

# Using **lsmeans**

Russell V. Lenth  
The University of Iowa

December 16, 2015

## Abstract

Least-squares means are predictions from a linear model, or averages thereof. They are useful in the analysis of experimental data for summarizing the effects of factors, and for testing linear contrasts among predictions. The **lsmeans** package provides a simple way of obtaining least-squares means and contrasts thereof. It supports many models fitted by R core packages (as well as a few key contributed ones) that fit linear or mixed models, and provides a simple way of extending it to cover more model classes.

## 1 Introduction

Least-squares means (LS means for short) for a linear model are simply predictions—or averages thereof—over a regular grid of predictor settings which I call the *reference grid*. They date back at least to Harvey (1960) and his associated computer program LSML (Harvey, 1977) and the contributed SAS procedure named **HARVEY** (Harvey, 1976). Later, they were incorporated via LSMEANS statements for various linear model procedures such as **GLM** in the regular SAS releases. See also Goodnight and Harvey (1997) and SAS Institute Inc. (2012) for more information about the SAS implementation.

In simple analysis-of-covariance models, LS means are the same as covariate-adjusted means. In unbalanced factorial experiments, LS means for each factor mimic the main-effects means but are adjusted for imbalance. The latter interpretation is quite similar to the “unweighted means” method for unbalanced data, as presented in old design books.

LS means are not always well understood, in part because the term itself is confusing. Searle *et al.* (1980) discusses exactly how they are defined for various factorial, nested, and covariance models. Searle *et al.* suggest the term “predicted marginal means” (or PMMs) as a better descriptor. However, the term “least-squares means” was already well established in the SAS software, and it has stuck.

The most important things to remember are:

- LS means are computed relative to a *reference grid*.
- Once the reference grid is established, LS means are simply predictions on this grid, or marginal averages of a table of these predictions.

A user who understands these points will know what is being computed, and thus can judge whether or not LS means are appropriate for the analysis.

## 2 The reference grid

Since the reference grid is fundamental, it is our starting point. For each predictor in the model, we define a set of one or more *reference levels*. The reference grid is then the set of all combinations of reference levels. If not specified explicitly, the default reference levels are obtained as follows:

- For each predictor that is a factor, its reference levels are the unique levels of that factor.
- Each numeric predictor has just one reference level—its mean over the dataset.

So the reference grid depends on both the model and the dataset.

### 2.1 Example: Orange sales

To illustrate, consider the **oranges** data provided with **lsmeans**. This dataset has sales of two varieties of oranges (response variables **sales1** and **sales2**) at 6 stores (factor **store**), over a period of 6 days (factor **day**). The prices of the oranges (covariates **price1** and **price2**) fluctuate in the different stores and the different days. There is just one observation on each store on each day.

For starters, let's consider an additive covariance model for sales of the first variety, with the two factors and both **price1** and **price2** as covariates (since the price of the other variety could also affect sales).

```
R> library("lsmeans")
R> oranges.lm1 <- lm(sales1 ~ price1 + price2 + day + store, data = oranges)
R> anova(oranges.lm1)
```

Analysis of Variance Table

```
Response: sales1
      Df Sum Sq Mean Sq F value    Pr(>F)
price1   1  516.6   516.6   29.100 1.76e-05
price2   1   62.7    62.7    3.533 0.07287
day       5  422.2    84.4    4.757 0.00395
store     5  223.8    44.8    2.522 0.05835
Residuals 23  408.3    17.8
```

The **ref.grid** function in **lsmeans** may be used to establish the reference grid. Here is the default one:

```
R> ( oranges.rg1 <- ref.grid(oranges.lm1) )
```

'ref.grid' object with variables:

```
price1 = 51.222
price2 = 48.556
day = 1, 2, 3, 4, 5, 6
store = 1, 2, 3, 4, 5, 6
```

As outlined above, the two covariates **price1** and **price2** have their means as their sole reference level; and the two factors have their levels as reference levels. The reference grid thus consists of the  $1 \times 1 \times 6 \times 6 = 36$  combinations of these reference levels. LS means are based on predictions on this reference grid, which we can obtain using **predict** or **summary**:

```
R> summary(oranges.rg1)
```

price1	price2	day	store	prediction	SE	df
51.2222	48.5556	1	1	2.91841	2.71756	23
51.2222	48.5556	2	1	3.84880	2.70134	23
51.2222	48.5556	3	1	11.01857	2.53456	23
51.2222	48.5556	4	1	6.09629	2.65137	23
51.2222	48.5556	5	1	12.79580	2.44460	23
51.2222	48.5556	6	1	8.74878	2.78618	23
51.2222	48.5556	1	2	4.96147	2.37774	23
51.2222	48.5556	2	2	5.89187	2.33558	23
51.2222	48.5556	3	2	13.06163	2.41645	23
51.2222	48.5556	4	2	8.13935	2.35219	23
51.2222	48.5556	5	2	14.83886	2.46615	23
51.2222	48.5556	6	2	10.79184	2.33760	23
51.2222	48.5556	1	3	3.20089	2.37774	23
51.2222	48.5556	2	3	4.13128	2.33558	23
51.2222	48.5556	3	3	11.30105	2.41645	23
51.2222	48.5556	4	3	6.37876	2.35219	23
51.2222	48.5556	5	3	13.07828	2.46615	23
51.2222	48.5556	6	3	9.03126	2.33760	23
51.2222	48.5556	1	4	6.19876	2.36367	23
51.2222	48.5556	2	4	7.12915	2.35219	23
51.2222	48.5556	3	4	14.29891	2.43168	23
51.2222	48.5556	4	4	9.37663	2.38865	23
51.2222	48.5556	5	4	16.07614	2.51909	23
51.2222	48.5556	6	4	12.02912	2.36469	23
51.2222	48.5556	1	5	5.54322	2.36312	23
51.2222	48.5556	2	5	6.47361	2.33067	23
51.2222	48.5556	3	5	13.64337	2.36367	23
51.2222	48.5556	4	5	8.72109	2.33760	23
51.2222	48.5556	5	5	15.42060	2.39554	23
51.2222	48.5556	6	5	11.37358	2.35232	23
51.2222	48.5556	1	6	10.56374	2.36668	23
51.2222	48.5556	2	6	11.49413	2.33925	23
51.2222	48.5556	3	6	18.66390	2.34784	23
51.2222	48.5556	4	6	13.74161	2.34130	23
51.2222	48.5556	5	6	20.44113	2.37034	23
51.2222	48.5556	6	6	16.39411	2.37054	23

## 2.2 LS means as marginal averages over the reference grid

The ANOVA indicates there is a significant `day` effect after adjusting for the covariates, so we might want to do a follow-up analysis that involves comparing the days. The `lsmeans` function provides a starting point:

```
R> lsmeans(oranges.rg1, "day") ## or lsmeans(oranges.lm1, "day")
```

day	lsmean	SE	df	lower.CL	upper.CL
1	5.56442	1.76808	23	1.90686	9.22197

```

2    6.49481 1.72896 23    2.91818 10.07143
3   13.66457 1.75150 23   10.04131 17.28783
4    8.74229 1.73392 23    5.15540 12.32918
5   15.44180 1.78581 23   11.74758 19.13603
6   11.39478 1.76673 23    7.74003 15.04953

```

Results are averaged over the levels of: store  
Confidence level used: 0.95

These results, as indicated in the annotation in the output, are in fact the averages of the predictions shown earlier, for each day, over the 6 stores. The above LS means are not the same as the overall means for each day:

```

R> with(oranges, tapply(sales1, day, mean))

      1      2      3      4      5      6
7.87275 7.10060 13.75860 8.04247 12.92460 11.60365

```

These unadjusted means are not comparable with one another because they are affected by the differing `price1` and `price2` values on each day, whereas the LS means are comparable because they use predictions at uniform `price1` and `price2` values.

Note that one may call `lsmeans` with either the reference grid or the model. If the model is given, then the first thing it does is create the reference grid; so if the reference grid is already available, as in this example, it's more efficient to make use of it.

## 2.3 Altering the reference grid

The `at` argument may be used to override defaults in the reference grid. The user may specify this argument either in a `ref.grid` call or an `lsmeans` call; and should specify a `list` with named sets of reference levels. Here is a silly example:

```

R> lsmeans(oranges.lm1, "day", at = list(price1 = 50,
      price2 = c(40,60), day = c("2","3","4")))

day    lsmean      SE df lower.CL upper.CL
2      7.72470 1.73517 23   4.13524  11.3142
3     14.89446 1.75104 23  11.27217  18.5168
4      9.97218 1.76613 23   6.31866  13.6257

```

Results are averaged over the levels of: price2, store  
Confidence level used: 0.95

Here, we restricted the results to three of the days, and used different prices. One possible surprise is that the predictions are averaged over the two `price2` values. That is because `price2` is no longer a single reference level, and we average over the levels of all factors not used to split-out the LS means. This is probably not what we want.<sup>1</sup> To get separate sets of predictions for each `price2`, one must specify it as another factor or as a `by` factor in the `lsmeans` call (we will save the result for later discussion):

---

<sup>1</sup>The *default* reference grid produces LS means exactly as described in Searle *et al.* (1980). However, an altered reference grid containing more than one value of a covariate, such as in this example, departs from (or generalizes, if you please) their definition by averaging with equal weights over those covariate levels. It is not a good idea here, but there is an example later in this vignette where it makes sense.

```
R> org.lsm <- lsmeans(oranges.lm1, "day", by = "price2",
  at = list(price1 = 50, price2 = c(40,60), day = c("2","3","4")) )
R> org.lsm
```

```
price2 = 40:
  day    lsmean      SE df lower.CL upper.CL
  2      6.23623 1.88711 23  2.33245  10.1400
  3     13.40599 2.11938 23  9.02173  17.7903
  4      8.48371 1.86651 23  4.62254  12.3449
```

```
price2 = 60:
  day    lsmean      SE df lower.CL upper.CL
  2      9.21317 2.10945 23  4.84944  13.5769
  3     16.38293 1.90522 23 12.44169  20.3242
  4     11.46065 2.17805 23  6.95500  15.9663
```

Results are averaged over the levels of: store  
Confidence level used: 0.95

Note: We could have obtained the same results using any of these:

```
R> lsmeans(oranges.lm1, ~ day | price, at = ... )      # Ex 1
R> lsmeans(oranges.lm1, c("day","price2"), at = ... )  # Ex 2
R> lsmeans(oranges.lm1, ~ day * price, at = ... )     # Ex 3
```

Ex 1 illustrates the formula method for specifying factors, which is more compact. The `|` character replaces the `by` specification. Ex 2 and Ex 3 produce the same results, but their results are displayed as one table (with columns for `day` and `price`) rather than as two separate tables.

## 3 Working with the results

### 3.1 Objects

The `ref.grid` function produces an object of class `"ref.grid"`, and the `lsmeans` function produces an object of class `"lsmobj"`, which is a subclass of `"ref.grid"`. There is really no practical difference between these two classes except for their `show` methods—what is displayed by default—and the fact that an `"lsmobj"` is not (necessarily) a true reference grid as defined earlier in this article. Let's use the `str` function to examine the `"lsmobj"` object just produced:

```
R> str(org.lsm)

'lsmobj' object with variables:
  day = 2, 3, 4
  price2 = 40, 60
```

We no longer see the reference levels for all predictors in the model—only the levels of `day` and `price2`. These *act* like reference levels, but they do not define the reference grid upon which the predictions are based.

