Update in Commercial Kidney Transplantation

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Objectives

1. To provide an update on organ trafficking and transplant commercialism to 2016 (since 2014)

2. To describe the short-term and long-term complications of commercial kidney transplantation

3. To emphasize that short-term and long-term complications are not necessarily related
Definitions

- **Organ trafficking**: Recruitment, transport, transfer, harboring or receipt of living/deceased persons or their organs by coercion/deception or through third party payments or benefits to achieve control over donor organs.

- **Transplant commercialism**: Policy or practice in which an organ is treated as a commodity by being bought or sold or used for material gain.

- **Travel for transplantation**: Movement of organs, donors, recipients, or transplant professionals across borders for transplant purposes.

- **Transplant tourism**: Travel for transplantation + Organ trafficking/Transplant commercialism.
Case 1:

- MRSA (wound)
- Aspergillus (wound, blood)
- E. Coli (wound, blood)
- Enterobacter (wound)
- Pseudomonas (blood, wound, lungs)

- Graft survived 3 months (Tx nephrectomy)
- Patient survived 5 months
Case 2: 6 months post-transplantation

Septic shock, disseminated Aspergillus
Died at 6 months (with graft function)
Complications in SMH Recipients 1998-2005

52% opportunistic infections
38% pyelonephritis including multi-drug resistant *E. coli*
23% CMV
19% fungal infections
14% tuberculosis
5% cerebral abscess
5% spinal abscess

25% wound infection
10% allograft nephrectomy
10% wound dehiscence
10% lymphocele
5% obstructive hydronephrosis
5% urine leak
5% metastatic cancer

*Prasad et al, Transplantation 2006*
Three-year Graft Survival

% Graft Survival

Time Post-Transplant (months)

STRATA:  
- Living biologically related - Canada  
- Living emotionally related - Canada  
- Non-biologically related, non-emotionally related

Prasad et al, Transplantation, 2006
Three Year Death-Censored Graft Survival

% Patient Survival

Time Post-Transplant (months)

SIRATA: _____ Living biologically related = Canada _____ Living emotionally related = Canada

_____ Non-biologically related, non-emotionally related

Local biologically- and emotionally related

Non-biologically, non-emotionally related

Prasad et al, Transplantation, 2006
Commercial Kidney Donors in the News
## Donor Outcomes

<table>
<thead>
<tr>
<th>Group (first author)</th>
<th>Year</th>
<th>n</th>
<th>Country</th>
<th>Average amount received</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naqvi [39]</td>
<td>2007</td>
<td>239</td>
<td>Pakistan</td>
<td>USD 1,377</td>
<td>88% of the donors had no economic improvement in their lives and 98% reported deterioration in general health status. Future vending was encouraged by 35% to pay off debts and freedom from bondage.</td>
</tr>
<tr>
<td>Goyal [40]</td>
<td>2002</td>
<td>305</td>
<td>India</td>
<td>USD 1,070</td>
<td>Average family income declined by one-third after nephrectomy. 86% reported deterioration in their health status. 79% would not recommend others to sell a kidney.</td>
</tr>
<tr>
<td>Zargooshi [41]</td>
<td>2001</td>
<td>300</td>
<td>Iran</td>
<td>USD 160</td>
<td>Poverty prevented 79% of vendors from attending follow-up visits, and vending caused negative effects on employment in 63%. 71% had severe de novo postoperative depression and 60% anxiety. Vending caused somewhat (20%) to very (66%) negative financial effects. It also had negative effects on the physical abilities in 60% of vendors who were mainly unskilled laborers, and 80% were dissatisfied with postoperative physical stamina, which was decreased mostly by depression. Of the vendors, 37% concealed the truth about the sale of their kidney from everyone, 14% disclosed it only to spouses, 43% to first-generation relatives and 94% were unwilling to be known as donors.</td>
</tr>
<tr>
<td>Zargooshi [42]</td>
<td>2001</td>
<td>100</td>
<td>Iran</td>
<td>USD 1,219</td>
<td>51% of donors hated the recipients and 82% were unsatisfied with their behavior. Motivations for donating were purely financial in 43% of cases and mainly financial with a minor altruistic component in another 40%. Of the donors, 76% agreed that kidney sale should be banned and if there was another chance they would prefer to beg (39%) or obtain a loan from usurers (60%).</td>
</tr>
</tbody>
</table>
Economic and health consequences of selling a kidney in India (Goyal M et al, JAMA 2002)

