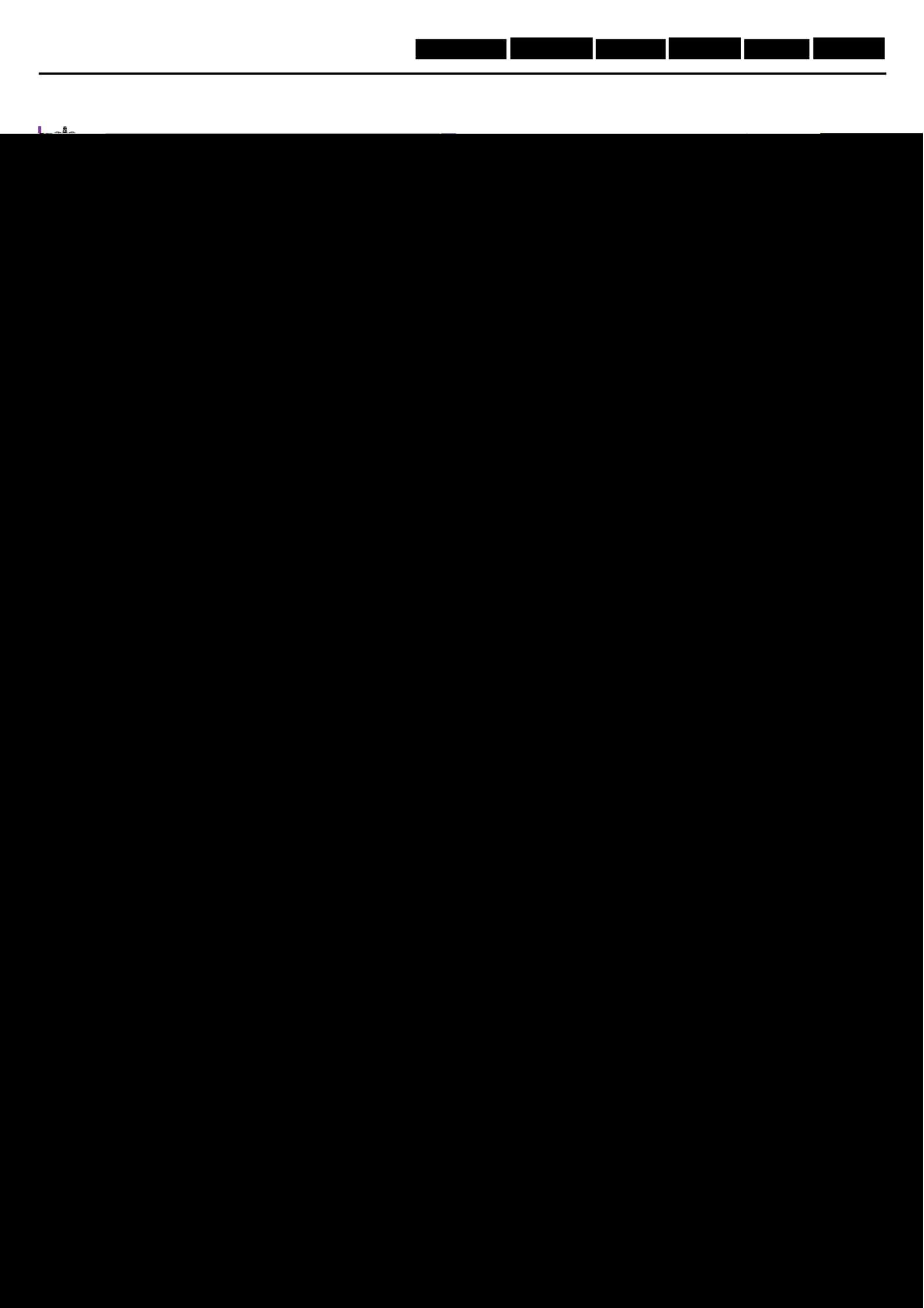

It is likely that changes in connective tissue chemistry impact many disease processes. For example, changes in crosslinking and glycation in the collagen of arterial walls are expected to lead to increased stiffening leading to increased blood pressure, an increased incidence of aneurisms and arterial valve stenosis. With respect to ageing, the stiffening of joints and tendons would also be expected as a consequence of increased collagen crosslinking and glycation. The treatment of aspects of diseases not necessarily liked to ageing, such as lung damage in cystic fibrosis and poor wound healing and tendon ruptures in diabetes may also benefit from this research.

The mice are not expected to exceed a severity of Mild.

use of animals wherever possible. Many of the animals used are to provide fresh aged tissues for study after they have been killed.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?

We typically start experiments with a small number (5 to 10) animals in each group, collect the required data and then collaborate with a statistician to decide if we need to increase the number of animals used. We then collect data from additional animals and add this to the original data set, if appropriate.

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

Where possible we keep the carcasses of the animals that we use so that we can sample tissue from different organs. This helps to minimise animal usage and allows us to build up a picture of changes in the connective tissue across the whole body of individual animals. For example, this potentially will allow us to correlate changes seen in skin with changes in the aorta, tendon or bone.

Where old and young animals are killed by other researches for tissues and the carcasses are unwanted, we often take these and keep the remaining tissues that could be of use in our own experiments.

Refinement

Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.

Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

The mice are allowed to age normally under this project and so they should not experience anything that a normal healthy mouse would not.

Where we require cardiovascular ultrasound measurements the mice will be put under general anaesthesia.

We have limited the time that commercially available genetically modified animals can be kept to minimise the potential for suffering or distress. The genetically modified strains required are extensively used by others and the phenotypes characterised.

Why can't you use animals that are less sentient?