BST02: Using R for Statistics in Medical Research

Part D: Statistics with R

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In this Section

- Common statistical tests
  - for continuous data
  - for categorical data
- (Generalized) linear regression
- Useful functions for regression models
- Modelling non-linear effects

t-test: `t.test()`

One-sample t-test

- compares the **mean of one sample** with a fixed value μ

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Two sample / independent samples t-test

- compares the **difference between the means** of two samples with a fixed value μ

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Two sample / independent samples t-test

- compares the **difference between the means** of two samples with a fixed value μ

Related samples t-test

- compares the **mean of the difference** between related observations with a fixed value μ (same as one-sample t-test)

Wilcoxon Test: `wilcox.test()`

Wilcoxon Signed Rank Test

- tests if **one sample** (or the difference between two paired samples) is **symmetric about** μ

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Wilcoxon Rank Sum Test / Mann-Whitney test

- test for a **location shift between the distributions** of two independent samples

See also BBR Sections 7.2 & 7.3 (http://hbiostat.org/doc/bbr.pdf)

Kruskal-Wallis Rank Sum Test: `kruskal.test()`

- **extension** of the Wilcoxon rank sum test for **more than two groups**
- test for a **difference in location** of a continuous variable between multiple groups
- the **Wilcoxon rank sum test is a special case** of the Kruskal-Wallis rank sum test

Other tests for continuous data

- **Kolmogorov-Smirnov Test:** `ks.test()`
  tests if two samples are drawn from the same continuous distribution
- **Shapiro-Wilk Normality Test:** `shapiro.test()`
- **Friedman Rank Sum Test:** `friedman.test()`
  non-parametric test for two or more related samples
- ...

Tests for Continuous Data

Demo

- Tests for Continuous Data
  R html

Tests for Categorical Data / Proportions

One-sample Proportion Test

- tests if the **proportion in one sample** is equal to a fixed value p
- `prop.test()` and `binom.test()`

Tests for Categorical Data / Proportions

One-sample Proportion Test

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Tests for Proportions in Multiple (independent) Groups

- tests if the **proportions in several samples** are equal
- `chisq.test()` and `fisher.test()` (when there are cells with 0)

See also BBR Sections 5.7 & 6 (http://hbiostat.org/doc/bbr.pdf)

Tests for Categorical Data / Proportions

Related Samples: McNemar Test

- Tests for **symmetry** in a 2×2 table
- `mcnemar.test()`

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3-Dimensional Contingency Table

- Cochrane-Mantel-Haenszel Test
- χ^2 test for **independence** of two nominal variables **within each stratum**
- `mantelhaen.test()`

Tests for Categorical Data

Demo

- Tests for Categorical Data
  R **html**

Practical

- Statistical Tests
  html

Useful Functions: Statistical Tests

Continuous Outcomes

- `t.test()`
- `wilcox.test()`
- `kruskal.test()`
- `ks.test()`
- `friedman.test()`
- `shapiro.test()`

Categorical Outcomes

- `prop.test()`
- `binom.test()`
- `chisq.test()`
- `fisher.test()`
- `mcnemar.test()`
- `mantelhaen.test()`

Pairwise tests

- `pairwise.prop.test()`
- `pairwise.t.test()`
- `pairwise.wilcox.test()`

Variance and Correlation

- `cor.test()`
- `bartlett.test()`
- `var.test()`

Multiple Testing Adjustment

- `p.adjust()`

Linear Regression

A standard linear regression model has the form

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p + \varepsilon \qquad \text{with} \quad \varepsilon \sim N(0, \sigma^2)$$

where

- y is the **outcome** variable ("dependent variable")
- $x_1, \ldots, x_p$ are the **covariates** ("independent variables")
- $\beta_0, \ldots, \beta_p$ are the **regression coefficients**
  - β_0 is the intercept
  - $\beta_1, \ldots, \beta_p$ estimate the effects of the covariates
- ε is a vector of **residuals**, which we assume to be (approximately) normally distributed.