Table 1. Participant Characteristics (N = 305)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (Median, Range)</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>35 (35, 20-55)</td>
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<tr>
<td>Female, %</td>
<td>71</td>
</tr>
<tr>
<td>Education, y</td>
<td>2.7 (0, 0-12)</td>
</tr>
<tr>
<td>Annual family income, $</td>
<td>420 (381, 0-1730)</td>
</tr>
<tr>
<td>Income below poverty line, %</td>
<td>71</td>
</tr>
<tr>
<td>Time since nephrectomy</td>
<td>6.0 y (6.4 y, 2 wk-19 y)</td>
</tr>
<tr>
<td>No. of people in household</td>
<td>4.2 (4.0, 1-8)</td>
</tr>
</tbody>
</table>

Table 2. Reasons for Selling a Kidney*

<table>
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<tr>
<th>Reason</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Pay off debts</td>
<td>292 (96)</td>
</tr>
<tr>
<td>Food/household expenses</td>
<td>160 (55)</td>
</tr>
<tr>
<td>Rent</td>
<td>71 (24)</td>
</tr>
<tr>
<td>Marriage expenses</td>
<td>65 (22)</td>
</tr>
<tr>
<td>Medical expenses</td>
<td>54 (18)</td>
</tr>
<tr>
<td>Funeral expenses</td>
<td>23 (8)</td>
</tr>
<tr>
<td>Business expenses</td>
<td>23 (8)</td>
</tr>
<tr>
<td>Other debts</td>
<td>49 (17)</td>
</tr>
<tr>
<td>Future marriage expenses</td>
<td>10 (3)</td>
</tr>
<tr>
<td>for daughters</td>
<td></td>
</tr>
<tr>
<td>Extra cash</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Start business</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Other reason</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

*Percentages do not add up to 100% because some participants had more than 1 reason for selling or more than 1 source of debt.

Table 3. Health Status Before and After Nephrectomy

<table>
<thead>
<tr>
<th>Health Before Nephrectomy</th>
<th>Excellent</th>
<th>Very Good</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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<tbody>
<tr>
<td>Excellent</td>
<td>11</td>
<td>16</td>
<td>15</td>
<td>58</td>
<td>50</td>
</tr>
<tr>
<td>Very good</td>
<td>0</td>
<td>14</td>
<td>16</td>
<td>53</td>
<td>39</td>
</tr>
<tr>
<td>Good</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Fair</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
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<td>0</td>
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</tbody>
</table>
The Declaration of Istanbul

In 2008, a group of leading medical experts from around the world met in Istanbul, Turkey to develop strategies to prevent organ trafficking and transplant tourism.

The group well appreciates the desperation felt by many patients in need of a transplant. It put forth a number of principles and proposals designed to promote both deceased and living donor transplantation around the world in a manner that protects the health and welfare of both recipients and donors while ending exploitation. They developed a policy document called The Declaration of Istanbul.

In 2010, the Declaration of Istanbul Custodian Group (DICG) was formed to promote the principles of the Declaration internationally. The DICG is sponsored by two major international professional organizations, The Transplantation Society (ITS) and the International Society of Nephrology (ISN). More than 80 international professional societies and governmental agencies have endorsed the Declaration of Istanbul.

For more information:
DECLARATION OF ISTANBUL CUSTODIAN GROUP
www.declarationofistanbul.org

Introduction

For many patients with end-stage kidney disease transplantation is the treatment of choice. Transplantation is a sophisticated procedure requiring an experienced team of surgeons and nephrologists in an advanced hospital environment. Kidneys transplants may come from a deceased donor or a living donor.

The availability of a deceased donor kidney and its allocation to you will depend on practices that are specific to your country of residence and are not discussed further here.

A living kidney donor is typically a close blood relative. In some countries a legal or emotional relationship (such as a spouse, partner, or friend) may be acceptable for donation. In each of these cases the act of donation is done willingly as an expression of love, trust, and mutual concern. The donor and recipient each care that the other has a safe and successful outcome. Transplants like this are performed openly and legally, and the outcome is typically excellent for both the recipient and the donor from a medical, psychological, and social point of view.