## 3.2 Summaries

There are several methods for "ref.grid" (and hence also for "lsmobj") objects. One already seen is `summary`. It has a number of arguments—see its help page. In the following call, we summarize `days.lsm` differently than before. We will also save the object produced by `summary` for further discussion.

```
R> ( org.sum <- summary(org.lsm, infer = c(TRUE,TRUE),
                        level = .90, adjust = "bon", by = "day") )
```

day = 2:

price2	lsmean	SE	df	lower.CL	upper.CL	t.ratio	p.value
40	6.23623	1.88711	23	2.33245	10.1400	3.305	0.0062
60	9.21317	2.10945	23	4.84944	13.5769	4.368	0.0005

day = 3:

price2	lsmean	SE	df	lower.CL	upper.CL	t.ratio	p.value
40	13.40599	2.11938	23	9.02173	17.7903	6.325	<.0001
60	16.38293	1.90522	23	12.44169	20.3242	8.599	<.0001

day = 4:

price2	lsmean	SE	df	lower.CL	upper.CL	t.ratio	p.value
40	8.48371	1.86651	23	4.62254	12.3449	4.545	0.0003
60	11.46065	2.17805	23	6.95500	15.9663	5.262	<.0001

Results are averaged over the levels of: store

Confidence level used: 0.9

Conf-level adjustment: bonferroni method for 2 estimates

P value adjustment: bonferroni method for 2 tests

The `infer` argument causes both confidence intervals and tests to be produced; the default confidence level of .95 was overridden; a Bonferroni adjustment was applied to both the intervals and the *P* values; and the tables are organized the opposite way from what we saw before.

What kind of object was produced by `summary`? Let's see:

```
R> class(org.sum)
```

```
[1] "summary.ref.grid" "data.frame"
```

The "summary.ref.grid" class is an extension of "data.frame". It includes some attributes that, among other things, cause additional messages to appear when the object is displayed. But it can also be used as a "data.frame" if the user just wants to use the results computationally. For example, suppose we want to convert the LS means from dollars to Russian rubles (at the July 13, 2014 exchange rate):

```
R> transform(org.sum, lsrubles = lsmean * 34.2)
```

	day	price2	lsmean	SE	df	lower.CL	upper.CL	t.ratio	p.value	lsrubles
1	2	40	6.23623	1.88711	23	2.33245	10.1400	3.30465	6.19070e-03	213.279
2	3	40	13.40599	2.11938	23	9.02173	17.7903	6.32544	3.74162e-06	458.485
3	4	40	8.48371	1.86651	23	4.62254	12.3449	4.54523	2.89206e-04	290.143
4	2	60	9.21317	2.10945	23	4.84944	13.5769	4.36757	4.50464e-04	315.090
5	3	60	16.38293	1.90522	23	12.44169	20.3242	8.59899	2.43159e-08	560.296
6	4	60	11.46065	2.17805	23	6.95500	15.9663	5.26188	4.88377e-05	391.954

Observe also that the summary is just one data frame with six rows, rather than a collection of three data frames; and it contains a column for all reference variables, including any `by` variables.

Besides `str` and `summary`, there is also a `confint` method, which is the same as `summary` with `infer=c(TRUE,FALSE)`, and a `test` method (same as `summary` with `infer=c(FALSE,TRUE)`, by default). The `test` method may in addition be called with `joint=TRUE` to obtain a joint test that all or some of the linear functions are equal to zero or some other value.

There is also an `update` method which may be used for changing the object's display settings. For example:

```
R> org.lsm2 <- update(org.lsm, by.vars = NULL, level = .99)
R> org.lsm2
```

day	price2	lsmean	SE	df	lower.CL	upper.CL
2	40	6.23623	1.88711	23	0.938488	11.5340
3	40	13.40599	2.11938	23	7.456193	19.3558
4	40	8.48371	1.86651	23	3.243791	13.7236
2	60	9.21317	2.10945	23	3.291240	15.1351
3	60	16.38293	1.90522	23	11.034351	21.7315
4	60	11.46065	2.17805	23	5.346122	17.5752

Results are averaged over the levels of: store  
Confidence level used: 0.99

### 3.3 Plots

Confidence intervals for LS means may be displayed graphically, using the `plot` method. For example:

```
R> plot(org.lsm, by = "price2")
```

The resulting display is shown in Figure 1. This function requires that the **lattice** package be installed.

## 4 Contrasts and comparisons

### 4.1 Contrasts in general

Often, people want to do pairwise comparisons of LS means, or compute other contrasts among them. This is the purpose of the `contrast` function, which uses a `"ref.grid"` or `"lsmobj"` object as input. There are several standard contrast families such as `"pairwise"`, `"trt.vs.ctrl"`, and `"poly"`. In the following command, we request `"eff"` contrasts, which are differences between each mean and the overall mean:

```
R> contrast(org.lsm, method = "eff")
```

```
price2 = 40:
  contrast estimate      SE df t.ratio p.value
2 effect  -3.13908 1.41529 23  -2.218  0.0551
3 effect   4.03068 1.44275 23   2.794  0.0310
4 effect  -0.89160 1.42135 23  -0.627  0.5366
```

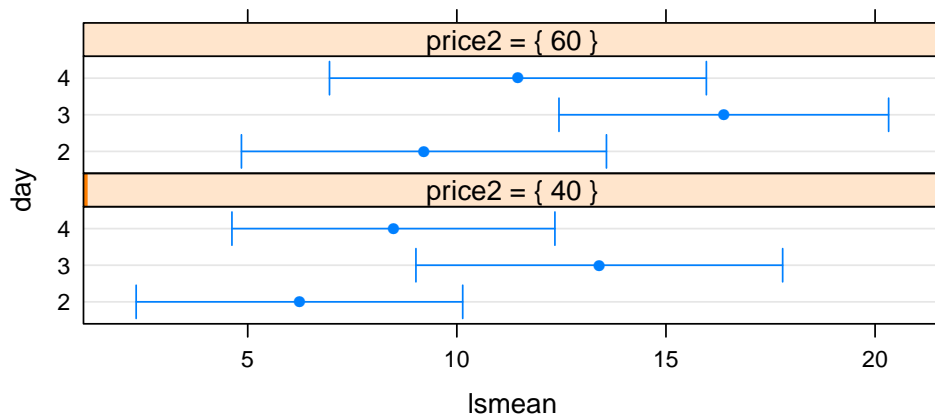


Figure 1: Confidence intervals for LS means in the `oranges` example.

```
price2 = 60:
  contrast estimate      SE df t.ratio p.value
2 effect  -3.13908 1.41529 23  -2.218  0.0551
3 effect   4.03068 1.44275 23   2.794  0.0310
4 effect  -0.89160 1.42135 23  -0.627  0.5366
```

Results are averaged over the levels of: store  
P value adjustment: fdr method for 3 tests

Note that this preserves the `by` specification from before, and obtains the effects for each group. In this example, since it is an additive model, we obtain exactly the same results in each group. This isn't wrong, it's just redundant.

Another popular method is Dunnett-style contrasts, where a particular LS mean is compared with each of the others. This is done using `"trt.vs.ctrl"`. In the following, we obtain (again) the LS means for days, and compare each with the average of the LS means on day 5 and 6.

```
R> days.lsm <- lsmeans(oranges.rg1, "day")
R> ( days_contr.lsm <- contrast(days.lsm, "trt.vs.ctrl", ref = c(5,6)) )
```

```
contrast      estimate      SE df t.ratio p.value
1 - avg(5,6) -7.853877 2.19424 23  -3.579  0.0058
2 - avg(5,6) -6.923486 2.12734 23  -3.255  0.0125
3 - avg(5,6)  0.246279 2.15553 23   0.114  0.9979
4 - avg(5,6) -4.676003 2.11076 23  -2.215  0.1184
```

Results are averaged over the levels of: store  
P value adjustment: dunnettx method for 4 tests

For convenience, `"trt.vs.ctrl1"` and `"trt.vs.ctrlk"` methods are provided for use in lieu of `ref` for comparing with the first and the last LS means. The `"dunnettx"` adjustment is a good



approximation to the exact Dunnett  $P$  value adjustment. If the exact adjustment is desired, use `adjust = "mvt"`; but this can take a lot of computing time when there are several tests.

Note that by default, `lsmeans` results are displayed with confidence intervals while `contrast` results are displayed with  $t$  tests. One can easily override this; for example,

```
R> confint(contrast(days.lsm, "trt.vs.ctrlk"))
```

(Results not shown.)

In the above examples, a default multiplicity adjustment is determined from the contrast method. This may be overridden by adding an `adjust` argument.

## 4.2 Pairwise comparisons

Often, users want pairwise comparisons among the LS means. These may be obtained by specifying "pairwise" or "revpairwise" as the `method` argument in the call to `contrast`. For group labels  $A, B, C$ , "pairwise" generates the comparisons  $A - B, A - C, B - C$  while "revpairwise" generates  $B - A, C - A, C - B$ . As a convenience, a `pairs` method is provided that calls `contrast` with `method="pairwise"`:

```
R> pairs(org.lsm)
```

```
price2 = 40:
```

contrast	estimate	SE	df	t.ratio	p.value
2 - 3	-7.16976	2.47970	23	-2.891	0.0216
2 - 4	-2.24748	2.44234	23	-0.920	0.6333
3 - 4	4.92228	2.49007	23	1.977	0.1406

```
price2 = 60:
```

contrast	estimate	SE	df	t.ratio	p.value
2 - 3	-7.16976	2.47970	23	-2.891	0.0216
2 - 4	-2.24748	2.44234	23	-0.920	0.6333
3 - 4	4.92228	2.49007	23	1.977	0.1406

Results are averaged over the levels of: store

P value adjustment: tukey method for comparing a family of 3 estimates

There is also a `cld` (compact letter display) method that lists the LS means along with grouping symbols for pairwise contrasts. It requires the **multcompView** package (Graves *et al.*, 2012) to be installed.

```
R> cld(days.lsm, alpha = .10)
```

day	lsmean	SE	df	lower.CL	upper.CL	.group
1	5.56442	1.76808	23	1.90686	9.22197	1
2	6.49481	1.72896	23	2.91818	10.07143	1
4	8.74229	1.73392	23	5.15540	12.32918	12
6	11.39478	1.76673	23	7.74003	15.04953	12
3	13.66457	1.75150	23	10.04131	17.28783	2
5	15.44180	1.78581	23	11.74758	19.13603	2

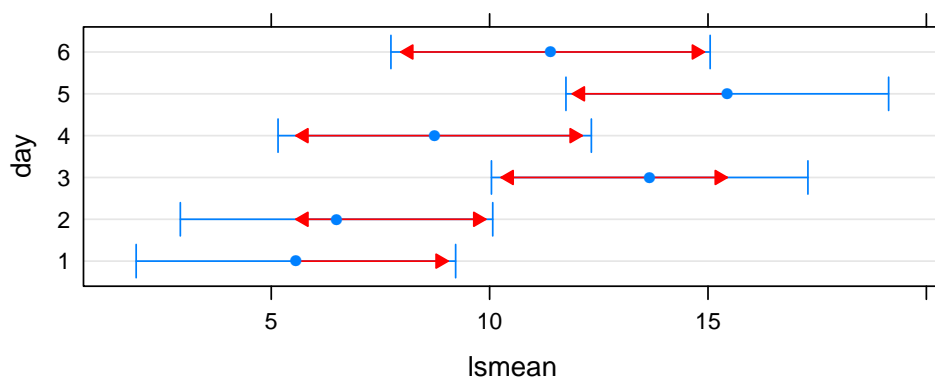


Figure 2: Graphical comparisons of the LS means for days.

