What is already known on this topic

The impact of reduced heroin supply on injecting drug use (where this is the drug of choice) has not previously been determined

What this study adds

Reduced heroin supply is associated with reduced injecting drug use

in heroin supply.[4] Nearly all such infections are related to injecting drug use, and there are no alternative explanations for the decrease in notifications, which was not predicted by mathematical models of the hepatitis C epidemic in Australia.[5] However, the true impact of reduced supply is unlikely to be detectable for some time. Reduction in injecting drug use, as indicated by reduced output in the needle and syringe programmes, would be consistent with reduction in such infections at the population level. We are currently exploring further impacts of the shortage on overdose, treatment, and crime.

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Contributors: CD (guarantor), LD, and WH conceived the study. LD supervised the research. CD led the writing. SG conducted the analysis for the study. All authors helped to conceptualise ideas, interpret findings, and review drafts of the manuscript.

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Competing interests: None declared.

Ethical approval: The study was approved by the University of New South Wales human research ethics committee and the human research ethics committees of the South Eastern Sydney Area Health Service, South Western Area Health Service, and Central Sydney Area Health Service.

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DRUG POINTS

Fatal liver failure associated with pioglitazone

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Thiazolidinediones are peroxisomal proliferator activated receptor γ agonists. Troglitazone is associated with idiosyncratic hepatic reaction, liver failure, and death and is withdrawn.[1 2] The toxicity of troglitazone is unlikely to be a class effect of thiazolidinediones since rosiglitazone and pioglitazone have shown little evidence of hepatic toxicity.[3] Some patients taking pioglitazone, however, have had liver failure, but no deaths are associated with it.[4]

A 63 year old white man with no history of alcohol misuse was admitted to hospital with jaundice after feeling unwell for three weeks. Three months before, doctors changed his gliclazide to pioglitazone. He had also taken lercanidipine for some years and a cephalosporin antibiotic for a few days. Blood investigations found concentrations of 522 µmol/l bilirubin, 472 IU/l alkaline phosphatase, 1053 IU/l aspartate aminotransferase, 1984 IU/l alanine aminotransferase, 455 µmol/l creatinine, and 28 g/l albumin. His prothrombin time was 56 seconds. He developed encephalopathy and acidosis 36 hours after admission and doctors transferred him to intensive care.

He had no stigmata of chronic liver disease, and hepatitis surface antigen, hepatitis A IgM, and hepatitis C antibody were negative. Ultrasound images showed normal parenchymal reflectivity with patent vessels and no biliary dilatation. When stabilised, doctors transferred him to the regional liver unit. He died nine days later.

The histopathology report describes parenchymal damage with steatohepatitis including Mallory bodies superimposed on a severely fibrotic liver. The cause is not certain, but the degree of fibrosis suggests a chronic process, and the type of necroinflammatory activity raises the possibility of alcohol related liver injury. Alternatively the changes could be drug induced damage superimposed on chronic liver disease related to diabetes, and the time scale indicates that pioglitazone is the likely cause.

We know of no previous cases of death associated with pioglitazone, although liver failure has been reported.

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