the command computes a confidence interval for the transformed parameter $g_h(\theta)$, with estimates and lower and upper confidence limits corresponding to the confidence level specified by the `level()` option, which defaults to `level(95)`. The estimate, lower confidence limit, and upper confidence limit for the untransformed parameter $c_k(\theta)$ are then derived by transforming the estimate, lower confidence limit, and upper confidence limit, respectively, for the transformed parameter (in the case of `margprev` and `regpar`) or by transforming the estimate, upper confidence limit, and lower confidence limit, respectively, for the transformed parameter (in the case of `punaf` and `punafcc`).

Table 3. Untransformed parameters expressed as functions of transformed parameters

<table>
<thead>
<tr>
<th>Package</th>
<th>Parameter formulas</th>
<th>Parameter names</th>
</tr>
</thead>
<tbody>
<tr>
<td>margprev</td>
<td>(c_1(\theta) = \text{invlogit}{g_1(\theta)})</td>
<td>Scenario 1 prevalence</td>
</tr>
<tr>
<td>regpar</td>
<td>(c_1(\theta) = \text{invlogit}{g_1(\theta)})</td>
<td>Scenario 0 prevalence</td>
</tr>
<tr>
<td></td>
<td>(c_2(\theta) = \text{invlogit}{g_2(\theta)})</td>
<td>Scenario 1 prevalence</td>
</tr>
<tr>
<td></td>
<td>(c_3(\theta) = \tanh{g_3(\theta)})</td>
<td>PAR</td>
</tr>
<tr>
<td>punaf</td>
<td>(c_1(\theta) = 1 - \exp{g_1(\theta)})</td>
<td>PAF (cohort or cross-sectional)</td>
</tr>
<tr>
<td>punafcc</td>
<td>(c_1(\theta) = 1 - \exp{g_1(\theta)})</td>
<td>PAF (case–control or survival)</td>
</tr>
</tbody>
</table>
4 Examples

4.1 Scenario comparisons in the lbw data using regpar

`lbw.dta` was discussed by Hosmer, Lemeshow, and Klar (1988) and is posted on the Stata Press website. It has one observation for each of a sample of 189 pregnancies and data on the birthweight of the baby and on a list of predictive variables. The most interesting of these variables is probably the mother’s smoking status during pregnancy, coded as the binary variable `smoke`, which is equal to 1 if the mother smoked during pregnancy and 0 otherwise. We will estimate scenario comparisons from a logistic regression model to predict the binary variable `low`, indicating that the baby’s birthweight was below 2,500 grams.

After loading the `lbw` data, we fit a logistic model of `low` with respect to the exposure factor `smoke` and the confounding factor `race` (1 for white, 2 for black, or 3 for other):

```
use http://www.stata-press.com/data/r12/lbw.dta
(logit lbw i.race i.smoke, or vce(robust))
```

```
Iteration 0:  log pseudolikelihood =  -117.336
Iteration 1:  log pseudolikelihood =  -110.10441
Iteration 2:  log pseudolikelihood =  -109.98749
Iteration 3:  log pseudolikelihood =  -109.98736
Iteration 4:  log pseudolikelihood =  -109.98736

Logistic regression Number of obs =  189
Wald chi2(3) =  14.30
Prob > chi2 = 0.0025
Log pseudolikelihood =  -109.98736 Pseudo R2 = 0.0626

|       | Odds Ratio | Std. Err. | z   |  P>|z|  | 95% Conf. Interval |
|-------|------------|-----------|-----|------|-------------------|
| race  |            |           |     |      |                   |
| 2     | 2.956742   | 1.420439  | 2.26| 0.024| 1.153162          | 7.581175   |
| 3     | 3.030001   | 1.187272  | 2.83| 0.005| 1.405753          | 6.530954   |
| smoke |            |           |     |      |                   |
| 1     | 3.052631   | 1.10296   | 3.09| 0.002| 1.503568          | 6.197631   |
| _cons| .1587319   | .0515235  | -5.67| 0.000| .0840173          | .2998882   |
```