Results are averaged over the levels of: store  
 Confidence level used: 0.95  
 P value adjustment: tukey method for comparing a family of 6 estimates  
 significance level used: alpha = 0.1

Two LS means that share one or more of the same grouping symbols are not significantly different at the stated value of **alpha**, after applying the multiplicity adjustment (in this case Tukey's HSD). By default, the LS means are ordered in this display, but this may be overridden with the argument **sort=FALSE**. **cld** returns a "summary.ref.grid" object, not an **lsmobj**.

Another way to display pairwise comparisons is via the **comparisons** argument of **plot**. When this is set to **TRUE**, arrows are added to the plot, with lengths set so that the amount by which they overlap (or don't overlap) matches as closely as possible to the amounts by which corresponding confidence intervals for differences cover (or don't cover) the value zero. This does not always work, and if there are discrepancies, a message is printed. But it usually works.

```
R> plot(days.lsm, comparisons = TRUE, alpha = .10)
```

Figure 2 shows the result. Note that the pairs of means having overlapping arrows are the same as those grouped together in the **cld** display. However, these comparison arrows show more about the degree of significance in the comparisons. The lowest and highest LS mean have arrows pointing only inward, as the others are not needed. If the confidence intervals and arrows together look too cluttered, one can add the argument **intervals = FALSE**, then only the arrows will be displayed.

### 4.3 Multiplicity adjustments—changing the family

You may have noticed that in the preceding examples where *P*-value adjustments were implemented, those adjustments were made *separately* for each sub-table when a **by** variable is active. Some users prefer that all the adjusted tests together as one family—or even combine more than one family of tests into one family for purposes of adjustment. This may be done using the **rbind** method (similar to using **rbind** to combine matrices).

On the flip side, perhaps we want to exclude some tests. This may be used using the **[]** operator: simply specify the row indexes of the tests to include.

To illustrate, consider the previously obtained `org.lsm` object. In `pairs(org.lsm)`, we obtain the same results twice (as seen above) because the model is additive. For the same reason, if we change the `by` variable to `"day"`, we'll obtain three copies of the same comparison of the two `price2`s. If we want to consider the three `day` comparisons and the one `price2` comparison together as one family of four tests, we can do:

```
R> rbind(pairs(org.lsm)[1:3], pairs(org.lsm, by = "day")[1])
```

contrast	price2	day	estimate	SE	df	t.ratio	p.value
1	40	.	-7.16976	2.47970	23	-2.891	0.0292
2	40	.	-2.24748	2.44234	23	-0.920	0.7585
3	40	.	4.92228	2.49007	23	1.977	0.1875
1	.	1	-2.97694	1.99466	23	-1.492	0.4056

Results are averaged over the levels of: store  
P value adjustment: mvt method for 4 tests

Note that by default, the `"mvt"` adjustment level is used; for complicated families like this, ordinary Tukey and Dunnett adjustments are usually not appropriate.

We arrived at this point by a circuitous path. In the additive model, the above conditional results are the same as the marginal ones:

```
R> rbind(pairs(lsmeans(org.lsm, "day")), pairs(lsmeans(org.lsm, "price2")))
```

contrast	estimate	SE	df	t.ratio	p.value
1	-7.16976	2.47970	23	-2.891	0.0292
2	-2.24748	2.44234	23	-0.920	0.7585
3	4.92228	2.49007	23	1.977	0.1875
1	-2.97694	1.99466	23	-1.492	0.4057

Results are averaged over the levels of: store, price2  
P value adjustment: mvt method for 4 tests

## 5 Multivariate models

The `oranges` data has two response variables. Let's try a multivariate model for predicting the sales of the two varieties of oranges, and see what we get if we call `ref.grid`:

```
R> oranges.mlm <- lm(cbind(sales1,sales2) ~ price1 + price2 + day + store,
                     data = oranges)
R> ref.grid(oranges.mlm)
```

'ref.grid' object with variables:

```
price1 = 51.222
price2 = 48.556
day = 1, 2, 3, 4, 5, 6
store = 1, 2, 3, 4, 5, 6
rep.meas = multivariate response levels: sales1, sales2
```

What happens is that the multivariate response is treated like an additional factor, by default named `rep.meas`. In turn, it can be used to specify levels for LS means. Here we rename the multivariate response to "variety" and obtain day means (and a compact letter display for comparisons thereof) for each variety:

```
R> org.mlsm <- lsmeans( oranges.mlm, ~ day | variety, mult.name = "variety")
R> cld(org.mlsm, sort = FALSE)
```

variety = sales1:

day	lsmean	SE	df	lower.CL	upper.CL	.group
1	5.56442	1.76808	23	1.906856	9.22197	1
2	6.49481	1.72896	23	2.918183	10.07143	12
3	13.66457	1.75150	23	10.041308	17.28783	23
4	8.74229	1.73392	23	5.155403	12.32918	123
5	15.44180	1.78581	23	11.747576	19.13603	3
6	11.39478	1.76673	23	7.740031	15.04953	123

variety = sales2:

day	lsmean	SE	df	lower.CL	upper.CL	.group
1	7.71566	2.32649	23	2.902962	12.52836	12
2	3.97645	2.27500	23	-0.729758	8.68265	1
3	16.59781	2.30467	23	11.830240	21.36539	2
4	11.04454	2.28153	23	6.324832	15.76425	12
5	14.99079	2.34981	23	10.129837	19.85174	2
6	12.04878	2.32470	23	7.239777	16.85779	12

Results are averaged over the levels of: store

Confidence level used: 0.95

P value adjustment: tukey method for comparing a family of 6 estimates

significance level used: alpha = 0.05

## 6 Contrasts of contrasts

With the preceding model, we might want to compare the two varieties on each day:

```
R> org.vardiff <- update(pairs(org.mlsm, by = "day"), by = NULL)
```

The results (not yet shown) will comprise the six `sales1-sales2` differences, one for each day. The two `by` specifications seems odd, but the one in `pairs` specifies doing a separate comparison for each day, and the one in `update` asks that we convert it to one table with six rows, rather than 6 tables with one row each. Now, let's compare these differences to see if they vary from day to day.

```
R> cld(org.vardiff)
```

contrast	day	estimate	SE	df	t.ratio	p.value	.group
sales1 - sales2	3	-2.933243	2.69411	23	-1.089	0.2875	1
sales1 - sales2	4	-2.302251	2.66706	23	-0.863	0.3969	1
sales1 - sales2	1	-2.151248	2.71961	23	-0.791	0.4370	1
sales1 - sales2	6	-0.654002	2.71752	23	-0.241	0.8120	1

```

sales1 - sales2 5      0.451016 2.74688 23    0.164  0.8710  1
sales1 - sales2 2      2.518361 2.65943 23    0.947  0.3535  1

```

Results are averaged over the levels of: store

P value adjustment: tukey method for comparing a family of 6 estimates

significance level used: alpha = 0.05

There is little evidence of variety differences, nor that these differences vary from day to day.

## 7 Interfacing with multcomp

The **multcomp** package (Hothorn *et al.*, 2013) supports more options for simultaneous inference than are available in **lsmeans**. Its **glht** (general linear hypothesis testing) function and associated "glht" class are similar in some ways to **lsmeans** and "lsmobj" objects, respectively. So **lsmeans** provides an **as.glht** function to do the conversion.

To illustrate, let us convert the **days\_contr.lsm** object (produced earlier) to a **glht** object, and use it to obtain adjusted *P* values under Westfall's adjustment procedure (not available in **lsmeans**):

```

R> library("multcomp")
R> days.glht <- as.glht(days_contr.lsm)
R> summary(days.glht, test = adjusted("Westfall"))

```

### Simultaneous Tests for General Linear Hypotheses

Linear Hypotheses:

	Estimate	Std. Error	t value	Pr(> t )
1 - avg(5,6) == 0	-7.854	2.194	-3.58	0.0062
2 - avg(5,6) == 0	-6.923	2.127	-3.25	0.0099
3 - avg(5,6) == 0	0.246	2.156	0.11	0.9100
4 - avg(5,6) == 0	-4.676	2.111	-2.22	0.0697

(Adjusted p values reported -- Westfall method)

In addition, **lsmeans** provides an **lsm** function that may be called from within a call to **glht**. Thus, another way to obtain the same **glht** object is to use

```

R> days.glht1 <- glht( oranges.lm1,
                      lsm("day", contr = "trt.vs.ctrl", ref = c(5,6)))

```

By the way, the following two statements will produce the same results:

```

R> summary(days_contr.lsm, adjust = "mvt")
R> summary(days.glht)

```

That is, the "mvt" adjust method in **lsmeans** is the same as the default single-step *P* value adjustment in **multcomp**.

One additional detail: If there is a **by** variable in effect, **glht** or **as.glht** returns a list of **glht** objects—one for each **by** level. There is a courtesy **summary** method for this "glht.list" class to make things a bit more user-friendly. Recall the earlier example result **org.lsm**, which contains information for LS means for three **days** at each of two values of **price2**. Suppose we are interested in pairwise comparisons of these LS means, by **price2**. If we call

```
R> summary(as.glht(pairs(org.lsm)))
```

(results not displayed) we will obtain two `glht` objects with three contrasts each, so that the results shown will incorporate multiplicity adjustments for each family of three contrasts. If, on the other hand, we want to consider those six contrasts as one family, use

```
R> summary(as.glht(pairs(org.lsm), by = NULL))
```

... and note (look carefully at the parentheses) that this is *not* the same as

```
R> summary(as.glht(pairs(org.lsm, by = NULL)))
```

which removes the *by* grouping *before* the pairwise comparisons are generated, thus yielding  $\binom{6}{2} = 15$  contrasts instead of just six.

## 8 A new example: Oat yields

Orange-sales illustrations are probably getting tiresome. To illustrate some new features, let's turn to a new example. The `Oats` dataset in the `nlme` package (Pinheiro *et al.*, 2013) has the results of a split-plot experiment discussed in Yates (1935). The experiment was conducted on six blocks (factor `Block`). Each block was divided into three plots, which were randomized to three varieties (factor `Variety`) of oats. Each plot was divided into subplots and randomized to four levels of nitrogen (variable `nitro`). The response, `yield`, was measured once on each subplot after a suitable growing period.

