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## Report to California Legislature

### **Title**

Analysis of Assembly Bill 228: Transplantation Services, Human Immunodeficiency Virus

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**CALIFORNIA**  
HEALTH BENEFITS REVIEW PROGRAM

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Analysis of Assembly Bill 228  
Transplantation Services:  
Human Immunodeficiency Virus

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A Report to the 2005-2006 California Legislature  
April 7, 2005

CHBRP 05-02



Established in 2002 to implement the provisions of Assembly Bill 1996 (*California Health and Safety Code*, Section 127660, et seq.), the California Health Benefits Review Program (CHBRP) responds to requests from the State Legislature to provide independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit mandates. The statute defines a health insurance benefit mandate as a requirement that a health insurer and/or managed care health plan (1) permit covered individuals to receive health care treatment or services from a particular type of health care provider; (2) offer or provide coverage for the screening, diagnosis, or treatment of a particular disease or condition; or (3) offer or provide coverage of a particular type of health care treatment or service, or of medical equipment, medical supplies, or drugs used in connection with a health care treatment or service.

A small analytic staff in the University of California's Office of the President supports a task force of faculty from several campuses of the University of California, as well as Loma Linda University, the University of Southern California, and Stanford University, to complete each analysis within a 60-day period, usually before the Legislature begins formal consideration of a mandate bill. A certified, independent actuary helps estimate the financial impacts, and a strict conflict-of-interest policy ensures that the analyses are undertaken without financial or other interests that could bias the results. A National Advisory Council, made up of experts from outside the state of California and designed to provide balanced representation among groups with an interest in health insurance benefit mandates, reviews draft studies to ensure their quality before they are transmitted to the Legislature. Each report summarizes sound scientific evidence relevant to the proposed mandate but does not make recommendations, deferring policy decision making to the Legislature. The State funds this work through a small annual assessment of health plans and insurers in California. All CHBRP reports and information about current requests from the California Legislature are available at CHBRP's Web site, [www.chbrp.org](http://www.chbrp.org).

**A Report to the 2005-2006 California State Legislature**

**Analysis of Assembly Bill 228  
Transplantation Services:  
Human Immunodeficiency Virus**

**April 7, 2005**

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## PREFACE

This report provides an analysis of the medical, financial, and public health impacts of AB 228, a bill to mandate the coverage of transplantation services for an enrollee infected with the human immunodeficiency virus, if the enrollee's physician deems him or her an acceptable candidate for transplant surgery. In response to a request from the California Assembly Committee on Health on February 4, 2005, the California Health Benefits Review Program (CHBRP) undertook this analysis pursuant to the provisions of Assembly Bill 1996 (2002) as chaptered in Section 127660, et seq. of the California Health and Safety Code.

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Jay Ripps, FSA, MAAA, of Milliman recused himself from contributing to this and all other CHBRP analyses, beginning March 1, 2005. His recusal is valid through his duration as acting chief actuary at Blue Shield of California.

CHBRP gratefully acknowledges all of these contributions but assumes full responsibility for all of the report and its contents. Please direct any questions concerning this report to CHBRP:

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## EXECUTIVE SUMMARY

### California Health Benefits Review Program Analysis of Assembly Bill 228

The California Legislature has asked the California Health Benefits Review Program to conduct an evidence-based assessment of the medical, financial, and public health impacts of Assembly Bill (AB) 228: Transplantation Services: Human Immunodeficiency Virus.

AB 228 proposes to address perceived inequities in access to transplantation services. It would prohibit a health plan or insurer from denying coverage for the costs of solid organ or tissue transplantation services on the basis of whether the enrollee is infected with the human immunodeficiency virus (HIV) if the surgeon and attending physician determine that the enrollee is an acceptable transplant candidate. AB 228 would apply to health care services plans licensed by Knox-Keene<sup>1</sup> and to health insurance policies regulated under the California Insurance code<sup>2</sup>.

Insurance coverage is one of four factors identified in CHBRP's analysis as potentially relevant to HIV-positive (HIV+) persons' access to transplantation. The other three factors are:

- The medical effectiveness of transplantation among HIV+ persons compared with other populations;
- The overall availability of organs and tissue for transplantation and the process for allocating them to individuals who need them.
- The willingness and ability of transplant centers provide transplantation services for HIV+ persons.

CHBRP's analysis of the likely medical, financial, and public health impacts of AB 228 reported in this document suggests that each of these latter three factors is more relevant in determining whether a HIV+ person receives needed transplantation services, than health insurance coverage alone. This is because:

- CHBRP found that all 20.4 million persons enrolled in health plans and insurance policies that would be subject to AB 228 currently have coverage for transplantation services.
- Looking at transplant experience to-date, HIV status does not predict medical outcome. HIV+ patients undergoing certain organ transplant surgeries are surviving at rates comparable to those who are HIV-negative (HIV-). Furthermore, they are not experiencing organ rejection at any rates different than those who are HIV-. However, these results are based on (1) a small number of cases, (2) different types of organs and tissues, and (3) only a few years of post-operative experience. Finally, these early cases may not be representative of all HIV+ persons needing transplants since the transplant centers have chosen HIV+ individuals deemed to be "good risk."
- Current national policy states asymptomatic HIV+ persons are eligible to receive an organ or tissue for transplantation. However, the need for solid organs exceeds their availability, thus waiting lists are used to allocate all solid organs.
- The prevailing assumption among most transplant centers is that transplantation is contraindicated for HIV+ persons. Moreover, because of this assumption and because transplant surgeries for this population began relatively recently, few centers have the experience or protocols to perform transplants on this population.

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<sup>1</sup> Health maintenance organizations in California are licensed under the Knox-Keene Health Care Services Plan Act, which is part of the California Health and Safety Code.

<sup>2</sup> AB 228 adds Section 1374.17 to the Health and Safety Code and Section 10123.21 to the Insurance Code relating to health coverage. AB 228 would not apply to specialized health care service plans, such as vision or dental plans.



## I. Medical Effectiveness

There are no randomized controlled trials relevant to the analysis of the effectiveness of the proposed mandate. A review of evidence from observational studies and case reports of organ transplantation in patients with HIV reveals that:

### *Outcomes*

- Advances in highly active antiretroviral therapy (HAART) since 1996 have made transplantation a viable possibility for many HIV+ patients. However, transplantation experience in the HIV+ population is still limited. Long-term outcomes remain unknown.
- Patients with HIV undergoing kidney transplantation have survival rates comparable with survival rates of patients without HIV. Graft survival in HIV+ patients meeting selection criteria is also similar to graft survival in HIV- patients. Although HIV+ kidney transplant patients have higher rates of rejection, this complication can usually be treated and managed without requiring retransplantation.
- In the hepatitis C–negative (HCV–) population, patient and graft survival rates after liver transplantation are similar regardless of HIV status. The available evidence concerning the survival of HIV+ patients with hepatitis C as the cause of liver failure after liver transplantation is mixed. Data from some centers suggest that the survival rates of liver transplant patients infected with both HIV and HCV is comparable. Data from other centers suggest that liver transplant patients with dual infections fare worse. Regardless of HIV status, the shorter post-transplant survival of HCV+ patients has also been documented.
- There are limited data suggesting that remission can be achieved in patients with HIV-related lymphoma who undergo autologous stem cell transplant (ASCT)<sup>3</sup>. Regimen-related toxicity does not appear to be increased when HAART therapy is combined with ASCT. However, patients are at a high risk of liver damage, which can be severe.
- Evidence concerning HIV-related outcome measures among HIV+ transplant recipients includes the following findings:
  - The amount of virus (viral load) remains undetectable after transplantation in many HIV+ patients on HAART<sup>4</sup> therapy.
  - HIV+ patients on HAART therapy maintain satisfactory levels of CD4 cells<sup>5</sup>.

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<sup>3</sup> The term “autologous stem cell transplants” (ASCT) refers to bone marrow stem cells that are collected from a patient and returned to that same patient following high dose chemotherapy. This is in contrast to “allogeneic stem cell transplants,” which refers to bone marrow stem cells that are collected from a healthy donor and given to a patient.

<sup>4</sup> Anti-HIV (also called antiretroviral) medications are used to control the reproduction of the virus and to slow the progression of HIV-related disease. Highly active antiretroviral therapy (HAART) is the recommended treatment for HIV infection. HAART combines three or more anti-HIV (antiretroviral) medications in a daily regimen. Anti-HIV medications do not cure HIV infection, and individuals taking these medications can still transmit HIV to others.

<sup>5</sup> CD4 T-cells (also called helper cells) are a type of white blood cell that leads the attack against infections in the body. These cells become infected with HIV. The lower the count of CD4 cells, the more likely the person will get sick, whereas a high CD4 cell count protects the patient against the risk of opportunistic infections (see footnote 7 below) associated with AIDS.





- Opportunistic infections related to acquired immune deficiency syndrome (AIDS) occasionally appear in transplant patients on HAART therapy, but these infections are usually controlled after adjustments in medications.
- Several investigators have reported rapid progression of human papilloma virus (HPV)-associated anal lesions in HIV+ patients who have undergone transplantation.

### *Caveats*

There are important caveats in interpreting the evidence from the studies reviewed:

- The available studies of organ transplantation in HIV+ patients consist primarily of studies of kidney and liver transplantation, with only rare reports of heart transplantation, multiple organ transplantation, and autologous stem cell transplantation for lymphoma after high-dose chemotherapy.
- Most studies came from institutions that impose strict selection criteria on HIV+ patients before transplantation. Only patients with evidence of a minimum level of immune function (CD4 T-cell<sup>5</sup> counts greater than 100/ml) and undetectable HIV RNA<sup>6</sup> levels were considered for transplantation. The major exceptions were patients with end-stage liver disease who could not tolerate drug therapy because of liver toxicity. Patients who were HIV+ also were required to be free of opportunistic infections<sup>7</sup>.
- Only a few centers in the United States perform solid organ transplantation on HIV+ patients, and they report data in the literature in the form of case reports and case series. As stated above, there are no randomized controlled trials.
- Several of the reports that inform the effectiveness analysis of the proposed mandate are collaborations among transplantation centers performing transplants on HIV+ patients. These transplant centers report their findings as they gain more experience and accumulate more data on both new and old patients. The result is that data on many of the same patients are repeated in multiple papers. In cases in which details of particular patients are provided, the same patient can be identified in different reports with a reasonable degree of certainty. However, there remains some uncertainty regarding the degree of duplicate reporting on HIV+ patients undergoing transplantation.
- The prevailing assumption in most transplant centers is that HIV+ status is a contraindication for transplantation. Those patients who received transplants were carefully selected as being “good risks” and were more likely to be adherent to postoperative treatment regimens. The skill and experience of clinicians in major transplantation centers may also be a contributing factor.

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<sup>6</sup> HIV RNA is the genetic material of the virus that causes HIV and acquired immune deficiency syndrome (AIDS). HAART controls replication of HIV, rendering viral levels undetectable or very low.

<sup>7</sup> HIV kills patients by weakening the body’s ability to fight disease. Infections that are rarely seen in people with normal immune systems are deadly to patients with HIV. People with HIV can get many serious infections called opportunistic infections: opportunistic infections (OI) do not affect patients with intact immune systems. These infections can be deadly in HIV patients, and they require immediate treatment.



## II. Utilization, Cost, and Coverage Impacts

- An analysis using publicly available California hospital claims data from 2001-2002, indicates there were 4,206 transplants performed in the state, including 1,862 bone marrow, 1,062 kidney, 789 liver, 299 heart, 144 lung, 39 simultaneous pancreas and kidney, and 11 pancreas transplants.
- Of these 4,206 transplants, the data record that 11 were performed on HIV+ patients. Because California's has privacy laws designed to prevent the dissemination of HIV status, these estimates likely underreport the true number of transplants performed on HIV+ patients. Other estimates based on conversations with transplant centers and reported below support this hypothesis.
- According to the health plans that responded to CHBRP's survey, all HIV+ members currently have coverage for transplant services. Most transplant centers in California do not accept HIV+ patients, however, because they do not currently have the protocols in place to handle surgeries for HIV+ patients and/or consider HIV status a contraindication for transplantation surgery.
- CHBRP was unable to determine how many, if any, HIV+ patients in California have been denied access to transplants annually. The Department of Managed Health Care reports one case that was reviewed under the Independent Medical Review process for denied coverage of transplant surgery in 2002 but has reported no cases since then. In addition, conversations with the two largest regional transplant networks in California indicate no denial of services on the basis of HIV status as far as they are aware. Conversations with two of the three transplant centers (that have conducted 42 of the 44 transplants have been reported to be conducted on HIV+ patients) also indicate that in recent years, carriers have not been denying coverage for patients deemed to be acceptable candidates. CHBRP therefore estimates that the number of new HIV+ transplant cases will not increase as a result of AB 228.
- All 20,368,000 Californians enrolled in health plans or insurance policies that would be subject to AB 228 currently have coverage for transplants. The mandate will not increase the number of insured individuals with coverage for transplants.