We see that maternal smoking triples the odds of low birthweight and that having a mother of either of the two nonwhite maternal races has a similar effect on the odds. However, few of the public really understand odds ratios. They might understand more easily the difference that might result if all mothers quit smoking before pregnancy, but their racial mix remained the same as in the real world. The `regpar` command can estimate this difference, using the stored estimation results:
. regpar, at(smoke=0)
Scenario 0: (asobserved)  _all
Scenario 1: smoke=0
Symmetric confidence intervals for the logit proportions
under Scenario 0 and Scenario 1
and for the z-transformed population attributable risk (PAR)
Total number of observations used: 189

|                | Coef.  | Std. Err. | z     | P>|z| | [95% Conf. Interval] |
|----------------|--------|-----------|-------|------|----------------------|
| Scenario_0     | -.789997 | .1519305 | -5.20 | 0.000 | -1.087775 - .4922187 |
| Scenario_1     | -1.215955 | .2051031 | -5.93 | 0.000 | -1.61795 - .8139606  |
| PAR            | .0837153   | .0266196 | 3.14  | 0.002 | .0315419 - .1358887  |

Asymmetric 95% CIs for the untransformed proportions
under Scenario 0 and Scenario 1
and for the untransformed population attributable risk (PAR)

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario_0</td>
<td>.31216931</td>
<td>.25203743</td>
<td>.37937104</td>
</tr>
<tr>
<td>Scenario_1</td>
<td>.22864901</td>
<td>.16548776</td>
<td>.30704715</td>
</tr>
<tr>
<td>PAR</td>
<td>.08352031</td>
<td>.03153146</td>
<td>.13505843</td>
</tr>
</tbody>
</table>

regpar starts its output by specifying scenarios 0 and 1 in the language of the at() option of margins. Scenario 0 is (asobserved) _all, implying that all covariates and factors are as observed in our real-world sample. Scenario 1 is smoke=0, implying that no mothers smoke, but (by default) the factor race is distributed as in our real-world sample. regpar then displays the logit proportions with low birth rate under scenarios 0 and 1 and the z transform of the difference between these proportions, known as the PAR, with their standard errors, z statistics, p-values, and symmetric confidence limits. Finally, it displays the more comprehensible asymmetric confidence intervals for the untransformed scenario proportions and for their difference. We see that in the real world (Scenario_0), 31.2% of babies are expected to have a low birthweight but that in the dream scenario where no mothers smoke and their races stay the same (Scenario_1), only 22.9% of babies are expected to have a low birthweight. The difference between these scenario percentages (PAR) is 8.4%, with confidence limits from 3.2% to 13.5%. The PAR can be interpreted as the proportion of all babies that have low birthweight because they were born in scenario 0 instead of in scenario 1.

Alternatively, we might want to communicate our message to an audience of smoking mothers, who might want to know how much they could do for their children if only they quit smoking before pregnancy. To answer this, we might use regpar with a subpop() option to compute an exposed-population attributable risk for the subpopulation of smoking mothers:
Attributable and unattributable risks and fractions

```
.regpar, at(smoke=0) subpop(if smoke==1)
Scenario 0: (asobserved) _all
Scenario 1: smoke=0
Symmetric confidence intervals for the logit proportions
under Scenario 0 and Scenario 1
and for the z-transformed population attributable risk (PAR)
Total number of observations used: 189

|              | Coef.     | Std. Err. | z    | P>|z| | [95% Conf. Interval] |
|--------------|-----------|-----------|------|-----|---------------------|
| Scenario_0   | -.3829923 | .2373852  | -1.61| 0.107| -.8482587 .0822742 |
| Scenario_1   | -1.436486 | .2279922  | -6.30| 0.000| -1.883343 -.9896299|
| PAR          | .2166422  | .0707321  | 3.06 | 0.002| .0780098 .3552746 |

Asymmetric 95% CIs for the untransformed proportions
under Scenario 0 and Scenario 1
and for the untransformed population attributable risk (PAR)

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario_0</td>
<td>.40540541</td>
<td>.29979827</td>
<td>.52055695</td>
</tr>
<tr>
<td>Scenario_1</td>
<td>.19209003</td>
<td>.13200536</td>
<td>.27098519</td>
</tr>
<tr>
<td>PAR</td>
<td>.21331537</td>
<td>.07785194</td>
<td>.34104503</td>
</tr>
</tbody>
</table>
```