Linear Regression

To fit a **linear regression** in R we use the function `lm()`.

The most important arguments are

- `formula`:
  a `formula` object
- `data`:
  a `data.frame` (optional, but usually needed)
- `subset`:
  a `vector` specifying which observations should be used (optional)
  (works like the `subset` argument of the function `subset()`)

Model Formula

A `formula` object has the form

```
outcome ~ linear predictor
```

for example

```
y ~ x1 + x2 + x3
```

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```
y ~ x1 + x2 + x3
```

- Variables are separated by "`+`" signs.
- An intercept is automatically included.
- One-sided formulas (omitting the outcome) are possible (used for random effects specification).

Model Formula: Interactions

Interaction terms are written using "`:`" or "`*`".

"`*`" includes the main effects and interaction terms, i.e.,

```
y ~ x1 * x2
```

is equivalent to

```
y ~ x1 + x2 + x1:x2
```

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```

Interactions between multiple variables can be written using "`()`", i.e.,

```
y ~ x1 * (x2 + x3)
```

is equivalent to

```
y ~ x1 * x2 + x1 * x3
```

Model Formula: Interactions

To specify a **higher level interaction** "^" is used.

For example:

```
y ~ (x1 + x2 + x3)^3
```

will create all interactions up to 3-way and is equivalent to

```
y ~ x1 * x2 * x3
```

and equivalent to

```
y ~ x1 + x2 + x3 + x1:x2 + x1:x3 + x2:x3 + x1:x2:x3
```

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and equivalent to

```
y ~ x1 + x2 + x3 + x1:x2 + x1:x3 + x2:x3 + x1:x2:x3
```

and

```
y ~ (x1 + x2 + x3)^2
```

will create all two-way interactions and is equivalent to

```
y ~ x1 + x2 + x3 + x1:x2 + x1:x3 + x2:x3
```

Model Formula: Removing terms

The "–" sign can be used to remove terms from a model formula.

For example

```
y ~ x1 * x2 * x3 - x2 - x1:x3
```

is equivalent to

```
y ~ x1 + x3 + x1:x2 + x2:x3 + x1:x2:x3
```

Model Formula: Removing terms

The "`-`" sign can be used to remove terms from a model formula.

For example

```
y ~ x1 * x2 * x3 - x2 - x1:x3
```

is equivalent to

```
y ~ x1 + x3 + x1:x2 + x2:x3 + x1:x2:x3
```

The **intercept** can be removed from a formula by using "`-1`" or "`+0`", i.e.

