Supplementary Material

Drug-Related Deaths in China: an Analysis of a Spontaneous Reporting System

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### Supplementary Table 1. Geographical and time distribution of ICSRs with an outcome of death in the Pan-pearl Platform

| Province   | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | Total (%,
|            |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | n=1731) |
|------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|---------|
| Fujian     | 0    | 0    | 1    | 9    | 4    | 18   | 7    | 7    | 2    | 2    | 2    | 7    | 2    | 6    | 3    | 5    | 0    | 75      | (4.33)  |
| Guangdong  | 0    | 4    | 13   | 13   | 43   | 27   | 27   | 26   | 19   | 17   | 22   | 28   | 45   | 39   | 56   | 39   | 14   | 432     | (24.96) |
| Guanxi     | 0    | 0    | 2    | 2    | 14   | 9    | 23   | 12   | 8    | 8    | 9    | 13   | 19   | 6    | 12   | 16   | 1    | 154     | (8.90)  |
| Guizhou    | 0    | 0    | 1    | 0    | 1    | 5    | 2    | 8    | 2    | 9    | 15   | 6    | 4    | 6    | 7    | 10   | 3    | 79      | (4.56)  |
| Hainan     | 0    | 0    | 1    | 10   | 5    | 2    | 5    | 2    | 3    | 0    | 3    | 4    | 3    | 8    | 3    | 7    |      | 56      | (3.24)  |
| Hebei      | 0    | 0    | 0    | 5    | 5    | 3    | 7    | 1    | 1    | 3    | 6    | 4    | 11   | 2    |      |      |      |        | 48      | (2.77)  |
| Henan      | 0    | 0    | 4    | 5    | 13   | 5    | 1    | 0    | 1    | 2    | 9    | 7    | 8    | 4    | 4    |      |      |        | 63      | (3.64)  |
| Hunan      | 0    | 0    | 11   | 15   | 18   | 20   | 18   | 22   | 22   | 37   | 51   | 53   | 41   | 28   | 25   | 26   | 3    | 390     | (22.53) |
| Jiangxi    | 0    | 0    | 1    | 12   | 10   | 4    | 11   | 5    | 2    | 2    | 10   | 2    | 1    |      |      |      |      |        | 63      | (3.64)  |
| Shaanxi    | 0    | 0    | 0    | 1    | 1    | 5    | 9    | 6    | 15   | 4    | 2    |      |      |      |      |      |      |      | 43      | (2.48)  |
| Sichuan    | 0    | 0    | 6    | 7    | 7    | 9    | 11   | 9    | 10   | 3    | 13   | 17   | 23   | 12   |      |      |      |        | 127     | (7.34)  |
| Yunnan     | 0    | 0    | 0    | 0    | 6    | 18   | 23   | 14   | 7    | 18   | 18   | 32   | 31   | 21   | 13   |      |      |        | 201     | (11.61) |
| Total      | 0    | 4    | 40   | 79   | 127  | 125  | 144  | 112  | 92   | 108  | 160  | 173  | 188  | 132  | 123  | 103  | 21   | 1731    | (100.00)|

ICSRs, Individual Case Safety Reports.
Supplementary Figure 1. Annual numbers of ICSRs reported and the percentage of death ICSRs in 5 provinces with all data available during the whole period.
**Supplementary Table 2.** Detailed information on death ICSRs related to drug use of female reproductive disorders