This time, the option `subpop(if smoke==1)` restricts the prediction to the subpopulation of smoking mothers, but scenarios 0 and 1 are defined as before. Once again, `regpar` displays the incomprehensible symmetric confidence intervals for the transformed parameters followed by the asymmetric confidence intervals for the transformed parameters, which are probably more easily explained to smoking mothers. We see that the children of smoking mothers have a 40.1% prevalence of low birthweight, which might be reduced to 19.2% if their mothers quit smoking before pregnancy, while their racial mix remained the same. The difference is 21.3% with confidence limits from 7.8% to 34.1%.

Another possibility is to compare our zero-smoking dream scenario not with the intermediate world in which we live but with the nightmare scenario where all mothers started smoking. This is done by using the `atzero()` option, which can be used to reset scenario 0, as follows:
Roger B. Newson

. regpar, at(smoke=0) atzero(smoke=1)
Scenario 0: smoke=1
Scenario 1: smoke=0
Symmetric confidence intervals for the logit proportions
under Scenario 0 and Scenario 1
and for the z-transformed population attributable risk (PAR)
Total number of observations used: 189

|               | Coef. | Std. Err. | z     | P>|z|  | [95% Conf. Interval] |
|---------------|-------|-----------|-------|------|---------------------|
| Scenario_0    | -.1697027 | .2464163 | -0.69 | 0.491 | -0.6526697, .3132642 |
| Scenario_1    | -1.215955 | .2051031 | -5.93 | 0.000 | -1.61795, -.8139606 |
| PAR           | .2331622  | .0759652  | 3.07  | 0.002 | .0842732, .3820612  |

Asymmetric 95% CIs for the untransformed proportions
under Scenario 0 and Scenario 1
and for the untransformed population attributable risk (PAR)

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario_0</td>
<td>.45767584</td>
<td>.34238817</td>
<td>.57768182</td>
</tr>
<tr>
<td>Scenario_1</td>
<td>.22864901</td>
<td>.16548776</td>
<td>.30704715</td>
</tr>
<tr>
<td>PAR</td>
<td>.22902683</td>
<td>.08407429</td>
<td>.36448745</td>
</tr>
</tbody>
</table>

We see that scenario 0 is set by the `atzero()` option to `smoke=1`, while scenario 1 is still `smoke=0`. Once again, `regpar` displays the symmetric confidence intervals for the transformed parameters followed by the asymmetric confidence intervals for the untransformed parameters. We see that if all mothers smoked and the racial mix stayed the same, then 45.8% of children might have low birthweight. The dream scenario prevalence, where no mothers smoke and the racial mix stays the same, is still 22.9%, as before. The difference in prevalence between the nightmare scenario 0 and the dream scenario 1 is 22.9% with confidence limits from 8.4% to 36.4%.