There is however, another source of living donor kidneys. Some people, in dire financial distress, may be willing to sell one of their kidneys. The buying and selling of kidneys is called "transplant commercialism", and it is illegal in almost all countries of the world. Kidneys taken from executed prisoners are also sometimes sold.

This brochure discusses some of the implications for you in buying a kidney and is meant to discourage you from taking this step even out of desperation.

What exactly is transplant commercialism and tourism?

In transplant commercialism, there is an exchange of money or some other form of significant material benefit between the recipient and the donor, either directly or, more frequently, through a middleman or broker who collects a fee for "services." The donor (really a "kidney seller") also receives money, usually much less than what the broker collects. As a result the amount of money spent by the recipient is more than would be paid for a legal transplant. Most medical insurance does not cover commercial transplantation.

Leaving your country of residence to undergo transplantation is commonly called "transplant tourism." Most transplant professionals disapprove of the practice and are also concerned that the level of care you receive will be inferior to that you will receive in your own country.

Why is transplant commercialism illegal?

- Many countries have laws that specifically ban transplant commercialism.
- Most likely it is illegal in the country where you live.
- Transplant commercialism results in more harm than good.
- It exposes donors and recipients to unnecessary dangers and undermines the healthy development of organ donation in both the home country of the recipient and the country they travel to purchase a kidney.
Policy Statement of Canadian Society of Transplantation and Canadian Society of Nephrology on Organ Trafficking and Transplant Tourism

John S. Gill,1,10 Aviva Goldberg,7 G. V. Ramesh Prasad,3 Marie-Chantal Fortin,4 Tom-Blydt Hansen,2 Adeera Levin,2 Jagbir Gill,1 Marcello Tonelli,5 Lee Anne Tibbles,6 Greg Knoll,7 Edward H. Cole,8 and Timothy Caulfield9

PREAMBLE
The Declaration of Istanbul on Organ Trafficking and Transplant Tourism (1) was developed after a directive from the World Health Assembly in 2004 (resolution 57.18), which urged member states: "to take measures to protect the poorest and vulnerable groups from transplant tourism and the sale of tissues and organs, including attention to the wider problem of international trafficking in human tissues and organs" (2). The Declaration of Istanbul (1) states that organ trafficking and transplant tourism should be prohibited, because they violate the principles of equity, justice, and respect for human dignity. The Declaration (1) aims to combat these activities that threaten the legacy of organ transplantation and the nobility of organ donation and calls for each country to develop a legal and professional framework to govern organ donation and transplantation activities. The Declaration (1) calls for increased oversight of donation and transplant activity in member states to ensure donor and recipient safety and prohibition of unethical practices.

In response to The Declaration (1), members of the Canadian Society of Transplantation and the Canadian Society of Nephrology developed this policy document that will help to establish a unified and consistent approach to deter transplant tourism by Canadian healthcare providers, and in so doing, will ensure the optimal care of Canadian patients with end organ failure. This policy document was produced with guidance of experts in Canadian medical law and bioethics. Where appropriate, the document refers directly to existing documents that are accepted in Canadian medical practice such as the Canadian Medical Association Code of Ethics (3). The document summarizes the official Policy of the Canadian Society of Transplantation and The Canadian Society of Nephrology and is intended to assist members of these professional societies in their interactions with patients. The recommendations provide healthcare professionals with a framework to approach the subject of transplant tourism and organ trafficking with patients. Healthcare providers should be aware of the legal and regulatory requirements that govern medical practice in their jurisdictions.

TARGET AUDIENCE
This document is relevant for Canadian healthcare providers involved in the care of patients who are candidates for solid organ transplantation or recipients of a solid organ transplant. Although kidneys are the most common organ involved in organ trafficking, the trafficking of livers and hearts is also known to occur (4). Therefore, the information in this document is also relevant for healthcare providers involved in the care of any patient with end organ failure.