We will fit a model using the `lmer` function in the `lme4` package (Bates *et al.*, 2013). This will be a mixed model with random intercepts for `Block` and `Block:Variety` (which identifies the plots). A logarithmic transformation is applied to the response variable (mostly for illustration purposes, though it does produce a good fit to the data). Note that `nitro` is stored as a numeric variable, but we want to consider it as a factor in this initial model.

```
R> data("Oats", package = "nlme")
R> library("lme4")
R> Oats.lmer <- lmer(log(yield) ~ Variety*factor(nitro) + (1|Block/Variety),
  data = Oats)
R> anova(Oats.lmer)
```

Analysis of Variance Table

	Df	Sum Sq	Mean Sq	F value
Variety	2	0.0750	0.0375	2.008
factor(nitro)	3	2.1350	0.7117	38.110
Variety:factor(nitro)	6	0.0451	0.0075	0.402

Apparently, the interaction is not needed. But perhaps we can further simplify the model by using only a linear or quadratic trend in `nitro`. We can find out by looking at polynomial contrasts:

```
R> contrast(lsmmeans(Oats.lmer, "nitro"), "poly")
```

NOTE: Results may be misleading due to involvement in interactions

contrast	estimate	SE	df	t.ratio	p.value
linear	1.50565129	0.1440469	45	10.453	<.0001
quadratic	-0.14510997	0.0644197	45	-2.253	0.0292
cubic	0.00273198	0.1440469	45	0.019	0.9850

Results are averaged over the levels of: Variety

(A message is issued when we average over predictors that interact with those that delineate the LS means. In this case, it is not a serious problem because the interaction is weak.) Both the linear and quadratic contrasts are pretty significant. All this suggests fitting an additive model where `nitro` is included as a numeric predictor with a quadratic trend.

```
R> Oats.lmer2 <- lmer(log(yield) ~ Variety + poly(nitro,2)
+ (1|Block/Variety), data = Oats)
```

Remember that `nitro` is now used as a quantitative predictor. But for comparing with the previous model, we want to see predictions at the four unique `nitro` values rather than at the average of `nitro`. This may be done using `at` as illustrated earlier, or a shortcut is to specify `cov.reduce = FALSE`, which tells `ref.grid` to use all the unique values of numeric predictors.

```
R> Oats.lsm2 <- lsmeans(Oats.lmer2, ~ nitro | Variety, cov.reduce = FALSE)
R> Oats.lsm2
```

Variety = Golden Rain:

nitro	lsmean	SE	df	lower.CL	upper.CL
0.0	4.35458	0.0770328	11.77	4.18637	4.52279
0.2	4.57770	0.0745363	10.34	4.41235	4.74304
0.4	4.72826	0.0745363	10.34	4.56292	4.89361
0.6	4.80627	0.0770328	11.77	4.63806	4.97448

Variety = Marvellous:

nitro	lsmean	SE	df	lower.CL	upper.CL
0.0	4.41223	0.0770328	11.77	4.24402	4.58044
0.2	4.63535	0.0745363	10.34	4.47000	4.80069
0.4	4.78591	0.0745363	10.34	4.62057	4.95126
0.6	4.86392	0.0770328	11.77	4.69571	5.03213

Variety = Victory:

nitro	lsmean	SE	df	lower.CL	upper.CL
0.0	4.27515	0.0770328	11.77	4.10694	4.44336
0.2	4.49827	0.0745363	10.34	4.33292	4.66361
0.4	4.64883	0.0745363	10.34	4.48349	4.81418
0.6	4.72684	0.0770328	11.77	4.55863	4.89505

Results are given on the log scale.

Confidence level used: 0.95

These LS means follow the same quadratic trend for each variety, but with different intercepts.<sup>2</sup>

---

<sup>2</sup>This is the promised example where our generalization of Searle *et al.* (1980)'s definition of LS means makes

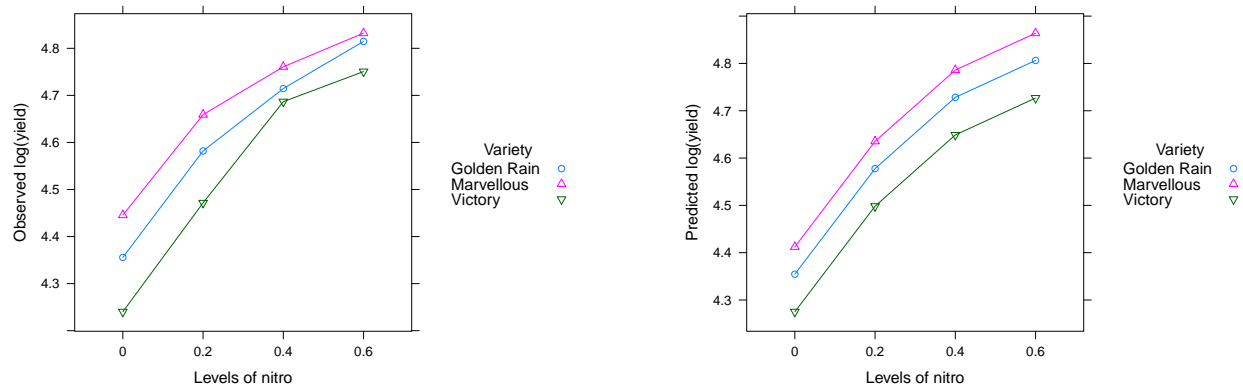


Figure 3: Interaction plots for the cell means and the fitted model, **Oats** example.

Fractional degrees of freedom are displayed in these results. These are obtained from the **pbkrtest** package (Halekoh and Højsgaard, 2013), and they use the Kenward-Rogers method. (The degrees of freedom for the polynomial contrasts were also obtained from **pbkrtest**, but the results turn out to be integers.)

## 9 Displaying LS means graphically

We have already seen the use of the **plot** function to display confidence intervals and/or comparison arrows. The **lsmeans** package also includes a function **lsmip** that displays predictions in an interaction-plot-like manner. It uses a formula of the form

```
curve.factors ~ x.factors / by.factors
```

This function also requires the **lattice** package. In the above formula, **curve.factors** specifies factor(s) used to delineate one displayed curve from another (i.e., groups in **lattice**'s parlance). **x.factors** are those whose levels are plotted on the horizontal axis. And **by.factors**, if present, break the plots into panels.

To illustrate, consider the first model we fitted to the **Oats** data. Let's do a graphical comparison of the two models we have fitted to the **Oats** data.

```
R> lsmip(Oats.lmer, Variety ~ nitro, ylab = "Observed log(yield)")
```

```
R> lsmip(Oats.lsm2, Variety ~ nitro, ylab = "Predicted log(yield)")
```

The plots are shown in Figure 3. Note that the first model fits the cell means perfectly, so its plot is truly an interaction plot of the data. The other displays the parabolic trends we fitted in the revised model.

---

sense. Suppose we want to compare the LS means for **Variety** with those in the original model **Oats.lmer** where **nitro** was a factor, we want to average equally over the four **nitro** levels, even though **nitro** is a covariate in this second model.



## 10 Transformations

When a transformation or link function is used in fitting a model, `ref.grid` (also called by `lsmeans`) stores that information in the returned object, as seen in this example:

```
R> str(Oats.lsm2)

'lsmlm' object with variables:
  nitro = 0.0, 0.2, 0.4, 0.6
  Variety = Golden Rain, Marvellous, Victory
Transformation: "log"
```

This allows us to conveniently unravel the transformation, via the `type` argument in `summary` or related functions such as `lsmip` and `predict`. Here are the predicted yields for (as opposed to predicted log yields) for the polynomial model:

```
R> summary(Oats.lsm2, type = "response")

Variety = Golden Rain:
  nitro response      SE    df lower.CL upper.CL
  0.0   77.8340  5.99577  11.77  65.7834  92.0921
  0.2   97.2902  7.25165  10.34  82.4632 114.7831
  0.4  113.0989  8.42998  10.34  95.8627 133.4343
  0.6  122.2751  9.41920  11.77 103.3439 144.6742
```

```
Variety = Marvellous:
  nitro response      SE    df lower.CL upper.CL
  0.0   82.4529  6.35158  11.77  69.6871  97.5571
  0.2  103.0637  7.68199  10.34  87.3568 121.5946
  0.4  119.8106  8.93024  10.34 101.5515 141.3527
  0.6  129.5313  9.97816  11.77 109.4766 153.2596
```

```
Variety = Victory:
  nitro response      SE    df lower.CL upper.CL
  0.0   71.8907  5.53794  11.77  60.7602  85.0601
  0.2   89.8612  6.69793  10.34  76.1664 106.0184
  0.4  104.4629  7.78628  10.34  88.5428 123.2454
  0.6  112.9383  8.69996  11.77  95.4527 133.6271
```

Confidence level used: 0.95

It is important to realize that the statistical inferences are all done *before* reversing the transformation. Thus, *t* ratios are based on the linear predictors and will differ from those computed using the printed estimates and standard errors. Likewise, confidence intervals are computed on the linear-predictor scale, then the endpoints are back-transformed.

This kind of automatic support for transformations is available only for certain standard transformations, namely those supported by the `make.link` function in the **stats** package. Others require more work—see the documentation for `update` for details.

## 11 More on tests

The default settings for `test` yield traditional two-tailed  $t$  (or  $z$ ) tests of significance against zero. So if  $\theta^{(j)}$  is the  $j$ th parameter (e.g., LS mean or contrast) being estimated, we are testing the null hypothesis  $H_0 : \theta^{(j)} = 0$  versus the alternative  $H_1 : \theta^{(j)} \neq 0$ . We can, however, specify different types of tests in the `test` or `summary` functions.

### 11.1 Nonzero null values

If we wish to use nonzero null values, i.e., test  $H_0 : \theta^{(j)} = \theta_0^{(j)}$ , use `test` or `summary` with the `null` argument set to the desired  $\theta_0^{(j)}$  values. For example, in the Oat-yield example, suppose we want to test each of the `Variety` yields against 100 (actually  $\log 100$  since the response was transformed):

```
R> Oats.Vlsm = lsmeans(Oats.lmer2, "Variety")
R> test(Oats.Vlsm, null = log(100), type = "response")
```

Variety	response	SE	df	null	t.ratio	p.value
Golden Rain	105.8528	7.95052	10.65	100	0.757	0.4653
Marvellous	112.1345	8.42233	10.65	100	1.525	0.1564
Victory	97.7701	7.34343	10.65	100	-0.300	0.7698

Tests are performed on the linear-predictor scale

Note that `null` should always be given on the linear-predictor scale (in this case  $\log$  yield), even when specifying `type="response"`. We could have specified different null values for each hypothesis by providing a vector of three numbers.