```
y ~ x1 + x2 - 1
y ~ x1 + x2 + 0
```

Generalized Linear Regression (GLM)

A **generalized linear regression** model has the form

$$g(\mathbb{E}(y)) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p$$

where $g(\,)$ is a link function and y is from the exponential family.

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where $g(\,)$ is a link function and y is from the exponential family.

For example **logistic regression** for binary y:

$$\log\left(\frac{P(y=1)}{1-P(y=1)}\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p$$

$\log\left(\frac{p}{1-p}\right)$ is the **logit** link.

Generalized Linear Regression (GLM)

To fit a **GLM** in R we use the function `glm()`.

The most important arguments are

- `formula`:
  a `formula` object
- `family`:
  a `family` object or name of the family function, describing the error distribution and link function
- `data`:
  a `data.frame` (optional, but usually needed)
- `subset`:
  a `vector` specifying which observations should be used (optional)

Families and Link Functions

Common families & available links in R: (see also `?family`)

family	link
`binomial`	`logit`, `probit`, `cauchit`, `log`, `cloglog`
`gaussian`	`identity`, `log`, `inverse`
`Gamma`	`inverse`, `identity`, `log`
`poisson`	`log`, `identity`, `sqrt`

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The `family` argument in `glm()` can be specified in the following ways:

- `binomial(link = "logit")`
- `binomial()`
- `binomial`
- `"binomial"`

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Common families & available links in R: (see also `?family`)

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The `family` argument in `glm()` can be specified in the following ways:

- `binomial(link = "logit")`
- `binomial()`
- `binomial`
- `"binomial"`

Note:
When the link is not explicitly specified (i.e. options 2-4), the default link is used.

Regression

Demo

- Regression Basics
  R html

Practical

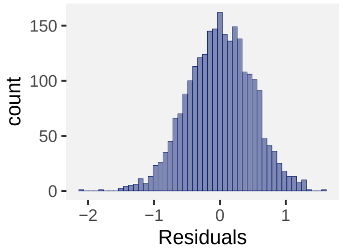
- Linear Regression html

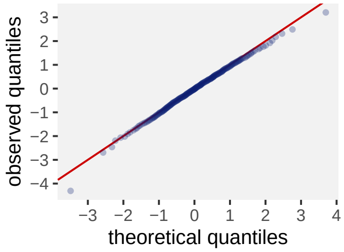
Model Evaluation

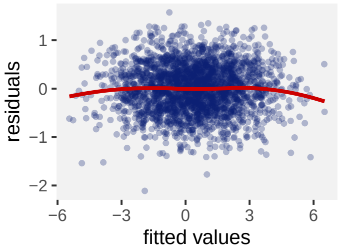
Linear model:

Evaluate the **assumptions** of a linear regression model visually, for example:

- Histogram of residuals
- Normal QQ-plot of residuals
- Scatterplot residuals vs fitted values







Model Comparison

Nested models:

- model is a **special case** of the other, i.e.,
- model B is a special case of model A when B can be obtained by setting some regression coefficients in A to zero

Comparison using a **likelihood ratio (LR) test**, for example:

```r
anova(modelA, modelB)
anova(modelA, modelB, test = "LRT") # for a glm
```

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```

Non-nested models:

Comparison using information criteria, e.g.