`regpar` might be even more useful if we had a large number of confounders instead of the single confounder `race`. In that case, we might want to reduce the potentially infinite-dimensioned confounder space to a finite-dimensioned confounder space by defining a propensity score for smoking, as recommended by Rosenbaum and Rubin (1983). Such a propensity score might be defined by using a logistic regression model to regress `smoke` with respect to the multiple confounders, then by using `predict` to define the smoking propensity score for each subject as the predicted probability of smoking for that subject. We might then define a grouping variable for the propensity score by using `xtile` (see [D] `pctile`) and then use the propensity-group variable in a second logistic regression model with `low` as the outcome and with smoking exposure and smoking-propensity group as the predictors. A problem with using propensity scores or groups as covariates in a logistic regression model is that the conditional odds ratio with respect to exposure, adjusted for the propensity score, is not the same quantity as the conditional odds ratio with respect to exposure, adjusted for the original confounders. This is in contrast to conditional mean differences (including prevalence differences) between exposed and unexposed subjects, where the mean difference conditional on the propensity score is equal to the mean difference conditional on the original covariates. Austin et al. (2007) argue that if we use the propensity-adjusted odds ratio to estimate the confounder-adjusted odds ratio, then our estimate is likely to be biased toward the null hypothesis that the odds ratio is 1, leading to an underestimation of the magnitude
of the exposure effect. This problem can be arguably solved by fitting a logistic regression of disease with respect to exposure propensity and exposure and then by using \texttt{regpar} to define the exposure effect as a difference in marginal disease prevalences between a nightmare scenario where exposure propensity stays the same and all subjects are exposed and a dream scenario where exposure propensity stays the same and all subjects are unexposed.

4.2 Scenario comparisons in the lbw data using \texttt{punaf}

Then again, we might want to estimate the possibility for disease prevention as a proportion of the total disease burden of low birthweight instead of as a proportion of all babies. This can be done by using \texttt{punaf} after the same logistic regression model as before. \texttt{punaf} compares scenario arithmetic means (including scenario prevalences) by using ratios instead of differences. These ratios, known as PUFs, can then be subtracted from 1 to obtain PAFs. As a simple example, we compare the smoking-free dream scenario to the real world once again:

```
. punaf, at(smoke=0) eform
Scenario 0: (asobserved) _all
Scenario 1: smoke=0
Confidence intervals for the means under Scenario 0 and Scenario 1
and for the population unattributable fraction (PUF)
Total number of observations used: 189

|               | Mean/Ratio | Std. Err. | z      | P>|z| | [95% Conf. Interval] |
|---------------|------------|-----------|--------|-----|---------------------|
| Scenario_0    | .3121693   | .0326225  | -11.14 | 0.000 | .2543534 .3831271   |
| Scenario_1    | .228649    | .0361738  | -9.33  | 0.000 | .1676887 .3117704   |
| PUF           | .7324519   | .0818807  | -2.79  | 0.005 | .5883333 .911874    |
```

95% CI for the population attributable fraction (PAF)

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAF</td>
<td>.2675481</td>
<td>.08812601</td>
<td>.41166675</td>
</tr>
</tbody>
</table>

We see that the scenarios, as in our first example with \texttt{regpar}, and the scenario means, computed by using \texttt{punaf}, are the same as the untransformed scenario prevalences using \texttt{regpar}. The confidence limits are slightly different because they are computed by using the log transform instead of the logit transform. The PUF is the ratio between the scenario 1 mean and the scenario 0 mean and represents the fraction of the scenario 0 disease burden that would remain if the babies were born in scenario 1. (Note that the \texttt{eform} option ensures that we see confidence intervals for the scenario means and their ratio instead of for their logs.) Finally, \texttt{punaf} subtracts the PUF (and its lower and upper confidence limits) from 1 to obtain the PAF (and its lower and upper confidence limits) and displays these in the bottom line of output. We see that 26.8% of the disease burden of low birthweight might be eliminated by eliminating maternal smoking, assuming that the racial mix stays the same, with confidence limits from 8.8% to 41.2%.
4.3 margprev and marglmean in the lbw data

We can also estimate marginal prevalences and means without comparing them between different scenarios. The margprev command can estimate marginal odds and the corresponding marginal prevalences from the current estimation results. For instance, the marginal odds and prevalence of low birthweight in a world of smoking mothers with the existing race distribution could be estimated as follows:

```
. margprev, at(smoke==1) eform
Scenario 1: smoke==1
Confidence interval for the marginal odds
under Scenario 1
Total number of observations used: 189

|        | Odds  | Std. Err. | z     | P>|z|  | [95% Conf. Interval] |
|--------|-------|-----------|-------|-----|---------------------|
| Scenario_1 | .8439156 | .2079545 | -0.69 | 0.491 | .5206539 1.367883 |

Asymmetric 95% CI for the untransformed marginal prevalence
under Scenario 1

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario_1</td>
<td>.45767584</td>
<td>.34238817</td>
<td>.57768182</td>
</tr>
</tbody>
</table>
```

This time, only scenario 1 is specified because there is no scenario 0. margprev displays first the marginal odds (not the marginal log odds, because eform has been specified) and then a confidence interval for the marginal prevalence, which is the same as the one calculated for the same nightmare scenario by regpar.