### 11.2 Equivalence tests

The preceding results say that none of the variety means differs significantly from 100, after transforming. But this is not the same as saying that we have evidence that the means are close to 100 (that is, absence of proof is not proof of absence). To make a strong statement that an effect is small, we should use an equivalence test, which more-or-less turns the hypotheses around:

$$H_0 : |\theta^{(j)} - \theta_0^{(j)}| \geq \delta \quad \text{versus} \quad H_1 : |\theta^{(j)} - \theta_0^{(j)}| < \delta$$

where  $\delta$  is a specified threshold of equivalence. A common test procedure is the two one-sided test (TOST) method (Schuirmann, 1987), whereby we obtain equivalence only if we can establish both that  $\theta^{(j)} - \theta_0^{(j)} > -\delta$  and that  $\theta^{(j)} - \theta_0^{(j)} < \delta$ . In `lsmeans`, we do this by pre-identifying the less significant of these two tests:

$$t = \frac{|\hat{\theta}^{(j)} - \theta_0^{(j)}| - \delta}{SE(\hat{\theta}^{(j)})}$$

and the  $P$  value is the *left*-tail probability of this quantity from the central  $t$  distribution.

In `test` or `summary`, an equivalence test is requested by specifying a nonzero `delta` argument, which in turn is used as the threshold  $\delta$ . In the Oat-yield example, the following results are obtained using a threshold of  $\delta = 0.20$ :

```
R> test(Oats.Vlsm, null = log(100), delta = 0.20, type = "r")
```

Variety	response	SE	df	null	t.ratio	p.value
Golden Rain	105.8528	7.95052	10.65	100	-1.905	0.0420
Marvellous	112.1345	8.42233	10.65	100	-1.138	0.1400
Victory	97.7701	7.34343	10.65	100	-2.363	0.0192

Statistics are tests of equivalence with a threshold of 0.2

P values are left-tailed

Tests are performed on the linear-predictor scale

So two of the three Variety means are established as being within .20 of log 100. The natural log scale has the special property that small increments on the log scale translate to approximate percentage differences of the same size. That is, a threshold of .20 corresponds to about a 20% difference:  $\log 80 - \log 100 = \log .8 \approx -.223$ , and  $\log 120 - \log 100 = \log 1.2 \approx .182$ .

### 11.3 One-sided tests, noninferiority, nonsuperiority

The `side` argument is also available to specify one-sided tests. A right-tailed alternative may be requested using `side` partially matching one of "+", "right", ">", +1, 1, "superiority", or (see later) "noninferiority". Similarly, a left-tailed alternative may be specified using `side` equal to "-", "left", "<", -1, "inferiority", or "nonsuperiority". (And for completeness, a two-sided alternative is specified using 0, 2, "!=", "both", "two-sided", "equivalence", or "=".) In the following example, we test to see if either Golden Rain or Marvellous has better yield than Victory:

```
R> test(contrast(Oats.Vlsm, "trt.vs.ctrlk"), side = ">")
```

contrast	estimate	SE	df	t.ratio	p.value
Golden Rain - Victory	0.0794312	0.0686844	10	1.156	0.2556
Marvellous - Victory	0.1370802	0.0686844	10	1.996	0.0725

Results are given on the log scale.

P value adjustment: sidak method for 2 tests

P values are right-tailed

The one-sided version of an equivalence test is called a noninferiority or nonsuperiority test. It is obtained by specifying both `side` and a nonzero `delta`. For example, to test whether Victory is as good as the other two within a 25% threshold, use

```
R> test(contrast(Oats.Vlsm, "trt.vs.ctrlk"), side = "nonsup", delta = .25)
```

contrast	estimate	SE	df	t.ratio	p.value
Golden Rain - Victory	0.0794312	0.0686844	10	-2.483	0.0321
Marvellous - Victory	0.1370802	0.0686844	10	-1.644	0.1269

Results are given on the log scale.

P value adjustment: sidak method for 2 tests

Statistics are tests of nonsuperiority with a threshold of 0.25

P values are left-tailed

We find strong evidence that, with the stated threshold of .25, Golden Rain is nonsuperior to Victory (so that Victory is noninferior to Golden Rain); but not strong evidence that Victory is noninferior to Marvellous.

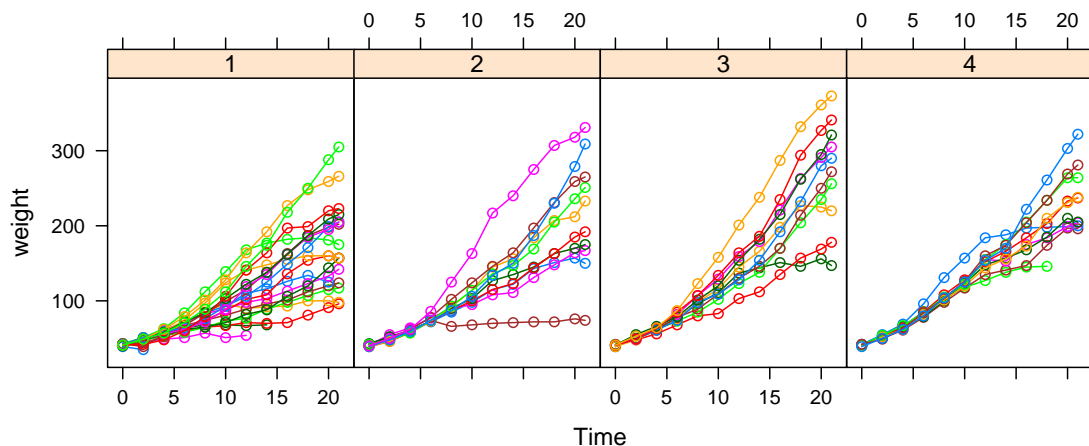


Figure 4: Growth curves of chicks, dataset `ChickWeight`.

## 12 Trends

The `lsmeans` package provides a function `lstrends` for estimating and comparing the slopes of fitted lines (or curves). To illustrate, consider the built-in R dataset `ChickWeight` which has data on the growths of newly hatched chicks under four different diets. The following code produces the display in Figure 4.

```
R> require("lattice")
R> xyplot(weight~Time | Diet, groups = ~ Chick, data = ChickWeight,
          type = "o", layout=c(4, 1))
```

Let us fit a model to these data using random slopes for each chick and allowing for a different average slope for each diet:

```
R> Chick.lmer <- lmer(weight ~ Diet * Time + (0 + Time | Chick),
                     data = ChickWeight)
```

We can then call `lstrends` to estimate and compare the average slopes for each diet.

```
R> ( Chick.lst <- lstrends (Chick.lmer, ~ Diet, var = "Time") )
```

Diet	Time.trend	SE	df	lower.CL	upper.CL
1	6.33856	0.610488	49.86	5.11227	7.56484
2	8.60914	0.838003	48.28	6.92447	10.29380
3	11.42287	0.838003	48.28	9.73821	13.10753
4	9.55583	0.839245	48.56	7.86892	11.24273

Confidence level used: 0.95

Here we obtain estimates and pairwise comparisons of the slopes using a compact letter display.

```
R> cld (Chick.lst)
```

	Diet	Time.trend	SE	df	lower.CL	upper.CL	.group
1		6.33856	0.610488	49.86	5.11227	7.56484	1
2		8.60914	0.838003	48.28	6.92447	10.29380	12
4		9.55583	0.839245	48.56	7.86892	11.24273	2
3		11.42287	0.838003	48.28	9.73821	13.10753	2

Confidence level used: 0.95

P value adjustment: tukey method for comparing a family of 4 estimates

significance level used: alpha = 0.05

According to the Tukey HSD comparisons (with default significance level of .05), there are two groupings of slopes: Diet 1's mean slope is significantly less than 3 or 4's, Diet 2's slope is not distinguished from any other.

Note: `lstrends` computes a difference quotient based on two slightly different reference grids. Thus, it must be called with a model object, not a `ref.grid` object.

## 13 User preferences

`lsmeans` sets certain defaults for displaying results—for example, using .95 for the confidence coefficient, and showing intervals for `lsmeans` output and test statistics for `contrast` results. As discussed before, one may use arguments in `summary` to change what is displayed, or `update` to change the defaults for a given object. But suppose you want different defaults to begin with. These can be set using the `lsm.options` statement. For example:

```
R> lsm.options(ref.grid = list(level = .90),
               lsmeans = list(),
               contrast = list(infer = c(TRUE, TRUE)))
```

This requests that any object created by `ref.grid` be set to have confidence levels default to 90%, and that `contrast` results are displayed with both intervals and tests. No new options are set for `lsmeans` results, and the `lsmeans` part could have been omitted. These options are stored with objects created by `ref.grid`, `lsmeans`, and `contrast`. For example, even though no new defaults are set for `lsmeans`, future calls to `lsmeans` on a model object will be displayed with 90% confidence intervals, because `lsmeans` calls `ref.grid`. However, calling `lsmeans` on an existing "ref.grid" object will inherit that object's setting.

Certain other options are available; for example, the "estble.tol" option sets the tolerance for determining estimability of linear contrasts. To see its current value:

```
R> get.lsm.option("estble.tol")
```

```
[1] 1e-08
```

Defaults for this and some other parameters are saved in `lsm.default`.

## 14 Two-sided formulas

In its original design, the only way to obtain contrasts and comparisons in `lsmeans` was to specify a two-sided formula, e.g., `pairwise ~ treatment`, in the `lsmeans` call. The result is then a list of `lsmobj` objects. In its newer versions, `lsmeans` offers a richer family of objects that can be

re-used, and dealing with a list of objects can be awkward or confusing, so its continued use is not encouraged. Nonetheless, it is still available for backward compatibility.

Here is an example where, with one command, we obtain both the LS means and pairwise comparisons for `Variety` in the model `Oats.lmer2`:

```
R> lsmeans(Oats.lmer2, pairwise ~ Variety)
```

```
$lsmeans
  Variety      lsmean      SE    df lower.CL upper.CL
Golden Rain 4.66205 0.0751092 10.65  4.52676  4.79734
Marvellous  4.71970 0.0751092 10.65  4.58441  4.85499
Victory      4.58262 0.0751092 10.65  4.44733  4.71791
```

Results are given on the log scale.

Confidence level used: 0.9

```
$contrasts
  contrast      estimate      SE df  lower.CL upper.CL t.ratio p.value
Golden Rain - Marvellous -0.0576490 0.0686844 10 -0.2164788 0.101181 -0.839 0.6883
Golden Rain - Victory    0.0794312 0.0686844 10 -0.0793986 0.238261  1.156 0.5036
Marvellous - Victory     0.1370802 0.0686844 10 -0.0217496 0.295910  1.996 0.1636
```

Results are given on the log scale.

Confidence level used: 0.9

Conf-level adjustment: tukey method for comparing a family of 3 estimates

P value adjustment: tukey method for comparing a family of 3 estimates

This example also illustrates the effect of the preceding `lsm.options` settings. Let us now return to the default display for contrast results.

```
R> lsm.options(ref.grid = NULL, contrast = NULL)
```

## 15 Messy data

To illustrate some more `lsmeans` capabilities, consider the dataset named `nutrition` that is provided with the `lsmeans` package. These data come from Milliken and Johnson (1992), and contain the results of an observational study on nutrition education. Low-income mothers are classified by race, age category, and whether or not they received food stamps (the `group` factor); and the response variable is a gain score (post minus pre scores) after completing a nutrition training program.

