progressing to cirrhosis and of developing hepatocellular carcinoma. Tiredness was increased in individuals homozygous for the Cys282Tyr mutation that could have important repercussions in the workplace setting.

Health economic considerations are vital to decisions regarding screening programmes. An economic analysis of this programme is currently ongoing. If genetic screening is shown to be cost effective, it should be implemented since hereditary haemochromatosis can be prevented by simple measures and, as shown in our study, the risks of such screening are very low and genetic discrimination need not occur.

Contributors

All authors participated in the design, implementation, analysis, and interpretation of the study. M B Delatycki, K J Allen, A E Nisselle, V Collins, and R Williamson participated in all phases of the study. S Metcalfe, M A Aitken, and A A Gason had specific responsibilities for educational aspects of the study. D du Sart, A Wakefield, and A Ritchie were responsible for the design and implementation of the molecular genetic aspects of the study. J Halliday had specific responsibilities in questionnaire design and data analysis and interpretation. I Macciocca and V Hill had specific responsibilities in genetic counselling. A J Nicoll undertook follow-up of homozygous individuals needing liver biopsy. L W Powell provided input to study design and data interpretation. M B Delatycki, K J Allen, A E Nisselle, V Collins, and R Williamson wrote the report with input from all other investigators.

Conflict of interest statement

We declare that we have no conflict of interest.

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Safer injection facility use and syringe sharing in injection drug users

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Safer injection facilities provide medical supervision for illicit drug injections. We aimed to examine factors associated with syringe sharing in a community-recruited cohort of illicit injection drug users in a setting where such a facility had recently opened. Between Dec 1, 2003, and June 1, 2004, of 431 active injection drug users 49 (11·4%, 95% CI 8·5–14·3) reported syringe sharing in the past 6 months. In logistic regression analyses, use of the facility was independently associated with reduced syringe sharing (adjusted odds ratio 0·30, 0·11–0·82, p=0·02) after adjustment for relevant sociodemographic and drug-use characteristics. These findings could help inform discussions about the merits of such facilities.

Vancouver, Canada, like many urban centres, has been the site of continuing HIV and overdose epidemics in illicit injection drug users.[1] In response to these public health problems, health officials in Vancouver opened North America's first medically supervised safer injection facility in September, 2003.[1,2] As previously described,[1] injection drug users in the facility can access sterile injecting equipment, inject preobtained illicit drugs under the supervision of nurses, and access nursing care and addictions counselling. Although such facilities exist in several European settings and in Sydney, Australia, few formal epidemiological analyses have been done of their effects on reported HIV risk behaviours, such as syringe sharing.[1,3,4] In Vancouver, a continuing prospective cohort study of injection drug users allowed us to examine factors associated with syringe sharing in local users after the opening of the safer injection facility.

We obtained data for these analyses from the Vancouver Injection Drug Users Study,[5] a prospective cohort that has been described previously. The study has been approved by the University of British Columbia and Providence Health Care ethics review boards, and all study participants provided written consent before enrolment. To be consistent with earlier analyses,[6] and to provide sufficient statistical power, syringe sharing was defined as borrowing or lending a used syringe in the

past 6 months. Data from participants seen between Dec 1, 2003, and June 1, 2004, were assessed in our study. We used univariate and multivariate statistics to determine factors associated with syringe sharing in the past 6 months. The associations between independent variables and the dependent variable were first analysed by univariate logistic regression. To adjust for potential confounding between use of the safer injection facility and syringe sharing, variables that were found to be significantly associated with syringe sharing ($p<0·05$) were then considered in a fixed logistic regression model, which included all variables that met this criteria as well as the facility use variable. We did all statistical analyses using SAS software version 8.0 (SAS, Cary, NC, USA).

We selected sociodemographic and drug use characteristics in these analyses on the basis of previous investigations of syringe sharing in injection drug users in Vancouver,[6,7] including: age, HIV serostatus, limited access to sterile syringes, need for help with injections, binge drug use, frequency of cocaine and heroin injection, and methadone maintenance treatment. Variable definitions were consistent with previous analyses: individuals who reported using cocaine or heroin once a day or more were defined as frequent cocaine or heroin users.[6] Bingeing was defined as periods in which drugs were used more often than usual.[6] To evaluate the effect of needle exchange programme access on syringe sharing, we compared participants who did and did not report accessing sterile syringes from such a programme. To consider the effect of the safer injection facility, we compared participants who reported undertaking all, most, or some of their injections at the facility with those participants who reported undertaking few or none of their injections at the facility.

431 active injection drug users were seen for follow-up during the study period, of whom 90 (20·9%, 95% CI 17·1–24·7) reported that all, most, or some of their injections were at the safer injection facility. 49 (11·4%, 8·5–14·3) individuals reported sharing syringes during this same period. Univariate analyses showed that need for help with injecting (odds ratio [OR] 2·94, 95% CI 1·59–5·42, p=0·01), bingeing (OR 2·04, 1·05–3·95, p=0·03), frequent heroin (OR 1·72, 0·95–3·13, p=0·07) or cocaine injection (OR 1·70, 0·93–3·06, p=0·08) were positively associated with syringe sharing, whereas younger age (OR 0·95 per year, 0·92–0·99, p=0·01) and use of the safer injection facility (OR 0·39, 0·15–1·03, p=0·05) were negatively associated with syringe sharing. In a logistic regression model, need for help injecting and binge drug use were positively associated with syringe sharing, whereas younger age and use of the facility were independently associated with reduced syringe sharing (table).