## III. Public Health Impacts

- In California, the two transplant centers that perform organ transplants on an ongoing basis on persons who are HIV+ report that since 2000, they have performed 42 transplants on HIV+ patients. In addition another transplant center is reported to have conducted two kidney transplants on HIV+ patients in the last year. Because the organization that administers the organ allocation process does not keep data on patients' HIV status, it is unknown how many HIV+ Californians are currently on the waiting list for organ transplants.
- AB 228 is not expected to have an impact on community health as defined in AB 1996, the legislation that led to CHBRP's creation. If AB 228 were to become law, the supply of organs (liver and kidney)—both from cadavers and live donors—is not expected to increase; the demand for transplants by HIV+ patients is not expected to increase; the distribution pattern of organ transplants is not expected to shift from HIV- to HIV+ patients; the number of transplant centers in California with transplant protocols for HIV+ patients is not expected to grow rapidly, and available evidence indicates that HIV+ patients are not excluded from insurance coverage for



transplantation.

- Blacks have substantially higher rates of HIV/AIDS and suffer greater morbidity and mortality from HIV compared with Whites. In addition, HIV+ Blacks have higher prevalence rates of end-stage liver disease compared with Whites. Available evidence indicates there would be no increase in the number of organ transplants to HIV+ persons following the mandate. Therefore, although there is evidence of gender and racial disparities with regards to HIV status and related health outcomes, we conclude that AB 228 will have no impact on reducing these disparities.
- Although evidence indicates that organ failure leads to premature death among HIV+ persons, CHBRP concludes that AB 228 would not have an impact on mortality since the bill would not increase the number of organ transplants performed on this population.
- End-stage organ disease is also associated with significant economic loss through lost productivity. However, because available evidence indicates this bill would not increase the number of organ transplants to HIV+ persons, CHBRP concludes that AB 228 will have no impact on these economic losses.



## INTRODUCTION

Assembly Bill (AB) 228 proposes to address perceived inequities in access to transplantation services by mandating that insured patients who are human immunodeficiency virus (HIV) positive (HIV+) and recommended for transplantation by their physicians and surgeons have the same insurance coverage for organ transplantation. AB 228 would mandate that a health care service plan or insurer “not deny coverage that is otherwise available under the plan contract for the costs of solid organ or other tissue transplantation services based upon the enrollee or subscriber being infected with the human immunodeficiency virus, if the enrollee or subscriber is deemed to be an acceptable transplant candidate by his or her attending physician and surgeon and by the physician and surgeon who will perform the transplantation services.”

AB 228 would apply to health care services plans licensed by Knox-Keene<sup>8</sup> and to health insurance policies regulated under the California Insurance code.<sup>9</sup> The bill would impose no new restrictions on health plans’ and insurers’ ability to decide which transplant centers and surgeons may perform covered transplantation services, thus leaving health plans and insurers free to negotiate with these providers over allowed reimbursement rates or to steer patients to designated “centers of excellence” that perform a certain volume of procedures and/or have established a record of good patient outcomes.

Currently, no other states have a similar mandate existing in law. However, over the last few years, there has been activity within various state and federal appeals processes throughout the United States. Appeals have effectively overturned the denials of transplant surgeries for HIV+ patients by the Massachusetts Medicaid managed care organization in 2001, the Pennsylvania’s Medicaid program in 2003, Kaiser Foundation Health Plan of Colorado in 2003, and the U.S. Department of Veteran’s Affairs in Iowa in 2004. In 2002, the California Department of Managed Health Care (DMHC) Independent Medical Review (IMR) program decided in favor of a HIV+ member who was denied transplant surgery based on an external review of the case by independent experts. Since 2002, however, the DMHC have received no appeals regarding denied transplantation services for HIV+ enrollees.

### *Demand, Supply, and the Organ Allocation Process*

Organs for transplantation are in high demand, but the supply is relatively scarce. As of 2004, 6,207 people died without transplantation nationally with 87,751 people currently remaining on the waiting lists for cadaver organs.<sup>10</sup> The following table provides a breakdown of the California waiting list by organ and waiting time. The number of the candidates on the waiting list who are HIV+ is not known because the United Network for Organ Sharing (UNOS) does not currently maintain that data.

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<sup>8</sup> Health maintenance organizations in California are licensed under the Knox-Keene Health Care Services Plan Act, which is part of the California Health and Safety Code.

<sup>9</sup> AB 228 adds Section 1374.17 to the Health and Safety Code and Section 10123.21 to the Insurance Code relating to health coverage. AB 228 would not apply to specialized health care service plans, such as vision or dental plans.

<sup>10</sup> Organ Procurement and Transplantation Network (OPTN) data, Reasons for Removal from Waiting List by Year, January 1995-December 31, 2004. see <http://www.optn.org>



## Organ by Waiting Time, California, as of March 20, 2005

	All Organs	Kidney	Liver	Pancreas	Kidney / Pancreas	Heart	Lung	Heart / Lung	Intestine
All Time	18,536	13,576	3,838	149	475	427	381	19	19
< 30 Days	623	475	88	11	28	15	17	1	1
30 to < 90 Days	1,596	1,342	171	6	35	25	31	2	4
90 Days to < 6 Months	1,993	1,624	269	22	45	28	40	1	7
6 Months to < 1 Year	2,868	2,242	462	29	117	26	53	3	0
1 Year to < 2 Years	3,976	3,090	669	33	131	58	58	3	4
2 Years to < 3 Years	2,900	2,225	503	19	72	49	58	4	2
3 Years to < 5 Years	3,527	2,534	810	26	37	74	64	1	0
5 or More Years	2,499	1,375	905	3	14	152	64	4	1

Source: <http://www.optn.org>, analysis conducted March 22, 2005

Note: "All Organs" may not be equal to the totals since a person may be on multiple waiting lists

When a person is deemed a candidate for transplant surgery, his or her care is coordinated with a transplant center in the person's region. The transplant center would then place the person on a national waiting list. The person's medical profile is maintained in the Organ Procurement and Transplantation Network (OPTN) data system which is administered by UNOS.<sup>11</sup> When a donor becomes available, the OPTN system compares the candidates on the list and ranks them by specific medical criteria. People on the regional waiting list will have first priority and the organ will become available outside the region if there is no match.

According to the California Transplant Donor Network (which covers Northern and Central California, and the Reno/Tahoe area of Northern Nevada), several factors can influence the match of an available organ to the person on the waiting list—including "tissue match, blood type, severity of medical condition and the immune status." Immune status, in this case means whether the existing reactive antigens in the donor and recipients blood would generate an acute rejection of the organ. Immune status for the purpose of matching does not include a CD4 T-cell count. If a person has a relative who presents as a live organ or tissue donor, the person will bypass the waiting list. If a person is uninsured, it is likely that a transplant center would not place him or her on the waiting list.

### *Transplant Centers: Perceptions and Protocols*

People who are HIV+ have traditionally been considered poor transplant candidates because use of scarce organs could not be justified given the high death rate from acquired immune deficiency syndrome (AIDS). In addition, it was feared that post-transplant immunosuppression might accelerate progression of HIV-related diseases. In 1997, approximately 88% of U.S. renal transplant centers stated they would not conduct a kidney transplant for a HIV+ patient who was otherwise a good candidate for surgery (Spital, 1998).

HIV+ patients are surviving longer due to effective antiretroviral therapy, specifically, highly active antiretroviral therapy (HAART). The UNOS policy that was adopted in 1992 states, "A potential

<sup>11</sup> OPTN is the unified transplant network established by the United States Congress under the National Organ Transplant Act (NOTA) of 1984. The act called for the network to be operated by a private, nonprofit organization under federal contract. UNOS administers the OPTN under contract with the Health Resources and Services Administration of the U.S. Department of Health and Human Services.



candidate for organ transplantation whose test for HIV-Ab [HIV antibodies] is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation” (UNOS, 1992).

In 1999, five transplants for HIV+ patients were reported to UNOS and 11 were reported in 2000. According to claims data available to CHBRP, in the 2001 and 2002 calendar years, 4,206 transplants were performed in California, of which 11 were HIV+ patients. These figures likely underreport the number because of privacy laws in several states, including California, designed to prevent the dissemination of individuals’ HIV status. Data gathered by CHBRP directly from transplant centers in the state that serve HIV+ persons and reported elsewhere in this document support the hypothesis that CHBRP’s estimate of 11 transplants in HIV+ persons in 2000 is too low. The limitations imposed by state privacy laws also means that UNOS data on transplants among patients with HIV is likely to be incomplete.

Discussions with the California regional transplant networks and three high-volume transplant centers<sup>12</sup> in California reveal that only the University of California, San Francisco (UCSF) Medical Center currently conducts transplants for HIV+ patients on an ongoing basis. Cedars-Sinai Medical Center in Los Angeles has begun to conduct such transplants as part of their participation in a solid organ transplant clinical trial sponsored by UCSF and supported by the National Institute of Allergy and Infectious Disease (NIAID); three have been performed at that institution already.<sup>13</sup> Based on conversations with transplant experts, transplant centers in California are not conducting such surgeries because they have not yet developed protocols. Developing such a protocol entails appropriate training for multidisciplinary surgery teams whose level of exposure when conducting surgery would be different than for surgeries on patients without infectious diseases. Currently, these centers still consider HIV+ status a contraindication for transplant.

### *Health Plans and Insurer’s Coverage*

Nationally, health insurer’s coverage behavior has varied. The Empire Blue Cross and Blue Shield of the Greater New York area adopted a policy in 2002 to cover transplantation surgery for HIV+ patients, as long as they were considered appropriate candidates for transplant surgery by their physician (EBCBS, 2002). However, as recently as February, 2005, Horizon Blue Cross and Blue Shield is reported to have denied coverage for a Baltimore patient who was accepted to be on the University of Pittsburg Medical Center’s transplant waiting list. The plan administrator denied the request, stating that “liver transplantation in HIV+ patients remains investigational at this time.”<sup>14</sup>

CHBRP surveyed the seven major health plans in California, of which five responded. The responding plans stated that their members currently have coverage for transplant services regardless of HIV status. Responding health plans acknowledge that up until a few years ago, transplantation for HIV+ patients would have been considered experimental or investigational and thus denied as a general exclusion under

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<sup>12</sup> Personal communications with Ronald W. Busuttill, MD, PhD, Chief of the Division of Liver and Pancreas Transplantation Surgery at the Dumont-UCLA Transplant Center 14 March 2005, Fred Poordad, MD, Chief, Hepatology, the Center for Liver Disease and Transplantation, 30 March 2005; Michelle Roland, MD, Assistant Professor of Clinical Medicine, UCSF AIDS Program, San Francisco General Hospital, 17 March 2005; Laurie Carlson, RN, Clinical Study Coordinator, Transplant Service UCSF, 1 April 2005; Phyllis Weber, Executive Director, California Transplant Donor Network, 25 March 2005; and Tom Moan, Executive Director, One Legacy, 22 March 2005.

<sup>13</sup> Seventeen centers nationally are participating in this clinical trail; two from California. More information can be obtained at <http://clinicaltrials.gov/ct/gui/show/NCT00074386?order=1>

<sup>14</sup> Source: <http://www.lambdalegal.org/cgi-bin/iowa/news/press.html?record=1649>, accessed March 25, 2005



the terms of the policy. However, they state current coverage policy does not discriminate on the basis of HIV status. Health plans responded that they either incorporate the protocol established by the transplant center(s) they use or defer decision making to those centers. Most transplant centers in California do not accept HIV+ patients, however, because they do not currently have the protocols in place to handle surgeries for HIV+ patients and/or consider HIV status a contraindication for transplantation surgery. As mentioned, the DMHC reports one case that came under IMR in 2002 but has reported no cases since then. In addition, conversations with the two largest regional transplant networks in California indicate no denial of services on the basis of HIV status as far as they are aware. Conversations with two of the three transplant centers (that have conducted most of the surgeries to be performed on HIV+ patients) also indicate that in recent years, carriers have not been denying coverage for patients deemed to be acceptable candidates. From this it appears that the health plans outside of California may be denying coverage for transplants based on HIV status when the enrollee has been designated an appropriate candidate for transplant surgery, but this does not appear to be the case in California. For an insured HIV+ patient deemed an appropriate candidate for transplant surgery, the barrier to transplantation is more likely to be a combination of the limited supply of organs and the number of transplant centers currently equipped to conduct such surgeries in California.

## I. MEDICAL EFFECTIVENESS

As previously mentioned, patients who are HIV+ have traditionally been considered poor transplant candidates because use of scarce organs could not be justified given the high death rate from AIDS. In addition, it was feared that post-transplant immunosuppression might accelerate progression of HIV-related diseases. However, HIV+ patients are surviving longer in this era of effective antiretroviral therapy, specifically, HAART. Nevertheless, such patients are at increased risk of end-stage kidney and liver disease as a result of HIV, its treatments, and other health conditions and, thus, could become candidates for transplantation.