The marglmean command can estimate general marginal means for general nonnegative variables, using the log transform to calculate confidence intervals. For instance, we might fit a gamma-family regression model for the nonnegative variable bwt, representing birthweight in grams, with respect to race and smoking status, as follows, using the glm command detailed in Hardin and Hilbe (2012):
### Attributable and unattributable risks and fractions

```
> glm bwt i.race i.smoke, family(gamma) link(log) eform vce(robust)
```

Iteration 0: log pseudolikelihood = -1698.0172
Iteration 1: log pseudolikelihood = -1697.9741
Iteration 2: log pseudolikelihood = -1697.9741

Generalized linear models
Optimization : ML
   No. of obs = 189
   Residual df = 185
   Scale parameter = .0555296
Deviance = 12.0823644 (1/df) Deviance = .06531
   Pearson = 10.27297009 (1/df) Pearson = .0555296
   Variance function: V(u) = u^2
   [Gamma]
   Link function : g(u) = ln(u)
   [Log]
   AIC = 18.01031
   BIC = -957.6409

|   | Robust exp(b) | Std. Err. | z  | P>|z| | [95% Conf. Interval] |
|---|--------------|-----------|----|------|----------------------|
| bwt |             |           |    |      |                      |
| race |             |           |    |      |                      |
| 2   | .8594198    | .042562   | -3.06 | 0.002 | .7799205 .9470227   |
| 3   | .863627     | .0360104  | -3.52 | 0.000 | .795855 .9371702   |
| 1.smoke |     |           |    |      |                      |
| _cons | 3332.454    | 97.62645  | 276.88 | 0.000 | 3146.499 3529.398   |

The parameters are a baseline arithmetic mean _cons (in grams) for the babies of nonsmoking white mothers, two arithmetic mean ratios for the babies of black and miscellaneous-race mothers, and an arithmetic mean ratio for the babies of smoking mothers compared with the babies of nonsmoking mothers of the same race. We can now use `marglmean` to estimate the marginal arithmetic mean, with asymmetric confidence limits, that would be expected if all mothers smoked and the race distribution remained the same:

```
> marglmean, at(smoke=1) eform
```

Scenario 1: smoke=1
Asymmetric confidence interval for the marginal mean under Scenario 1
Total number of observations used: 189

|   | Mean  | Std. Err. | z    | P>|z| | [95% Conf. Interval] |
|---|-------|-----------|------|------|----------------------|
| Scenario_1 | 2702.087 | 80.18231  | 266.28 | 0.000 | 2549.416 2863.902   |

We see that the mean birthweight in this scenario would be 2,702 grams with confidence limits from 2,549 grams to 2,864 grams. We could also use `punaf` to estimate the ratio (or PUF) between this scenario mean and the scenario mean where no mothers smoked (not shown to save space).

#### 4.4 punafcc in case–control and survival data

The punafcc command calculates unattributable and attributable fractions for case–control and survival data. The unattributable fraction in this case is a mean between-
scenario odds ratio for cases (if used after a logistic estimation) or a mean between-scenario hazard ratio for lifetimes that terminated from the cause of interest (if used after a Cox survival regression) instead of a ratio of scenario means. Currently, the only scenarios that can be compared in this way are scenario 1 and the world in which we sampled the data.

downs.dta is an example of a case–control study dataset, described and used in epitab (see [ST] epitab) to demonstrate the cci command. The data are from Rothman, Greenland, and Lash (2008) and represent a case–control study whose outcome variable is Down syndrome in infants, with maternal spermicide use as the exposure and maternal age group as a confounding factor. The dataset has eight observations and four variables. These variables are three binary key variables (case, exposed, and age) identifying the eight observations uniquely and indicating case status, exposure status, and maternal age at or above 35 years, respectively, and one integer variable (pop) containing frequency weights for the combination of case status, exposure status, and age group indicated by the three key variables.