```r
AIC(modelA, modelB)
BIC(modelA, modelB)
```

The model with the **smaller** AIC (or BIC) has the **better** fit.

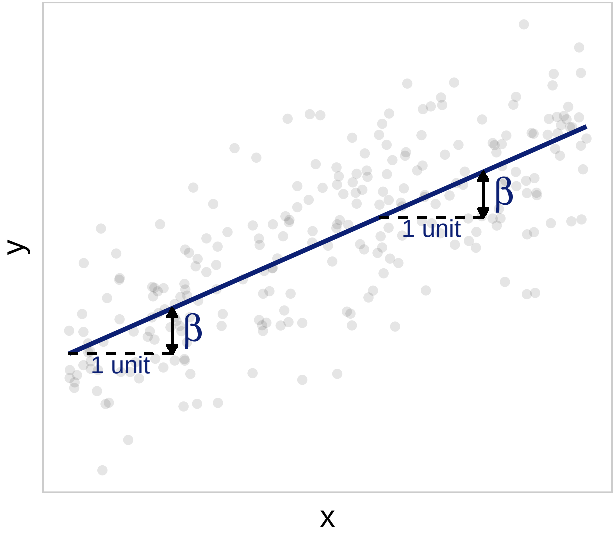
Model Evaluation

Demo

- Model Evaluation **R** **html**

Non-linear Effects

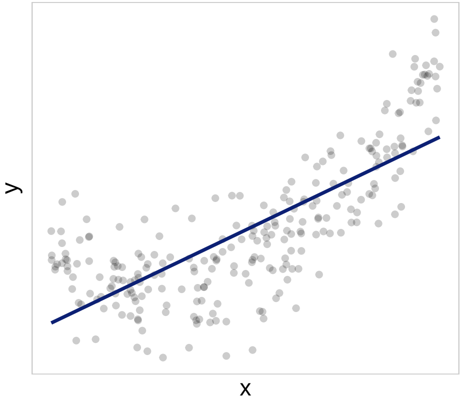
Default assumption: **linear effect**, i.e., $x \rightarrow y$ ➡ $x + 1 \rightarrow y + \beta, \quad \forall x$

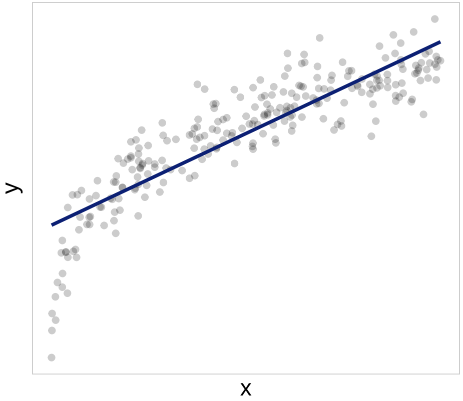


Non-linear Effects

Default assumption: **linear effect**, i.e., $x \rightarrow y$ ➡ $x + 1 \rightarrow y + \beta, \quad \forall x$

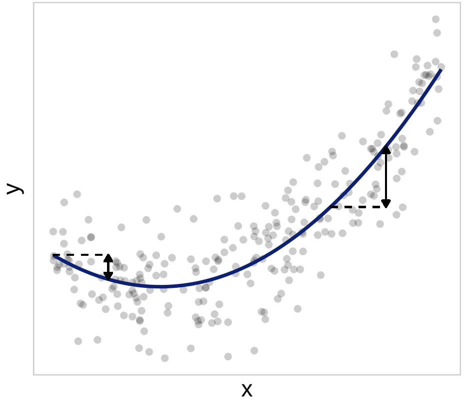
This may not always be the case:

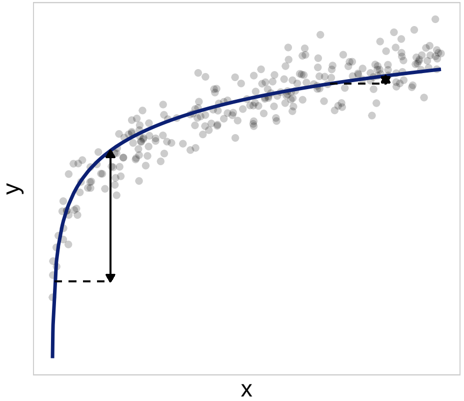




Non-linear Effects

Here, we would like to allow the **effect** of a one-unit increase **of x** to **change with the value of x**:





Non-linear Effects

Sometimes, we can use

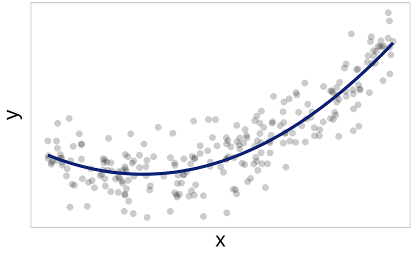
- a **transformation of x**, or
- x as well as **a polynomial** of x (or a transformation).

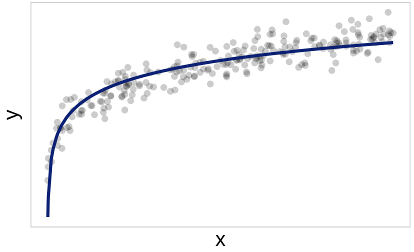
For example:

```
y ~ x + I(x^2)
```

or

```
y ~ log(x)
```





Non-linear Effects: `I()`

The function `I()` is needed to distinguish between operators that need to be interpreted as

- arithmetic operators and
- formula operators

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- arithmetic operators and
- formula operators

Example:

```r
y ~ I(a + b)
```

would be the same as

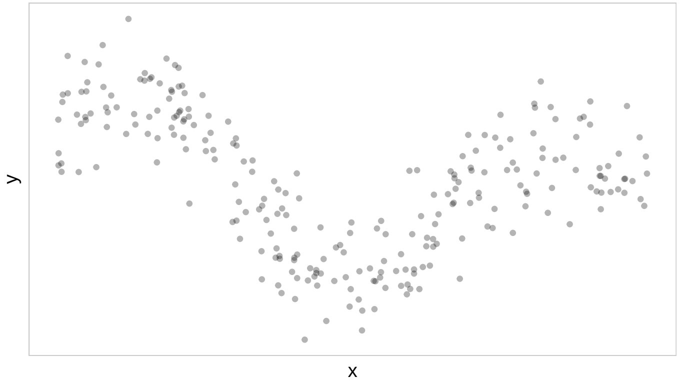
```r
z <- a + b
y ~ z
```

but not the same as

