assigned remotely – by telephone or computer – for a patient confirmed as eligible to participate in the study. Another way is to use a series of numbered envelopes, each containing an allocation – when a patient is eligible for a study, the next envelope in the series is opened to reveal what the allocation is. For this system to work, the envelopes have to be opaque so that doctors can't 'cheat' by holding the envelope up to the light to see the allocation inside.

This approach is recognized today as a key feature of fair tests of treatments. Studies in which random numbers are used to allocate treatments are known as 'randomized trials' (see box in Chapter 3, p26).

Concealing treatment allocation in a trial using telephone randomization.

Ways of using unbiased (random) allocation in treatment comparisons

Random allocation for treatment comparisons can be used in various ways. For example, it can be used to compare different treatments given at different times in random order to the same patient – a so-called 'randomized cross-over trial'. So, to assess whether an inhaled drug could help an individual patient with a persistent, dry cough, a study could be designed to last a few months. During some weeks, chosen randomly, the patient

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would use an inhaler containing a drug; during the other weeks the patient would use an identical-looking inhaler which did not contain the drug. Tailoring the results of research to individual patients in this way is clearly desirable if it can be done. But there are many circumstances in which such crossover studies are simply not possible. For example, different surgical operations cannot be compared in this way, and nor can treatments for 'one-off', acute health problems, such as severe bleeding after a road crash.

Random allocation can also be used to compare different treatments given to different parts of the same patient. So, in a skin disorder such as eczema or psoriasis, affected patches of skin can be selected at random to decide which should be treated with ointment containing a drug, and which with ointment without the active ingredients. Or in treating illness in both eyes, one of the eyes could be selected at random for treatment and comparison made with the untreated eye.

Another use of random allocation is to compare different treatments given to different populations or groups – say, all the people attending each of a number of primary care clinics

	Mon	Tues	Weds	Thurs	Fri
May week 1	A	B	A	B	B
May week 2	A	A	B	B	A
May week 3	B	A	B	A	A
May week 4	B	A	B	B	A
May week 5	A	B	A	B	B

Randomize days within a person

Randomize eyes within a person

Randomize communities within a region

Randomize individuals within a group

Different possible units for random allocation.

or hospitals. These comparisons are known as 'cluster (or group) randomized trials'. For example, to assess the effects of the Mexican universal health insurance programme, researchers matched 74 pairs of healthcare catchment areas – clusters that collectively represented 118,000 households in seven states. Within each matched pair one was allocated at random to the insurance programme.[6]

However by far the most common use of random allocation is its use to decide which patient will receive which treatment.

Following up everyone in treatment comparisons

After taking the trouble to assemble comparison groups to ensure that like will be compared with like, it is important to avoid introducing the bias that would result if the progress of some patients were to be ignored. As far as possible, all the patients allocated to the comparison groups should be followed up and included in the main analysis of the results of the group to which they were allocated, irrespective of which treatment (if any) they actually received. This is called an 'intention-to-treat' analysis. If this is not done, like will no longer be compared with like.

At first sight it may seem illogical to compare groups in which some patients have not received the treatments to which they were assigned, but ignoring this principle can make the tests unfair and the results misleading. For example, patients who have partial blockages of blood vessels supplying the brain and who experience dizzy spells are at above average risk of having a stroke. Researchers conducted a test to find out whether an operation to unclog blood vessels in these patients would reduce subsequent strokes. They rightly compared all the patients allocated to have the operation, irrespective of whether they survived the surgery, with all those allocated not to have it. If they had recorded the frequency of strokes only among patients who survived the immediate effects of the operation, they would have missed the important fact that the surgery itself can cause stroke and death and, other things being equal, the surviving patients in this group will have fewer strokes. That would have been an unfair test of the effects of the operation, the risks of which need to be factored into the assessment.

The outcomes of surgery and medical treatment shown in the