We start by loading downs.dta and fitting a full logistic regression model, allowing age odds ratios and different exposure odds ratios for the two age groups:

```plaintext
  . webuse downs, clear
  . logit case i.age i.exposed i.age#i.exposed [fweight=pop], or vce(robust)
Iteration 0:  log pseudolikelihood =  -85.885722
Iteration 1:  log pseudolikelihood =  -82.752975
Iteration 2:  log pseudolikelihood =  -81.552365
Iteration 3:  log pseudolikelihood =  -81.451562
Iteration 4:  log pseudolikelihood =  -81.451332
Iteration 5:  log pseudolikelihood =  -81.451332
Logistic regression Number of obs =  1270
 Wald chi2(3) =  11.64
  Prob > chi2 = 0.0087
Log pseudolikelihood =  -81.451332 Pseudo R2 =  0.0516

                      Robust            
                     case | Odds Ratio  Std. Err.     z   P>|z|  [95% Conf. Interval]
-------------------|----------|-----------------|--------|---------|------------------------
 1.age             |     4.10  |      2.78       |  2.09  | 0.037   | 1.090465               |
 1.exposed         |     3.39  |      2.29       |  1.81  | 0.070   | 0.904392               |
 age#exposed       |     1.69  |      2.39       |  0.37  | 0.711   | 1.05541                | 27.034
  _cons             |     0.008 |      0.002      | -14.24 | 0.000   | 0.0044086              | 0.0163831
```
Attributable and unattributable risks and fractions

```
. punafcc, at(exposed=0) eform vce(unconditional)
Scenario 0: (asobserved) _all
Scenario 1: exposed=0
Confidence interval for the population unattributable faction (PUF)
Total number of observations used: 1270

| Ratio   | Std. Err. | z   | P>|z| | 95% Conf. Interval |
|---------|-----------|-----|------|-------------------|
| PUF     | 0.816142  | 0.1181495 | -1.40 | 0.160 | 0.6145268 1.083903 |
```

95% CI for the population attributable fraction (PAF)

<table>
<thead>
<tr>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAF</td>
<td>0.18385804</td>
<td>-0.08390349</td>
</tr>
</tbody>
</table>

We see from the PUF that in a fantasy scenario where no mothers were exposed to spermicide, we might expect the rate of Down syndrome to be 81.6% of that observed in the population from which our cases and controls were sampled with 95% confidence limits from 61.5% to 108.4%. This allows the possibility that spermicide use might even be slightly protective, at least at some maternal ages. The PAF is computed by subtracting the PUF from 1 and therefore has confidence limits from $-8.4\%$ to 38.5%. These limits are wide enough to include 0 and even a small range of negative values.

Similarly, we can estimate unattributable and attributable fractions in the Stanford heart transplant dataset `heart3`, with one observation per study subject per time interval, where the time interval can be a pretransplant interval (present for all subjects) or a posttransplant interval (present only for subjects who received a transplant). We will fit the Cox regression model used in `stcox` (see `[ST] stcox`), where death is regressed with respect to the quantitative covariates `year` (year of acceptance) and `age` (age in years at start) and the binary variables `posttran` (indicating that the interval is post-transplant) and `surgery` (indicating prior heart surgery on entry). We do not need to use `stset`, because this has already been done to the dataset.
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. use http://www.stata-press.com/data/r12/stan3, clear
(Heart transplant data)
. stcox age posttran surg year, vce(robust)
         failure _d: died
         analysis time _t: t1
         id: id
Iteration 0: log pseudolikelihood = -298.31514
Iteration 1: log pseudolikelihood = -289.7344
Iteration 2: log pseudolikelihood = -289.53498
Iteration 3: log pseudolikelihood = -289.53378
Iteration 4: log pseudolikelihood = -289.53378
Refining estimates:
Iteration 0: log pseudolikelihood = -289.53378
Cox regression -- Breslow method for ties
No. of subjects = 103 Number of obs = 172
No. of failures = 75
Time at risk = 31938.1
Wald chi2(4) = 19.68
Log pseudolikelihood = -289.53378 Prob > chi2 = 0.0006
             (Std. Err. adjusted for 103 clusters in id)