The outcomes of transplantation of organs in HIV+ patients, as well as other outcome indicators, that are relevant to the proposed mandate include:

- Patient survival
  - Death rate
  - Median survival rate
  - Overall survival rate
  
- Graft survival
  - Pathologic evidence of rejection
    - Biopsy of liver, heart (endocardium), kidney, etc
    - Laboratory tests reflecting acute or chronic rejection (i.e., elevated liver function tests, leukocytosis,<sup>15</sup> elevated blood urea nitrogen (BUN),<sup>16</sup> and creatinine<sup>17</sup>)
  
  - Functional status

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<sup>15</sup> Leukocytosis refers to an increase in the total number of white blood cells (WBCs) from any cause.

<sup>16</sup> Blood urea nitrogen (BUN) is a waste product usually excreted by the kidneys. BUN values can rise when your kidneys are not working properly or when you are dehydrated.

<sup>17</sup> Creatinine is a protein produced by muscle and released into the blood. The amount produced is relatively stable in a given person. The creatinine level in the serum is therefore determined by the rate it is being removed, which is roughly a measure of kidney function.



Graft failure (infection, thrombosis, leaks, bleeding)  
Oxygenation (PO<sub>2</sub>) levels, functional capacity (forced vital capacity) in lung transplant patients  
Blood urea nitrogen (BUN) and creatinine levels in kidney patients  
Diabetic control (blood glucose and hemoglobin A<sub>1c</sub> [HbA<sub>1c</sub>]<sup>18</sup> levels in pancreatic transplant patients)  
Patient-based assessments of functional status and quality of life (e.g., SF-36<sup>19</sup> measures)

The published literature on transplantation in HIV+ patients focuses mostly on kidney and liver transplants. There was one case report each of cardiac transplantation and combined kidney-pancreas transplantation in HIV+ patients. There were no available studies or patient reports on lung or other solid organ transplantation, or corneal transplants in the HIV+ patient. There was one report reporting successful outcomes with autologous stem cell transplantation in patients with HIV-associated lymphomas after high-dose chemotherapy.

The outcomes reported in the literature include patient death and survival rates, graft survival rates, hepatitis recurrence rates in patients undergoing liver transplants, and outcomes indicative of adequacy of control of HIV, such as CD4 levels, viral load, and incidence of opportunistic infections. The authors of the papers generally did not report information on the functional status outcomes mentioned above.

The literature search for the present analysis was conducted through PubMed and the Cochrane Library for literature published during the period from 1996 through the present. A description of the methods used to conduct the medical effectiveness review and the process used to “grade” the evidence for each outcome measure can be found in Appendix A: Literature Review Methods. Summary tables with detailed findings and evidence from the literature can be found in Appendix B: Summary of Findings on Medical Effectiveness.

## **Kidney Transplantation in HIV+ Patients**

### Patient survival rates in HIV+ patients undergoing kidney transplantation

End-stage kidney disease patients who are HIV+ and well controlled on HAART regimens and who undergo kidney transplantation have survival rates similar to those of HIV negative (HIV-) kidney transplant recipients. Using United States Renal Data System (USRDS) data from 2002, Abbott et al. (2004) found that the risk of death was slightly lower for HIV+ patients than for HIV- patients. The survival rate of HIV+ patients was greater than 95% over three years in contrast to the survival rate of 87% for patients overall, but this difference was not statistically significant. Other authors also found nonsignificant differences in survival rates of their patient populations in comparison with HIV- patients from UNOS. Although Stock et al. (2003) did not present data from a comparison group, 10 of 10 HIV + kidney transplant patients presented in the paper survived at least until publication.

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<sup>18</sup> HbA<sub>1c</sub> is a test that measures the amount of glycosylated hemoglobin in your blood. The test gives a good estimate of how well diabetes is being managed over time. It measures the number of glucose molecules attached to hemoglobin, a substance in red blood cells.

<sup>19</sup> The SF-36 is a “short form” general health survey.





*In summary, based on the available published studies, the prognosis for survival after kidney transplantation in HIV+ patients was at least as good as survival in patients without HIV.*

### Graft survival rates in HIV+ kidney transplant patients

Findings from the studies reviewed show that graft survival in HIV+ kidney transplant patients meeting selection criteria is similar to that of HIV- patients. In the paper by Abbott et al. (2004), 46 of 47 grafts in HIV+ patients were intact. The percentage for HIV+ patients (97.9 %) compares favorably with the percentage of surviving grafts in the general kidney transplant patient population regardless of HIV status (93.2%). Other authors also report similarly high graft survival rates, but concede that their reports are based on small numbers (Roland and Stock, 2003; Stock et al., 2003).

*The evidence suggests that kidney graft survival does not differ between kidney transplant recipients who are HIV+ and those who are HIV-, when HIV+ recipients are well controlled with HAART.*

### Kidney rejection rates in HIV+ patients

The evidence on kidney rejection rates in HIV+ patients is mixed in the available studies that were reviewed. Abbott et al. (2004) found that the rejection rates in HIV+ patients compared favorably with the overall population of patients undergoing cadaver kidney transplantation. Roland and Stock in their various papers (Roland et al., 2003; Roland and Stock, 2003; Stock et al., 2003; Stock et al., 2001) all report elevated rates of rejection episodes, which are usually treated without loss of the graft. Stock et al. (2003) reported that the rejection rate seen in HIV+ patients is at least twice the rate seen in HIV- patients.

*In summary, the evidence is mixed concerning the rate of rejection in HIV+ patients undergoing kidney transplantation. However, rejection in most of these patients can be treated so that they do not lose their grafts.*

## **Liver Transplantation in HIV+ Patients**

### Patient survival rates in HIV+ patients undergoing liver transplantation

Patients who are HIV+ are at increased risk of being positive for hepatitis B (HBV+) and hepatitis C (HCV+). They are consequently at increased risk for end-stage liver disease due to hepatitis infections in comparison with the general population. Norris and colleagues (2004) reported on the results in patients from their transplant unit at King's College Hospital in London and found that seven of seven HIV+/HCV- (five patients were HBV+) liver transplant patients had survived, with follow-up ranging between 668 and 2,661 days. They conclude that HIV+ patients who are HCV- (and some who are HBV+) have survival rates similar to that of their HIV-/HCV- patients. Ragni et al. (2003) similarly report that nine of nine of their HIV+/HCV- patients were alive at the time of publication (between one and three years post-transplant). The only deceased patient in their study who did not have HCV-related liver disease died of recurrent thrombosis of the hepatic artery and septicemia.

These findings are in contrast to the situation with patients who are positive for both HIV and HCV. Although Neff et al. (2003) report favorable findings for HIV+ patients undergoing liver transplantation



regardless of HCV status (14/16 patients survived with one death in an HCV+ patient and one in an HCV- patient), several studies suggest that survival is significantly poorer among HIV+ patients with end-stage liver disease caused by HCV. In a study by Ragni et al. (2003), 15 HCV+ patients had approximately a 50% survival in comparison with a 100% survival in patients without HCV co-infection. However, it should be noted that even in the HIV- population, survival after liver transplantation is better for HBV+ patients than it is for HCV+ patients.

The other studies reviewed included even smaller numbers of patients, and it was difficult to draw conclusions from these studies about the effect of HCV status on mortality. Moreno et al. (2005) reported on four liver transplant patients with a median follow-up of 510 days. All of the patients had HCV-related liver disease, and one succumbed to fibrosing cholestatic hepatitis, a complication of HCV+ hepatitis, at 17 months.

Survival rates also vary widely in the reported studies, a result of either small numbers of patients in each study or different practices at different transplant centers. For example, Radecke et al. (2005) report a 40% survival rate for five HIV+ patients, four of whom had HCV-related liver disease.

*In summary, survival among HIV+/HCV- liver transplant recipients in most transplant centers reporting in the literature is comparable to that of HIV-/HCV- transplant recipients. However, HIV+ patients who are also HCV+ appear to have poorer outcomes than their counterparts who are not HIV+, but this finding is not consistent across all studies.*

#### Graft survival rates in HIV+ liver transplant patients

HIV+ patients who are HCV- have graft survival rates similar to those of HIV-/HCV- patients in the studies reviewed, but most investigators report that HIV+/HCV+ patients fare more poorly. Norris et al. (2004) report 100% and 33% graft survival rates for seven HIV+/HCV- patients and six HIV+/HCV+ patients, respectively. In contrast, Neff et al. (2003) reported that liver graft survival in 14 of 16 HIV+ patients (87.5%) compared favorably with graft survival in non-HIV+ populations (comparison data were not provided by the authors). However, most papers either do not include a comparison group or report lower graft survival for HIV+/HCV+ patients in comparison with HIV-/HCV- or HIV-/HCV+ patients.

*In summary, the evidence suggests that graft survival in HIV+/HCV- liver transplantation is comparable to liver graft survival in HIV-/HCV- patients, with the caveat that there is some evidence consistent with the conclusion that graft survival may be poorer in HIV+/HCV+ patients than in those who are HIV-/HCV- or HIV-/HCV+.*

#### Liver graft rejection rates in HIV+ patients

The liver graft rejection rates in the studies reviewed varied from 0% (four patients in the study by Stock et al., 2003) to 35.7% in the study by Norris et al. (2004). However, in the study by Norris et al. (2004), graft function was normal at the time of publication in all surviving patients. Neff et al. (2003) reported that in all survivors, transplantation reversed the symptoms of acute and chronic liver failure. Roland et al. (2003) reported that abnormal liver function tests normalized with changes in medications in patients experiencing graft rejection. Comparison group data were not presented in most of the studies, making it difficult to compare liver graft rejection in HIV+ and HIV- patient populations.



## Recurrence of hepatitis C

Norris et al. (2004) reported that HCV recurrence is a major problem among all HCV+ patients undergoing liver transplantation, regardless of HIV status. Six of seven HIV+ patients with HCV+ liver disease experienced recurrence of HCV. HIV+ patients also experience a more accelerated return of HCV disease. Moreno et al. (2005) reported a 75% recurrence (3 of 4 patients).

*In summary, recurrence of HCV is a major problem, not only in HIV+ patients undergoing transplantation, but also in their HIV- counterparts.*

## **Cardiac Transplantation in an HIV+ Patient**

### Patient survival rate for HIV+ patient with cardiac transplantation

The literature review yielded only one paper (Calabrese et al., 2003) concerning cardiac transplantation in HIV+ populations. The paper describes one patient who is HIV+ and surviving at least 24 months until the time of publication with a high quality of life despite episodes of rejection.

### Cardiac graft survival rate

Calabrese et al. (2003) report only one patient with an intact cardiac graft. The patient has a high quality of life, but has suffered from numerous episodes of rejection that have responded to therapy.

## **Kidney-Pancreas Transplant in an HIV+ Patient**

### Patient survival rate for HIV+ patient undergoing kidney-pancreas transplant

The literature contains only one report, by Toso et al. (2003), of a patient undergoing a successful kidney-pancreas transplant. However, this was not a typical HIV+ patient, but a “long term non-progressor” who is not in need of HAART. The evidence is insufficient to draw conclusions.

### Kidney-pancreas graft survival rate/graft rejection rate

Toso et al. (2003) reported on one HIV+ patient with a surviving kidney-pancreas graft. With information on only one patient, the evidence for survival of a kidney-pancreas transplant graft is inconclusive. This patient had not experienced rejection at the time of publication.

## **Autologous Stem Cell Transplantation (ASCT) for HIV-Associated Lymphoma**

### Patient survival following high-dose chemotherapy with ASCT

One series of 19 patients reported good outcomes for high-dose chemotherapy (HDC)/ASCT for patients in this study with HIV-related lymphomas if treated early in the course of disease (Krishnan et al., 2003) and maintained on HAART. In the study by Krishnan et al. (2003), the survival rate was 16/19 (84%) with follow-up from 6-57.5 months. All patients experienced hepatotoxicity, mostly mild. However, 3/19 (16%) experienced grade 3-4 hepatotoxicity.



## **HIV Viral Loads in Surviving HIV+ Patients Maintained with HAART Post-transplantation**

A major concern has been that immunosuppressive treatment to suppress organ rejection in HIV+ transplant recipients would lead to increased viral replication with progression to clinical AIDS with opportunistic infections. The review of the literature suggests that post-transplant HIV+ patients who are closely monitored can maintain low or undetectable viral loads on a combination of HAART and other medications necessary to prevent rejection of the graft. Most of the studies reported, however, include small numbers of patients. Neff et al. (2003) reported that 14 of 15 patients (not including a patient who succumbed very quickly) showed undetectable levels of HIV. Moreno et al. (2005) reported undetectable viral loads in three of four patients. One patient experienced a rebound of viremia prior to death when HAART was discontinued. Similarly, Radecke et al. (2005) reported that the two surviving patients had undetectable viral loads. The viral loads in the three deceased patients were low until HAART had to be discontinued due to medical complications.