Consider the model that includes all main effects and two-way interactions. A Type-II (hierarchical) analysis-of-variance table is also shown.

```
R> nutr.lm <- lm(gain ~ (age + group + race)^2, data = nutrition)
R> library("car")
R> Anova(nutr.lm)
```

Anova Table (Type II tests)

```
Response: gain
      Sum Sq Df F value    Pr(>F)
age      82.4  3   0.961    0.414
```

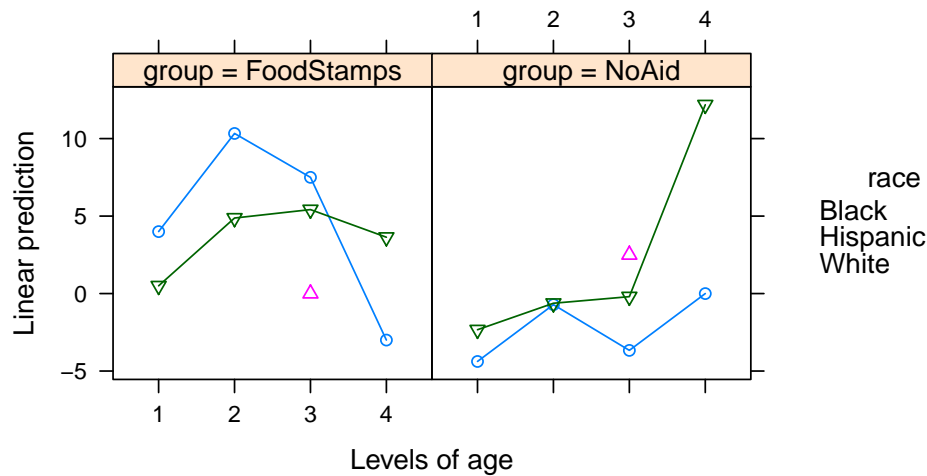


Figure 5: Predictions for the nutrition data

```
group      658.1  1  23.044  6.1e-06
race       11.2  2   0.196   0.823
age:group   91.6  3   1.069   0.366
age:race    87.3  3   1.019   0.388
group:race  113.7  2   1.991   0.142
Residuals 2627.5 92
```

One main effect (`group`) is quite significant, and there is possibly an interaction with `race`. Let us look at the `group` by `race` LS means:

```
R> lsmip(nutr.lm, race ~ age | group)
R> lsmeans(nutr.lm, ~ group*race)
```

group	race	lsmean	SE	df	lower.CL	upper.CL
FoodStamps	Black	4.70826	2.36812	92	0.00497136	9.41154
NoAid	Black	-2.19040	2.49058	92	-7.13689810	2.75610
FoodStamps	Hispanic	NA	NA	NA	NA	NA
NoAid	Hispanic	NA	NA	NA	NA	NA
FoodStamps	White	3.60768	1.15562	92	1.31252147	5.90284
NoAid	White	2.25634	2.38927	92	-2.48896668	7.00164

Results are averaged over the levels of: age  
Confidence level used: 0.95

Figure 5 shows the predictions from this model. One thing the output illustrates is that `lsmeans` incorporates an estimability check, and returns a missing value when a prediction cannot be made uniquely. In this example, we have very few Hispanic mothers in the dataset, resulting in empty cells. This creates a rank deficiency in the fitted model, and some predictors are thrown out.

We can avoid non-estimable cases by using `at` to restrict the reference levels to a smaller set. A useful summary of the results might be obtained by narrowing the scope of the reference levels

to two races and the two middle age groups, where most of the data lie. However, always keep in mind that whenever we change the reference grid, we also change the definition of the LS means. Moreover, it may be more appropriate to average the two ages using weights proportional to their frequencies in the data set. The simplest way to do this is to add a `weights` argument.<sup>3</sup> With those ideas in mind, here are the LS means and comparisons within rows and columns:

```
R> nutr.lsm <- lsmeans(nutr.lm, ~ group * race, weights = "proportional",
  at = list(age = c("2", "3"), race = c("Black", "White")))
```

So here are the results

```
R> nutr.lsm
```

group	race	lsmean	SE	df	lower.CL	upper.CL
FoodStamps	Black	8.275710	2.917880	92	2.48055	14.070871
NoAid	Black	-2.858277	1.678104	92	-6.19114	0.474582
FoodStamps	White	5.270305	0.868032	92	3.54632	6.994292
NoAid	White	-0.316369	1.010292	92	-2.32290	1.690158

Results are averaged over the levels of: age

Confidence level used: 0.95

```
R> summary(pairs(nutr.lsm, by = "race"), by = NULL)
```

contrast	race	estimate	SE	df	t.ratio	p.value
FoodStamps - NoAid	Black	11.13399	3.55123	92	3.135	0.0023
FoodStamps - NoAid	White	5.58667	1.33198	92	4.194	0.0001

Results are averaged over the levels of: age

```
R> summary(pairs(nutr.lsm, by = "group"), by = NULL)
```

contrast	group	estimate	SE	df	t.ratio	p.value
Black - White	FoodStamps	3.00540	3.01639	92	0.996	0.3217
Black - White	NoAid	-2.54191	1.95876	92	-1.298	0.1976

Results are averaged over the levels of: age

The general conclusion from these analyses is that for age groups 2 and 3, the expected gains from the training are higher among families receiving food stamps. Note that this analysis is somewhat different than the results we would obtain by subsetting the data before analysis, as we are borrowing information from the other observations in estimating and testing these LS means.

## 15.1 More on weighting

The `weights` argument can be a vector of numerical weights (it has to be of the right length), or one of four text values: `"equal"` (weight the predictions equally when averaging them, the default), `"proportional"` (weight them proportionally to the observed frequencies of the factor combinations

---

<sup>3</sup> It may also be done by specifying a custom function in the `fac.reduce` argument, but for simple weighting, `weights` is simpler.



```
R> lsmeans(nutr.lm, "race", weights = "equal")
```

race	lsmean	SE	df	lower.CL	upper.CL
Black	1.25893	1.64600	92	-2.010175	4.52803
Hispanic	NA	NA	NA	NA	NA
White	2.93201	1.34661	92	0.257519	5.60650

Results are averaged over the levels of: age, group  
Confidence level used: 0.95

```
R> lsmeans(nutr.lm, "race", weights = "prop")
```

race	lsmean	SE	df	lower.CL	upper.CL
Black	1.92655	1.39403	92	-0.842112	4.69522
Hispanic	NA	NA	NA	NA	NA
White	2.52282	0.60446	92	1.322310	3.72333

Results are averaged over the levels of: age, group  
Confidence level used: 0.95

```
R> lsmeans(nutr.lm, "race", weights = "outer")
```

race	lsmean	SE	df	lower.CL	upper.CL
Black	2.54667	1.431362	92	-0.296136	5.38948
Hispanic	NA	NA	NA	NA	NA
White	3.14294	0.749415	92	1.654536	4.63134

Results are averaged over the levels of: age, group  
Confidence level used: 0.95

```
R> lsmeans(nutr.lm, "race", weights = "cells")
```

race	lsmean	SE	df	lower.CL	upper.CL
Black	0.380952	1.166180	92	-1.93518	2.69709
Hispanic	1.666667	3.085422	92	-4.46125	7.79458
White	2.795181	0.586592	92	1.63016	3.96020

Results are averaged over the levels of: age, group  
Confidence level used: 0.95

Figure 6: Comparison of four different weighting methods

being averaged over), "outer" (weight according to the outer products of the one-factor marginal counts), or "cells" (weight each mean differently, according to the frequencies of the predictions being averaged). Figure 6 shows the LS means for **race** using the four different weighting schemes. (Note: If the model itself has weights, then the total weights are used instead of counts.)

Note there are four different sets of answers. The "equal" weighting is self-explanatory. But what's the distinction between "proportional" and "outer"? To clarify, consider:

```
R> temp = lsmeans(nutr.lm, c("group", "race"), weights = "prop")
R> lsmeans(temp, "race", weights = "prop")
```

race	lsmean	SE	df	lower.CL	upper.CL
Black	2.54667	1.431362	92	-0.296136	5.38948
Hispanic	NA	NA	NA	NA	NA
White	3.14294	0.749415	92	1.654536	4.63134

Results are averaged over the levels of: age, group  
Confidence level used: 0.95

The previous results using "outer" weights are the same as those using "proportional" weights on one factor at a time. Thus, if only one factor is being averaged over, "outer" and "proportional" are the same. Another way to look at it is that outer weights are like the expected counts in a chi-square test; each factor is weighted independently of the others.

The results for "cells" weights stand out because everything is estimable—that's because the empty cells in the data were given weight zero. These results are the same as the unadjusted means:

```
R> with(nutrition, tapply(gain, race, mean))
```

Black	Hispanic	White
0.380952	1.666667	2.795181

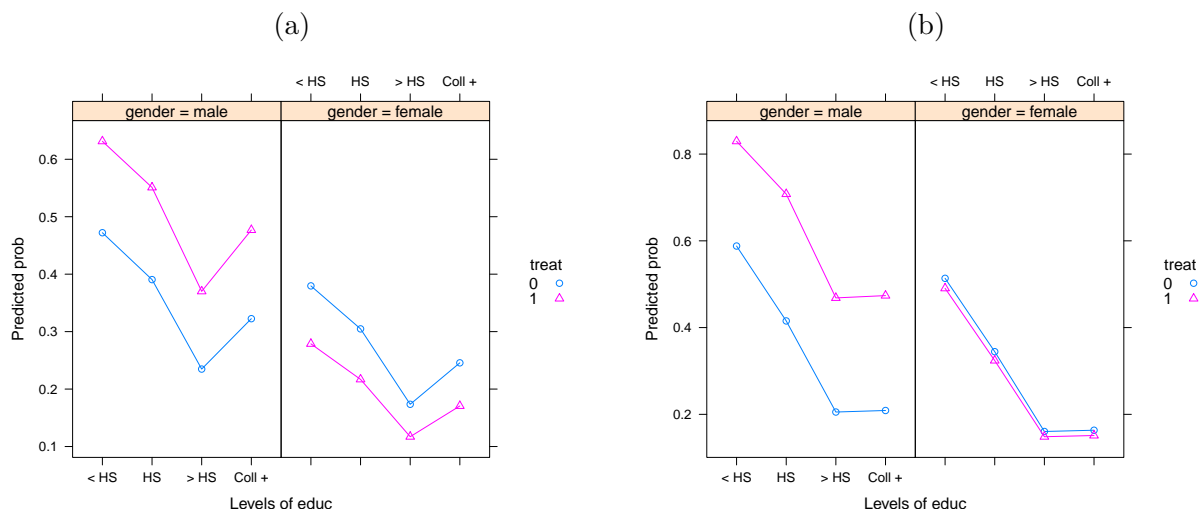


Figure 7: Estimated responses for the **framing** data. (a) Holding **emo** constant at its mean; (b) Using predictions of **emo** for each **treat**.