	Adjusted odds ratio (95% CI)	p
Age (per year older)	0·95 (0·92–0·98)	0·01
Use of safer injection facility	0·30 (0·11–0·82)	0·02
Need for help injecting	2·95 (1·57–5·55)	0·01
Binge drug use	2·04 (1·02–4·08)	0·04
Intercept (constant)	(–0·79)	0·19

Model adjusted for all variables shown.

Table: **Multivariate logistic regression of factors associated with syringe sharing**

The protective effect of safer injection facility use remained independently associated with reduced syringe sharing when we further adjusted the model to include frequent heroin and cocaine injection (adjusted OR 0·29, 0·11–0·78, p=0·01). Although our logistic models included a small number of syringe sharing events, a goodness of fit test indicated that the estimated models fit the data.

We realised that despite multivariate adjustment, our findings could be due to residual confounding if the safer injection facility had selected injection drug users who were inherently at a lower risk of syringe sharing. To test for this, we examined the rate of syringe sharing for those who did use the facility and those who did not during their follow-up visit immediately before its opening on Sept 22, 2003. Rates of syringe sharing were similar in these populations before the opening (χ^2 0·46, 1 degree of freedom, p=0·50), and the differences only emerged during follow-up after the facility had opened.

We have shown that use of a medically supervised safer injection facility was independently associated with reduced syringe sharing in a community-recruited sample of injection drug users who had similar rates of syringe sharing before the facility's opening. Our study has several limitations. First, although previous studies have indicated that the Vancouver Injection Drug Users Study cohort is representative of local users,[6] it is not a random sample. Second, although it is highly plausible that provision of sterile injecting equipment and medical supervision of injection drug use could be causally related with reduced syringe sharing, our study is limited by its cross-sectional design and hence we caution against inferring such a causal relation. However, our prospective approach showed that differences in the rate of syringe sharing only emerged after the facility opened. It is noteworthy that ethical issues will probably prevent interventional study designs that could completely resolve the issues of selection effects and unmeasured confounding. It should also be noted that we probably underestimated rates of syringe sharing and borrowing because of socially desirable responding, and we were forced to use a combined endpoint of lending and borrowing to obtain adequate statistical power. We have justified this approach previously, and we applied a rigorous approach in our attempts to control for potential confounders.[6] Future prospective analyses with nominal data about recent use

of safer injection facilities are needed to further elucidate the relation between their use and syringe sharing. Our findings could help to inform discussions in the UK and elsewhere, where the potential public-health benefits of such facilities are of growing interest.[1,8]

Contributors

T Kerr and E Wood designed the study. K Li and T Kerr did statistical analyses. T Kerr drafted the report and incorporated all suggestions. J Montaner and M Tyndall contributed to conception and design of the analyses, interpretation of data, and drafting of the report, and all authors approved the version to be published.

Conflict of interest statement

We declare that we have no conflict of interest.

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Reduced intensity conditioning for allograft after cytoreductive autograft in metastatic breast cancer

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The benefits of allografting noted in some malignant diseases might be safely extended to metastatic breast cancer by a combination of cytoreduction with high-dose chemotherapy (HDT) and autologous stem-cell transplant (ASCT) with graft-versus-tumour effect mediated by transplanted donor immune cells with nonmyeloablative allografting (reduced intensity conditioning transplantation, RICT). 17 patients with heavily pretreated disease were given tandem transplants. 13 patients sustained donor engraftment. Three had partial remission after HDT and ASCT and complete remission after RICT; they achieved full chimerism and all developed graft-versus-host disease (GVHD) before regression of cancer. Another patient did not respond to HDT and ASCT but had partial remission after RICT, giving an overall response rate of 24%. Five patients had grade II or higher acute GVHD and five had extensive chronic GVHD. No non-relapse-related deaths occurred during the first 100 days. Five patients (29%) were alive 90–2160 days (median 1320) after RICT. This two-step approach is feasible in patients with metastatic breast cancer.

Few patients with metastatic breast cancer have long-term disease-free survival, since the disease is not curable at this stage. For these patients, high-dose chemotherapy (HDT) and autologous stem-cell transplant (ASCT) is associated with a relatively high response rate, a high rate of recurrence, and very low non-relapse-related mortality (NRM). Data support the existence of a graft-versus-tumour effect after allografting in haematological and nonhaematological cancers.[1] Unfortunately, the morbidity and mortality associated with myeloablative allografting in patients with solid tumours has tempered the enthusiasm for these observations. However, reduced intensity conditioning transplantation (RICT) has renewed interest in allografting for these patients.[2]

We aimed to use HDT and ASCT to achieve maximum tumour reduction in patients before proceeding to RICT. This tactic could provide the benefit of a conventional allograft, but with reductions in the typical acute toxicities and associated mortality of myeloablative therapy.

Between September, 1997, and April, 2004, we enrolled 17 patients with metastatic breast adenocarcinoma (table 1). Median age was 41 years. To be enrolled, patients had to have evaluable disease but not brain metastases. At time of HDT/ASCT, the patients had received a median of 3 (range 2–5) previous chemotherapy lines; 14 patients had received hormone therapy, and seven patients had undergone radiotherapy on bone lesions. The study was approved by the ethics committee of San Martino