*In summary, studies have shown that post-transplant HIV+ patients on medications to prevent rejection of the new graft can also tolerate treatment with HAART to keep viral load low, provided drug dosages are carefully monitored.*

## **Impact of Transplantation on CD4 T-cell Counts in HIV+ Patients**

In the immediate post-transplant period, laboratory tests show that many patients have transient decreases in their CD4 T-cell counts, which temporarily predisposes them to infection. In general, as reported by Neff et al., 2003, Norris et al. (2004), and Roland et al. (2003), after the initial post-transplant period, most patients on HAART are able to maintain cell counts above 200, which is adequate to avoid the opportunistic infections that define AIDS.

## **AIDS-defining Opportunistic Infections in Transplant Patients**

Findings from studies reviewed show that opportunistic infections are not a major problem in transplant patients under treatment with both HAART and standard antirejection drugs. Moreno et al. (2005), Radecke et al. (2005), and Nowak et al. (2003) reported that none of their patients suffered from opportunistic infections. Other researchers found an occasional case of cytomegalovirus (CMV) (Neff et al., 2003) or candida esophagitis (Roland and Stock, 2003) that resolved after adjustments in the medication.

## **HPV-associated Anal Lesions in HIV+ Patients Undergoing Transplantation**

The risk of developing HPV-associated anal cancers and anal lesions is much higher in HIV+ transplant patients than in HIV+ patients who have not undergone transplantation (Roland et al., 2003, Stock et al., 2003) despite HAART. Stock et al. (2003) reported rapid progression of these lesions post-transplantation and described 12 patients who had undergone either kidney or liver transplantation and had been examined both before and after surgery. Nine (75%) had HPV-related abnormalities pre-transplantation. Four of the nine (44.4%) showed progression to a higher grade of anal intraepithelial neoplasia after surgery. The three patients who had originally been negative for HPV all tested positive for anal HPV on examination post-transplantation. The heart transplant patient described in Calabrese et al. (2003) also suffered from recurrent anal condylomata.



*In summary, solid organ transplantation appears to place HIV+ patients at greater risk than HIV+ patients who do not undergo organ transplantation of rapidly progressive HPV-associated anal lesions.*

## **Limitations of the Analysis**

There are two major caveats in the interpretation of the findings from this analysis. The studies available for review are all based on small numbers of patients undergoing transplantation at one of several transplantation centers. The investigators write occasional case reports on individual patients and report a small series of patients when they have sufficient numbers. As patients live longer, investigators write additional follow-up case series. Occasionally, investigators at various centers collaborate and write papers combining their series of patients. The result is a small number of patients who undergo transplantation and are who reported in two or more publications.

The other major limitation in the interpretation of the findings is that the transplantation centers currently performing transplants on HIV+ patients are among the largest, most well known, and respected centers that have pioneered organ transplantation over the years. Most transplants in HIV+ patients in the United States are performed by centers that participate in National Institute of Health (NIH) clinical trials of HIV and transplantation<sup>20</sup>. It is likely that the training and the experience of the transplant team, as well as careful patient selection, are significant factors in favorable outcomes for HIV+ patients. Although these centers report that HIV+ patients compare favorably with HIV- patients undergoing organ transplantation, it cannot be determined if these same findings would be true if the mandate were to become law and more transplantation centers entered into the field of transplantation for HIV+ patients.

## **Conclusions**

In summary, HIV+ patients undergoing kidney or liver transplantation have survival rates similar to their HIV- counterparts, except patients who are both HIV+ and HCV+, who fare more poorly. HCV-related liver disease is problematic even in the HIV- patient. Autologous stem cell transplantation after high-dose chemotherapy for patients with HIV-related lymphomas looks promising, especially if performed early in the course of disease, but the evidence is limited to one study. HAART is successful in post-transplant HIV+ patients in keeping viral loads low and CD4 T-cell levels high.

## **II. UTILIZATION, COST, AND COVERAGE IMPACTS**

### **Introduction**

According to CHBRP's estimates, there are 20,368,000 insured Californians currently enrolled in Knox-Keene plans or insured by health policies regulated under the insurance code that will be affected by AB 228. In the 2001 and 2002 calendar years, 4,206 transplants were performed in California, of which 11 were in HIV+ patients. These figures likely underreport the actual number of transplants in HIV+ patients because California's privacy laws prevent information on HIV status from being disseminated.

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<sup>20</sup> Personal communication, R. Busuttill, University of California, Los Angeles, 14 March, 2005.



CHBRP surveyed seven health plans in California, of which responses were received from five. The five stated that their members currently have coverage for transplant services regardless of HIV status. Responding health plans acknowledge that up until a few years ago, transplantation for HIV+ patients would have been considered experimental or investigational and thus denied as a general exclusion under the terms of the policy. However, they state current coverage policy does not discriminate on the basis of HIV status. Health plans responded that they either incorporate the protocol established by the transplant center(s) they use or defer decision making to those centers. Most transplant centers in California do not accept HIV+ patients, however, because they do not currently have the protocols in place to handle surgeries for HIV+ patients and/or consider HIV status a contraindication for transplantation surgery. As mentioned, the DMHC reports one case that came under IMR in 2002 but has reported no cases since then. In addition, conversations with the two largest regional transplant networks in California indicate no denial of services on the basis of HIV status as far as they are aware. Conversations with two of the three transplant centers (that have conducted most of the surgeries to be performed on HIV+ patients) also indicate that in recent years, carriers have not been denying coverage for patients deemed to be acceptable candidates. From this it appears that the health plans in California are not currently denying coverage for transplants based on HIV status when the enrollee has been designated an appropriate candidate for transplant surgery. Therefore, CHBRP estimates that the number of new HIV+ transplant cases will not increase as a result of AB 228.

## **Present Baseline Cost and Coverage**

### Current coverage of the mandated benefit (Section 3(i))

An estimated 20,368,000 Californians currently have coverage for the mandated benefit, including:

- 3,200,000 Medi-Cal recipients in HMOs;
- 494,000 Healthy Family recipients in HMOs;
- 795,000 CalPERS members in HMOs;
- 1,952,000 persons with individually purchased coverage;
- 13,927,000 persons with employment-based coverage.

### Current utilization levels and costs of the mandated benefit (Section 3(h))

During the period 2001-2002, 4,206 transplants were performed in California, including 1,862 bone marrow, 1,062 kidney, 789 liver, 299 heart, 144 lung, 39 simultaneous pancreas and kidney, and 11 pancreas transplants. Of these 4,206 transplants, 11 were performed on HIV+ patients according to the California hospital discharge database. These figures likely underreport the actual number of transplants on HIV+ patients because California's privacy laws prevent information on HIV status from being disseminated.

Thirty-seven hospitals in California performed transplants during the 2001-2002 period, although four hospitals (UCLA, City of Hope National Medical Center, UCSF, and Stanford) accounted for almost 60% of the total transplants performed during this period.

### The extent to which costs resulting from lack of coverage are shifted to other payers, including both public and private entities. (Section 3(f))

CHBRP estimates no shift in costs among different payers as a result of current coverage because all insured Californians have coverage for transplants regardless of HIV status.



### Public demand for coverage (Section 3(j))

Based on criteria specified under AB 1996 (2002), CHBRP is to report on the extent to which collective bargaining negotiates and the extent to which self-insured plans currently have coverage for the benefits specified under the proposed mandate. Based on conversations with the largest collective bargaining agents in California, there is no evidence that unions currently include such detailed provisions during the negotiations of their health insurance policies. In order to determine whether any local unions engage in negotiations at such detail, they would need to be surveyed individually.<sup>21</sup> Currently, the largest public self-insured plan, California Public Employees' Retirement System (CalPERS) preferred provider organization (PPO) plan covers transplantation services, regardless of HIV status, as long as services are preauthorized and conducted at a designated center of excellence.

### **Impacts of Mandated Coverage**

#### How will changes in coverage related to the mandate affect the benefit of the newly covered service and the per-unit cost? (Section 3(a))

AB 228 has the potential to substantially increase the per unit cost of transplantation. Because there is considerable excess demand (due to limited supply) for organ transplantation nationally, AB 228 could in theory create additional excess demand by increasing the number of HIV+ patients seeking transplantation. As discussed above, however, CHBRP has no evidence that HIV+ individuals are currently being denied coverage of transplantation services.

The average benefit of transplantation could also be affected by the mandate if HIV+ individuals had systematically different outcomes relative to HIV- individuals. However, the medical effectiveness literature presented above indicates that transplant outcomes do not differ significantly according to HIV status, at least for kidney and liver transplant patients.

Therefore, CHBRP estimates that AB 228 will not affect the average benefit or the per-unit cost of transplantation.

#### How will utilization change as a result of the mandate? (Section 3(b))

Because we find no evidence that insured enrollees who are HIV+ are currently being denied coverage of transplantation services once they have been deemed a candidate for surgery, CHBRP estimates no changes in utilization.

#### To what extent does the mandate affect administrative and other expenses? (Section 3(c))

CHBRP estimates no impact.

#### Impact of the mandate on total health care costs (Section 3(d))

CHBRP is not able to estimate any measurable impact of AB 228 on total health care expenditures because there is no evidence that HIV+ individuals are currently being denied coverage to transplantation. However, it is possible that the mandate could increase awareness among HIV+ individuals of their

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<sup>21</sup> Personal communication with SEIU and California Labor Federation on February 8, 2005



existing coverage for transplantation. Because transplantation involves life-threatening conditions, in contrast to elective procedures, CHBRP estimates that any increase in demand for transplantation due to increased awareness of its status as a covered benefit is likely to be minimal.

#### Costs or savings for each category of insurer resulting from the benefit mandate (Section 3(e))

Because CHBRP estimates no measurable impact on total health care expenditures, there are no effects on individual categories of insurers. Programs subject to the Health and Safety Code, specifically Medi-Cal, Healthy Families, and CalPERS, will experience no change in costs or utilization as a result of the mandate.

#### Impact on access and health service availability (Section 3(g))

AB 228 is unlikely to have any impact on the number of transplant centers that offer transplantation services to HIV+ patients because coverage does not appear to be a reason for the current dearth of transplant centers without protocols necessary to treat HIV+ patients. Therefore, access to transplantation among HIV+ patients is not likely to change.

If HIV+ patients were more likely to seek transplantation as a result of AB 228, this increased demand could affect overall access to transplanted organs because of the severely limited supply of organs. Under these circumstances, AB 228 would change the distribution of benefits, given the relatively fixed supply of organs, with HIV+ patients having a higher likelihood of transplantation after the mandate and HIV- patients having a lower likelihood of transplantation. These potential distributional consequences are discussed further below in the Public Health Impact section.

### **III. PUBLIC HEALTH IMPACTS**

#### **Present Baseline Health Outcomes**

As the life expectancy of persons with HIV has increased, end-organ disease has become more of a threat than the HIV disease itself (Roland and Havlir, 2003). Because persons who are HIV+ are at risk for end-stage renal disease (ESRD) and end-stage liver disease (ESLD), the two types of organ transplants most commonly performed on HIV patients are kidney and liver transplants. It is estimated that between 3.5% and 6.9% of persons with HIV have ESRD (Roland and Stock, 2003). Kidney dialysis may shorten the life expectancy of persons with HIV, thus creating a need for kidney transplants in this population. Co-infection with HBV or HCV can lead to the development of ESLD among HIV+ patients. It is estimated that approximately 9% of HIV patients are co-infected with HBV and 23%-33% of HIV patients are co-infected with HCV (Roland and Stock, 2003).

Discussions with the California regional transplant networks and three high-volume transplant centers in California reveal that only the UCSF Medical Center currently conducts transplants for HIV+ patients on an ongoing basis. Cedars-Sinai Medical Center in Los Angeles has begun to conduct such transplants as part of their participation in a solid organ transplant clinical trial sponsored by UCSF and supported by the National Institute of Allergy and Infectious Disease (NIAID).<sup>22</sup> The UCLA Kidney Transplant Program has also begun to conduct such surgeries in the last year. UCSF reports that since 2000, they

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<sup>22</sup> Seventeen centers nationally are participating in this clinical trial; two are from California. More information can be obtained at <http://clinicaltrials.gov/ct/gui/show/NCT00074386?order=1>





have performed 39 transplants on HIV+ patients, Cedars-Sinai reports having performed three such transplants, and UCLA has performed two. UNOS maintains a national database of all persons on the waiting list for organ transplants, but their HIV status is not collected. Therefore we have no way of determining how many HIV+ Californians are currently on the waiting list for organ transplants.

## **Impact of the Proposed Mandate on Public Health**

### Impact on Community Health (Section 1A)

The review of the effectiveness literature found that HIV+ patients undergoing kidney or liver transplantation have survival rates similar to their non-HIV+ counterparts. The exception is patients who are both HIV+ and HCV+. The literature indicates that these patients may fare worse than noninfected patients, yet HCV+-related liver disease is problematic even in the HIV- patient. Thus, HIV+ patients with the appropriate indications and managed in settings such as those that have been used in the existing studies have outcomes comparable to those who are HIV-. Therefore, to the extent that this mandate increases the number of transplants to HIV+ patients, there is the possibility to extend the life expectancy of these persons.