Robust

| _t   | Haz. Ratio | Std. Err. | z   | P>|z| | [95% Conf. Interval] |
|------|------------|-----------|-----|------|----------------------|
| age  | 1.030224   | .0148771  | 2.06| 0.039| 1.001474 1.059799    |
| posttran | .9787243 | .2961736  | -0.07| 0.943| .5408498 1.771104    |
| surgery | .3738278  | .1304912  | -2.82| 0.005| .1886013 .7409665   |
| year  | .8873107   | .0613176  | -1.73| 0.084| .7749139 1.01601     |

We see the hazard ratios associated with each binary or quantitative covariate, with Huber (or robust) confidence limits.

We might want to know the fractions of mortality attributable and unattributable to subjects not having prior surgery. That is, we might want to ask how much the death rate in the study might have decreased if all patients had received heart surgery prior to joining the study and if acceptance years, ages, and transplant history during the study had been the same as in the real world, and to ask how much hazard would have remained. This can be done by using `punafcc` with the option `vce(unconditional)` as before because the covariate values of lifetimes that ended in death will be subject to sampling error, assuming that deaths do not occur by design.
From the PUF, we see that giving all the subjects prior surgery, and changing nothing else, might have reduced mortality to 42.4% of the level observed. When this PUF is subtracted from 100% to get a PAF, we conclude that 57.6% of the mortality observed is attributable to subjects not having prior surgery with confidence limits from 22.1% to 76.9%.

The option vce(unconditional), recommended here for use with punafcc, requires that the user must specify vce(robust) in the estimation command generating the parameter estimates. Also the interpretation of the unattributable and attributable fractions requires the assumption that the association between the outcome and the exposure altered in the fantasy scenarios is indeed causal, meaning that the outcome will change as predicted if we intervene to change the exposure.

4.5 Standardization as out-of-sample prediction

We can also compare outcomes between different models applied to the same scenario instead of between the same model applied to different scenarios. For instance, in a multicenter study, we might fit a logistic regression model of disease with respect to gender and age to the data from a center, input a dataset specifying a standard distribution of gender and age, and use margprev to estimate the marginal prevalence expected if the logistic model is applied to that standard population. This is an example of out-of-sample prediction, and the five commands introduced here have a noesample option to make this possible; this option is similar to the one of the same name for margins.

The Global Allergy and Asthma European Network (GA²LEN) survey is part of a multiregional European study on asthma and allergy in Europe. Sensitivity to a range of allergens was measured on a subsample of subjects in each region, using skin prick tests. We wanted to compare sensitivity prevalences, standardized to a common age distribution, between 13 European regions. To do this, we fitted a logistic regression model for sensitivity to each allergen in each region, with respect to gender and age, and then used margprev to estimate a standardized sensitivity prevalence.
For instance, in the case of sensitivity to cat allergen in the United Kingdom, the logistic model (fit by using sampling probability weights) was as follows:

```
. logit spt_cat male fquesagec [pweight=sampwt5], or
Iteration 0:  log pseudolikelihood = -1030.8768
Iteration 1:  log pseudolikelihood = -977.80033
Iteration 2:  log pseudolikelihood = -973.41056
Iteration 3:  log pseudolikelihood = -973.39866
Iteration 4:  log pseudolikelihood = -973.39866
Logistic regression
Number of obs = 159
Wald chi2(2) = 4.04
Prob > chi2 = 0.1328
Log pseudolikelihood = -973.39866 Pseudo R2 = 0.0558
```

| spt_cat | Odds Ratio | Robust Std. Err. | z  | P>|z|   | [95% Conf. Interval]  |
|---------|------------|------------------|----|-------|-----------------------|
| male    | 2.527963   | 1.535882         | 1.53| 0.127 | .7684525              | 8.316188       |
| fquesagec | .6700974  | .2209261         | -1.21| 0.225 | .3511585              | 1.278712      |
| _cons   | .0794547   | .0300632         | -6.69| 0.000 | .0378487              | .1667967      |