## 15.2 Alternative covariate adjustments

The **framing** data in the **mediation** package has the results of an experiment conducted by Brader *et al.* (2008) where subjects were given the opportunity to send a message to Congress regarding immigration. However, before being offered this, some subjects (**treat**=1) were first shown a news story that portrays Latinos in a negative way. Besides the binary response (whether or not they elected to send a message), we also measured **emp**, the subjects' emotional state after the treatment was applied. There are various demographic variables as well.

Before fitting a logistic regression model, I will change the labels for **educ** to shorter strings.

```
R> library("mediation")
R> levels(framing$educ) = c("NA", "Ref", "< HS", "HS", "> HS", "Coll +")
R> framing.glm = glm(cong_mesg ~ age + income + educ + emo + gender * factor(treat),
  family = binomial, data = framing)
```

The left-hand plot in Figure 7 displays the conventional adjusted means, where predictions are made with the covariates **age**, **income**, and **emo** set to their mean values:

```
R> lsmip(framing.glm, treat ~ educ | gender, type = "response")
```

This plot is rather implausible because the displayed treatment effects are the opposite for females as for males, and the effect of education isn't monotone as one might expect.

However, **emo** is a post-treatment measurement. This means that the treatment could have affected it (it is a *mediating* covariate). If it is indeed affected by **treat**, then Figure 7(a) would be misleading because **emo** is held constant. Instead, consider making the predictions where **emo** is set to its predicted value at each combination of **treat** and the demographic variables. This is easily done by setting **cov.reduce** to a formula for how to predict **emo**:

```
R> lsmip(framing.glm, treat ~ educ | gender, type = "response",
  cov.reduce = emo ~ treat*gender + age + educ + income)
```

This plot is shown in Figure 7(b). It is quite different, suggesting that `emo` does indeed play a strong mediating role. (The **mediation** package has functions for estimating the strength of these effects.) The predictions suggest that, taking emotional response into account, male subjects exposed to the negative news story are more likely to send the message than are females or those not seeing the negative news story. Also, the effect of `educ` is (almost) monotone. You can see what values of `emo` are used in these predictions by looking at the `grid` slot in the reference grid:

```
R> ref.grid(framing.glm,
  cov.reduce = emo ~ treat*gender + age + educ + income)@grid
```

	age	income	educ	emo	gender	treat	.wgt.
1	47.766	10.7962	< HS	8.32779	male	0	6
2	47.766	10.7962	HS	7.27257	male	0	32
3	47.766	10.7962	> HS	6.47527	male	0	24
4	47.766	10.7962	Coll +	5.26561	male	0	34
5	47.766	10.7962	< HS	8.55422	female	0	8
6	47.766	10.7962	HS	7.49899	female	0	37
7	47.766	10.7962	> HS	6.70169	female	0	23
8	47.766	10.7962	Coll +	5.49203	female	0	33
9	47.766	10.7962	< HS	9.99963	male	1	2
10	47.766	10.7962	HS	8.94440	male	1	9
11	47.766	10.7962	> HS	8.14711	male	1	13
12	47.766	10.7962	Coll +	6.93745	male	1	6
13	47.766	10.7962	< HS	9.61805	female	1	4
14	47.766	10.7962	HS	8.56282	female	1	14
15	47.766	10.7962	> HS	7.76552	female	1	10
16	47.766	10.7962	Coll +	6.55587	female	1	10

whereas the overall mean of 6.974 is used as the value of `emo` in Figure 7(a).

Another use of formulas in `cov.reduce` is to create representative values of some covariates when others are specified in `at`. For example, suppose there are three covariates  $x_1, x_2, x_3$  in a model, and we want to see predictions at a few different values of  $x_1$ . We might use

```
R> rg <- ref.grid(my.model, at = list(x1 = c(5,10,15)),
  cov.reduce = list(x2 ~ x1, x3 ~ x1 + x2))
```

(When more than one formula is given, they are processed in the order given.) The values used for  $x_2$  and  $x_3$  will depend on  $x_1$  and should in some sense be more realistic values of those covariates as  $x_1$  varies than would be the overall means of  $x_2$  and  $x_3$ . Of course, it would be important to display the values used—available as `rg@grid`—when reporting the analysis.

## 16 Other types of models

### 16.1 Models supported by `lsmeans`

The `lsmeans` package comes with built-in support for several packages and model classes:

```
stats : "lm", "mlm", "aov", "aovlist", "glm"
nlme : "lme", "gls", "nlme"
```

```

lme4 : "lmerMod", "glmerMod"
survival : "survreg", "coxph"
MASS : "polr"
gee, geepack : "gee", "geeglm", "geese"
ordinal : "clm", "clmm"
rms : "rms" and descendents such as "ols", "lrm", "orm", etc.

```

**lsmeans** support for all these models works similarly to the examples we have presented. Note that generalized linear or mixed models, and several others such as survival models, typically employ link functions such as **log** or **logit**. In most cases, the LS means displayed are on the scale of the linear predictor, and any averaging over the reference grid is performed on the linear-predictor scale; but there are exceptions. Some objects have optional arguments that can be specified in the `ref.grid` or `lsmeans` call: see `?models` for details.

## 16.2 Ordinal-data example

The `clm` and `clmm` functions in **ordinal**, as well as the `polr` function in **MASS**, fit polytomous regression models to Likert-scale data. They do this by modeling the ordinal response as a categorization of a continuous latent variable  $S$ , then estimating thresholds for this categorization and fitting a generalized linear model to the cumulative probabilities for each threshold. By default, **lsmeans** produces predictions of the latent variable.

The example shown here is based on the **housing** data in the **MASS** package, where the response variable is satisfaction (**Sat**) on a three-point scale of low, medium, high; and predictors include **Type** (type of rental unit, four levels), **Infl** (influence on management of the unit, three levels), and **Cont** (contact with other residents, two levels). We will assume that the latent variable is normally distributed (by specifying a probit link).

```

R> library("ordinal")
R> data(housing, package = "MASS")
R> housing.clm <- clm(Sat ~ (Infl + Type + Cont)^2,
                      data = housing, weights = Freq, link = "probit")
R> lsmip(housing.clm, Cont ~ Infl | Type, layout = c(4,1))

```

The plot is shown in Figure 8. Generally, the higher the influence, the higher the satisfaction. Overall  $F$  tests of the **Infl** effect suggest that it is strong for all four housing types:

```

R> test(pairs(lsmeans(housing.clm, ~ Infl | Type)), joint = TRUE)

```

	F	df1	df2	p.value
Tower	7.9378	2	NA	0.0004
Apartment	40.0412	2	NA	0.0000
Atrium	3.1349	2	NA	0.0435
Terrace	10.8234	2	NA	0.0000

The tests are asymptotic (signaled by `df2 = NA`), so they are actually chi-square tests for the statistics  $X^2 = df_1 \cdot F$  with  $df_1$  degrees of freedom. Higher contact also seems to be associated with higher satisfaction, but terrace apartments may be an exception. Let's see:

```

R> test(pairs(lsmeans(housing.clm, ~ Cont | Type)), joint = TRUE)

```

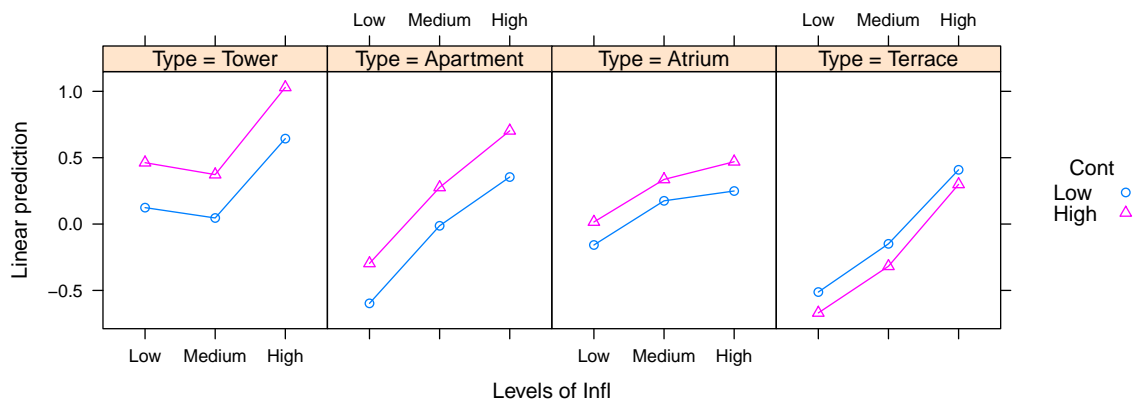


Figure 8: Interaction plot for the latent variable in the `housing` example.

	F	df1	df2	p.value
Tower	8.4661	1	NA	0.0036
Apartment	13.0978	1	NA	0.0003
Atrium	1.4211	1	NA	0.2332
Terrace	0.9310	1	NA	0.3346

So the effect is inconclusive for both atria and terraces.

The `mode` argument may be used to choose what to examine. Modes `"linear.predictor"` and `"cum.prob"` create an additional pseudo-factor named `cut` for the thresholds at which the predictions are made.

```
R> ref.grid(housing.clm, mode = "cum.prob")
```

'ref.grid' object with variables:

Infl = Low, Medium, High

Type = Tower, Apartment, Atrium, Terrace

Cont = Low, High

cut = multivariate response levels: Low|Medium, Medium|High

So here are our estimated marginal probabilities for `Infl` of being less than highly satisfied:

```
R> lsmeans(housing.clm, ~ Infl, at = list(cut = "Medium|High"),
  mode = "cum.prob")
```

Infl	cumprob	SE	df	asympt.LCL	asympt.UCL
Low	0.704649	0.0178354	NA	0.669692	0.739605
Medium	0.606165	0.0197268	NA	0.567501	0.644828
High	0.442192	0.0269420	NA	0.389386	0.494997

Results are averaged over the levels of: Type, Cont

Confidence level used: 0.95

Compare these results with those for the back-transformed linear predictor:

```
R> summary(lsmmeans(housing.clm, ~ Infl, at = list(cut = "Medium/High"),
  mode = "linear.predictor"), type = "response")
```

Infl	cumprob	SE	df	asympt.LCL	asympt.UCL
Low	0.716271	0.0185478	NA	0.678853	0.751465
Medium	0.609159	0.0202367	NA	0.568995	0.648191
High	0.439691	0.0275347	NA	0.386446	0.494052

Results are averaged over the levels of: Type, Cont  
Confidence level used: 0.95

The results are similar, but somewhat different because of the back-transformation coming before (first case) or after (second case) averaging or computing confidence limits.

### 16.3 Chick weights, revisited

Previously, we used the `ChickWeight` data to illustrate the use of `lstrends`. That example made the simplifying assumption that the growth trends are linear, which is clearly questionable. To do a better job of fitting the data, consider instead the idea of fitting a logistic curve to each chick's data. The `stats` package provides the `SSlogis` function for this purpose: it is an S-shaped curve (scaled from the cdf of a logistic distribution) having three parameters `asym` (the asymptotic value at which it levels off), `xmid` (the  $x$  coordinate of its inflection point), and `scal` (roughly the difference between the median and the .73rd quantile). Also, the `nlme` package's `nlme` function can fit a set of nonlinear curves such that the parameters of those curves may be modeled using a mixed-effects linear model.