There are three factors that were considered when exploring the potential of this mandate to increase the number of transplants to HIV+ patients: 1) distribution effects related to organ transplants, 2) transplant center barriers, and 3) insurance coverage barriers. In assessing distribution effects, it is necessary to look at liver and kidney transplants separately because the pool of donors is fixed for liver transplants but not for kidneys. This mandate would not change the number of overall liver transplants performed in California due to the fixed number of organs available for transplantation. Although the total number of liver transplants performed in California would remain the same, there would be a potential for a change in the distribution pattern of liver transplants to include a higher proportion of HIV+ patients. Kidney transplants are different from liver transplants in that organs come from both cadavers and live donors and thus the pool of donors is not fixed. According to utilization data provided by Milliman, approximately 43% of kidney transplants in California come from live donors. Thus, the pool of donors is not fixed for kidney transplants and this mandate could potentially increase the number of kidney transplants to HIV+ patients. The extent to which this mandate will result in a redistribution of organs from HIV- to HIV+ individuals or an increase in live donor kidney transplants to HIV+ persons depends on the transplant center and insurance coverage barriers described below.

The second factor considered in the calculation of the community health impact of this mandate was transplant center barriers. Interviews with transplant experts revealed that the lack of HIV+ transplant protocols at transplant centers is a barrier to performing transplants on HIV+ patients. In addition, most transplant centers would still consider HIV status a contraindication for transplant surgery. There are currently only two transplant centers in California that have implemented such protocols—one having done so in the last few months as part of their participation in the NIAID solid organ transplant clinical trial. Another center has also conducted such surgeries – two kidney transplant in the last year. There is no evidence that other centers will rapidly develop protocols. Therefore, the impact of AB 228 will be limited by the ability of patients to undergo transplants at one of these two centers.

Finally, the current level of health insurance coverage for transplants to HIV+ patients was assessed. Based on the survey responses of five<sup>23</sup> major health insurers in California, insurers do not appear to have

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<sup>23</sup> CHBRP surveyed the seven major California health plans and insurers and five responded.



policies that exclude coverage for transplants for HIV+ patients when they have been deemed a candidate for transplant surgery by their physician and surgeon. These patients are treated as others seeking transplants in terms of the criteria used to determine their eligibility. Therefore, no increase in the number of organ transplants to HIV+ patients is expected as a result of this mandate.

In conclusion, the analysis shows that AB 228 is not expected to have an impact on community health. The supply of organs (liver and kidney)—both cadaver and live donor—is not expected to increase; the demand for transplants by HIV+ patients is not expected to increase; the distribution pattern of organ transplants is not expected to shift from HIV- to HIV+ patients; the number of transplant centers in California with transplant protocols for HIV+ patients is not expected to grow rapidly, and available evidence indicates that HIV+ patients in California are not excluded from insurance coverage for transplantation.

### Impact on Community Health where Gender and Racial Disparities Exist (Section 1B)

Much of the literature on racial disparities within the HIV+ population concerns the differences between Blacks and Whites. Blacks have substantially higher rates of HIV/AIDS. Rates for Black men are seven times that for White men (CDC 2004). For women, the difference is even more striking: the rates of HIV/AIDS among Black women are 19 times higher than that of White women (CDC 2004). Additionally, Blacks suffer greater morbidity and mortality from HIV (CDC 2005; Fleishman and Hellinger, 2003; McGinnis et al., 2003).

Many researchers have examined racial differences in treatment for HIV+ patients. Palacio et al. (2002) conducted a literature review of the effect of race on the use of antiretrovirals and reported that 14 studies found a negative relationship between nonwhite race and antiretroviral use, 3 studies found a positive association, and 16 found no association. Subsequent studies have also found that, compared with Whites, Blacks with HIV were less likely to receive antiretrovirals (Gebo et al., 2005) and were less likely to participate in clinical trials (Stone et al., 1997).

In addition to treatment and outcome disparities for HIV, there is also a body of research that focuses on disparities for transplants. For kidney transplants, where Blacks and other minorities have significantly higher rates of end-stage renal disease (Nzerue et al., 2002), researchers have found that racial disparities in transplant outcomes have progressively decreased over time (Powe and Boulware, 2002; Smith and Butterly, 2002). Moore et al. (2004) examined a larger category of solid organ transplants and found no racial differences with regards to survival or health-related quality of life. Some literature has indicated, however, that disparities do exist with regard to who receives an organ for transplantation. Isaacs et al. (2000) found racial disparities among recipients of simultaneous pancreas-kidney transplants, with Whites receiving a disproportionately higher number of transplants. Additionally, Furth et al. (2000) found that Black children and adolescents wait longer for kidney transplants compared with White children.

Compared with racial disparities, there is less research on gender disparities surrounding HIV and transplants. There is some evidence to suggest that women with HIV are less likely than men to receive antiretrovirals (Gebo et al., 2005; Raine, 2000) and participate in AIDS clinical trials (Stone et al., 1997). With regard to transplants, Kayler et al. (2002) found that men were more likely than women to receive a living-donor kidney transplant, and Thamer et al. (2001) found when using written scenarios that nephrologists were less likely to recommend a transplant for women.

Although the literature reports both racial and gender disparities with respect to both HIV treatment and the receipt of transplants, there is little research that examines race and gender within the population of



HIV+ patients that receive transplants or may receive them. One study (Swanson et al., 2002) examined the 32 HIV+ patients who received kidney transplants from 1987 to 1997 and found that the HIV+ recipients were comparable to the HIV- kidney transplant population even though Blacks have much higher rates of end-stage renal disease due to HIV-associated nephropathy (Abbott et al., 2001; Daugas et al., 2005; Nzerue et al., 2002; Ross et al., 2000)

Available evidence indicates this mandate would not increase the number of organ transplants to HIV+ persons. Therefore, although there is evidence of gender and racial disparities with regard to HIV status and related health outcomes, we conclude that AB 228 will have no impact on reducing these disparities.

#### Reduction of Premature Death and the Economic Loss Associated with Disease (Section 1C)

Due to advances in treatment, the prognosis for HIV+ persons in developed countries has improved substantially in recent years. Consequently, a greater proportion of deaths within the HIV+ population are due to end-organ failure (Neff et al., 2004; Roland and Havlir, 2003; Valdez et al., 2001), particularly liver and kidney failure (Calabrese, 2001; Puoti et al., 2000). The heightened risk for liver disease among HIV+ patients has been attributed to the high rates of HBV and HCV within the HIV+ population (Borgia et al., 2003; Neff et al., 2003; Nowak et al., 2003; Puoti et al., 2000) and, to a lesser extent, the potential of hepatotoxicity as a side effect of some antiretroviral treatments (Clark et al., 2002).

The increased risk for kidney disease within the HIV+ population is predominately attributed to HIV-related conditions such as HIV-associated nephropathy (Daugas et al., 2005; Dellow et al., 2000; Krawczyk et al., 2004), which is primarily found among Blacks with HIV (Abbott et al., 2001; Daugas et al., 2005; Nzerue et al., 2002; Roland and Stock, 2003; Ross et al., 2000). Additionally, although antiretroviral therapy often improves HIV-related kidney complications, there are also potentially harmful side effects for certain antiretrovirals that can contribute to renal failure (Daugas et al., 2005; Dellow et al., 2000).

Although the evidence presented above indicates that organ failure leads to premature death in HIV+ persons, available evidence indicates this mandate would not increase the number of organ transplants to HIV+ persons. Therefore we conclude that AB 228 will have no impact on premature death.

It has been documented that both end-organ disease lead to economic loss in terms of lost-productivity (Campbell et al., 2002; Kaitelidou et al., 2005). However, available evidence indicates this mandate would not increase the number of organ transplants to HIV+ persons, therefore we conclude that AB 228 will have no impact on the economic loss associated with end-organ disease in HIV+ patients.



## APPENDIX A Literature Review Methods

AB 228 is an act to add Section 1374.17 to the Health and Safety Code, and to add Section 10123.21 to the Insurance Code relating to health care coverage. The proposed bill states that, *A health care service plan shall not deny coverage that is otherwise available under the plan contract for the costs of solid organ or other tissue transplantation services based upon the enrollee or subscriber being infected with the human immunodeficiency virus, if the enrollee or subscriber is deemed to be an acceptable transplant candidate by his or her attending physician and surgeon and by the physician and surgeon who will perform the transplantation services.*

Appendix A describes the literature search for studies that compare organ transplantation in HIV+ patients with organ transplantation in non-HIV infected patients. The studies focus primarily on kidney or liver transplants. HIV+ patients are at a very high risk of hepatitis, which can lead to end-stage liver disease. As HIV+ patients live longer, they also develop HIV-related end-stage kidney disease. The articles that were included in the analysis were those that provided information on outcomes of transplantation in HIV+ patients. These outcome measures are also discussed in this appendix.

To “grade” the evidence for all outcome measures, the CHBRP effectiveness team uses a system<sup>24</sup> with the following categories:

1. Favorable (statistically significant effect): Findings are uniformly favorable, and many or all are statistically significant.
2. Pattern<sup>25</sup> toward favorable (but not statistically significant): Findings are generally favorable, but there may be none that are statistically significant.
3. Ambiguous/mixed evidence: Some findings are significantly favorable, and some findings with sufficient statistical power show no effect.
4. Pattern toward no effect/weak evidence: Studies generally find no effect, but this may be due to a lack of statistical power.
5. No effect: There is statistical evidence of no clinical effect in the literature with sufficient statistical power to make this assessment.
6. Unfavorable: No findings show a statistically significant benefit, and some show significant harms.
7. Insufficient evidence to make a “call”: There are very few relevant findings, so that it is difficult to discern a pattern.

Studies of transplantation in HIV+ patients were identified from PubMed and Cochrane databases (January, 1996-January 2005). 1996 coincides with the expansion of highly active antiretroviral therapy (HAART) and the resulting increase in longevity, rendering earlier studies less applicable to the mandate. The scope of the literature search included all types of transplants performed in the United States today as well as laboratory tests, biopsies, and other technologies that gauge the functioning of the organ.

The *Medical Subject Headings* (MeSH) terms used by the librarian in the PubMed search were:

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<sup>24</sup>The foregoing system was adapted from the system used by the U.S. Preventive Services Task Force, available at <http://www.ahcpr.gov/clinic/3rduspstf/ratings.htm>. The medical effectiveness team also considered guidelines from the Centers for Medicare & Medicaid Services, (available at <http://www.cms.hhs.gov/mcac/8b1-i9.asp>) and guidelines from the Blue Cross and Blue Shield Association (available at <http://www.bcbs.com/tec/teccriteria.html>).

<sup>25</sup> In this instance, the word “trend” may be used synonymously with “pattern.”



Explode HIV Infections  
Explode Organ Transplantation (Searches include Bone Transplantation, Heart Transplantation, Kidney Transplantation, Liver Transplantation, Lung Transplantation, Pancreas Transplantation)  
Explode Organ Transplantation/Adverse Effects  
Explode Organ Transplantation/Mortality  
Explode Tissue Transplantation (Searches include Bone Marrow Transplantation, Corneal Transplantation, Skin Transplantation)  
Explode Tissue Transplantation/Adverse Effects  
Explode Tissue Transplantation/Mortality  
Transplants  
Kidney Failure/Complications/Surgery  
Liver Failure/Complications/Surgery  
Explode Host vs Graft Reaction (Searches include Graft Rejection, Graft Survival.)  
Infection  
Biological Markers  
Vision  
Biopsy  
Liver  
Heart  
Kidney  
Hemorrhage  
Leukocytosis  
Blood Urea Nitrogen  
Creatinine  
Blood Glucose  
Hemoglobin A, Glycosylated  
Survival  
Survival Rate  
Survival Analysis  
Mortality  
Quality of Life  
Activities of Daily Living  
Treatment Outcome  
Technology Assessment Biomedical  
Explode Clinical Trials

Keywords:

heart lung transplant\*  
kidney pancreas transplant\*  
small bowel transplant\*  
multi-visceral transplant\*  
forced vital capacity  
diabetic control  
systematic review

The search was limited to the following publication types:  
Meta-analyses, randomized controlled trials, clinical trials, and review articles.



In an effort to find newer references that have not been assigned MeSH terms, a search was performed using:

organ transplant\*, Bone transplant\*, heart transplant\* , heart lung transplant\*,  
kidney transplant\* , liver transplant\* , pancreas transplant\* , kidney pancreas transplant\*,  
tissue transplant\*, bone marrow transplant\*, corneal transplant\*, skin transplant\*,  
multi visceral transplant\*, graft survival, graft rejection, rejection, elevated liver function test\*,  
infection\*, vision, bleeding, hemorrhage, thrombosis, biopsy, liver, heart, kidney,  
laboratory test\*, leukocytosis, blood urea nitrogen, BUN, creatinine, blood glucose,  
Hemoglobin A, Glycosylated, HbA1c, PO<sub>2</sub>, FVC, forced vital capacity, functional status,  
diabetic control, survival rate, death rate, mortality, quality of life, functional status, activities  
of daily living, treatment outcome, technology assessment biomedical, randomized controlled  
trial\*, clinical trial\*, meta analysis, systematic review

Limited to searches to the following publication types:

Meta-analyses, clinical trials, randomized controlled trials, and review articles.