```r
y ~ a + b
```

Complex Non-linear Effects

Non-linear effects may be **more complex** than can be modelled with a simple transformation or polynomial.



Also: the shape may depend on other covariates in the model
➡ we do not always know the shape in advance
➡ **Regression Splines** / **B-Splines**

B-Splines

A **B-Spline** is a linear combination of a set of **basis functions**.

These basis functions are defined so that they are
- a **polynomial functions** inside a given interval, and
- zero outside that interval.

The intervals are defined by a set of **knots**.

The polynomial function have a certain **degree** (i.e., constant, linear, quadratic, ...)

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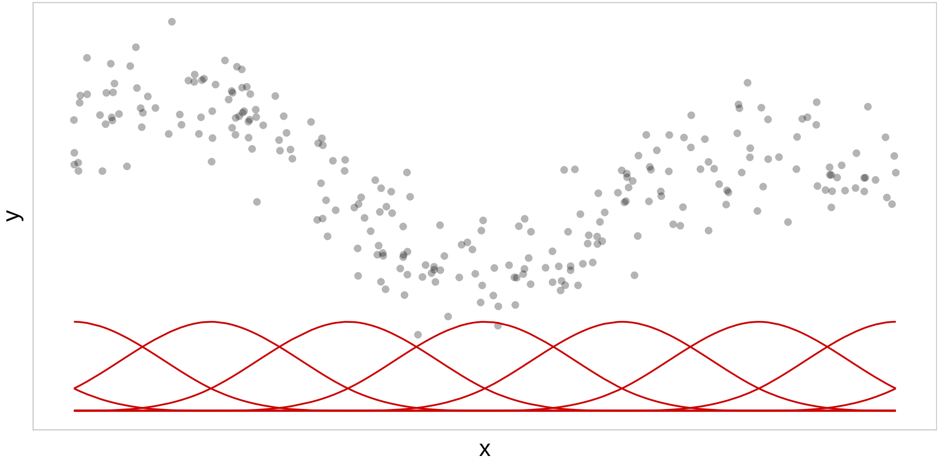
B-Splines in R

The R package **splines** provides the functions

- `bs()`: B-splines
- `ns()`: natural cubic (B-)splines

B-Splines

