Title: Low dead space syringes are just one component of an integrated package of care needed to tackle HCV and social exclusion among people who inject drugs

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**Summary:** The provision of low dead space syringes to prevent HIV/HCV transmission among people who inject drugs is insufficient without changing needle syringe programmes to reach the most marginalised and underserved populations. Interventions must be embedded within a broader strategy to tackle social exclusion among people who inject drugs and reduce health and social inequalities.

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It was encouraging to read Hancock et al.'s economic analysis of detachable low dead space syringes (LDSS), which concluded that the syringes are cost saving and lead to additional quality adjusted life years (QALY) in relation to hepatitis C (HCV) transmission and disease progression.[1] This is a useful addition to the growing body of evidence indicating the acceptability of LDSS among people who inject drugs (PWID), although, as Hancock et al. acknowledge, further epidemiological evidence is needed to demonstrate their effectiveness in reducing HCV/HIV acquisition at a population level.[2-4]

While the technological advances offered by LDSS are welcome, they are of limited use on their own. The provision of LDSS needs to occur alongside innovation within needle syringe programmes (NSP) to ensure unrestricted provision of injecting equipment and safe injecting advice reach underserved populations and those disengaged from services. LDSS must therefore be considered part of an integrated approach to alleviate social exclusion and reduce health inequalities faced by PWID.

There is a critical need to avert the growing health crisis faced by PWID in the United Kingdom. The recent increase in HIV infections linked to injecting drug use in Glasgow, concentrated among those who were homeless or injecting cocaine, occurred in the context of on-going provision of NSPs.[5] This illustrates the inadequacy of wider services for those living in precarious circumstances, repeating lessons from Vancouver that showed HIV/HCV epidemics can thrive despite wide availability of NSPs.[6] Hospitalisations for serious bacterial infections and drug-related deaths have been steadily increasing since 2012, in line with cuts to health and social care services that have compounded vulnerabilities among PWID, particularly among the growing homeless population. [7-10] Unstably housed PWID face increased risk of HIV/HCV infection, poor mental health, respiratory diseases, bacterial infections and invasive and infectious diseases.[5,11,12] Hancock et al. employ a QALY measure as is standard within cost-effectiveness analysis in the UK. However, a narrow focus on health outcomes is insufficient when dealing with people experiencing complex interrelated health and social issues as it does not take into account aspects of social exclusion that affect wellbeing.[13] Improving mental and physical health, reducing skin and soft tissue infections, and addressing social welfare needs must be equally prioritised.

For the most marginalised PWID, access to NSP needs to be improved. Women who inject drugs are at increased risk of HIV/HCV acquisition, violence and poorer mental health compared to their male counterparts, but they also face barriers to services related to stigma, concerns about confidentiality, loss of child custody and gendered power imbalances in injecting relationships.[14-16] People who inject crack cocaine are also at increased risk of HIV and HCV acquisition and are less likely to use LDSS.[3,5,12] Services need to adapt to reach these underserved populations, distributing injecting equipment via secondary distribution, through peer-led outreach and in homeless hostels. This is imperative not only to increase provision of LDSS, but to establish contact and facilitate access to housing and other critical social and welfare support services.

Hancock et al. model the impact of replacing high dead space syringes with LDSS distributed via the Bristol Drugs Project. This project is a very atypical service, as it is one of the last remaining fixed-site NSPs in the UK with a harm reduction focus, therefore limiting the generalisability of the study's findings. It is important to work with other providers including pharmacies and mobile outreach to distribute LDSS and provide appropriate training to staff around safe injecting advice.[4,17] Future cost-effectiveness analyses will then need to consider these modalities.

A key factor determining the relative health impact of LDSS is coverage; ensuring that PWID have sufficient supply of sterile equipment for each injection.[18] Recent data illustrate that often three or more attempts are necessary to obtain an injection among PWID.[19] The provision of multiple LDSS for each injection is needed to minimise risk of HCV, HIV, bacterial infections, venous damage and associated transitions to jugular and femoral injections. It is not clear what estimate of coverage is used in Hancock et al.'s analysis, but future analyses may need to revisit NSP coverage calculations to provide more accurate measures of cost-savings. Going forwards, it is essential to work with PWID to ensure that distribution of LDSS occurs through appropriate and diverse outlets with messaging that encourages the transition to LDSS by reflecting PWIDs' priorities, such as emphasising LDSS benefits in reducing drug solution wastage over health benefits.[4] These interventions must be embedded within a broader strategy to tackle social exclusion among PWID in order to halt the increase in deaths and improve the health and social welfare of the most marginalised in the UK.

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