The asterisk signifies that the term was truncated.

A total of 48 English language articles were found, of which 14 were ultimately found to provide data on patient outcomes. The only pertinent studies were observational studies and case reports. No meta-analyses were found. All pertinent studies and case reports from the United States and Western Europe that appeared in English were included. Opinion pieces, overviews, and basic science papers that did not report detailed information on patients by outcomes were not included in the analysis. References that were letters to the editor instead of peer-reviewed articles were also not included in the analysis. Despite efforts to find information on all types of transplants performed, including intestine, lung, and corneal transplants, only information on kidney, liver, cardiac (one case-report), and a combined kidney-pancreatic (one case-report) transplant were found. At least two reviewers screened the title and abstract of each citation returned by the literature search to determine eligibility for inclusion. Full-text articles were obtained and reviewers reapplied the initial eligibility criteria.



Several articles were rejected at least in part because they were based on data from the “pre-HAART” era, i.e., they were based on data on HIV+ patients from before highly active antiretroviral therapy changed the course of HIV/AIDS:

Bisleri G, Morgan JA, Deng MC, Mancini DM, Oz MC. (2003). Should HIV-positive recipients undergo heart transplantation? *Journal of Thoracic Cardiovascular Surgery*. 126:1639-1640.

Sayegh SE, Keller MJ, Huprikar S, Murphy B. (2004). Solid organ transplantation in HIV-infected recipients. *Pediatric Transplantation*. 8:214-221.

The major limitation with the medical effectiveness analysis is that of overlapping patients in the various studies. Every few years, the investigators write a new series with updates on old patients and with the addition of new patients. A few of the papers are collaborations among transplant surgeons at several major transplant centers. It cannot be determined if the patients in some articles include the same patients initially presented in other articles. To compound the problem, the number of HIV-infected patients undergoing organ transplantation is small.



**APPENDIX B**  
**Summary of Findings on Effectiveness of Transplantation in HIV+ Patients**

**Table B-1. Summary of Published Studies on Effects of Solid Organ Transplantation in HIV+ Patients**

Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Moreno et al., 2005	Observational study	<p>HIV+ patients undergoing liver transplantation</p> <p>(No comparison group)</p>	<p>Four patients with HIV infection and end - stage liver disease who met standard criteria for liver transplantation and had:</p> <ol style="list-style-type: none"> <li>1) CD4 T-cell count &gt; 100/ml</li> <li>2) HIV RNA levels &lt; 50 copies/ml (unless therapy was contraindicated due to liver toxicity)</li> <li>3) Did not have opportunistic infections or neoplasia</li> <li>4) Have not abused alcohol or illicit drugs for at least two years</li> </ol> <p>Patient characteristics:  Former intravenous drug users (n = 3)  HCV+ (n = 4)  Infected with HBV and hepatitis D virus (HDV) (n = 1)</p>	Spain





Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Abbott et al. 2004	Retrospective cohort study	<p>Only cases specified for HIV and HCV serology:</p> <p>Intervention group: HIV+ patients undergoing kidney transplant</p> <p>Control group: All patients undergoing kidney transplant</p>	<p>US adult deceased donor kidney transplant recipients from Jan 1, 1996 to May 31, 2001. Patients followed until October 31, 2001.</p> <p>27,851 adult recipients of deceased donor kidneys for whom serology (HCV and HIV) information on donor and recipient was available). Of these, 47 were HIV+.</p> <p>8,875 (6.8%) of all cadaveric kidney transplant patients were HCV+; 3 (6.4%) of all HIV-infected recipients were HCV+.</p> <p>7684 (27.6%) of all kidney transplant patients were African American, as opposed to only 6 (12.8%) of HIV+ patients.</p>	United States  (US kidney data system: USRDS)
Radecke et al., 2005	Observational study	<p>HIV patients undergoing liver transplantation</p> <p>No comparison group</p>	<p>Five HIV-infected patients with viral-induced liver cirrhosis.</p> <p>Patient characteristics: HBV (n = 1) HCV (n = 3) HCV/HBV/HDV (n = 1)</p>	Germany



Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Norris et al., 2004	Observational study	<p>Group 1: Patients co-infected with HCV (n = 7)</p> <p>Group 2: Patients without HCV (n = 7)</p> <p>Authors also provide some data for comparison purposes on other non-HIV patients undergoing liver transplants during same time period. HIV+ patients represented 1.1% of patients undergoing transplants in the time period for the study (n = ~1400)</p>	<p>Fourteen HIV-infected liver allograft recipients with:</p> <p>Patient characteristics:</p> <p>HCV cirrhosis (n = 7)  HBV (n = 3)  Acute HBV-related liver failure (n = 2)  Alcoholic liver disease (n = 2)</p> <p>All patients had transplants at the King's College Hospital program between 1995 and April 2003.</p>	London



<b>Citation</b>	<b>Type of Study</b>	<b>Intervention vs. Comparison Group</b>	<b>Population Studied</b>	<b>Location</b>
Calabrese et al., 2003	Case report	HIV+ patient undergoing cardiac transplantation	One patient with HIV in need of a cardiac transplant most likely related to daunorubicin-induced toxicity in the treatment of Kaposi's sarcoma.  (Patient is a biostatistician and one of the authors of the report [RZ])	Cleveland
Krishnan et al., 2003	Observational study	HIV+ patients undergoing ASCT for treatment of lymphoma  No comparison group	19 HIV+ lymphoma patients (Hodgkin's disease and non-Hodgkin's lymphoma)	California
Neff et al., 2003	Observational study	HIV+ patients in need of liver transplant  (No comparison group)	Sixteen HIV-infected allograft recipients (10 from Pittsburgh and 6 from Miami)  Patient characteristics Chronic HCV (n = 11) Chronic HBV (n = 3) Fulminant hepatic failure (n = 2) HCV with concomitant hepatocellular cancer (n = 1)	Pittsburgh and Miami



<b>Citation</b>	<b>Type of Study</b>	<b>Intervention vs. Comparison Group</b>	<b>Population Studied</b>	<b>Location</b>
Nowak et al., 2003	Observational study	HIV+ patients in need of liver transplant  (No comparison group)	Four HIV+ patients  Patient characteristics: Liver cirrhosis due to HCV (3) Liver failure due to primary billiary cirrhosis diagnosed with HIV at time of transplant (had previously tested negative) (1)	Sweden

<b>Citation</b>	<b>Type of Study</b>	<b>Intervention vs. Comparison Group</b>	<b>Population Studied</b>	<b>Location</b>
Ragni et al., 2003 <sup>26</sup>	Observational	Intervention group: 24 HIV+ patients undergoing liver transplant  Comparison group: Data from United Network of Organ Sharing (UNOS) on 13,574 individuals known to be HIV-	Twenty-four HIV + patients with end-stage liver disease (ESLD) who fulfilled standard criteria for liver transplantation  10 subjects (Pittsburgh)  6 (Miami)  4 (San Francisco)  3 (London)  1 (Minneapolis)  Patient characteristics: HCV (n = 15) HBV (n = 7) Fulminant hepatic failure (3)	Pittsburgh, PA  Miami, FL  San Francisco, CA  London, England  Minneapolis, MN

<sup>26</sup> This paper reviews experience with liver transplantation in HIV+ patients at several institutions, but it does not provide detailed information about individual patients. It cannot be determined if any of the patients reported in this paper are also included in other papers by Roland and Stock that are summarized in this analysis. Caution in interpretation of findings is advised.



Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Roland and Stock, 2003 <sup>27</sup>	Review (retrospective and prospective)	<p>HIV+ kidney and liver transplant patients</p> <p>(Limited summary statistics presented for comparison with HIV– patients using data from UNOS)</p>	<p>45 (26 kidney and 19 liver transplant patients) retrospective and prospective HIV-infected patients meeting standard transplant criteria and HIV-specific criteria:</p> <ol style="list-style-type: none"> <li>1) no history of OI</li> <li>2) CD4 T-cell counts &gt; 200 cells/ml for kidney recipients and &gt; 100 cells/ml for liver recipients</li> <li>3) HIV RNA &lt; 50 copies/ml (Liver recipients could have detectable HIV RNA ,provided the study HIV clinician predicted full virologic suppression post-transplant).</li> </ol>	San Francisco, CA

<sup>27</sup> This paper does not provide detailed information for each patient. It is expected that there is considerable overlap in patients with the other articles by these authors. Caution is advised in the interpretation.



Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Roland et al., 2003 <sup>28</sup>	Case reports and review	Two HIV+ transplant patients: One kidney and one liver	HIV+  Patient characteristics:  Kidney transplant—renal failure (n = 1) Liver failure—end -stage liver (HBV) (n = 1)	San Francisco
Stock et al., 2003	Observational study	Fourteen HIV + transplant patients: 10 kidney transplant, (mean follow-up 480 days); 4 liver transplant (mean follow-up 380 days).  (No comparison group)	HIV+ patients meeting standard transplant criteria and HIV-specific criteria:  1) Undetectable plasma HIV-1 RNA levels (viral load) for three months with ability to tolerate a stable antiretroviral (ARV) regimen for three months before transplant (kidney). 2) Predicted to achieve viral load suppression post-transplantation if unable to take HAART (liver). 3) CD4 T-cell counts > 200/ml for kidney recipients or > 100/ml for liver recipients 4) No history of opportunistic infections.	San Francisco, CA

<sup>28</sup> The kidney transplant patient in this review shares the same medical history with a patient in the study by Stock et al (2003) and is presumed to be the same patient. Roland is also a co-author on the paper by Stock et al. (2003). Caution should be exercised in interpretation of the data.



<b>Citation</b>	<b>Type of Study</b>	<b>Intervention vs. Comparison Group</b>	<b>Population Studied</b>	<b>Location</b>
Toso et al., 2003	Case report	One HIV+ patient undergoing kidney-pancreas transplant	One long-term non-progressor HIV+ patient with diabetes and end-stage renal failure without ARV undergoing kidney-pancreas transplant	Switzerland



Citation	Type of Study	Intervention vs. Comparison Group	Population Studied	Location
Stock et al., 2001	Observational study	<p>Nine HIV+ transplant patients: 6 kidney, (mean follow-up 480 days); 3 liver transplant patients (mean follow-up 380 days).</p> <p>No comparison group</p>	<p>HIV+ patients meeting standard criteria for transplantation with:</p> <ol style="list-style-type: none"> <li>1) Undetectable HIV viral load for 3 months</li> <li>2) CD4 T-cell counts &gt; 200/ml (kidney recipients) or &gt; 100/ml (liver recipients) for 6 months</li> <li>3) No history of opportunistic infections</li> <li>4) Tolerating a stable antiretroviral regimen</li> <li>5) No history of cancer except basal cell carcinoma or in-situ anogenital carcinoma</li> <li>6) No HCV+ status in kidney recipients with findings of cirrhosis on liver biopsy.</li> </ol> <p>Patients received solid organ transplantation (kidney or liver) during the previous year.</p>	San Francisco, CA





**Table B-2. Summary of Evidence of Effectiveness by Outcome for Solid Organ Transplantation in HIV+ Patients**

<b>Patient Survival Rate with Kidney Transplant, Pattern toward favorable</b>		
<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Abbott et al., 2004	<p>HIV+ patients: &gt; 95% survival rate (45/47) over three years; 4.3% ( 2/47) deceased over same period</p> <p>All patients: 87.2% survival rate over three years ( numbers of patients); 12.8% (3,569/27,851) deceased in same period</p> <p>Risk of death: lower for HIV+ patients (p = 0.31)</p>	<p>NS</p> <p>Favorable for HIV+ patients</p>
Roland and Stock, 2003	<p>HIV+ patients: 92.3% survival rate (24/26) in kidney recipients; 2/26 (7.7%) deaths:</p> <p>Ischemic bowel and enterococcal sepsis (n = 1)</p> <p>Chronic rejection and staphylococcal sepsis (n = 1)</p> <p>Median follow-up was 314 days (3-1,696).</p> <p>Subject survival rates in this small sample were similar to 1-year survival rates in the UNOS database</p>	<p>NS</p> <p>No difference in survival between HIV+ and HIV- patients)</p>
Roland et al., 2003	One HIV+ patient survival at follow-up 2.5 years	No comparison group
Stock et al., 2003	HIV+ patients: 100% survival rate (10/10): mean follow-up 480 days	No comparison group
Stock et al., 2001	HIV+ patients: 100% survival rate (6/6); follow-up 4-70 weeks)	No comparison group