Instead of $y \sim \beta_0 + \beta_1 x + \ldots$ we assume $y \sim \beta_0 + \sum_{\ell=1}^{d} \beta_\ell B_\ell(x) + \ldots$



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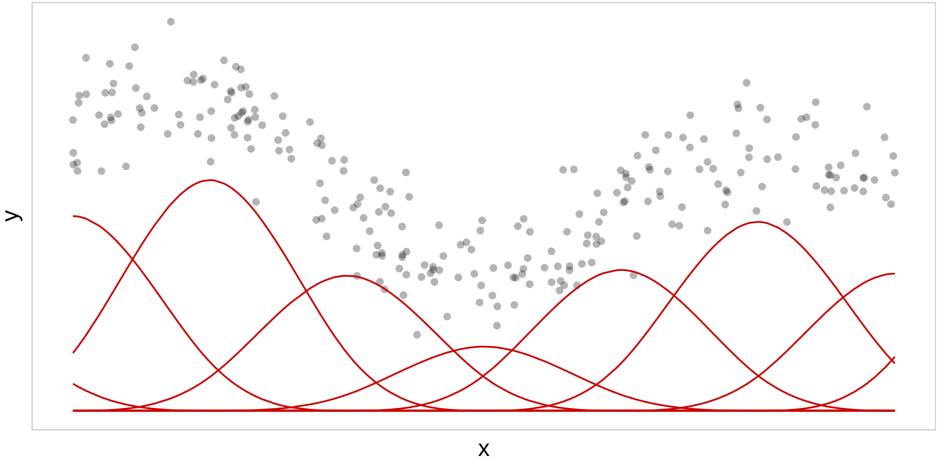

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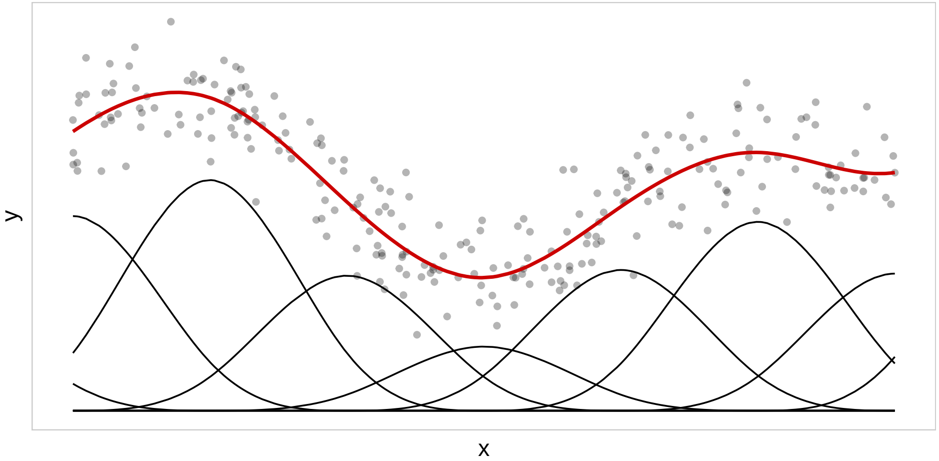
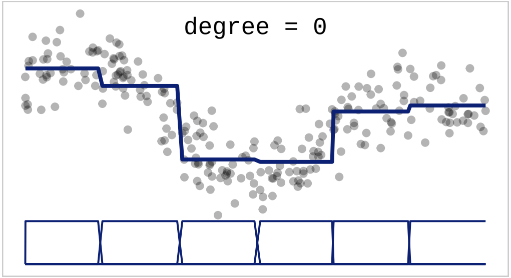
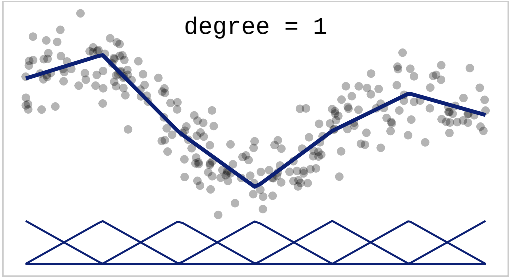
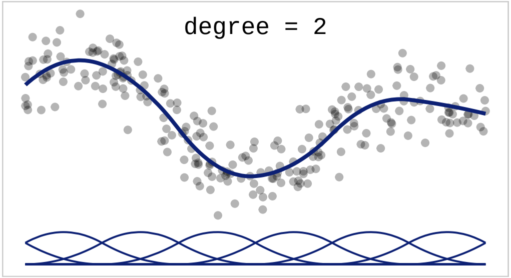
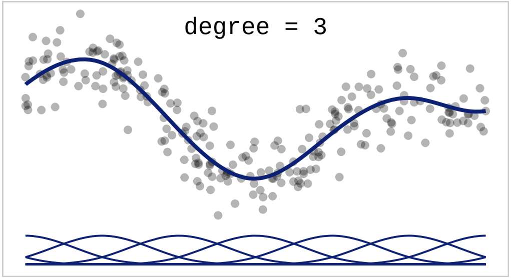


B-Splines: `degree`

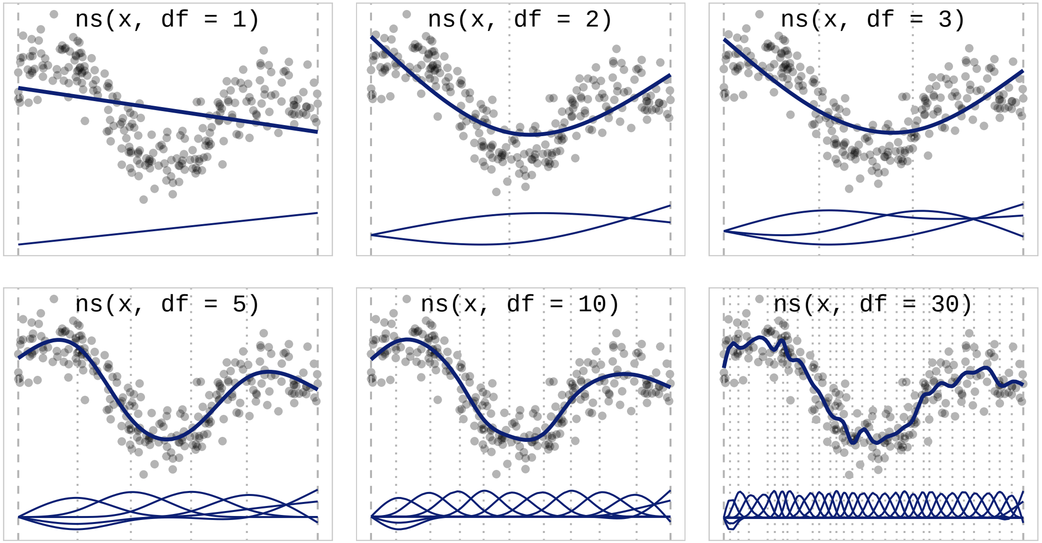








B-Splines: `df`



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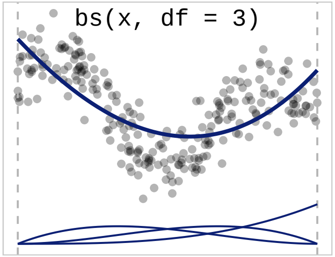

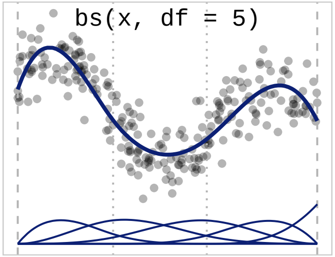

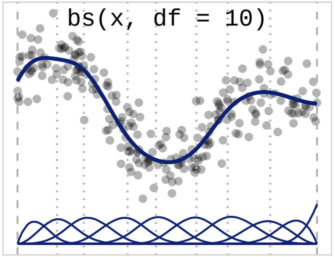

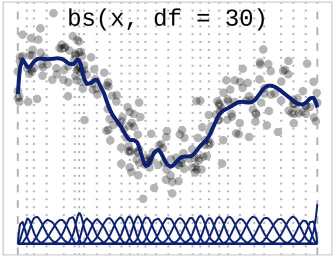

B-Splines in R: `bs()` & `ns()`

Important arguments of `ns()` and `bs()` are:

`degree`

- degree of the polynomial in each of the basis functions
- in `bs()`: default is 3
- in `ns()`: always 3 (“cubic”)

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`knots`

- position of (inner) knots
- if unspecified:
  - `df-degree` knots are used
  - positioned at equally spaced quantiles

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`Boundary.knots`

- by default: `range(x)`
- outside the `Boundary.knots` the fit is extrapolated

Non-linear Effects

Demo

- Splines R html

Practicals

- Logistic Regression & More html
- Logistic Regression II html
- Custom Model Summary Function html

Regression

Regression Models

- `lm()`
- `glm()`

Regression Results

- `summary()`
- `coef()`, `confint()`
- `fitted()`, `residuals()`, `rstandard()`
- `AIC()`, `BIC()`
- `anova()`

Plots

- `plot()`
- `qqnorm()`, `qqline()`, `qqplot()`

Formulas

- Formula operators: `+`, `-`, `*`, `:`, `^`
- `ns()`, `bs()`, `I()`
- `all.vars()`
- `update()`
- `as.formula()`