The variables `spt_cat` and `male` are binary indicators of skin-prick sensitivity to cat allergen and male gender, and the variable `fquesagec` is a continuous age centered by subtracting 48 years and divided by 10 years to be expressed in decades over 48 years. Therefore, the parameter `_cons` is a baseline sensitivity odds for 48-year-old women; the parameter `male` is a male-gender odds ratio; and the parameter `fquesagec` is a per-decade odds ratio for age, assuming the effect of age on odds to be exponential. To derive a standardized prevalence from these parameters, we first load (and list) a new dataset with one observation per gender per age group and data on the numbers of individuals in that gender and age group in a European standard population:
In this dataset, \textit{male} indicates male gender; \textit{agemin}, \textit{agemax}, and \textit{agemean} contain minimum, maximum, and mean ages in years; \textit{fquesagec} contains the mean age in decades centered at 48 years; and \textit{stanpop} contains the number of individuals with that gender and age group in the European standard population. We can now estimate the marginal odds and prevalence by applying our model to this dataset, using \textit{stanpop} as a frequency-weight variable:

\begin{verbatim}
. margprev [fweight=stanpop], eform noesample
Scenario 1: (asobserved) _all
Confidence interval for the marginal odds
under Scenario 1
Total number of observations used: 134000

| Scenario_1 | Odds | Std. Err. | z      | P>|z|    | [95% Conf. Interval] |
|------------|------|-----------|--------|--------|---------------------|
| 3.000      | 0.1782219 | 0.07486 | -4.11  | .000   | .0782391 .4059742   |

Asymmetric 95% CI for the untransformed marginal prevalence under Scenario 1

<table>
<thead>
<tr>
<th>Scenario_1</th>
<th>Estimate</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.000</td>
<td>0.15126346</td>
<td>0.07256191</td>
<td>0.2887494</td>
</tr>
</tbody>
</table>
\end{verbatim}

We see the marginal odds and the more comprehensible marginal prevalence of 15.1% (95% confidence interval: 7.3% to 28.9%). The marginal odds for this region (the United Kingdom) and the 12 others were entered into the Statistical Software Components \texttt{parmhet} package to compute heterogeneity statistics. The $I^2$ statistic of
Higgins and Thompson (2002) was 46.4%, with a p-value of 0.033, so there seems to be heterogeneity in cat allergy prevalence between European regions not attributable to heterogeneity in gender and age distribution.

5 Acknowledgments

I thank all at StataCorp for making the margins command available. In particular, I thank Kristin MacDonald, Jennifer Rolfs, Miguel Dorta, and Jeff S. Pitblado for handling the demanding and highly technical margins queries with which I routinely bombarded them during the development of the suite of commands described here. I also thank Dr. Mohammadreza Bozorgmanesh of the Research Institute for Endocrine Sciences, Tehran, Iran, for drawing my attention to the literature on the PAF, especially on extensions of the PAF to survival analyses. I also thank the administrators of the GA²LEN survey for allowing me to include the example of section 4.5 in this article. The GA²LEN conducted an epidemiological project from 2007 to 2009 to examine respiratory and allergic disease in Europe. This work involved 24 research centers in 15 countries across Europe and was funded by the European Union. My own work at Imperial College London is financed by the United Kingdom Department of Health.

6 References


**About the author**

Roger B. Newson is a lecturer in medical statistics at Imperial College London, UK, working principally in asthma research. He wrote the *margprev, marglmean, regpar, punaf, punafcc*, and *parmhet* Stata packages.