DEFINITIONS
a. Organ trafficking is the recruitment, transport, transfer, harboring, or receipt of living or deceased persons or their organs by means of the threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability, or of the giving to, or the receiving by, a third party of payments, or benefits to achieve the transfer of control over the potential donor, for the purpose of exploitation by the removal of organs for transplantation (1).
b. Transplant commercialism is a policy or practice in which an organ is treated as a commodity, including being bought or sold or used for material gain (1).
c. Travel for transplantation is the movement of organs, donors, recipients, or transplant professionals across jurisdictional borders for transplantation purposes.
Commercial kidney transplantation is an important risk factor in long-term kidney allograft survival

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1Division of Nephrology, St. Michael’s Hospital, Toronto, Ontario, Canada; and 2Renal Transplant Program, St. Michael’s Hospital, Toronto, Ontario, Canada

Transplant tourism, a form of transplant commercialization, has resulted in serious short-term adverse outcomes that explain reduced short-term kidney allograft survival. However, the nature of longer-term outcomes in commercial kidney transplantation recipients is less clear. To study this further, we identified 69 Canadian commercial transplant recipients of 72 kidney allografts transplanted during 1998 to 2013 who reported to our transplant center for follow-up care. Their outcomes to 8 years post-transplant were compared with 702 domestic living donor and 827 deceased donor transplant recipients during this period using Kaplan-Meier survival plots and multivariate Cox regression analysis. Among many complications, notable specific events included hepatitis B or C seroconversion (7 patients), active hepatitis and/or fulminant hepatic failure (4 patients), pulmonary tuberculosis (2 patients), and a type A dissecting aortic aneurysm. Commercial transplantation was independently associated with significantly reduced death-censored kidney allograft survival (hazard ratio 3.69, 95% confidence interval 1.88–7.25) along with significantly delayed graft function and eGFR 30 ml/min/1.73 m² or less at 3 months post-transplant. Thus, commercial transplantation represents an important risk factor for long-term kidney allograft loss. Concerted arguments and efforts using active recipient outcomes among the main premises are still required in order to eradicate transplant commercialization.


KEYWORDS: ethnicity; graft survival; transplant tourism

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RESULTS

A total of 69 commercial transplant recipients received 72 allografts between 1 January 1998 and 31 December 2013 from various countries in Asia, Africa, Europe, and South America, with 3 patients each receiving a second allograft, corresponding to an average rate of 4 to 5 transplants/year. Among these 69 patients were 20 who received 22 allografts received before 28 February 2005 (3 transplants/year) and whose survival to 3 years post-transplant has been reported previously. After this period, there were 49 recipients who received 50 allografts between 1 March 2005 and 31 December 2013, corresponding to a rate of 5 to 6 transplants/year. During the overall 1998 to 2013 study period, there were correspondingly 827 deceased donor and 702 living donor kidney transplants performed at our center and for which data were available. Thirty-four of 69 commercial transplant
Background

- Transplant tourism and organ trafficking are widely condemned
- Serious adverse outcomes in recipients have been compiled in many reports
- These adverse outcomes are typically early
- Reduced graft survival is attributed to these early events
- As transplant centres gather more experience, these early events may not be seen as often
- This presents a challenge to efforts to combat commercialization
- Nature of longer-term outcomes is less clear
Methods

- Review of St. Michael’s patients 1998-2013
- Follow-up through June 30, 2014
- Canadian citizens or permanent residents (eligible for transplant in Canada) proceeding abroad, transplanted, and returning to Canada for care
- Chart review supplemented by patient interview as needed
- For descriptive purposes two “eras”: 01/01/98-28/02/05 and 01/03/05-31/12/13
- Kaplan-Meier methodology and log-rank test
Results

• 69 patients received 72 allografts during 1998-2013
• Corresponds to 4-5 transplants/year
• Includes 20 patients/22 allografts 1998-2005 (3 transplants/year)
• From 1998-2013, 827 deceased donor and 702 living donor transplants at St. Michael’s
• 34/69 presented for pre-transplant assessment at St. Michael’s
• PRA 8-100%, wait time 3-192 months
• One patient Canadian-born
• Standard immunosuppressive therapy
Transplant Complications 2005-2013

• Hepatitis B seroconversion (2)
• Hepatitis C seroconversion (5)
• Active hepatitis (3)
• Fulminant hepatic failure (1)
• Pulmonary tuberculosis (2)
• ESBL E coli urosepsis (1)
• Abdominal wall hernia (2)
• Type A dissecting aortic aneurysm (1)
• Only one patient required immediate hospitalization compared to 7 in earlier era
Figure 1: Graft Survival (Death Counted as Loss)