**Kidney Graft Survival Rate, pattern toward favorable**

Citation	Results	Categorization of Results (Significance, Direction)
Abbott et al., 2004	HIV+ patients: 97.9% (46/47) graft survival rate for patients undergoing kidney transplant (between January 1, 1996 and May 31, 2001) 2.1 % graft loss  All patients: 93.2% (25,953/27,851) graft survival for patients undergoing kidney transplant (between January 1, 1996 and May 31, 2001) 6.8% graft loss	NS Favorable for HIV+ patients
Roland and Stock, 2003	HIV+ patients: 88.5% graft survival rate (23/26) ; 3/26 lost grafts: Rejection (n = 2) Thrombosis (n = 1) Survival rate in this small sample is similar to 1-year graft survival rate of 87.9% reported in UNOS database)	NS Favorable for HIV+ patients
Roland et al., 2003	One HIV+ patient graft survival at 2.5 years	No comparison group
Stock et al., 2003	HIV+ patients: 100% (10/10) graft survival rate; mean follow-up 480 days	No comparison group
Stock et al., 2001	HIV+ patients: 100% (6/6) graft survival	No comparison group

**Kidney Rejection Rate, mixed evidence**

Citation	Results	Categorization of Results (Significance, Direction)
Abbott et al.,	Rejection in first year: HIV+: 17.0% rejection rate (8/47 ) All patients: 18.8% (5,217/27,851)	NS Favorable for HIV+ patients
Roland and Stock, 2003	Rejection rate: HIV+ 38% (10/26)  (Most patients showing signs of rejection were treated and patients did not lose grafts)	No comparison information



**Kidney Rejection Rate, mixed evidence (cont.)**

Citation	Results	Categorization of Results (Significance, Direction)
Roland et al., 2003	One HIV+ (1/1) patient with acute rejection 2.5 years post-transplant (treated)	No comparison information
Stock et al., 2003	Rejection rate: HIV+ 50% (5/10) (at least two-fold the rate seen in HIV- patients undergoing transplantation with similar immunosuppressive protocols) treated	NS Unfavorable for HIV+ patients
Stock et al., 2001	Rejection rate: HIV+ 66.6% (4/6) Patients treated without loss of graft	No comparison group

**Patient Survival Rate with Liver Transplant: HIV+ plus HBV+ patients, pattern toward favorable HIV+/HCV+ patients, mixed evidence  
Antiretroviral intolerant patients, unfavorable**

Citation	Results	Categorization of Results (Significance, Direction)
Moreno et al., 2005	HIV + patients: 75% (3/4); follow-up at least one year Cause of death: 1) Fibrosing cholestatic hepatitis at 17 months	No comparison group



Citation	Results	Categorization of Results (Significance, Direction)
Radecke et al., 2005	<p>HIV+ 40% survival rate (2/5 alive at 23 and 61 months, respectively)</p> <p>Cause of death:</p> <ol style="list-style-type: none"> <li>1) Recurrent thrombosis of the hepatic artery three months post-transplant (n = 1)</li> <li>2) HCV-associated cholestatic hepatitis 10 months post-transplant (n = 1)</li> <li>3) Chemotherapy-induced liver damage due to Hodgkins disease diagnosed after transplantation 31 months post-transplant (n = 1)</li> </ol> <p>Both surviving patients: HCV+-related liver disease</p>	No comparison group



Citation	Results	Categorization of Results (Significance, Direction)
Norris et al., 2004	<p><u>HIV+/HCV- patients:</u> 7 HBV co-infected patients and patients transplanted for nonviral liver disease surviving with follow-up between 668 and 2,661 days</p> <p><u>Survival in HIV+/HCV+ patients:</u> 12 months post-transplant: 4/7 At 25 months: 2/7 alive</p> <p>Cause of deaths:</p> <ol style="list-style-type: none"> <li>1) Recurrent HCV, graft dysfunction, and sepsis (n = 3)</li> <li>2) Septicemia and allograft failure not related to HCV at three months post transplant (n = 1)</li> <li>3) Ruptured cerebral AV malformation in a background of HCV recurrence and allograft dysfunction (n = 1)</li> </ol> <p>Actuarial (cumulative) survival: HCV-/HIV+ patients<sup>29</sup>:</p> <ul style="list-style-type: none"> <li>1 year: 100%</li> <li>2 years: 100%</li> <li>5 years: 100%</li> </ul> <p>HBV+/HIV- patients:</p> <ul style="list-style-type: none"> <li>1 year: 86.4%</li> <li>2 years: 82%</li> <li>5 years: 80.4%</li> </ul> <p>HCV+/HIV+ patients:</p> <ul style="list-style-type: none"> <li>1 year: 57.1%</li> <li>25 months: 28.6%</li> </ul> <p>HCV+/HIV-</p> <ul style="list-style-type: none"> <li>1 year: 87.5%</li> <li>2 years: 83.9%</li> </ul> <p>(Authors report ~1,400 transplants in HIV- patients, but do not break down information by HCV status)</p>	<p>NS (small number of patients in study) Favorable for HIV+/HCV- patients</p> <p>Unfavorable for HIV+/HCV+ patients</p>

<sup>29</sup> Of the 7 HIV+/HCV- patients, 5 were HBV+.



Citation	Results	Categorization of Results (Significance, Direction)
Neff et al., 2003	<p>HIV+</p> <p>One-year survival rate: 94% (14/16) alive at time of publication of study; (1/16 was 6 months after transplant at time of publication of study)</p> <p>Actuarial survival rate at two years: 80%:</p> <p>Survival in this small group of patients is not significantly different from the survival of non-HIV+ transplant patients according to UNOS statistics.</p> <p>Cause of death:</p> <ol style="list-style-type: none"> <li>1) Noncompliance and resultant chronic rejection with recurrent HCV(n = 1)</li> <li>2) Acute rejection, sepsis, and multi-organ failure (HCV-) 12 days after transplant (n = 2).</li> </ol>	<p>NS</p> <p>Favorable for HIV+ patients with HBV and HCV</p>
Nowak et al., 2003	<p>HIV +</p> <p>Three of four alive (9 months, 14 months, and 3 years respectively) at time of publication of study.</p> <p>Survival rate: 75%</p> <p>Cause of death:</p> <ol style="list-style-type: none"> <li>1) Central nervous system disease of unknown origin considered not to be related to HIV infection at three months after transplant (n = 1)</li> </ol>	<p>No comparison group</p>



Citation	Results	Categorization of Results (Significance, Direction)
Ragni et al., 2003	<p>Cumulative survival among 24 HIV + recipients similar to that among age- and race-comparable HIV- recipients (p = 0.365)</p> <p>Proportions of HIV+ surviving at 12, 24, and 36 months after transplant were 87.1%, 72.8%, and 72.8%</p> <p>versus</p> <p>12, 24, and 36 months survival of 86.6%, 81.6%, and 77.9%, respectively for HIV- patients in the UNOS cohort (5,225 patients)</p> <p>Survival significantly poorer among six transplant recipients with post-transplant ARV intolerance (p = 0.044). Of 6 nonsurvivors, 4 (66.7%) had ARV intolerance in contrast to 2 (11.1 % of survivors). All had HCV.</p> <p>Survival significantly poorer among the HIV+ subjects with end-stage liver disease caused by HCV infection.</p> <p>HCV: 50% survival (15 patients were HCV+)</p> <p>Patients without HCV infection: 100.0%; (9 patients without HCV infection) (p = 0.023)</p>	<p>NS Favorable for HIV+ patients</p> <p>Sig Unfavorable for HIV+ patients with antiretroviral intolerance</p> <p>Sig Unfavorable for HIV+ patients with HCV infection</p> <p>Sig Unfavorable for HIV +patients with HCV</p>



Citation	Results	Categorization of Results (Significance, Direction)
Roland and Stock, 2003	<p>HIV+</p> <p>Survival rate liver recipients: 78.9% (15/19 )</p> <p>Cause of death:</p> <ol style="list-style-type: none"> <li>1) Recurrent HCV (n = 1)</li> <li>2) Rejection after protease inhibitor (PI) discontinued, but immunosuppression dose was not adjusted (n = 1)</li> <li>3): Postoperative pancreatitis (n = 1)</li> <li>4) Sinus thrombosis secondary to <i>Rhizopus</i> infection 4.5 years post-transplant) (n = 1)</li> </ol> <p>Patient and graft survival rates in this small sample (78.9% survival) were similar to but slightly lower than 1-year patient survival and graft survival rates in the UNOS database (87.9%)</p>	<p>NS</p> <p>Unfavorable for HIV+ patients</p>
Roland et al., 2003	HIV+ patient survival; 14-month follow-up	No comparison group
Stock et al., 2003	<p>HIV+:75% survival rate (3/4); mean follow-up 380 days</p> <p>Cause of death:</p> <p>Rapid reoccurrence of HCV co-infection at 445 days after transplant (n = 1)</p>	No comparison group





**Liver Graft Survival Rate: HBV+ patients, pattern toward favorable  
HCV- patients, pattern toward unfavorable**

Citation	Results	Categorization of Results (Significance, Direction)
Moreno et al., 2005	HIV+ Graft survival rate 75%? 3/4, length of follow-up? Cause of graft failure: 1) Fibrosing cholestatic hepatitis (n = 1)	No comparison group
Radecke et al., 2005	HIV+ Graft survival rate 60%? 3/5 liver graft failures:  Cause of graft failure: 1) Recurrent thrombosis of the hepatic artery 3 months after transplant (n = 1) 2) HCV-associated cholestatic hepatitis (n = 1) 3) Chemotherapy-induced liver damage due to Hodgkins disease diagnosed after transplantation (n = 1)	No comparison group
Norris et al., 2004	HIV + Graft survival rate: 100% (7/7 non-HCV patients)  33.3% (2/6 HCV patients (not counting patient ↓ arteriovenous malformation (cluster of abnormal blood vessels prone to hemorrhage) in the brain)	NS Favorable for HIV+/HCV- patients  Unfavorable for HIV+/HCV+ patients
Neff et al., 2003	HIV+ Subject and graft survival rate: 87.5% (14/16)  Cause of death: Acute cellular rejection (ACR) and HCV infection died (2)	NS
Nowak et al., 2003	HIV+ Subject and graft survival rate: 75% (3/4 functioning grafts) Cause of death: Reasons unrelated to graft function	No comparison group
Roland et al., 2003	1/1 (one patient with functioning graft)	No comparison group



Citation	Results	Categorization of Results (Significance, Direction)
Roland and Stock, 2003	<p>HIV+</p> <p>1/19 patient retransplanted because of small-for-size graft</p> <p>1/19 patients who died had complications after treatment for rejection</p> <p>(4/19 patients in total deceased including retransplanted patient)</p> <p>Patient and graft survival rates in this small sample (78.9% survival) were similar to 1-year patient survival and graft survival rates in the UNOS database (87.9%), but slightly lower</p>	<p>NS</p> <p>Slightly unfavorable for HIV+ patients</p>
Stock et al., 2003	<p>HIV+</p> <p>3/4 (75%) graft survival with mean follow-up 380 days</p> <p>One patient required (living donor patient) retransplantation with a cadaveric liver and kidney 28 days after transplantation secondary to poor liver function related to a small-for-size graft<sup>30</sup>.</p>	<p>No comparison group</p>

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<sup>30</sup> The patient mentioned here is likely the same patient mentioned in the Roland and Stock (2003)



**Liver Graft Rejection, pattern toward no effect (weak evidence)**

Citation	Results	Categorization of Results (Significance, Direction)
Moreno et al., 2005	HIV+ Rejection rate: 25% One of 4 patients (treated and controlled with no complications); 2 developed cholangitis	No comparison group
Norris et al., 2004	HIV+ and HIV– Rejection rate: 35.7% 5/14 (including 2 HCV+ patients) experienced at least one episode of rejection 5-34 days after transplantation (comparable to non-HIV patients transplanted at same time)  No patients had chronic rejection  Graft function normal in all surviving patients	Favorable for HIV+ patients
Neff et al., 2003	HIV+ 2/16 acute rejections leading to death  3 other patients with acute rejection (treated)  In all survivors, transplantation reversed symptoms of acute and chronic liver failure	No comparison group
Nowak et al., 2003	HIV+ 4 patients in study Information regarding rejection is not reported in this paper	
Roland et al., 2003	HIV+ Rejection rate: 0% (only one liver transplant patient in report) Abnormal liver function tests normalized with change in medications	No comparison group
Stock et al., 2003	HIV+ Rejection rate: 0% 0/4 All with normal liver function tests	No comparison group



<b>Recurrence Hepatitis C Virus (HCV), pattern toward unfavorable</b>		
<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Moreno et al., 2005	Rate of recurrence: 75% 3/4 patients with recurrent HCV infection	No comparison group
Norris et al., 2004	Rate of recurrence: 85.7% 6/7 In discussion, Norris et al. (2004) point out that HCV recurrence is a major problem among all HCV+ patients undergoing liver transplantation, regardless of HIV status. However, HIV+ patients experience a more accelerated return of HCV disease	NS Unfavorable for HIV+/HCV+ group
Neff et al., 2003	9/10 (not including patient who died 12 days after surgery)	No comparison group
<b>Survival with Cardiac Transplant, insufficient evidence to make call</b>		
<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Calabrese et al., 2003	Survival rate: 100% Case report of one patient	No comparison group
<b>Cardiac Graft Survival, insufficient evidence to make call</b>		
<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Calabrese et al., 2003	One patient with functioning graft Frequent episodes of rejection (treated)	No comparison group
<b>Survival with Kidney-Pancreas Transplant, insufficient evidence to make call</b>		
<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Toso et al., 2003	One patient undergoing successful transplant	No comparison group