| Case | Age (years) | Weight (kg) | Suspected drugs | ADR(s) reported (IT) | Primary diseases (ICD-10) \(^a\) |
|------|-------------|-------------|-----------------|----------------------|----------------------------------|
| 1    | 16          | NA          | Estradiol valerate tablet | Hepatic failure, Shock, Acidosis, Respiratory distress syndrome, Encephalopathy | Amenorrhea, unspecified (N91.2) |
| 2    | 23          | 55          | Misoprostol tablet | Anaphylactic shock | Spontaneous abortion: complete or unspecified, without complication (O03.9) |
| 3    | 25          | 65          | Mifepristone tablet | Uterine haemorrhage | Medical abortion: complete or unspecified, without complication (O04.9) |
| 4    | 28          | 50          | Oxytocin injection+ Misoprostol tablet+ Mifepristone tablet | Palpitations, Unconsciousness | Medical abortion: incomplete, without complication (O04.4) |
| 5    | 32          | 65          | Oxytocin injection + Calcium gluconate injection | Embolism pulmonary, Disseminated intravascular coagulation | Single spontaneous delivery, unspecified (O80.9) |
| 6    | 35          | 70          | Oxytocin injection | Anaphylactic shock | Prolonged pregnancy (O48) |
| 7    | 36          | 58          | Baofukang suppository \(^b\) | Fetal death | Infections of the genital tract in pregnancy (O23.5) |
|      |             |             | Oxytocin injection + Vitamin B1 injection + Calcium gluconate injection + Cefazolin sodium pentahydrate injection + Fat-soluble vitamin injection + Water-soluble vitamin injection | Anaphylactic shock | Diseases of the skin and subcutaneous tissue complicating pregnancy, childbirth and the puerperium (O99.7), Other specified noninflammatory disorders of uterus (N85.8) |
| 8    | 38          | 74          | Misoprostol tablet | Anaphylactic shock, Apnoea | Medical abortion: complete or unspecified, without complication (O04.9), Endocrine, nutritional and metabolic diseases complicating pregnancy, childbirth and the puerperium (O99.2) |
| 9    | 39          | 48          | Mifepristone tablet+ Misoprostol tablet | Anaphylactic shock | Medical abortion: complete or unspecified, without complication (O04.9) |

IT, WHO-ART included terms; \(^a\) ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision; NA, No information available; \(^b\) a vaginally administered traditional Chinese medicine made from zedoary turmeric oil and Borneol, others are conventional medicines.
**Supplementary Table 3.** Top 10 most frequently reported ADEs and the suspected drugs

| Code | System Organ Class         | ADEs (PT)                    | No. of records | Suspected drugs (No. of ICSRs)           |
|------|---------------------------|------------------------------|----------------|------------------------------------------|
| 1830 | Immune disorders and infections | Anaphylactic shock          | 763            | Cefoperazone Sodium and Sulbactam Sodium (39), Ceftriaxone Sodium (35), Iopromide (17), Benzylpenicillin (17), Benzathine Benzylpenicillin (14), Cefotaxime sodium (13), Dextran 40 (12), Qingkailing (11)b, Lidocaine Hydrochloride (9), Cefoperazone Sodium (8), Cefuroxime Sodium (8) |
| 1810 | Body as a whole-general disorders | Death                       | 235            | Low Calcium Peritoneal Dialysis Solution (lactate) (35), Ceftriaxone Sodium (9), Iloprost Solution for Inhalation (6), Moxifloxacin Hydrochloride (4), Iopromide (4), Itraconazole (3), Xiangdan (3) b |
| 1100 | Respiratory disorders      | Dyspnoea                     | 111            | Cefoperazone Sodium and Sulbactam sodium (5), Ceftriaxone Sodium (4), Moxifloxacin Hydrochloride (4), Qingkailing (3) b, Ceftazidime (3) |
| 1830 | Immune disorders and infections | Anaphylactoid reaction      | 70             | Ceftriaxone Sodium (3), Benzathine Benzylpenicillin (3), Clindamycin Phosphate (2), Benzylpenicillin Sodium (2), herba houttuyniae (2) |
| 1100 | Respiratory disorders      | Respiratory insufficiency    | 70             | Itraconazole (4) |
| 1000 | Cardiovascular disorders   | Cardiac arrest               | 64             | Iopromide (8), Vinpocetine Sodium Chloride (2), Iohexol Injection(2) |
| 1810 | Body as a whole-general disorders | Sudden death                | 62             | Diclofenac Sodium (3), Cefoperazone Sodium and Sulbactam Sodium (2), Ceftriaxone Sodium (2) |
| 1000 | Cardiovascular disorders   | Cyanosis                     | 39             | Cefoperazone Sodium and Sulbactam Sodium (2), Cefathiamidine (2) |
| 1810 | Body as a whole-general disorders | Chest pain                  | 39             | Cefoperazone Sodium and Sulbactam Sodium (2), Cervus and Cucumis Polypetide (2), Moxifloxacin Hydrochloride and Sodium Chlorid (2) |
| 0400 | Neurological disorders     | Muscle contractions involuntary | 38          | Cefoperazone Sodium and Sulbactam Sodium (2), Iopromide (2), Vinpocetine Sodium Chloride (2), Qingkailing (2) b |

PT, WHO-ART preferred terms; a Dosage form is injection except Iloprost solution for inhalation; b TCM, others are conventional drugs.