Prasad et al, Kidney Int 2016
Figure 2: Graft Survival (Death as Censoring Event)

Prasad et al, Kidney Int 2016
Figure 3: Patient Survival (Graft Loss Censored)

Prasad et al, Kidney Int 2016
Table 3  
Multivariate Cox regression analysis of factors affecting death-censored allograft survival

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate</th>
<th></th>
<th></th>
<th></th>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P-value</td>
<td>Hazard Ratio (95%</td>
<td>Paramater Estimate</td>
<td>Standard Error</td>
<td>Chi-Square</td>
<td>P-value</td>
<td>Hazard Ratio (95%</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Confidence Interval)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Confidence Interval)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>0.09</td>
<td>0.923</td>
<td>(0.839-1.015)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Second or greater transplant</td>
<td>0.55</td>
<td>1.153</td>
<td>(0.719-1.850)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Body mass index (per kg/m²)</td>
<td>0.52</td>
<td>0.992</td>
<td>(0.969-1.016)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Commercial transplant</td>
<td>&lt;0.001</td>
<td>3.356</td>
<td>(1.666-6.760)</td>
<td>1.305</td>
<td>0.344</td>
<td>14.327</td>
<td>&lt;0.001</td>
<td>3.688</td>
<td>(1.876-7.250)</td>
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<tr>
<td>Cause of end-stage renal disease</td>
<td>0.22</td>
<td>1.268</td>
<td>(0.867-1.856)</td>
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<tr>
<td>Ethnicity</td>
<td>0.80</td>
<td>0.968</td>
<td>(0.747-1.254)</td>
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<tr>
<td>Delayed graft function</td>
<td>&lt;0.0001</td>
<td>2.838</td>
<td>(2.075-3.881)</td>
<td>1.038</td>
<td>0.155</td>
<td>44.567</td>
<td>&lt;0.0001</td>
<td>2.826</td>
<td>(2.083-3.834)</td>
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<td>eGFR ≤ 30 ml/min/1.73 m² at 3 months</td>
<td>&lt;0.01</td>
<td>1.789</td>
<td>(1.259-2.543)</td>
<td>0.561</td>
<td>0.178</td>
<td>9.864</td>
<td>&lt;0.01</td>
<td>1.753</td>
<td>(1.253-2.487)</td>
<td></td>
</tr>
</tbody>
</table>

1 Reference group=first transplant
2 Diabetic nephropathy v others
3 Caucasian v others
4 eGFR= estimated glomerular filtration rate
Why Do Commercial Kidney Transplant Patients Fare Poorly?

• Poor donor and recipient health from improper screening
• Substandard clandestine operative environment for the transplant
• Self-selected group may be at higher immunological risk, compounded by poor cross-match techniques
• Inherent recipient characteristics that determined the decision to go abroad in the first place, with subsequent non-adherence
• Immunosuppressive regimens designed for short-term, not long-term benefit
• Lack of transfer information impacting care decisions
New Measures to Combat Transplant Tourism

• Council of Europe Convention against Trafficking in Human Organs (CoEC)
• Supplements the Palermo protocol and the WHO guiding principles by addressing action, means, purpose of human trafficking
• Call on governments to establish as a criminal offense the illegal removal of organs (live or deceased)
• Call on professionals to prevent transplant-related crimes
Conclusions

• Commercial transplant recipients are 4 times more likely to lose their graft or die within 8 years
• Transplant tourism and organ trafficking still exist today!
• Surviving transplant in the short term does not guarantee long-term survival
• Concerted arguments and efforts using adverse recipient outcomes as premises are STILL required in order to eradicate transplant commercialization
# Acknowledgements

<table>
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<tr>
<th>1998-2005 Study</th>
<th>1998-2013 Study</th>
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<td>Jeffrey Zaltzman</td>
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<tr>
<td>Ashutosh Shukla</td>
<td>Sailesh Ananth</td>
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<td>John Honey</td>
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<td>Michelle Nash</td>
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<td>Michael Huang</td>
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