**Kidney-Pancreas Graft Survival/ Rejection, insufficient evidence to make call**

Citation	Results	Categorization of Results (Significance, Direction)
Toso et al., 2003	Graft survival No evidence of rejection	No comparison group

**Survival following Autologous Stem Cell Transplantation (ASCT), favorable for ASCT**

Citation	Results	Categorization of Results (Significance, Direction)
Krishnan et al., 2003	<p>16 of 19 ASCT patients surviving and in remission with a median follow-up of 27.5 months (6-57.5 months)</p> <p>2 died from relapsed lymphoma 1 died from regimen related toxicity The patients who died had poorly controlled disease, one with a so-called anaplastic large-cell non-Hodgkin's lymphoma and the other with Burkitt's leukemia.</p> <p>Authors attribute their favorable findings to both HAART as well as early use of transplantation in comparison with unpublished information they obtained about another series.</p>	No comparison group

**Hepatotoxicity following ASCT, unfavorable for ASCT**

Krishnan et al., 2003	<p>19/19 patients developed hepatotoxicity (mostly grade 1-2)</p> <p>3 patients developed grade 3-4</p> <p>(Grading system for hepatotoxicity is not explained in the paper)</p>	No comparison group
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**HIV viral load levels in surviving patients maintained with HAART after transplantation (patients who survive have low viral loads, usually maintained on HAART therapy), pattern strongly toward favorable**

Citation	Results	Categorization of Results (Significance, Direction)
Moreno et al., 2005	<p>Undetectable levels: 75% HIV RNA remained undetectable in 3/4 patients</p> <p>One patient had rebound of viral load prior to death when HAART discontinued.</p>	<p>NS Favorable</p>
Radecke et al., 2005	<p>2 surviving patients: Undetectable viral levels</p> <p>3 deceased patients: Viral levels were low until HAART had to be discontinued because of complications</p>	<p>NS Favorable</p>
Norris et al., 2004	<p>HIV RNA remained undetectable in 8 patients</p> <p>HIV RNA level of 90 copies/ml in one patient</p>	<p>No comparison group</p> <p>Information not provided for deceased patients</p>
Calabrese et al., 2003	<p>HIV RNA remained undetectable (one patient)</p>	<p>No comparison group</p>
Nowak et al., 2003	<p>HIV RNA remained undetectable in 4/4 patients</p>	<p>No comparison group</p>
Neff et al., 2003	<p>HIV RNA remained undetectable in 14/15 patients (not including patient who succumbed quickly).</p> <p>In patient with HIV viremia, adjustments in HAART regimen resulted in undetectable viral loads at follow-up</p>	<p>No comparison group</p>



Citation	Results	Categorization of Results (Significance, Direction)
Ragni et al., 2003	<p>HIV RNA PCR load: copies/ml &lt; 400 (range of &lt; 400-179,000).</p> <p>Survival was poorer among those patients with a post-transplantation HIV load of &gt; 400 copies/ml than among those with post-transplantation HIV load of ≤ 400 copies/ml (p = 0.016)</p>	<p>Sig Favorable for patients with low HIV loads</p>
Roland et al., 2003	<p>Below limits of detection (2 patients)</p>	<p>NS Favorable</p>
Roland and Stock, 2003	<p>Viral load remained suppressed in most patients. median baseline HIV RNA in the liver recipients &lt;5 0 (&lt;5 0-115,776).</p>	<p>NS Favorable</p>
Stock et al., 2003	<p>Undetectable in all patients maintained on HAART</p> <p>One patient with severe recurrence HCV discontinued some meds because of hepatotoxicity leading to increased viral load up to 9,600 copies.</p>	<p>Favorable</p>



**Impact of Transplant on CD4 T-cell count in survivors (patients who survive have adequate CD4 T-cell count on HAART therapy), pattern strongly toward favorable**

Citation	Results	Categorization of Results (Significance, Direction)
Moreno et al., 2005	Significant decrease immediately post-transplant. Immunologic recovery began during month 3 and persisted during first year.	NS Favorable
Radecke et al., 2005	Stable CD4 T-cell counts on meds	NS Favorable
Norris et al., 2004	Surviving patients all have CD4 cell counts above 259	No comparison group
Calabrese et al., 2003	Occ decreases to < 100 cells but usually > 200.	No comparison group
Neff et al., 2003	Most patients have CD4 cell counts > 200 post-transplant/show signs of improvement.	No comparison group
Nowak et al., 2003	Increase in CD4 cells	No comparison group
Ragni et al., 2003	CD4 cell count (cells/ml):  188 (76–973)	NS Favorable





Citation	Results	Categorization of Results (Significance, Direction)
Roland and Stock, 2003	<p>Kidney: Pre-transplant CD4 T-cell counts: 441 (200–1,054) Post-transplant CD4 T-cell counts: 436 (3–975)</p> <p>Liver: Pre-transplant CD4 T-cell counts: 280 (103–973). Post-transplant CD4 T-cell counts: 218 (110–992)</p>	NS Favorable
Roland et al., 2003	<p>Kidney: Pre-transplant CD4 T-cell count: 407 cells/ml Post-transplant CD4 T-cell count: 249 cells/ml 4 days after the institution of anti-rejection therapy to 1011 cells/ml.</p> <p>Liver: Pre-transplant CD4 T-cell count 439 cells/ml. After transplant CD4 T-cell counts: 305 to 700 cells/ml and 405 cells at 20 months</p>	NS Favorable
Stock et al., 2003	<p>CD4 counts remained stable in patients not treated for rejection (after decreasing immediately post-transplant and rebounding).</p> <p>One patient with severe recurrence HCV discontinued some meds because of hepatotoxicity leading to decreased CD4 counts and death</p>	NS Favorable
Toso et al., 2003	CD4 cells remained in normal range (one patient)	No comparison group



**AIDS-defining opportunistic infections (OIs) in the transplant patient, Pattern toward favorable (HIV+ transplant recipients have very low incidence of OI when medication is appropriately adjusted)**

<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Moreno et al., 2005	No opportunistic infections	No comparison group
Radecke et al., 2005	No opportunistic infections mentioned.	No comparison group
Neff et al., 2003	1 Cytomegalovirus (CMV) (responded to tx)	No comparison group
Calabrese et al., 2003	None since transplant	No comparison group
Moreno et al., 2005	1 CMV (responded to treatment)	No comparison group
Nowak et al., 2003	None described in any of 4 patients	No comparison group
Roland and Stock, 2003	1 CMV 1 Candida esophagitis	No comparison group
Toso et al., 2003	No opportunistic infections	No comparison group

**HPV-associated Anal Lesions, pattern toward unfavorable**

<b>Citation</b>	<b>Results</b>	<b>Categorization of Results (Significance, Direction)</b>
Calabrese et al., 2003	Recurrent anal condylomata	
Roland et al., 2003	Kidney transplant patient: High-grade squamous intraepithelial neoplasia in anus 2.5 years post-transplantation. (Patient also had other warty lesions of the hand and a squamous cell carcinoma of the skin on his head)	Unfavorable

**HPV-associated Anal Lesions, pattern toward unfavorable**

Stock et al., 2003	12 patients examined pre and post-transplant: 9 (75%) had abnormalities pre-transplant Progression to higher grade of anal intraepithelial neoplasia post-transplant in 4/9 (44.4%) The 3 patients negative for anal HPV pre-transplant all positive for anal HPV post-transplant.	NS Unfavorable
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Citation	Results	Categorization of Results (Significance, Direction)
Stock et al., 2003	<p>Among 12 examined before transplantation: 9 (75%) had abnormal cytology or histological abnormalities and were positive for anal HPV</p> <p>Nine of 12 reexamined by publication: Progression to higher grade of anal intraepithelial neoplasia AIN in 4/9.</p> <p>Patients negative for anal lesions/ HPV at baseline all have detectable HPV post-transplant</p>	Pattern toward unfavorable



## APPENDIX C

### Cost Impact Analysis: General Caveats and Assumptions

This appendix describes general caveats and assumptions used in conducting the cost impact analysis. For additional information on the cost model and underlying methodology, please refer to the CHBRP Web site, <http://www.chbrp.org/costimpact.html>.

The cost analysis in this report was prepared by Milliman and University of California, Los Angeles, with the assistance of CHBRP staff. Per the provisions of AB 1996 (California Health and Safety Code, Section 127660, et seq.), the analysis includes input and data from an independent actuarial firm, Milliman. In preparing cost estimates, Milliman and UCLA relied on a variety of external data sources. The *Milliman Health Cost Guidelines* (HCG) were used to augment the specific data gathered for this mandate. The HCGs are updated annually and are widely used in the health insurance industry to estimate the impact of plan changes on health care costs. Although these data were reviewed for reasonableness, they were used without independent audit.

The expected costs in this report are not predictions of future costs. Instead, they are estimates of the costs that would result if a certain set of assumptions were exactly realized. Actual costs will differ from these estimates for a wide variety of reasons, including:

- Prevalence of mandated benefits before and after the mandate different from our assumptions.
- Utilization of mandated services before and after the mandate different from our assumptions.
- Random fluctuations in the utilization and cost of health care services.

Additional assumptions that underlie the cost estimates presented here are:

- Cost impacts are only shown for people with insurance.
- The projections do not include people covered under self-insurance employer plans because those employee benefit plans are not subject to state-mandated minimum benefit requirements.
- Employers and employees will share proportionately (on a percentage basis) in premium rate increases resulting from the mandate. In other words, the distribution of premium paid by the subscriber (or employee) and the employer will be unaffected by the mandate.

There are other variables that may affect costs, but which Milliman did not consider in the cost projections presented in this report. Such variables include, but are not limited to:

- Population shifts by type of health insurance coverage. If a mandate increases health insurance costs, then some employer groups or individuals may elect to drop their coverage. Employers may also switch to self-funding to avoid having to comply with the mandate.
- Changes in benefit plans. To help offset the premium increase resulting from a mandate, members or insured may elect to increase their overall plan deductibles or copayments. Such changes would have a direct impact on the distribution of costs between the health plan and the insured person, and may also result in utilization reductions (i.e., high levels of patient cost sharing result in lower utilization of health care services). Milliman did not include the effects of such potential benefit changes in its analysis.
- Adverse Selection. Theoretically, individuals or employer groups who had previously foregone insurance may now elect to enroll in an insurance plan postmandate because they perceive that it is to their economic benefit to do so.



- Health plans may react to the mandate by tightening their medical management of the mandated benefit. This would tend to dampen our cost estimates. The dampening would be more pronounced on the plan types that previously had the least effective medical management (i.e., FFS and PPO plans).
- Variation in existing utilization and costs, and in the impact of the mandate, by geographic area and delivery system models. Even within the plan types we modeled (HMO, PPO, POS, and FFS), there are variations in utilization and costs within California. One source of difference is geographic. Utilization differs within California due to differences in the health status of the local commercial population, provider practice patterns, and the level of managed care available in each community. The average cost per service would also vary due to different underlying cost levels experienced by providers throughout California and the market dynamic in negotiations between health plans and providers. Both the baseline costs prior to the mandate and the estimated cost impact of the mandate could vary within the state due to geographic and delivery system differences. For purposes of this analysis, however, we have estimated the impact on a statewide level.



**APPENDIX D**  
**Information Submitted by Outside Parties for Consideration for CHBRP Analysis**

In accordance with its policy to analyze evidence submitted by outside parties during the first two weeks of each 60-day review of a proposed benefit mandate, CHBRP received the following submissions:

*No information was submitted to date.*

CHBRP analyzes all evidence received during the public submission period according to its relevance to the proposed legislation and the program's usual methodological criteria. For more information about CHBRP's methods, to learn how to submit evidence relevant to an on-going mandate review, or to request email notifications of new requests CHBRP receives from the California Legislature, please visit: [www.chbrp.org](http://www.chbrp.org).



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## California Health Benefits Review Program Committees and Staff

A group of faculty and staff undertakes most of the analysis that informs reports by the California Health Benefits Review Program (CHBRP). The CHBRP **Faculty Task Force** comprises rotating representatives from six University of California (UC) campuses and three private universities in California. In addition to these representatives, there are other ongoing contributors to CHBRP from UC. This larger group provides advice to the CHBRP staff on the overall administration of the program and conducts much of the analysis. The CHBRP **staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and coordinates all external communications, including those with the California Legislature. The level of involvement of members of CHBRP's Faculty Task Force and staff varies on each report, with individual participants more closely involved in the preparation of some reports and less involved in others.

As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, Milliman, to assist in assessing the financial impact of each benefit mandate bill. Milliman also helped with the initial development of CHBRP's methods for assessing that impact.

The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance and thoughtful critiques provided by the members of the National Advisory Council. However, the Council does not necessarily approve or disapprove of or endorse this report. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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