Accordingly, let us fit a model where each chick has a logistic curve for which the `asym` parameter varies randomly for each chick, and for which both `asym` and `xmid` depend on the chick's diet. We chose starting values by examining the curves and making a rough judgment of the typical asymptotic value, midpoint, and scale for each diet. We need to keep firmly in mind how factors are coded; so we explicitly show that we intend to use `"contr.treatment"` coding, by which the first mean is estimated directly, and the remaining estimates are offsets from that. We need a set of four starting values for `asym` and `xmid`, and one for `scal`.

```
R> require("nlme")
R> options(contrasts = c("contr.treatment", "contr.poly"))
R> Chick.nlme = nlme(weight ~ SSlogis(Time, asym, xmid, scal),
  data = ChickWeight,
  fixed = list(asym + xmid ~ Diet, scal ~ 1),
  random = asym ~ 1 | Chick,
  start = c(200, 100, 200, 100, 10, 0, 0, 0, 7))
R> Chick.nlme
```

Nonlinear mixed-effects model fit by maximum likelihood

```
Model: weight ~ SSlogis(Time, asym, xmid, scal)
Data: ChickWeight
Log-likelihood: -2439.4
Fixed: list(asym + xmid ~ Diet, scal ~ 1)
asym.(Intercept)      asym.Diet2      asym.Diet3      asym.Diet4 xmid.(Intercept)
221.207493           75.235197           198.767610           90.692332           12.216286
```

xmid.Diet2	xmid.Diet3	xmid.Diet4	scal
1.870092	4.464178	0.929361	7.059857

Random effects:

Formula: `asym ~ 1 | Chick`

`asym.(Intercept) Residual`

StdDev: 66.9958 13.8516

Number of Observations: 578

Number of Groups: 50

Now we can use `lsmeans` to compare the parameters based on Diet:

```
R> cld(lsmeans(Chick.nlme, ~ Diet, param = "asym"))
```

Diet	lsmean	SE	df	lower.CL	upper.CL	.group
1	221.207	16.8641	520	188.077	254.338	1
2	296.443	24.3132	520	248.679	344.207	2
4	311.900	24.0879	520	264.578	359.221	2
3	419.975	29.4935	520	362.034	477.916	3

Confidence level used: 0.95

P value adjustment: tukey method for comparing a family of 4 estimates

significance level used: alpha = 0.05

```
R> cld(lsmeans(Chick.nlme, ~ Diet, param = "xmid"))
```

Diet	lsmean	SE	df	lower.CL	upper.CL	.group
1	12.2163	0.552564	520	11.1308	13.3018	1
4	13.1456	0.598941	520	11.9690	14.3223	12
2	14.0864	0.642599	520	12.8240	15.3488	2
3	16.6805	0.726923	520	15.2524	18.1085	3

Confidence level used: 0.95

P value adjustment: tukey method for comparing a family of 4 estimates

significance level used: alpha = 0.05

The result is that diet 3 has both a higher mean `asym` and a higher mean `xmid` than the other diets. This is compatible with the results of the earlier `lstrends` analysis, but grounded in terms of the parameters of the logistic curve.

## 16.4 Extending to more models

The functions `ref.grid` and `lsmeans` work by first reconstructing the dataset (so that the reference grid can be identified) and extracting needed information about the model, such as the regression coefficients, covariance matrix, and the linear functions associated with each point in the reference grid. For a fitted model of class, say, "`modelobj`", these tasks are accomplished by defining S3 methods `recover.data.modelobj` and `lsm.basis.modelobj`. The help page "`extending-lsmeans`" and the vignette by the same name provide details and examples.

Developers of packages that fit models are encouraged to include support for `lsmeans` by incorporating (and exporting) `recover.data` and `lsm.basis` methods for their model classes.

## 16.5 Bayesian models

Certain Bayesian models are now supported by **lsmeans**. For illustration, consider a two-factor Poisson regression example given in the **MCMCpack** package:

```
R> library("MCMCpack")
R> counts <- c(18, 17, 15, 20, 10, 20, 25, 13, 12)
R> outcome <- gl(3, 1, 9)
R> treatment <- gl(3, 3)
R> posterior <- MCMCpoisson(counts ~ outcome + treatment, mcmc = 1000)
```

The result is an `mcmc` object (defined in the **coda** package), but it has an added `"call"` attribute that enables **lsmeans** to do its work. Here are results for treatments, averaged over outcomes:

```
R> ( post.lsm <- lsmeans(posterior, "treatment") )
```

treatment	lsmean	SE	df	asympt.LCL	asympt.UCL
1	2.78820	0.158523	NA	2.47750	3.09890
2	2.80098	0.129532	NA	2.54711	3.05486
3	2.80179	0.138729	NA	2.52988	3.07369

Results are averaged over the levels of: outcome  
Confidence level used: 0.95

This is a frequentist summary, based on the mean and covariance of the regression parameters in the `posterior` sample. But **lsmeans** provides an `as.mcmc` method to obtain a sample from the posterior distribution of the LS means (that is, the original posterior sample of regression coefficients, transformed by the appropriate linear functions.)

```
R> library("coda")
R> summary(as.mcmc(post.lsm))
```

```
Iterations = 1:1000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 1000
```

1. Empirical mean and standard deviation for each variable,  
plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
treatment 1	2.79	0.159	0.00501	0.0233
treatment 2	2.80	0.130	0.00410	0.0160
treatment 3	2.80	0.139	0.00439	0.0167

2. Quantiles for each variable:

	2.5%	25%	50%	75%	97.5%
treatment 1	2.45	2.69	2.81	2.91	3.07
treatment 2	2.53	2.71	2.80	2.89	3.04
treatment 3	2.52	2.72	2.81	2.90	3.04

Since `as.mcmc` produces an `mcmc` object, any of the other available methods may be used with it.



## 17 Discussion

The design goal of **lsmeans** is primarily to provide the functionality of the LSMEANS statement in various SAS procedures. Thus its emphasis is on tabular results which, of course, may also be used as data for further analysis or graphics. By design, it can be extended with relative ease to additional model classes. A unique capability of **lsmeans** is its explicit reliance on the concept of a reference grid, which I feel is a useful approach for understanding what is being computed.

Some **lsmeans** capabilities exceed those of SAS, including the **lstrends** capability, more flexibility in organizing the output, and more built-in contrast families. In addition, SAS does not allow LS means for factor combinations when the model does not include the interaction of those factors; or creating a grid of covariate values using **at**.

There are a few other R packages that provide capabilities that overlap with those of **lsmeans**. The **effects** package (Fox, 2003; Fox and Hong, 2009) can compute LS means. However, for an unbalanced dataset, it does not use equal weights, but rather it appears to use “outer” weights, as described in Section 15.1. Also, it does not check estimability, so some results could be questionable. The emphasis of **effects** is on graphical rather than tabular displays. It has special strengths for curve-fitting models such as splines. In contrast, **lsmeans**’s strengths are more in the area of factorial models where one wants traditional summaries in the form of estimates, contrasts, and interaction plots.

The **doBy** package (Højsgaard *et al.*, 2013) provides an **LSmeans** function that has some of the capabilities of **lsmeans**, but it produces a data frame rather than a reusable object. In earlier versions of the package, this function was named **popMeans**. The package also has an **LSmatrix** function to obtain the linear functions needed to obtain LS means.

## References

- Bates D, Maechler M, Bolker B, Walker S (2013). *lme4: Linear Mixed-effects Models Using Eigen and S4*. R package version 1.1-0, URL <http://lme4.r-forge.r-project.org/>.
- Brader T, Valentino N, Suhay E (2008). “What triggers public opposition to immigration? Anxiety, group cues, and immigration threat.” *American Journal of Political Science*, **52**(4), 959–978.
- Fox J (2003). “Effect Displays in R for Generalised Linear Models.” *Journal of Statistical Software*, **8**(15), 1–27. URL <http://www.jstatsoft.org/v08/i15/>.
- Fox J, Hong J (2009). “Effect Displays in R for Multinomial and Proportional-Odds Logit Models: Extensions to the **effects** Package.” *Journal of Statistical Software*, **32**(1), 1–24. URL <http://www.jstatsoft.org/v32/i01/>.
- Goodnight JH, Harvey WR (1997). “Least squares means in the fixed effects general model.” *Technical Report SAS Technical Report R-103*, SAS Institute Inc.
- Graves S, Piepho HP, Selzer L, Dorai-Raj S (2012). *multcompView: Visualizations of Paired Comparisons*. R package version 0.1-5, URL <http://CRAN.R-project.org/package=multcompView>.
- Halekoh U, Højsgaard S (2013). *pbkrtest: Parametric Bootstrap and Kenward Roger Based Methods for Mixed Model Comparison*. R package version 0.3-8, URL <http://CRAN.R-project.org/package=pbkrtest>.
- Harvey W (1960). “Least-squares analysis of data with unequal subclass numbers.” *Technical Report ARS-20-8*, USDA National Agricultural Library.

- Harvey W (1976). “Use of the HARVEY Procedure.” In *SUGI Proceedings*. URL <http://www.sascommunity.org/sugi/SUGI76/Sugi-76-20%20Harvey.pdf>.
- Harvey WR (1977). *User’s guide for LSML 76. Mixed model least-squares and maximum likelihood computer program*. Ohio State University.
- Højsgaard S, Halekoh U, Robison-Cox J, Wright K, Leidi AA (2013). **doBy**: *Groupwise summary statistics, LSmeans, general linear contrasts, various utilities*. R package version 4.5-10, URL <http://CRAN.R-project.org/package=doBy>.
- Hothorn T, Bretz F, Westfall P (2013). **multcomp**: *Simultaneous Inference in General Parametric Models*. R package version 1.3-1, URL <http://CRAN.R-project.org/package=multcomp>.
- Milliken GA, Johnson DE (1992). *Analysis of Messy Data – Volume I: Designed Experiments*. Chapman & Hall/CRC. ISBN 0-412-99081-4.
- Pinheiro J, Bates D, R-core (2013). **nlme**: *Linear and Nonlinear Mixed Effects Models*. R package version 3.1-113, URL <http://CRAN.R-project.org/package=nlme>.
- SAS Institute Inc (2012). “LSMEANS Statement.” In *SAS/STAT(R) 9.3 User’s Guide*. URL [http://support.sas.com/documentation/cdl/en/statug/63962/HTML/default/viewer.htm#statug\\_introcom\\_a0000003362.htm](http://support.sas.com/documentation/cdl/en/statug/63962/HTML/default/viewer.htm#statug_introcom_a0000003362.htm).
- Schuurmann D (1987). “A Comparison of the Two One-Sided Tests Procedure and the Power Approach for Assessing the Equivalence of Average Bioavailability.” *Journal of Pharmacokinetics and Biopharmaceutics*, **15**(6), 657–680.
- Searle SR, Speed FM, Milliken GA (1980). “Population marginal means in the linear model: An alternative to least squares means.” *The American Statistician*, **34**(4), 216–221.
- Yates F (1935). “Complex Experiments.” *Journal of the Royal Statistical Society (Supplement)*, **2**, 181–247.